
*Immunity and how vaccines
work*

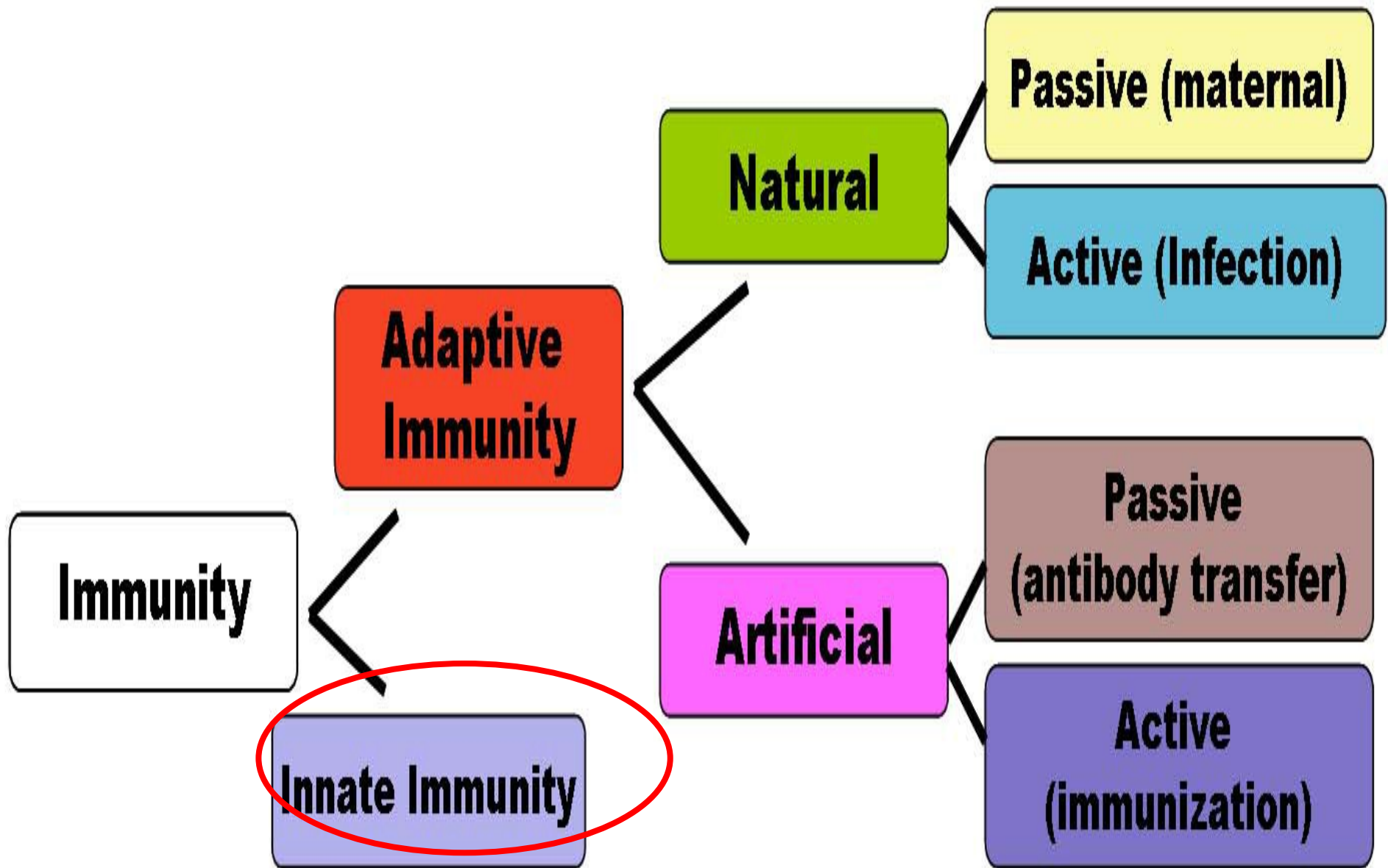
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Dublin Immunisation Study Day
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Overview

- The immune system
 - Innate immunity
 - Adaptive immunity
- How vaccines work
 - Different types of vaccines
 - Vaccine contents
- Herd immunity
- Adverse events
- Vaccine failure

The immune system

- The body recognises micro-organisms as 'foreign', not belonging inside the body, because of unique molecules on it's surface **-antigens**
- Once recognised, the immune system tries to destroy the micro-organisms
- There are two systems for doing this
 - the innate system and
 - the adaptive system



Innate immunity

- Physical barriers
 - Skin
 - Mucous membranes (mucous traps micro-organisms and cilia moves the mucous)
- Chemical barriers
 - Gastric and digestive enzymes
- Cellular and protein secretions
 - Lysozyme (in tears and saliva)
 - Complement (the complement cascade)
 - Macrophages
 - Mast cells (release histamine)
 - White blood cells (identify and remove foreign substances)
- **Defining characteristic: No memory persists afterwards**

Adaptive (acquired) immunity

- The micro-organism (foreign agent) is recognised in a specific manner and the immune system develops a memory of it
- The response increases in strength and effectiveness with each encounter

Active immunity - adaptive mechanisms

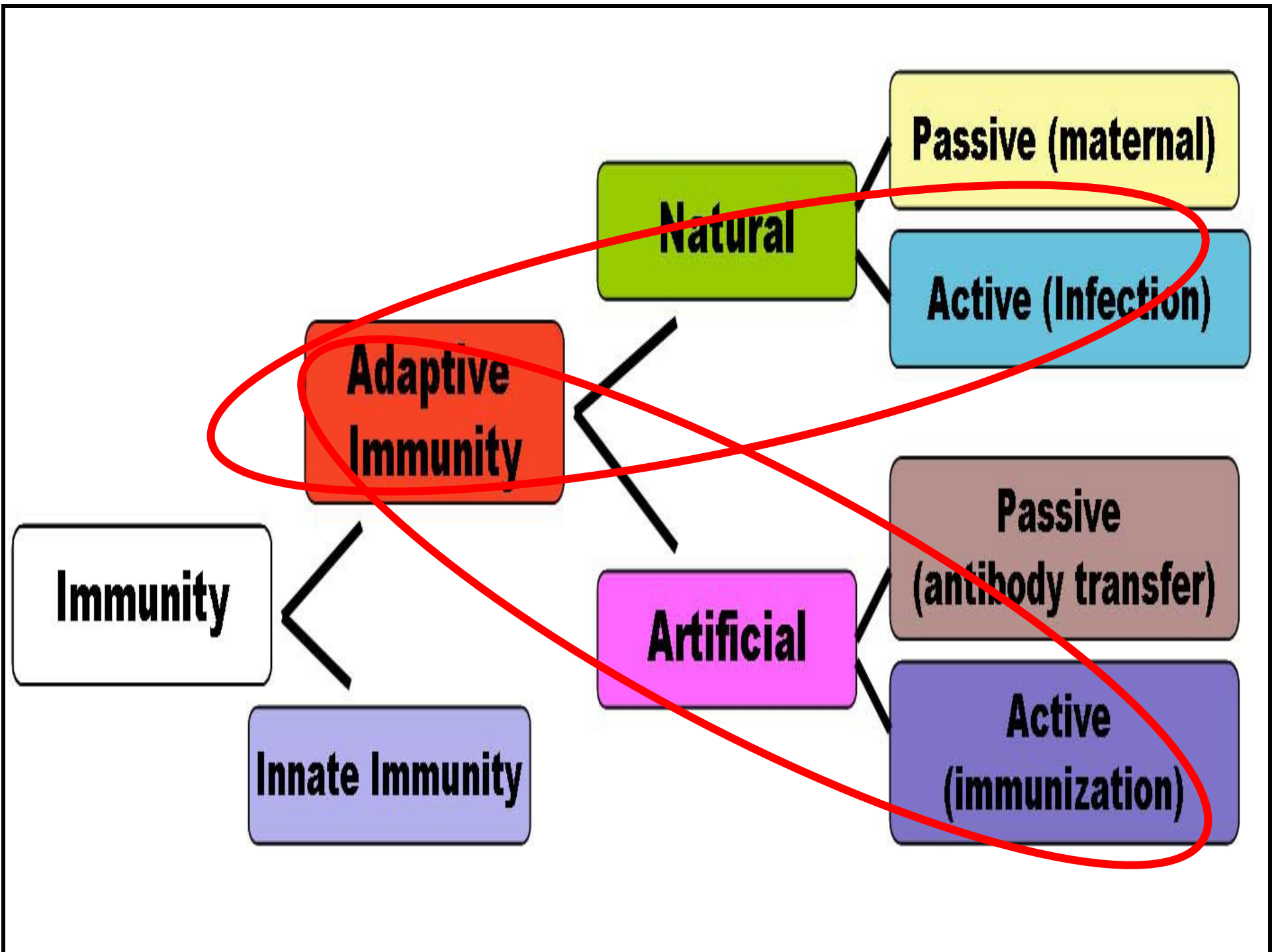
- **Natural**

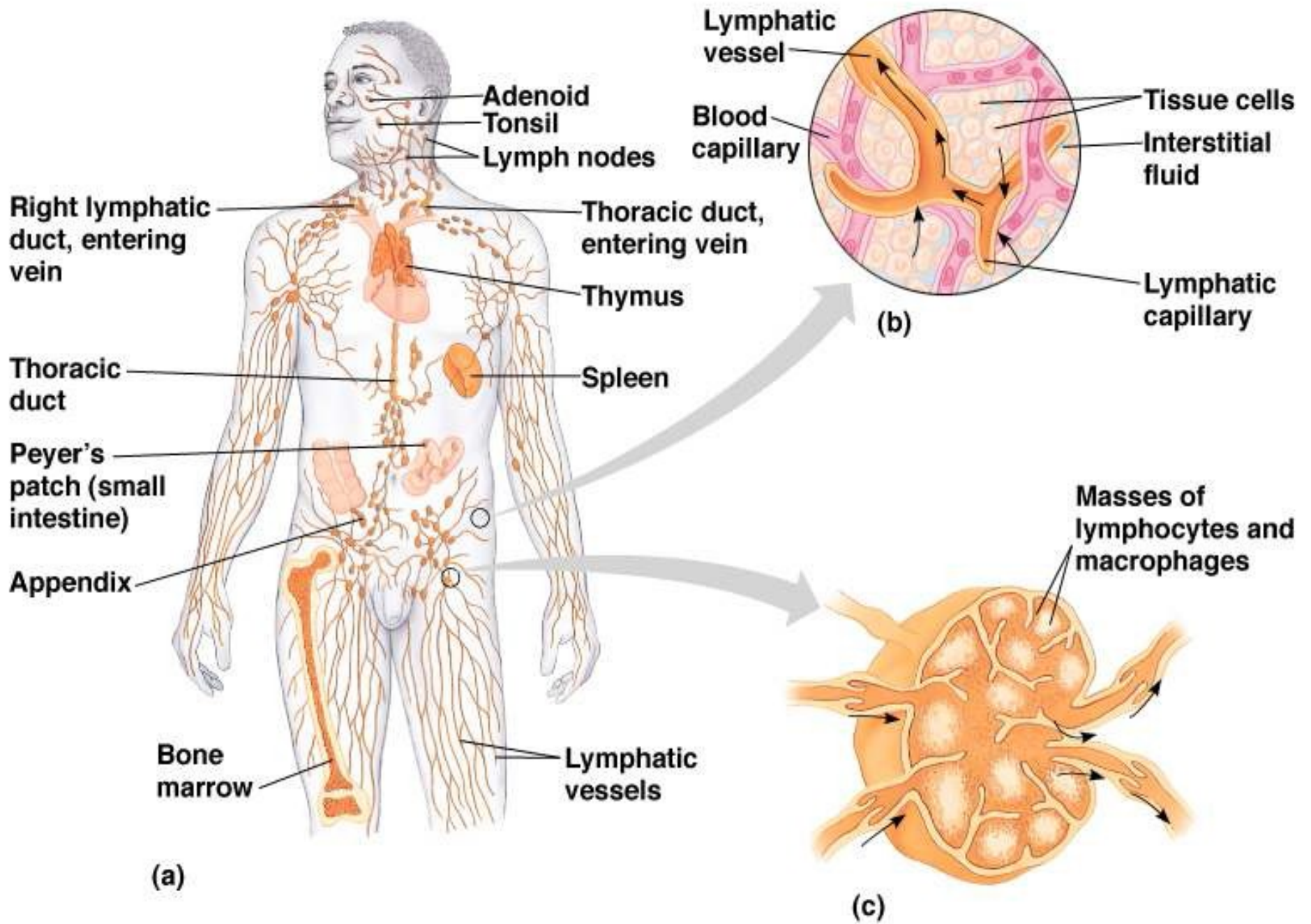
- Following infection with a micro-organism

- **Artificial**

- Following immunisation the administration of agent to stimulate immune response

- **Protection produced by individual's own immune system**
- **Protection often life-long but may need boosting**





Antigen

- A protein or polysaccharide capable of producing an immune response

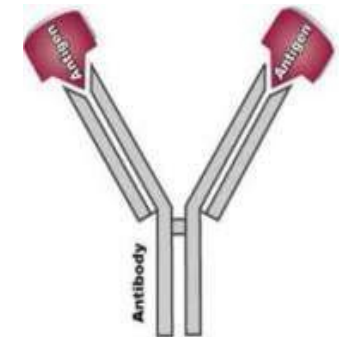
Active immunity

- Macrophages digest most of the micro-organism except the antigens. They 'regurgitate' the antigens displaying them on their surface so that WBCs called lymphocytes can take over the attack (T cells and B cells)
- Humoral / antibody mediated
 - B cells
- Cell mediated
 - T cells
 - Killer / cytotoxic destroy infected cells and micro-organisms
 - Helper stimulate and direct activity of B cells

Antibodies

Different types

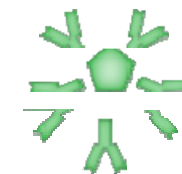
- IgM, IgG, IgA, IgD, IgE
- Each antibody is specific for its antigen
 - no cross protection
- We have millions of different antibodies
- When B cells come into contact with their matching antigen, they are stimulated to divide into larger cells called plasma cells, which secrete huge amounts of antibodies



Monomer
IgD, IgE, IgG



Dimer
IgA

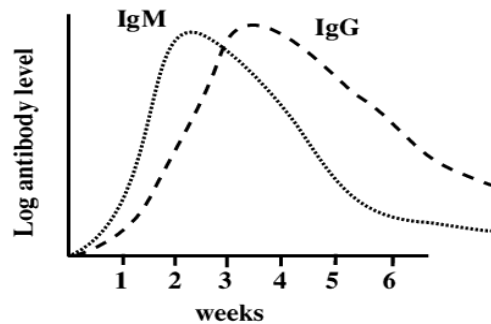


Pentamer
IgM

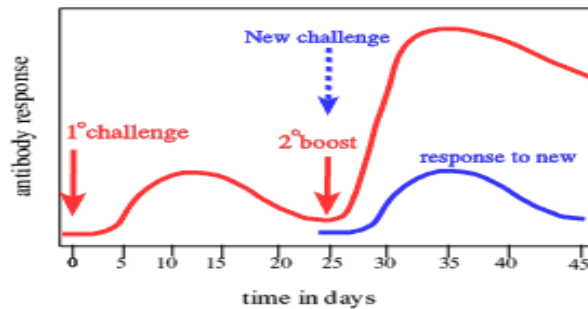
Functions of antibodies

- Neutralise toxins
- Block adhesion or cell entry of the antigen
- Neutralise and prevent viral replication

Active immunity - immune response



Specific memory is the hallmark of the adaptive immune response



- **Primary response**
rapid
mainly IgM
- **Secondary response**
faster and more powerful
mainly IgG

Memory persists afterwards

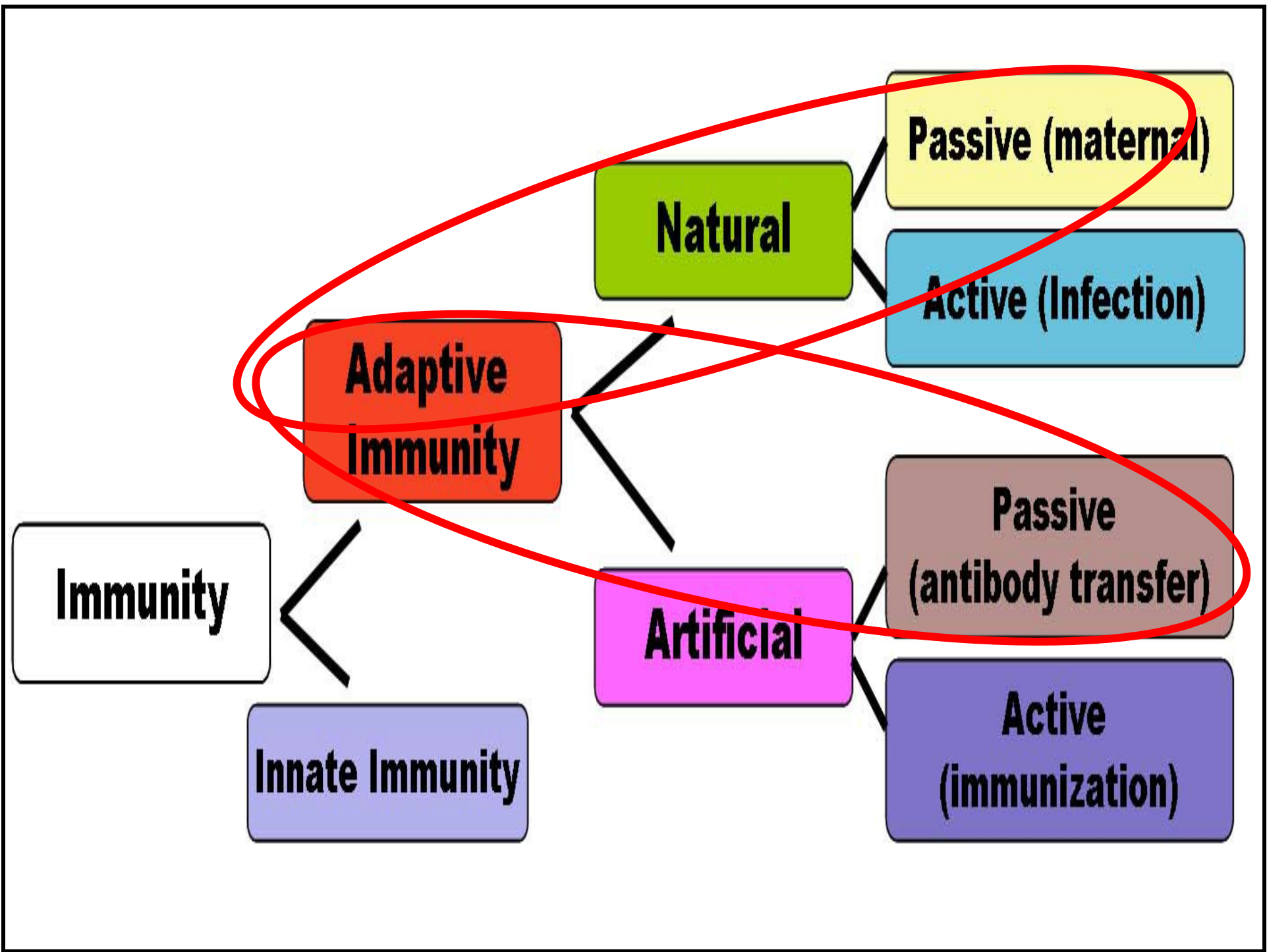
Passive immunity - adaptive mechanisms

- **Natural**

- Maternal transfer of immunity to an infant

- **Artificial**

- Administration of pre- formed substance to provide immediate but short-term protection (immunoglobulin, anti- toxin)
- Gives rapid protection within 48 hours
- Protection is temporary and wanes with time (usually few months)



Immunity

Innate Immunity

Adaptive Immunity

Natural

Passive (maternal)

Active (Infection)

Artificial

Passive (antibody transfer)

Active (immunization)

Natural passive immunity

- Maternal antibodies are transferred to the foetus across the placenta and to a baby in breast milk.

Artificial passive immunity

- Provided by administering Immunoglobulins for post-exposure prophylaxis e.g.
 - Human Normal Immunoglobulin (HNIG)
 - Collected from pooled human donations – contains antibodies to infectious agents common in the community,
 - Hepatitis B immunoglobulin (HBIG),
 - Varicella Zoster Immunoglobulin(VZIG)
 - Tetanus immunoglobulin (TIG)
 - Rabies Immunoglobulin
- Administration of anti-toxins
 - Diphtheria anti toxin
 - Botulism anti toxin

How vaccines work

- **Induce active immunity artificially**
 - Immunity and immunological memory similar to natural infection but without the risk of disease
- **Immunological memory allows**
 - Rapid recognition and response to the antigens of the micro-organism
 - Prevents or modifies effect of the disease

Vaccine Type

Vaccine Type	Explanation	Examples
Live Attenuated	Live organism with low virulence	MMR, BCG, OPV, Yellow fever, varicella
Inactivated (killed)	Organism with no virulence	Influenza, IPV, rabies
Inactivated toxins	“Toxoids”	Tetanus, diphtheria
Subcellular fraction (including conjugated vaccines)	No virulence	PCV, PPV, Hib, Men C
Genetically engineered	Contains no original antigen product	Hepatitis B, HPV

Live attenuated vaccines

- **Weakened viruses / bacteria**
 - Achieved by growing numerous generations in lab
 - Stimulates immune system to react as it does to natural infection
 - Produces long lasting immune response after one or two doses
 - Can cause mild form of the disease e.g. mini measles which is not transmissible
 - CANNOT be given to immuno-compromised persons
 - For example: BCG / MMR / Varicella / Yellow Fever

Inactivated vaccine and toxoids

- When adequate attenuation of live virus is not possible the vaccine is inactivated by chemical process or heat
- Toxoids are toxins that have been inactivated and chemically modified
- Cannot cause the disease they are designed to protect against
- Doses
 - Two or more doses plus booster doses usually required

Inactivated vaccine and toxoids

- Whole cell
 - Viruses (IPV, hep A, influenza)
- Sub-cellular fraction
 - Protein-based
 - Toxoid (diphtheria, tetanus)
 - Subunit (Hep B & HPV – genetically engineered, acellular pertussis, influenza)
 - Polysaccharide – pure (PPV) or conjugate (PCV, Men C, Hib)

Often require adjuvant or conjugation to stimulate immune response

Vaccine components 1

- Adjuvants

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

- For example.

- Hepatitis B vaccine
- Tetanus toxoid
- Diphtheria toxoid

Vaccine components 2

- **Suspension fluid**
 - Fluid (water, saline, tissue-culture mixture).
- **Preservatives, stabilisers, antimicrobial agents**
 - Trace amounts used to stabilise vaccine.
 - May cause allergic reaction.
- **Thiomersal**
 - Used in vaccine production since the 1930s
 - Contains ethyl mercury and is used in some vaccines to prevent bacterial and fungal growth. Unlike methyl mercury ethyl mercury is rapidly excreted from the body and is not toxic.
 - 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.
- **Conjugating agents**
 - Carrier proteins which combine with antigens to improve immunogenicity e.g. Men C, PCV, Hib.

Polysaccharide vaccines

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

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 interval of four weeks 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

- 1,000 bacteria on each cm² of skin
 - 1,000,000 bacteria on each cm² 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 following immunisation (AEFI)

- **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

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

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

Vaccine coverage for elimination

Infection / Infectious agent	Average age at infection, in years	Inter- epidemic period (years)	R_0	Critical vaccination coverage to block transmission, %
Measles	4 to 5	2	15-17	92-95
Pertussis	4 to 5	3 to 4	15-17	92-95
Mumps	6 to 7	3	10 to 12	90-92
Rubella	9 to 10	3 to 5	7 to 8	85-87
Diphtheria	11 to 14	4 to 6	5 to 6	80-85
Polio Virus	12 to 15	3 to 5	5 to 6	80-85

Source: HPA

Resources

- Immunity and how vaccines work. National Immunisation Office
http://www.immunisation.ie/en/Downloads/TrainingManual/PDFFile_16731_en.pdf
- Immunity and how vaccines work. Chapter 1 Green Book (UK)
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/144249/Green-Book-Chapter-1.pdf
- How Vaccines Work, NIH – National Institute of Allergy and Infectious Disease US
www.niaid.nih.gov/topics/vaccines/understanding/pages/howwork.aspx

THANK YOU!