Immunity and how vaccines work

Dr Mary O Meara
National Immunisation Office

www.immunisation.ie

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Objectives of session

An understanding of the following principles

- Overview of immunity
- Different types of vaccines and vaccine contents
- Vaccine failures
- Time intervals between vaccine doses
- Vaccine overload
- Adverse reactions
- Herd immunity

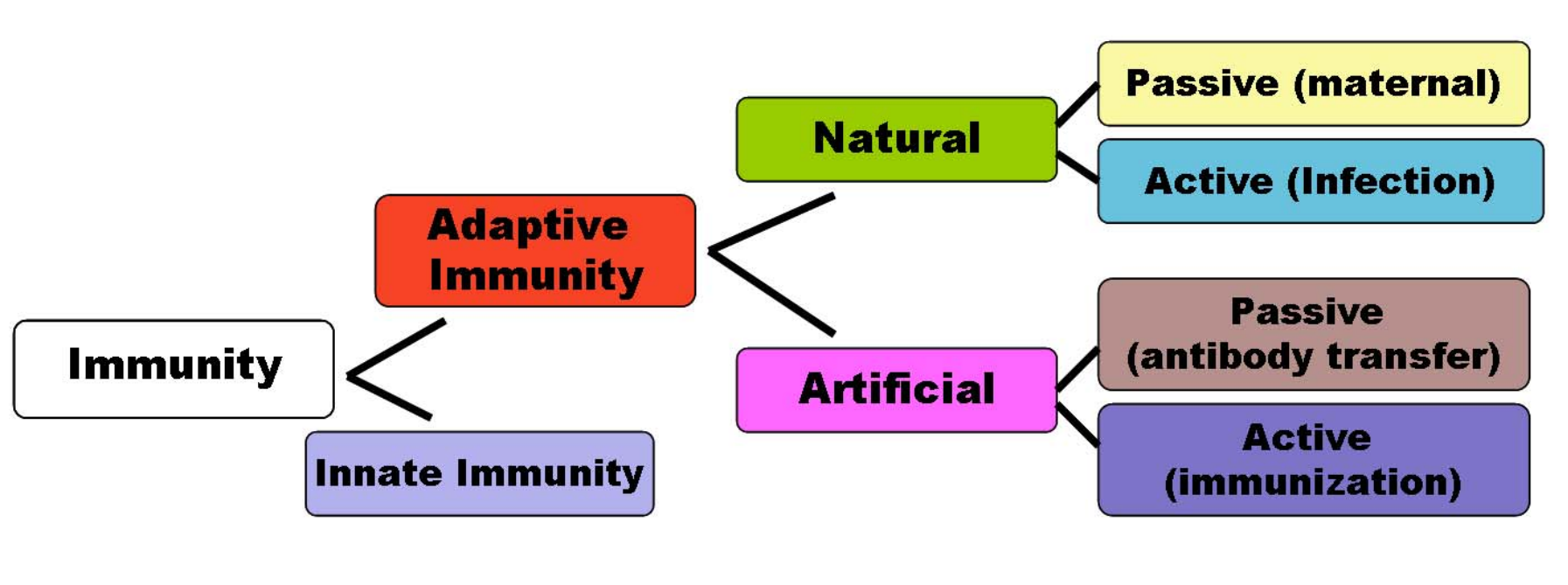
Immunity

– The ability of the human body to protect itself from infectious disease

The immune system

– Cells with a protective function in the
  - bone marrow
  - thymus
  - lymphatic system of ducts and nodes
  - spleen
  - blood

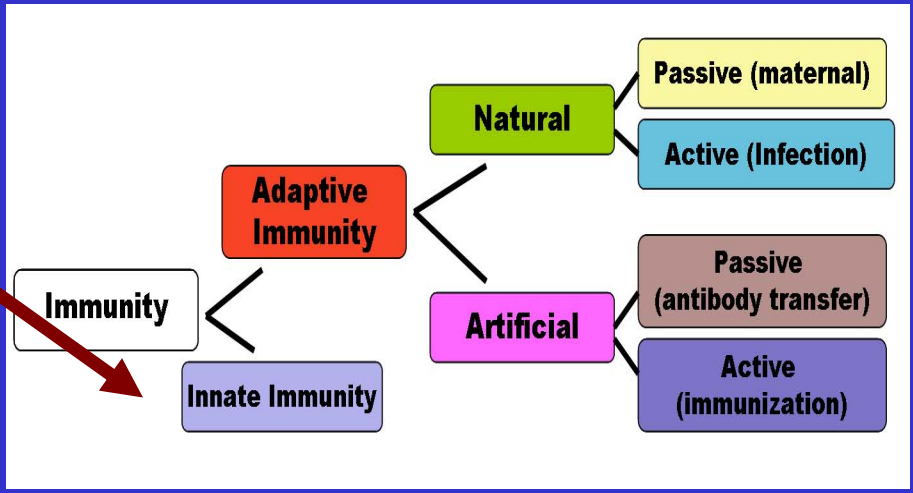
Types of immunity



Natural (innate) immunity

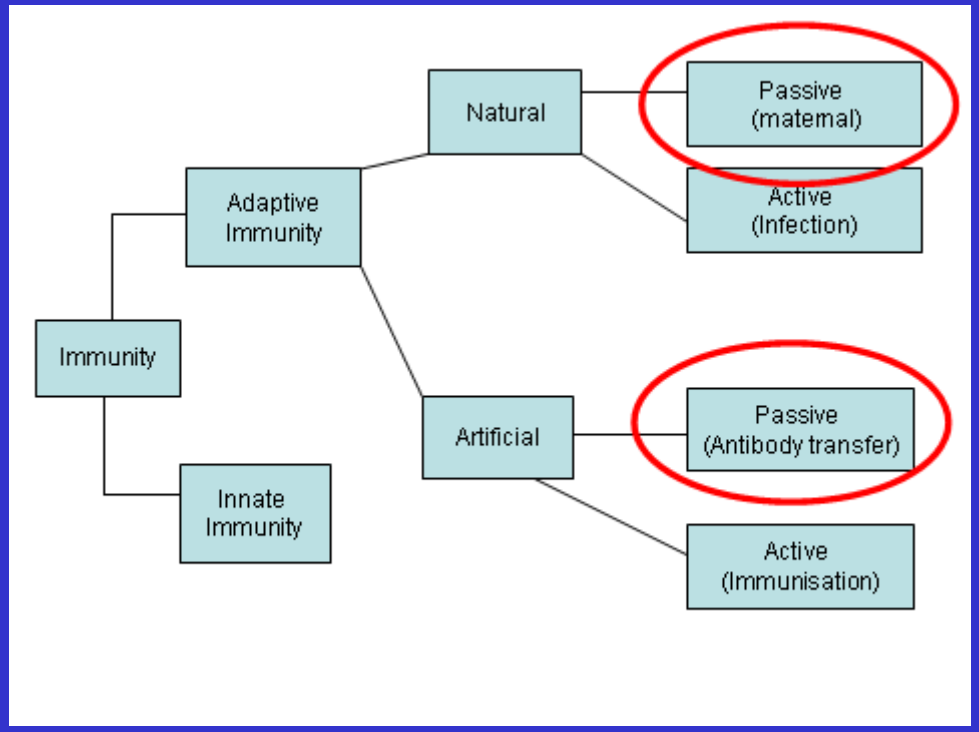
Non-specific mechanisms

- Physical barriers
  - skin and mucous membranes
- Chemical barriers
  - gastric and digestive enzymes
- Cellular and protein secretions
  - phagocytes, macrophages, complement system



** No “memory” of protection exists afterwards **

Passive immunity – adaptive mechanisms



Natural

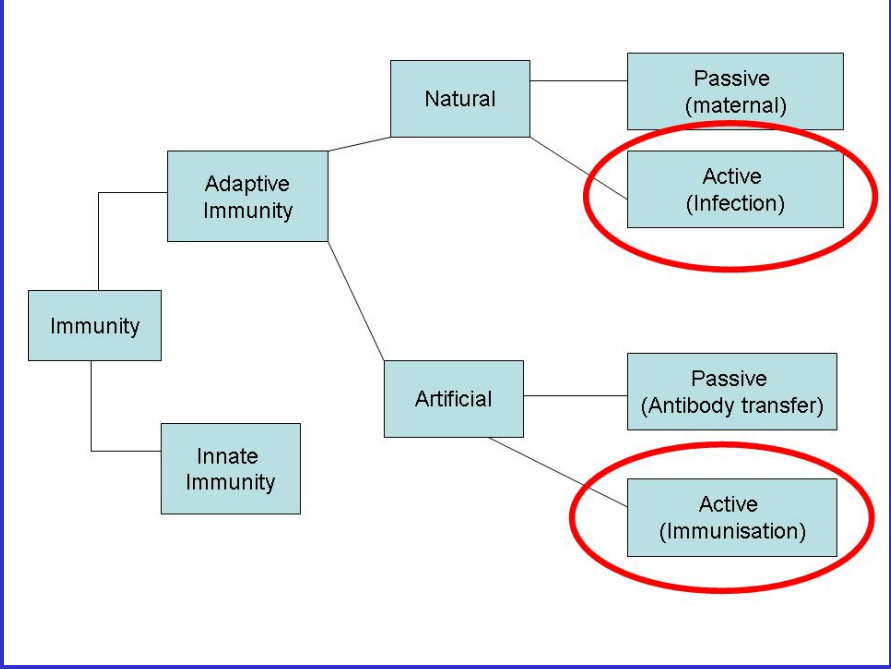
– maternal transfer of antibodies to infant via placenta

Artificial

– administration of pre-formed substance to provide immediate but short-term protection (anti-toxin, antibodies)

Protection is temporary and wanes with time (usually few months)

Active immunity – adaptive mechanisms



Natural
- following contact with organism

Artificial
- administration of agent to stimulate immune response (immunisation)

Acquired through contact with an micro-organism
Protection produced by individual's own immune system
Protection often life-long but may need boosting

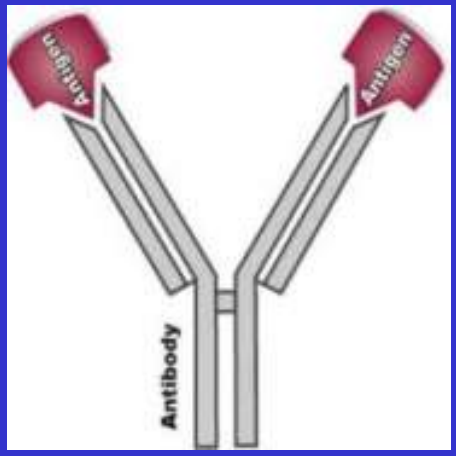
www.immunisation.ie

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Antigen

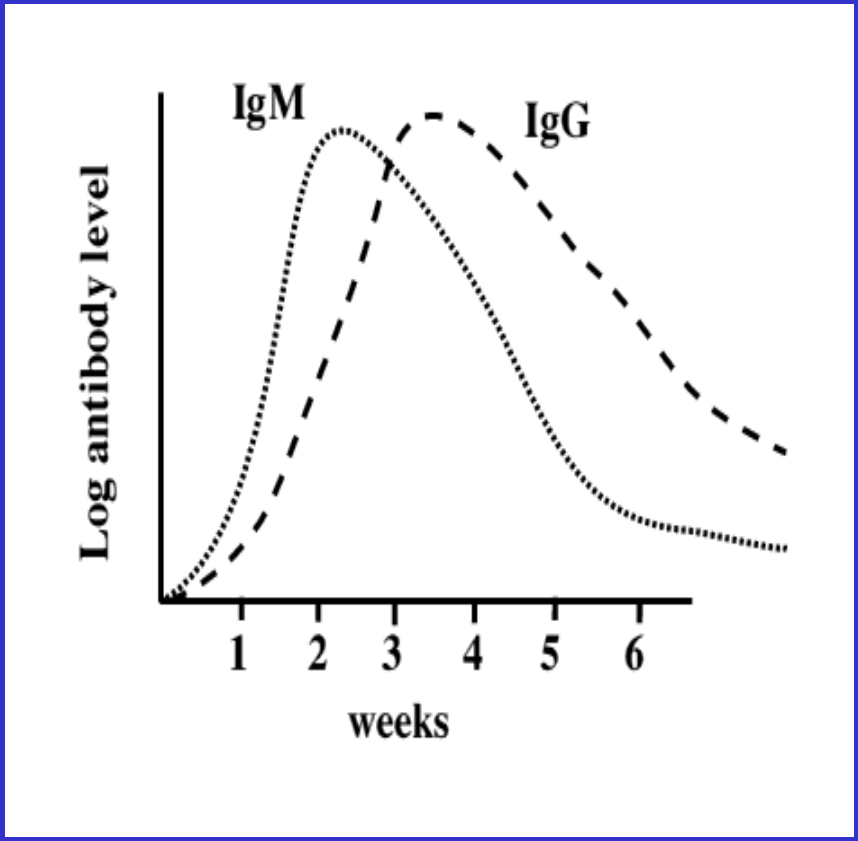
A live or inactivated substance (e.g. protein or polysaccharide) capable of producing an immune response

Antibodies



- Different types
  - IgM, IgG, IgA, IgD, IgE
- Functions
  - Neutralise toxins
  - Block adhesion/cell entry of the antigen
  - Neutralise and prevent viral replication
- Antigen specific
  - Cannot cross-protect different type of micro-organism

Immune response following exposure to antigen



Primary response

- rapid
- mainly IgM

Secondary response

- faster and more powerful
- mainly IgG

PROTECT HEALTH IMMUNISE

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Specific memory is the hallmark of the adaptive immune response

PROTECT HEALTH IMMUNISE

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

How vaccines work

- Induce active immunity
  - Immunity and immunologic memory similar to natural infection but without risk of disease

- Immunological memory allows
  - Rapid recognition and response to pathogen
  - Prevent or modify effect of disease

Classification of vaccines

- Live attenuated
- Inactivated
  - Whole cell
  - Fractionated
    - Protein based
      - Toxoid
      - Sub unit
    - Polysaccharide
      - Pure
      - Conjugate

Live attenuated vaccines

Weakened viruses /bacteria

- Achieved by growing numerous generations in laboratory
- Produces long lasting immune response after one or two doses
- Stimulates immune system to react as it does to natural infection
- Can cause mild form of the disease (e.g. mini measles which is non transmissible)
- CANNOT be given to immuno-compromised persons

e.g. BCG/ MMR/ Varicella/ Yellow fever

Inactivated vaccine and toxoids

- Cannot cause disease they are designed to protect against
- Doses
  - Two of more doses plus booster doses usually required
- Whole
  - Viruses (IPV, hepatitis A, influenza))
  - Bacteria (whole cell pertussis)
- Fractional
  - Protein-based
    - Toxoid (diphtheria, tetanus)
    - Subunit (Hepatitis B, acellular pertussis)
  - Polysaccharide–based
    - Pure
    - Conjugate

Polysaccharide vaccines

- Immunogenicity
  - Less immunogenic than toxoids
  - Response in children poor
- Duration of protection
  - Does not provide lifelong immunity, booster often needed

e.g.

  - Pneumococcal polysaccharide vaccine
  - Meningococcal ACWY polysaccharide vaccine (travel)

Vaccine components

- Conjugating agents
  - Carrier proteins which combine with antigens to improve immunogenicity

  E.g. Men C, PCV, Hib
- Suspension fluid
  - Fluid (water, saline, tissue-culture mixture)
- Preservatives, stabilisers, antimicrobial agents
  - Trace amounts used to stabilise vaccine
  - May cause allergic reaction

Vaccine components

- Adjuvants
  - Aluminium salt used to increase immunogenicity of vaccines containing inactivated micro-organisms or their products

  e.g.
    - Hepatitis B vaccine
    - Tetanus toxoid
    - Diphtheria toxoid

Vaccine components

- Thiomersal*
  - Used in vaccine production since the 1930s
  - Mercury containing compound used in some vaccines to prevent bacterial and fungal growth
  - Also used as inactivating agent in early stage of production of some killed vaccines
  - In 1999 EU and U.S. manufacturer's decision to decrease thiomersal levels in vaccines

*also known as thimerosal

www.immunisation.ie

PROTECT HEALTH IMMUNISE

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Vaccine failure

- Primary
  - Inadequate immune response to vaccine (e.g.MMR1)
  - Infection possible any time post vaccination
- Secondary
  - Adequate antibody response immediately after vaccination
  - Level of antibodies decrease with time
  - Booster doses usually required
  - Feature of many inactivated vaccines

Time intervals between vaccine doses

Antigen combination	Recommended minimal interval between doses
≥2 killed antigens	No minimum interval
Killed and live antigens	No minimum interval
≥2 live antigens	Four-week minimum interval if not administered simultaneously

Time intervals between vaccine doses

- 2 Live vaccines - Minimum one month interval required
  - Allows **each immune response to develop**
  - Allows the next response to be a true secondary response – i.e. faster and bigger and with higher affinity IgG
  - Diminishes immune interference

Vaccine overload

- The human body is composed of 10 trillion cells and contains 100 trillion bacteria
  - On average there are
    - 1000 bacteria on each cm^2 of skin
    - 1,000,000 bacteria on each cm^2 of the scalp
    - 100,000,000 bacteria per gram of saliva

- The maximum number of antigens in a vaccine was ~3000 (DTwP, most from wP)
- With the new vaccines this number is much lower still

- No evidence that vaccines can overload the immune system

http://www.schoolscience.co.uk/content/4/biology/abpi/immune/immune3

Adverse events

- Live vaccines:
  - frequency of adverse events falls with number of doses
  - If antibody is made -> neutralises small amount of vaccine virus in any subsequent vaccine dose
  - E.g. MMR

- Inactivated vaccines
  - frequency of adverse events increases with number of doses
  - Good antibody levels ->good secondary immune response
  - May be inflammatory (i.e. produce a sore arm)
  - E.g. tetanus, pertussis

Herd immunity

- Only applies to diseases which are passed from person to person
- For each disease
  - a certain level of immunity in the population which protects the whole population because the disease stops spreading in the community
- Provides indirect protection of unvaccinated as well as vaccinated individuals.
- May be the most important aspect of how vaccines work
  - MMR given to infants protects pregnant women from rubella.
  - Can eradicate disease even if some people remain susceptible

http://www.immunisation.nhs.uk/About_Immunisation/Science/How_immunisation_works_-_animation

Acknowledgements

Core Topic 2 Training slides,
Health Protection Agency, UK, Feb 2008
www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947391135

Understanding vaccines,
National Institutes of Health, US Jan 2008
www3.niaid.nih.gov/healthscience/healthtopics/vaccine/PDF/undvacc.pdf