# Immunity and How Vaccines Work

Kevin Connolly

# Learning Characteristics

- Active: “let’s try it out and see how it works”
- Reflective: “let’s think it through first”
- Visual:  learn best by seeing pictures, diagrams, or demonstrations
- Verbal: learn best by written or spoken words

# Definitions

**Antibody**: immunoglobulin produced mainly by plasma cells; identifies and neutralises pathogens

**Antigen**: substance that can provoke an immune response

**Clone**: group of identical decendents

**Epitope**: the specific piece of the antigen to which an antibody binds.

**Humoral**: relating to fluids

**Innate**: present from birth

# Definitions

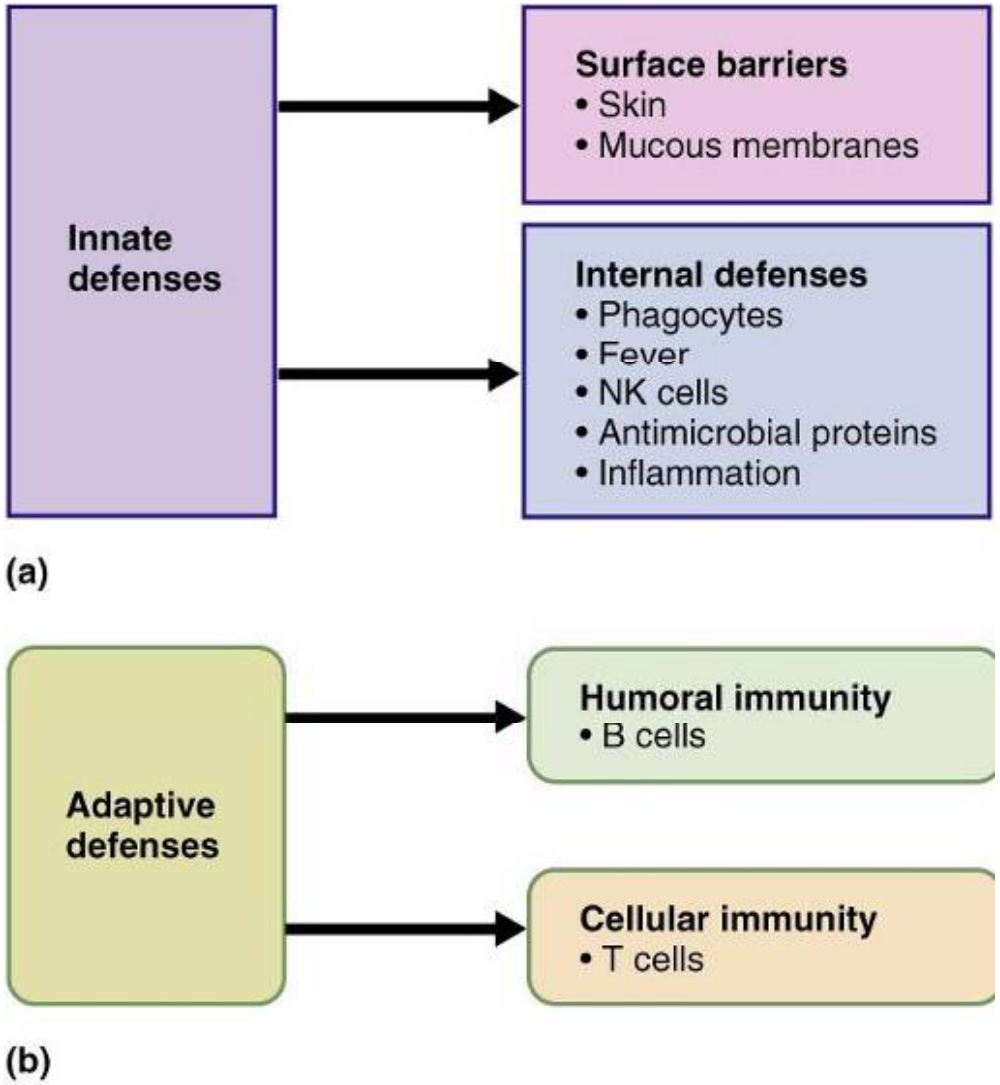
- **Immunity**: resistance to pathogens and their toxic effects (immunis - exempt, protected)
- **Immune system** - cells, tissues, and molecules that mediate resistance to infections
- **Immunology** - study of structure and function of the immune system
- **Immunity** - resistance of a host to pathogens and their toxic effects
- **Immune response** - coordinated response to introduction of foreign substances; mediated by cells and molecules of the immune system

# Role of Immune System

- Defense against microbes
- Defense against the growth of tumor cells
  - kills tumor cells
- Homeostasis
  - destruction of abnormal or dead cells
    (e.g. dead blood cells, Ag-Ab complex)

# Immune System Overview

- Hematopoietic
- Vasculature
- Lymphatic

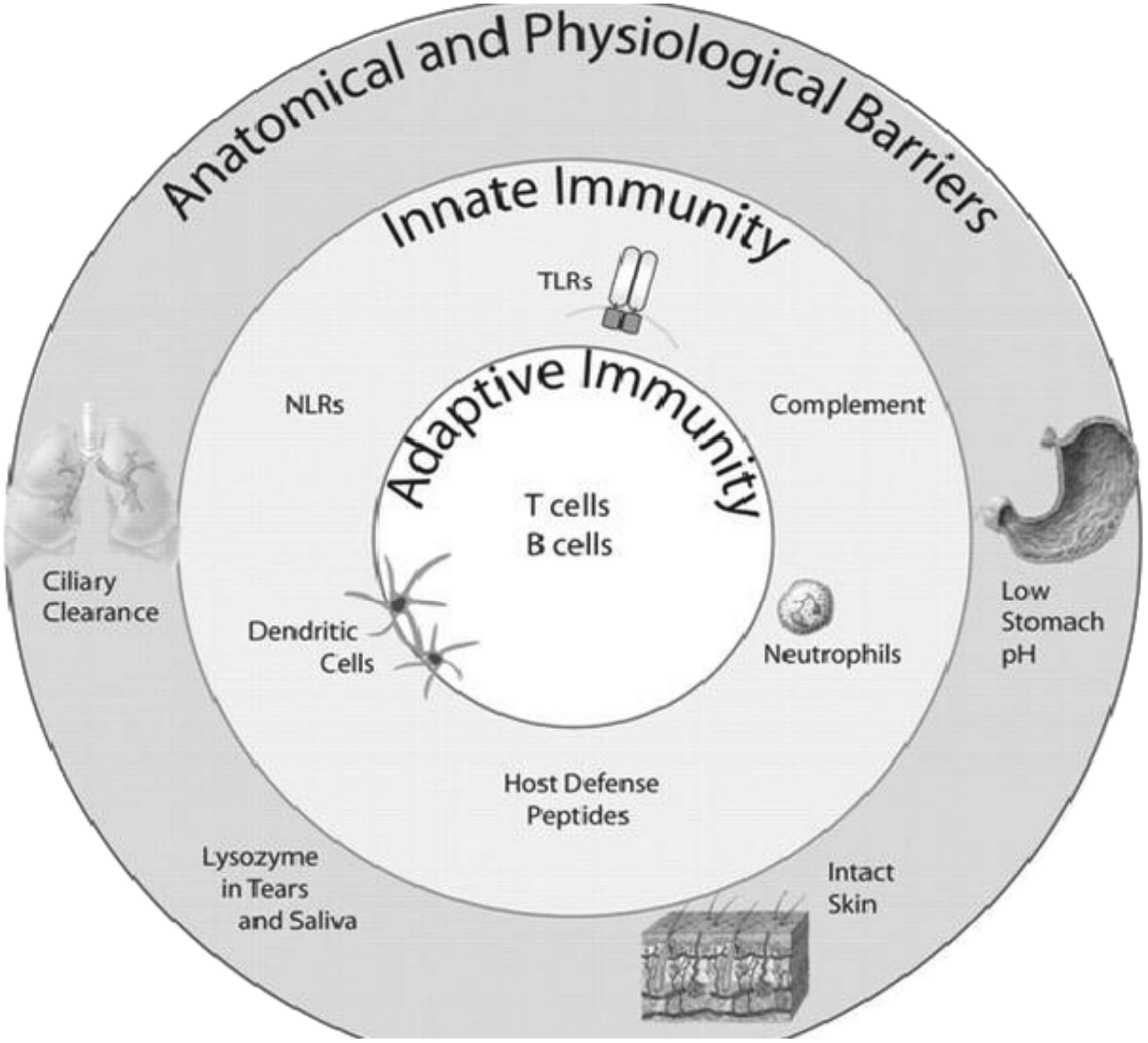


# Immune System

1. Organs
2. Cells
3. Molecules

# Innate Immunity

- Relies on already formed components
- Response within minutes to limit the infection
- Non-specific
  - same molecules / cells respond to a range of pathogens
- No memory
  - same response after repeated exposure
- Does not lead to clonal expansion


Anatomical and Physiological Barriers
Innate Immunity
TLRs
Adaptive Immunity
NLRs
Complement
T cells
B cells
Ciliary
Clearance
Dendritic
Cells
Neutrophils
Low
Stomach
pH
Host Defense
Peptides
Lysozyme
in Tears
and Saliva
Intact
Skin

# Immune System Organs

- Tonsils and adenoids
- Thymus
- Lymph nodes
- Spleen
- Payer’s patches
- Appendix
- Lymphatic vessels
- Bone marrow

# Immune System Cells

- Lymphocytes
  - T-lymphocytes
  - B-Lymphocytes, plasma cells
  - natural killer lymphocytes
- Monocytes, Macrophage
- Granulocytes
  - neutrophils
  - eosinophils
  - basophils

# Immune System Molecules

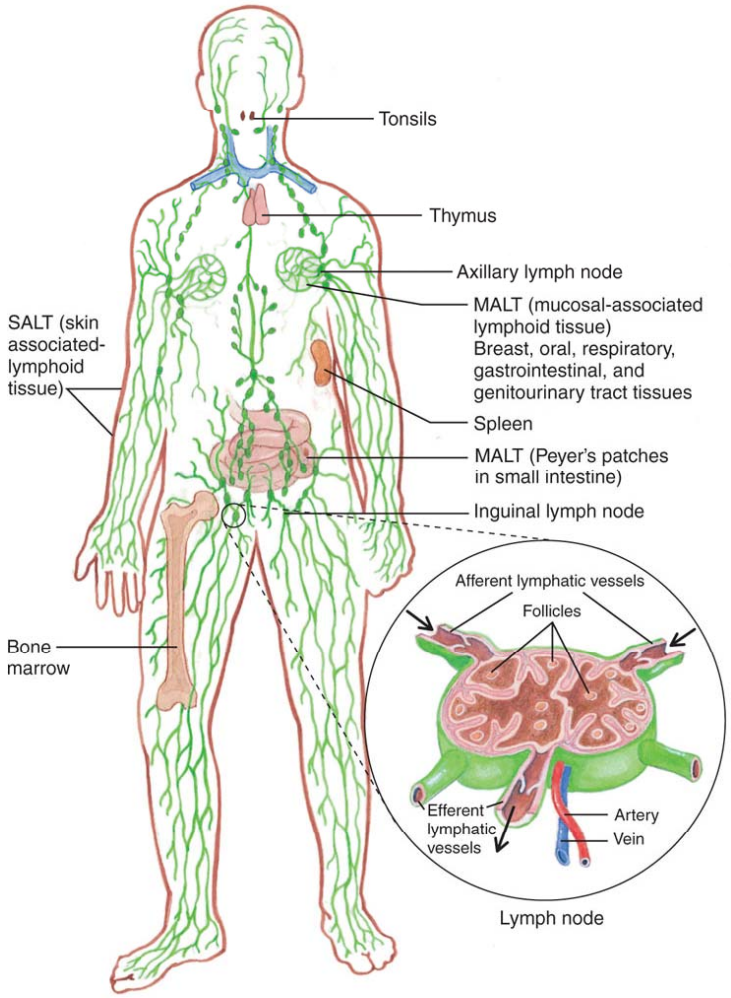
- Antibodies
- Complement
- Cytokines
- Interleukins
- Interferons
- etc

# Lymphoid System

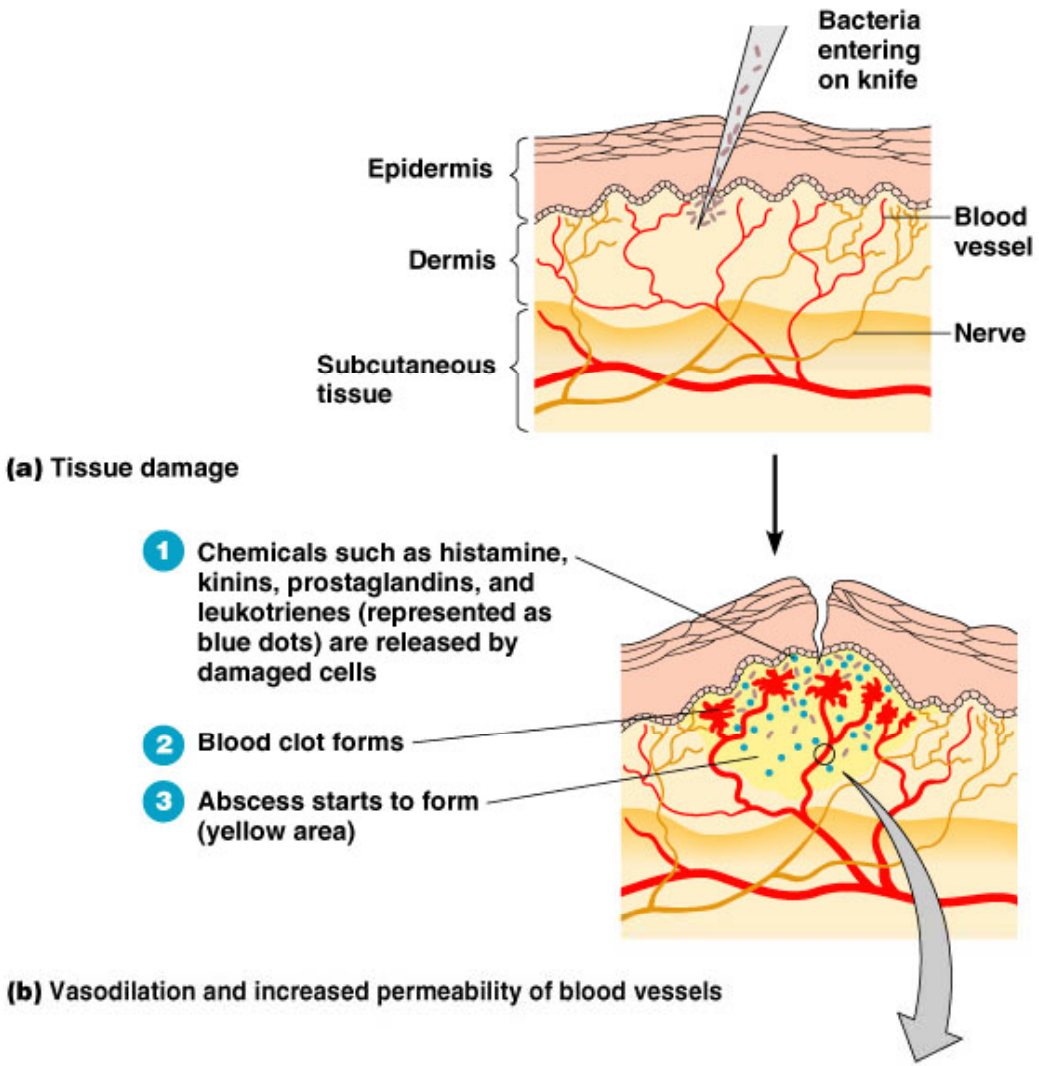
**Lymphoid organs:** Sites where lymphocytes gather to encounter antigens

Skin, lymph nodes, spleen, thymus, tonsils, adenoids
GIT

Situated to allow for initiation of immune response from nearly any place in body



# Inflammation



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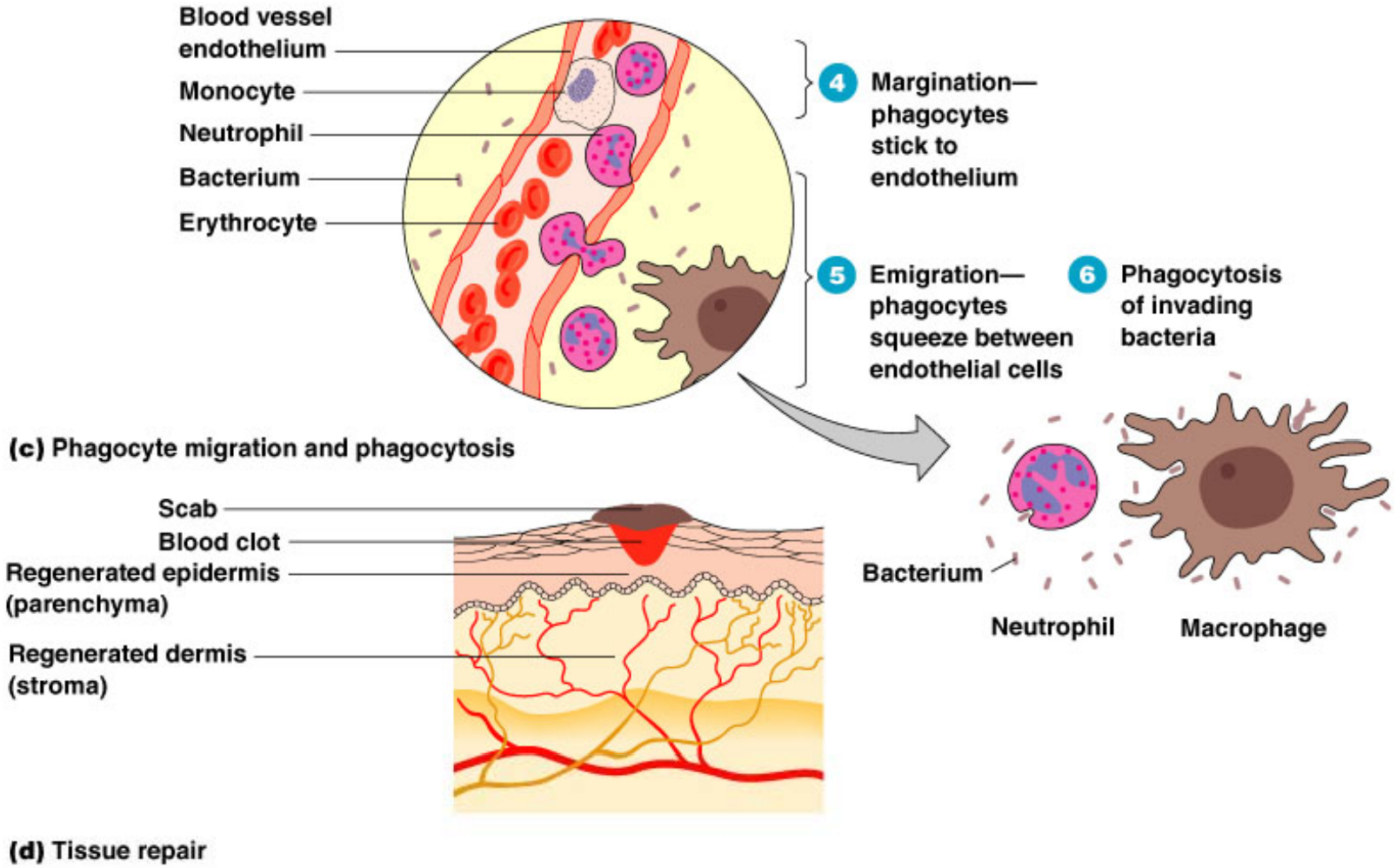
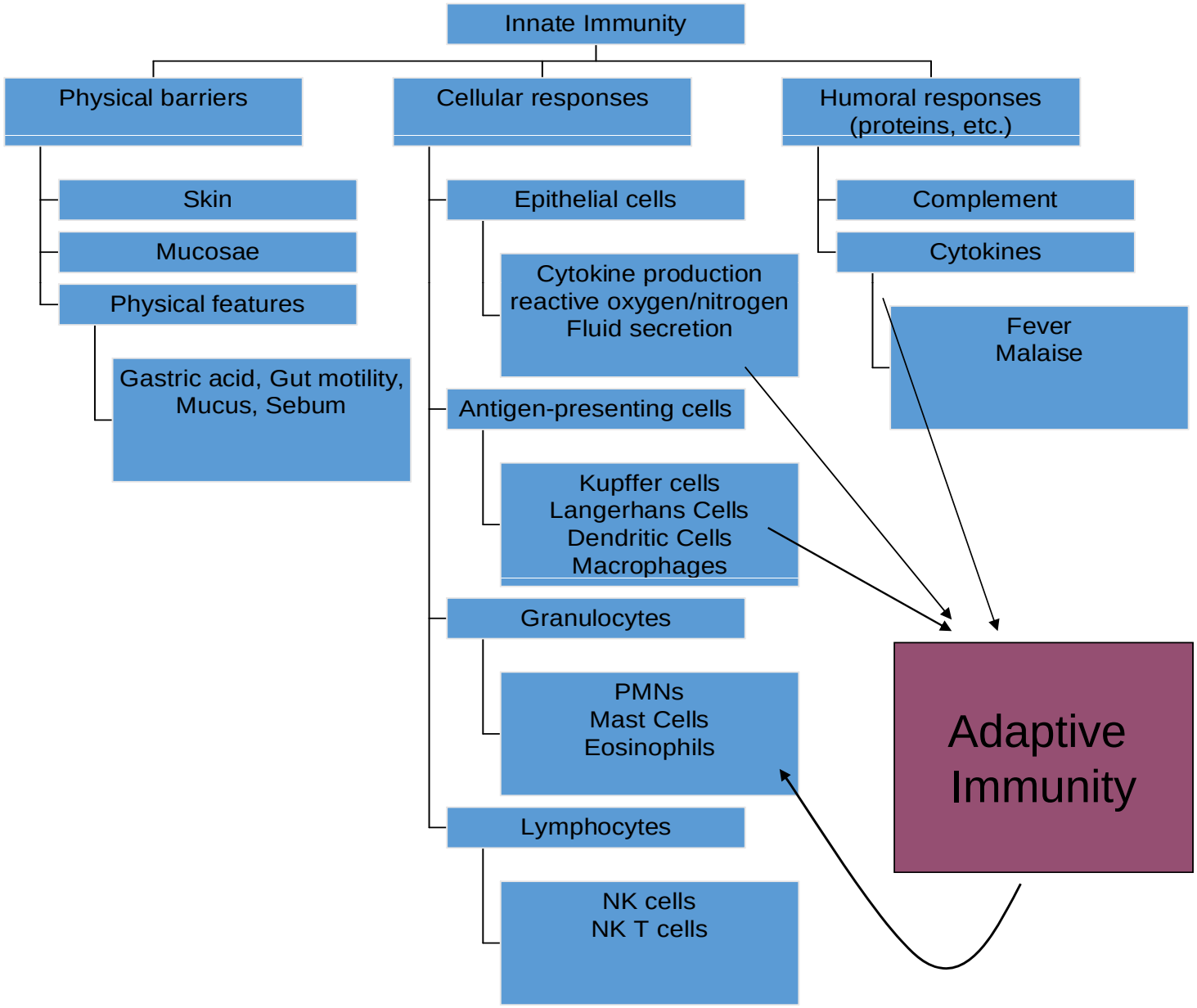
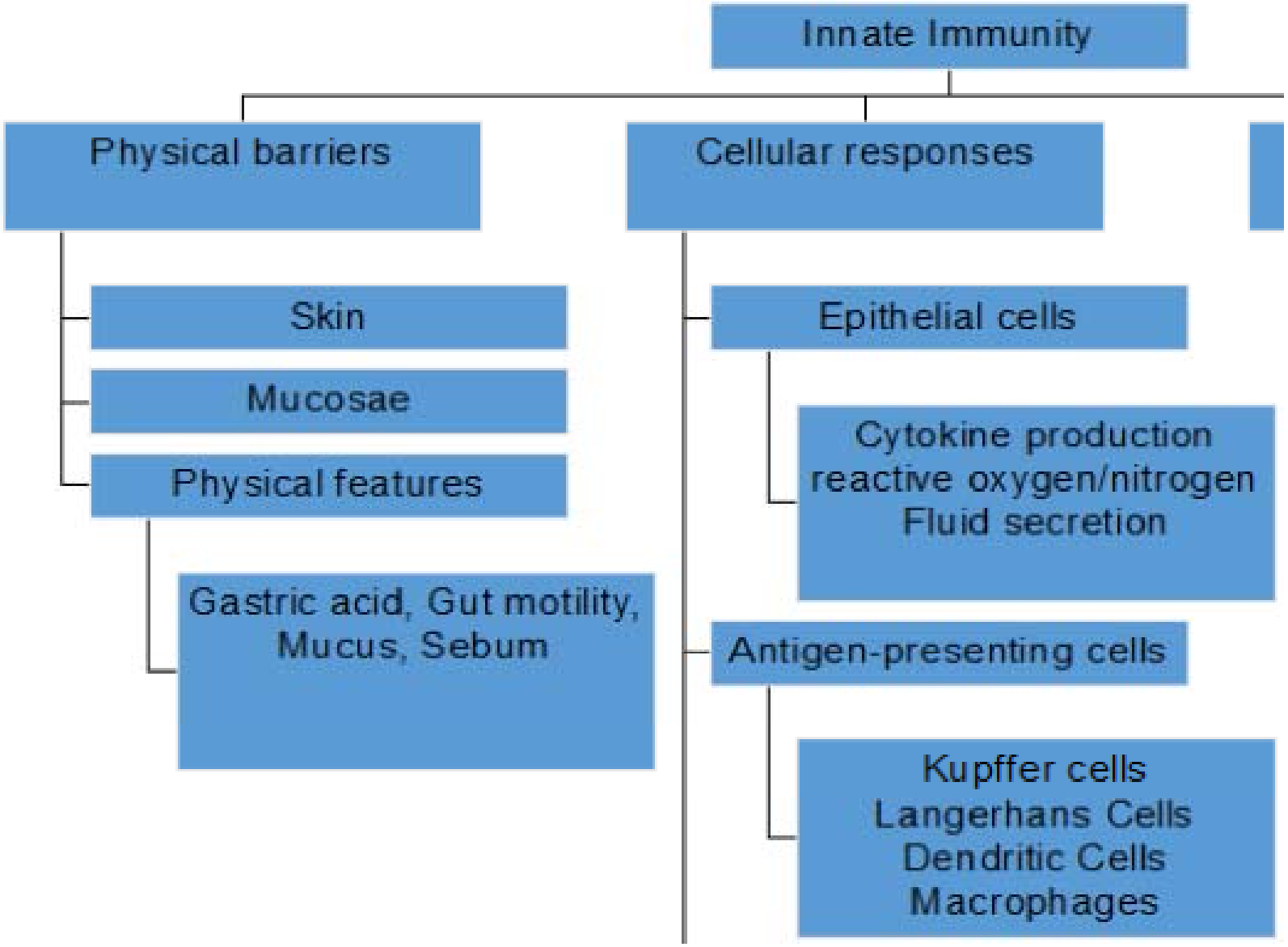



Innate Immunity
Physical barriers
Cellular responses
Humoral responses (proteins, etc.)
Skin
Mucosae
Physical features
Gastric acid, Gut motility, Mucus, Sebum
Epithelial cells
Cytokine production
reactive oxygen/nitrogen
Fluid secretion
Antigen-presenting cells
Kupffer cells
Langerhans Cells
Dendritic Cells
Macrophages
Granulocytes
PMNs
Mast Cells
Eosinophils
Lymphocytes
NK cells
NK T cells
Complement
Cytokines
Fever
Malaise
Adaptive Immunity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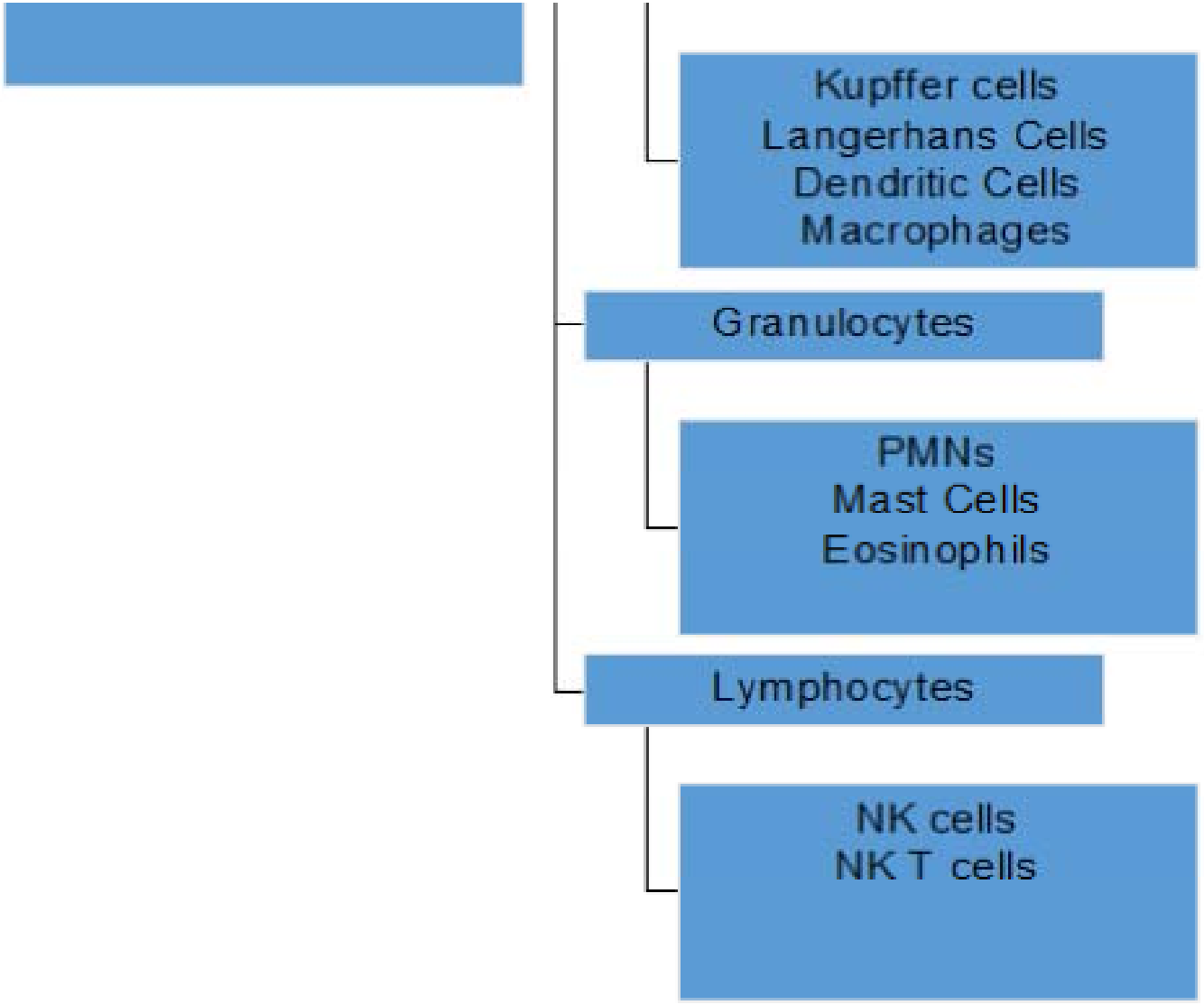
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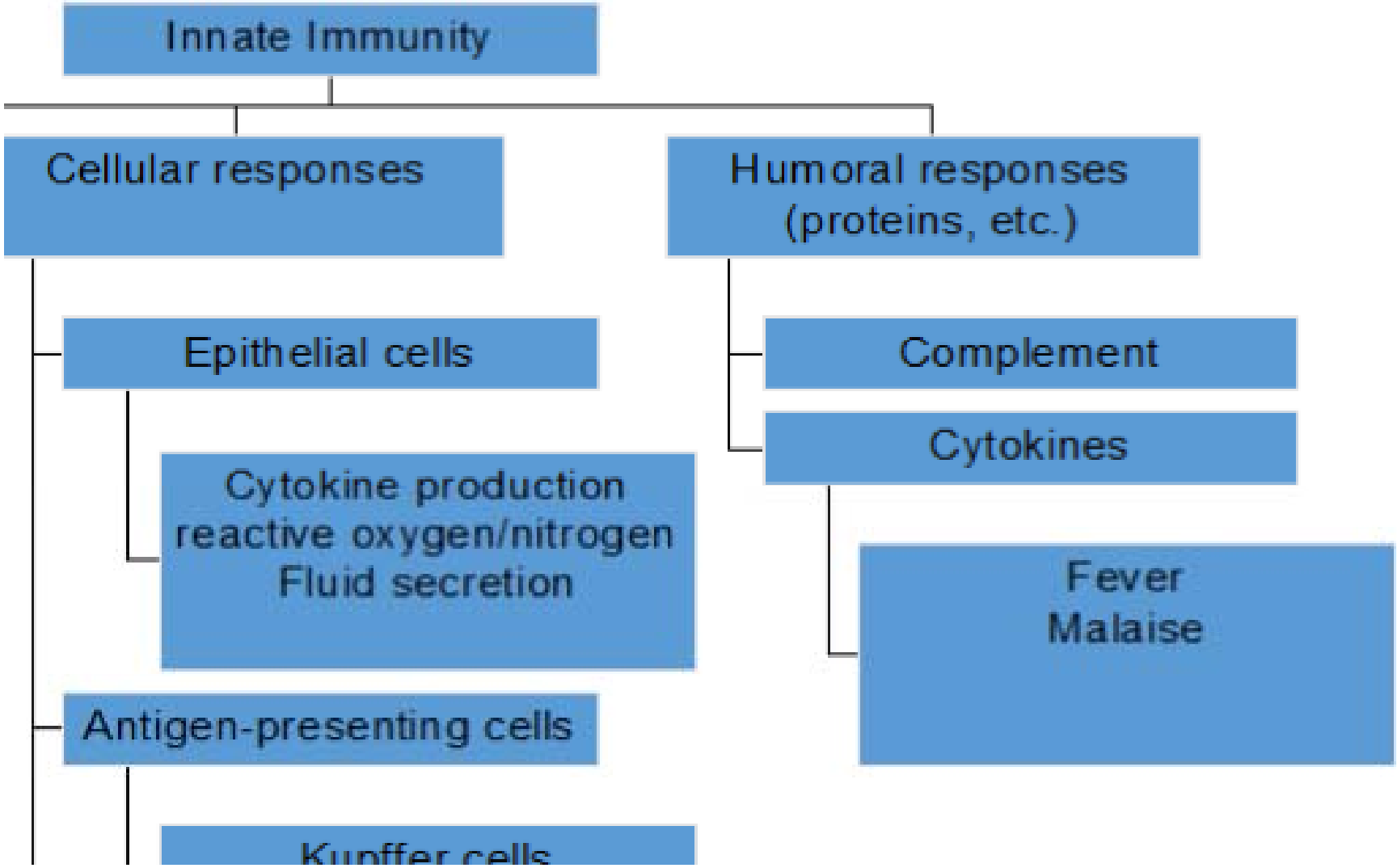
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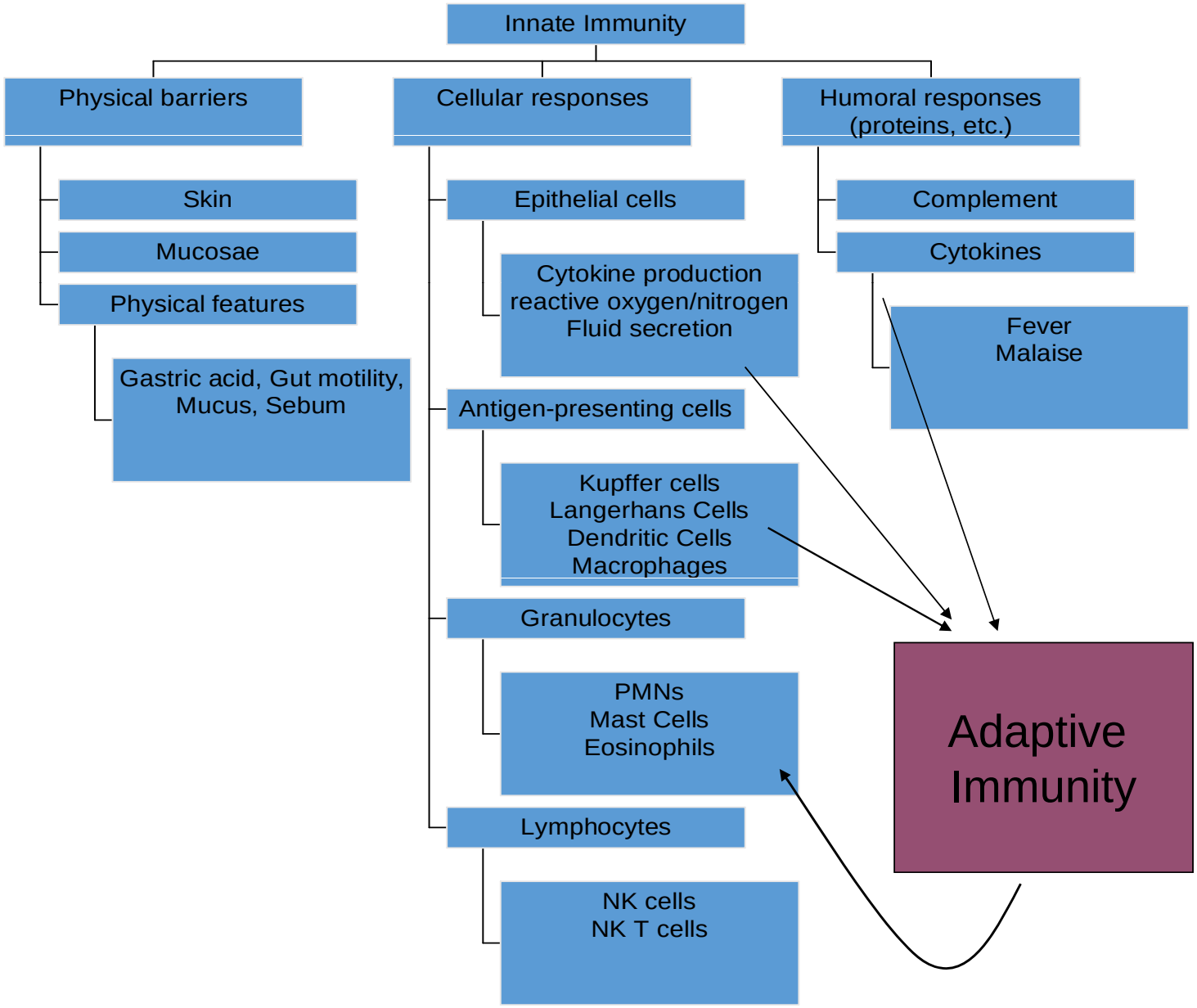
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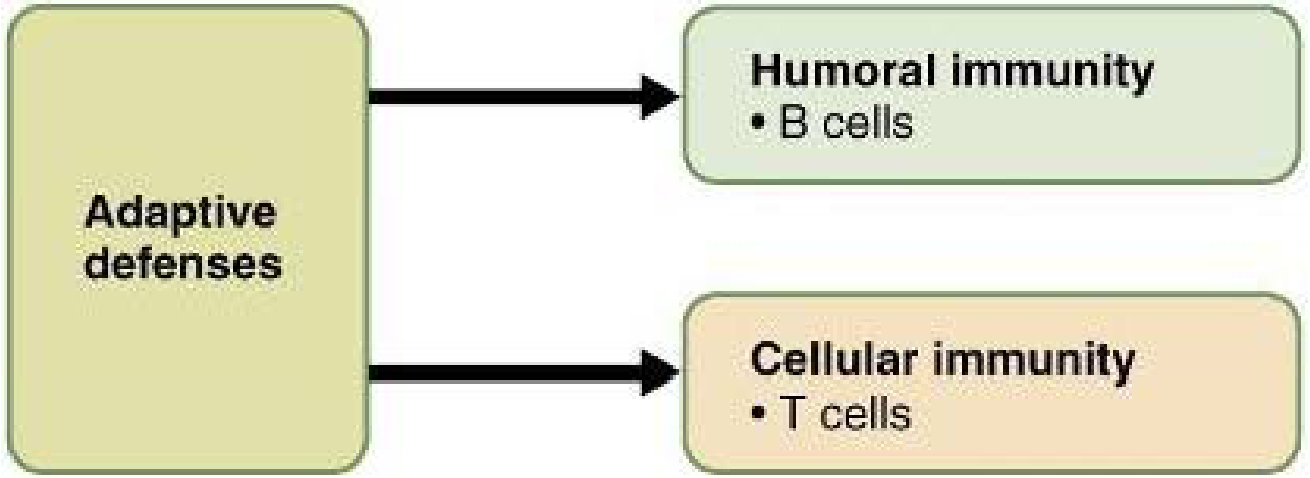
Adaptive Immunity

# Adaptive Immune System

- Adaptive: responds to specific foreign substances



# Adaptive Immunity

**Immune system adapts to previously unseen molecules**

Induction by infection, vaccination

Immune system mounts response

Immune response must:

Recognise micro-organism as foreign

Respond by producing specific antibodies, lymphocytes

Mediate elimination of organisms

Form memory

# Adaptive Immune System: Cells

**Antigen Presenting Cells (APCs)**

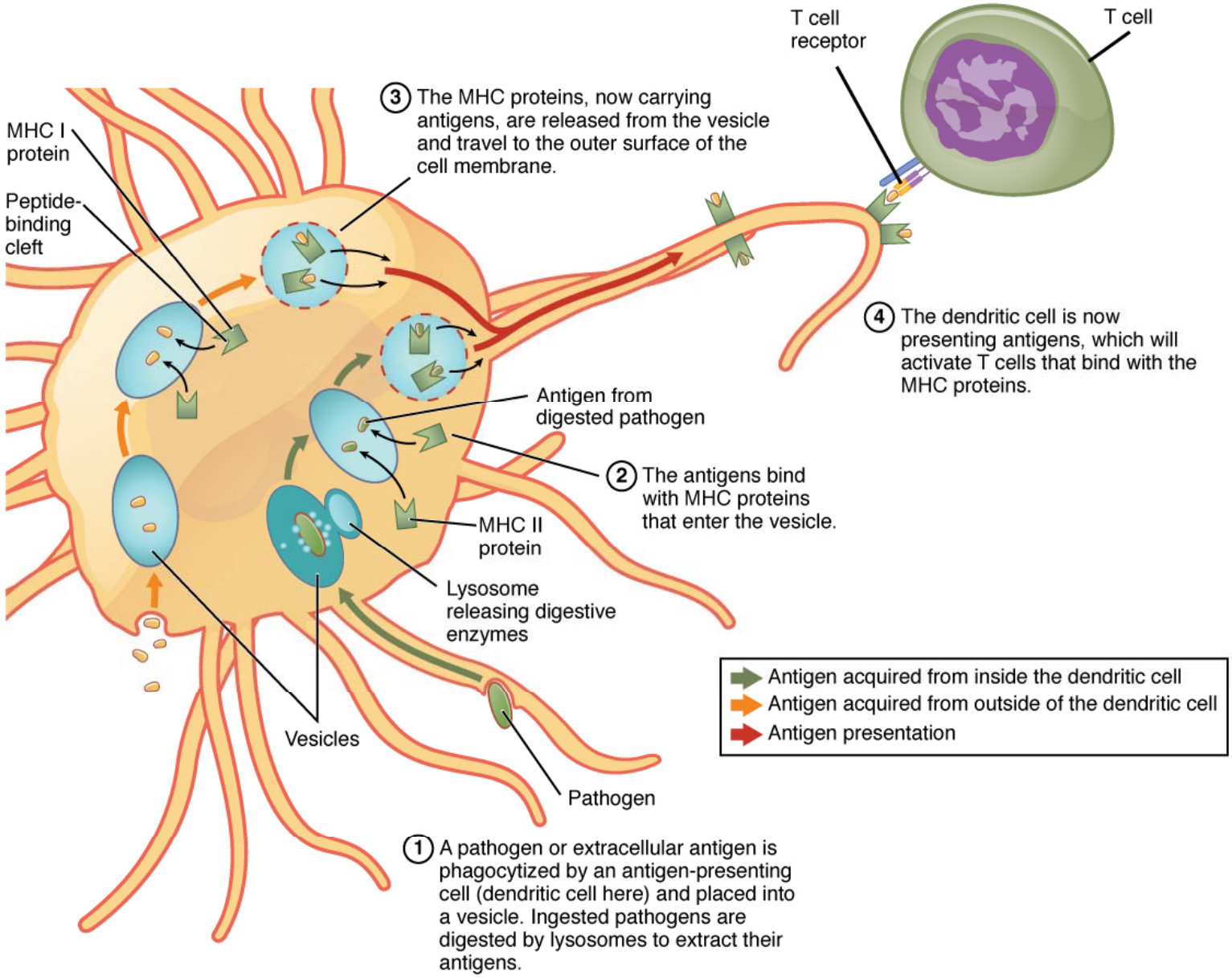
Macrophages & B lymphocytes

Ingest foreign material

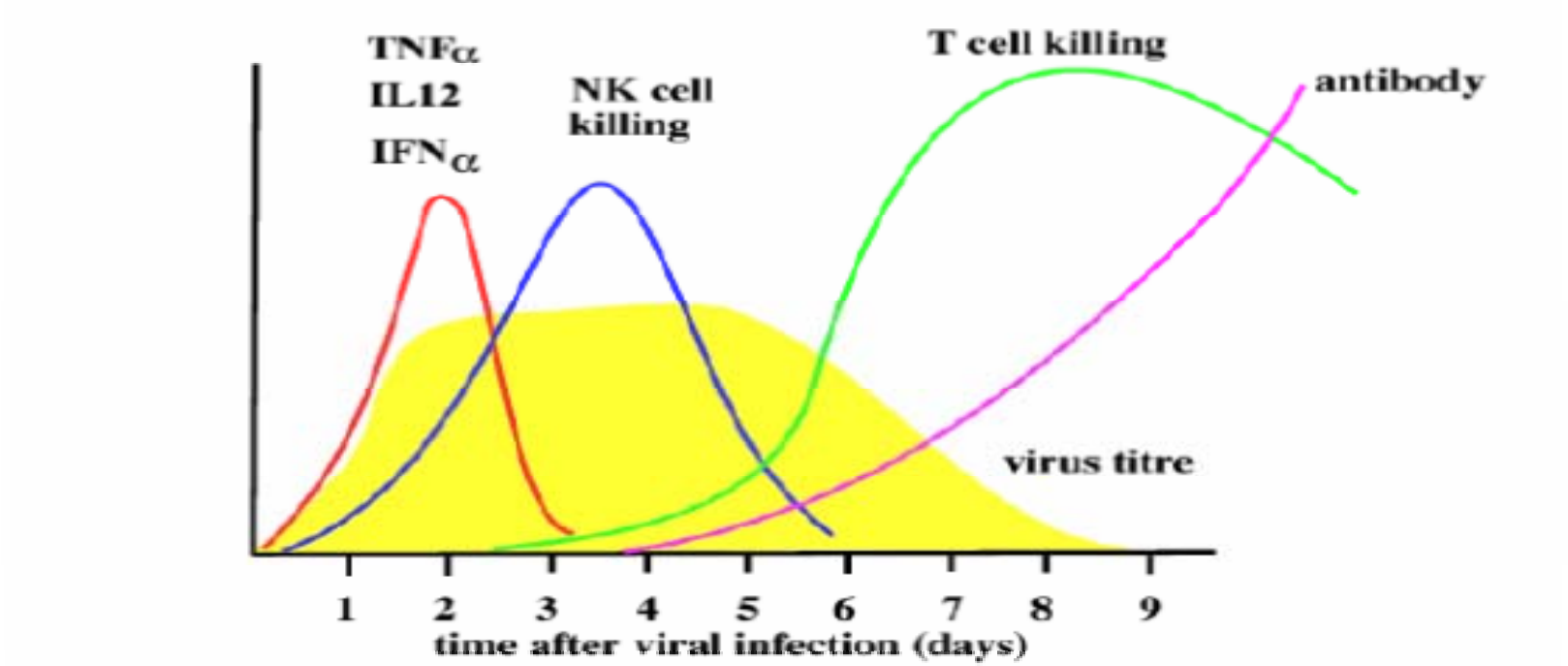
Present antigenic fragments on their cell

Fragments recognised by T-cells.

# Antigen Presenting Cell



# Innate and Adaptive Immunity Work Together



# Adaptive Immunity: active and passive

| | Active Immunity | Passive Immunity |
|---|---|---|
| Natural | Clinical, sub-clinical infection | via breast milk, placenta |
| | | |
| Artificial | Vaccination:<br>Live, non-live | Immune serum, immune cells |

# Cell-mediated Immune Response

## Primary response

- Production of specific clones of effector T cells and memory clones
- Develops in several days
- Does not limit the infection

## Secondary response

- more pronounced, faster
- more effective at limiting the infection

# Generation of Immune Response

~ 4-7 days to generate **primary immune response**

- IgM produced then IgG
- After ~3 weeks primary response turned off
- Ab-producing cells, memory B cells formed
- Memory B cells secrete Ab when same agent encountered again
- This is **secondary immune response**
- **Memory** lasts weeks / years

# Adaptive System: T Cells

Sorted in the Thymus

Manage the immune response

Eliminate microbes that survive within phagocytes or other infected cells

Produce memory cells

# T lymphocytes

Two types

- Helper T- lymphocytes ($T_H$L)

  -activate phagocytes to kill microbes

  -activate B cell

- Cytotoxic T-lymphocyte (CTL)

  -destroy infected cells containing microbes

# Functions of $T_H$ Cells

## Orchestrate immune response

- Recognize antigen presented by APC
- Cytokines are delivered
- Cytokines activate APC to destroy antigen

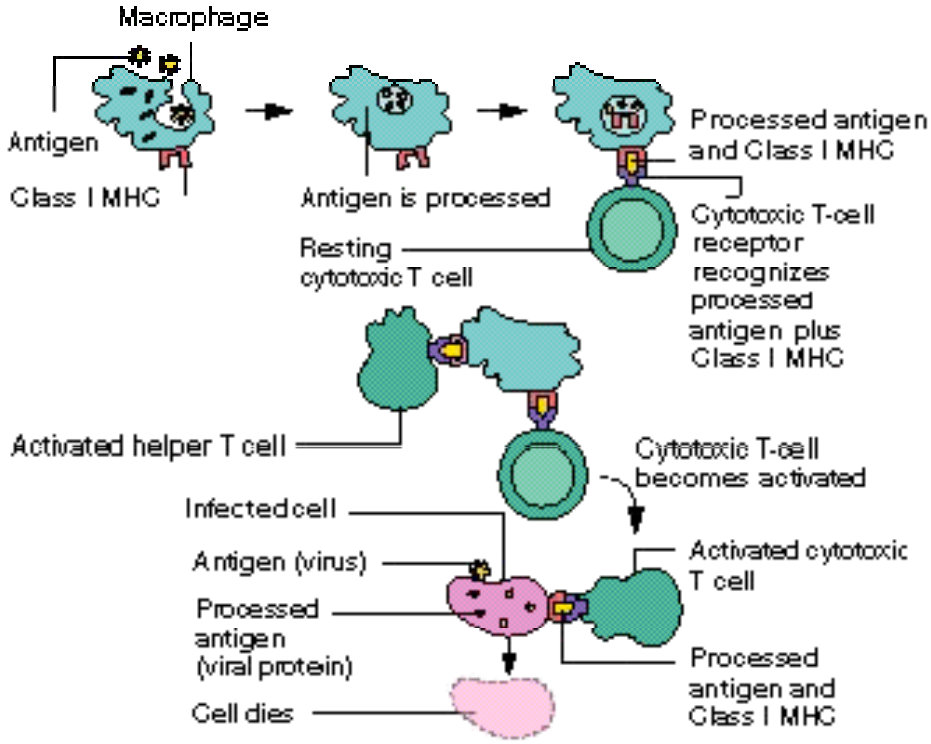
## Activate B cell

If $T_H$ cell encounters B cell bearing antigen

- $T_H$ cell produces cytokines
- Cytokines activate B cell
- B cell proliferates
- Drives formation of B memory cells

# Cell-mediated Immune Response

1. T-cell
   - recognizes antigen on macrophage
   - identifies molecules on cell surfaces
2. T-cell goes into effector stage that can kill infected cells



## Slide 32

**I1** Is this sentence right?
Suzi Lyons, 20/03/2006

# Adaptive System: B Cells

- Eliminate extra-cellular microbes and their toxins
- Are APCs and Ab-producing cells

Antigen binds to B-cell receptors

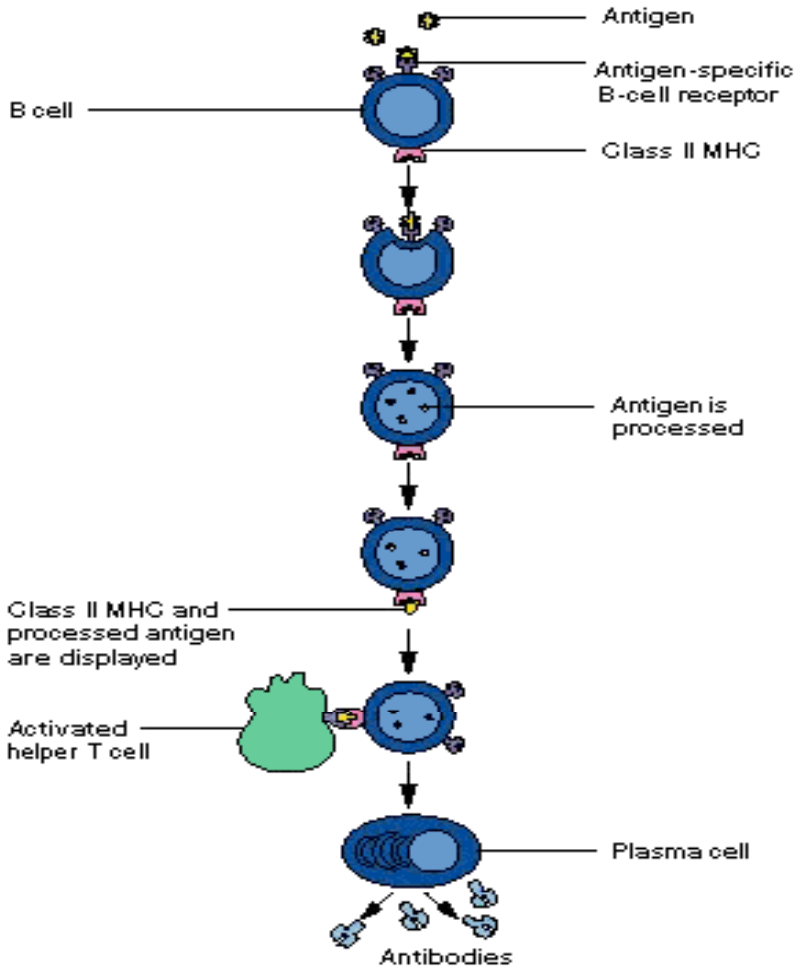
Antigen ingested by B-cell

B cell presents antigen to T-cell

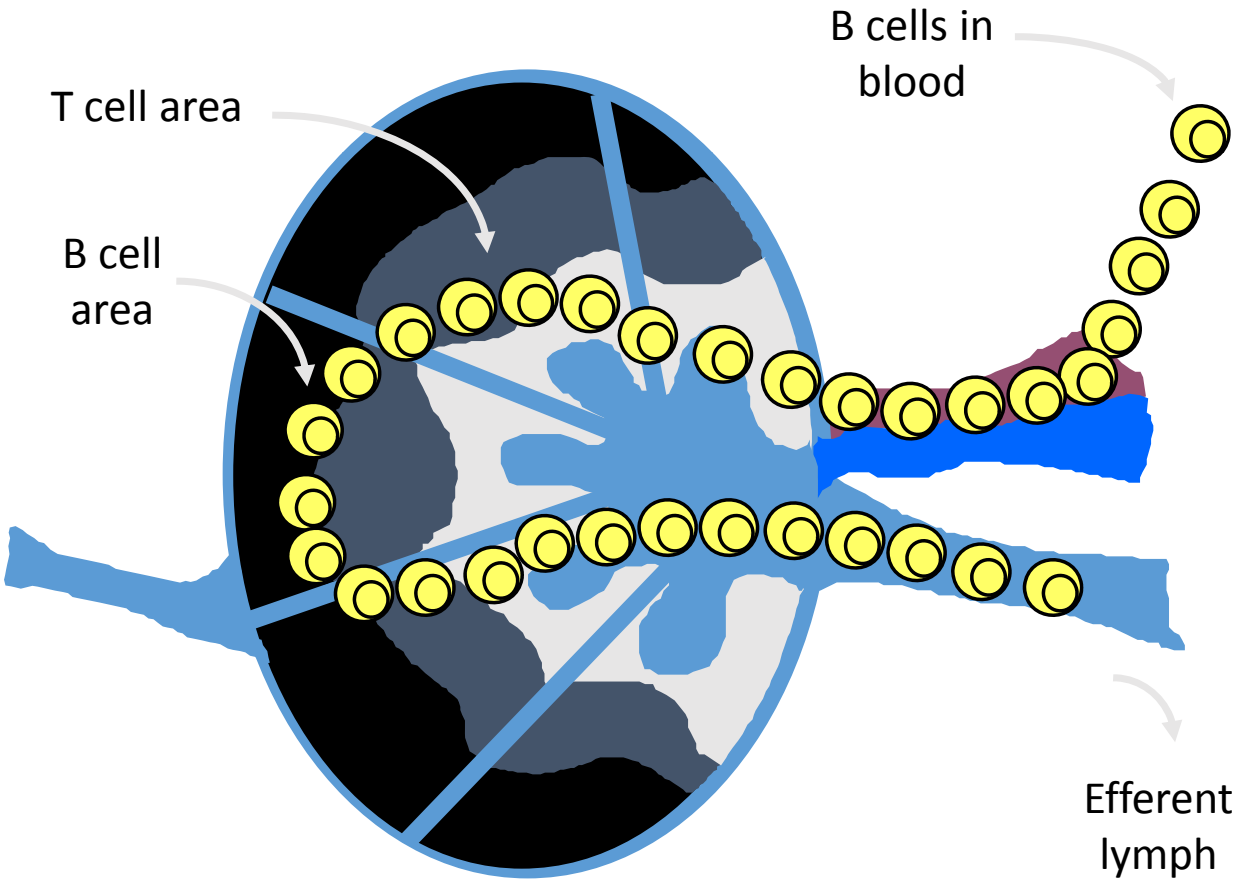
B cell produces antibody

# Humoral (B cell) Immune Response

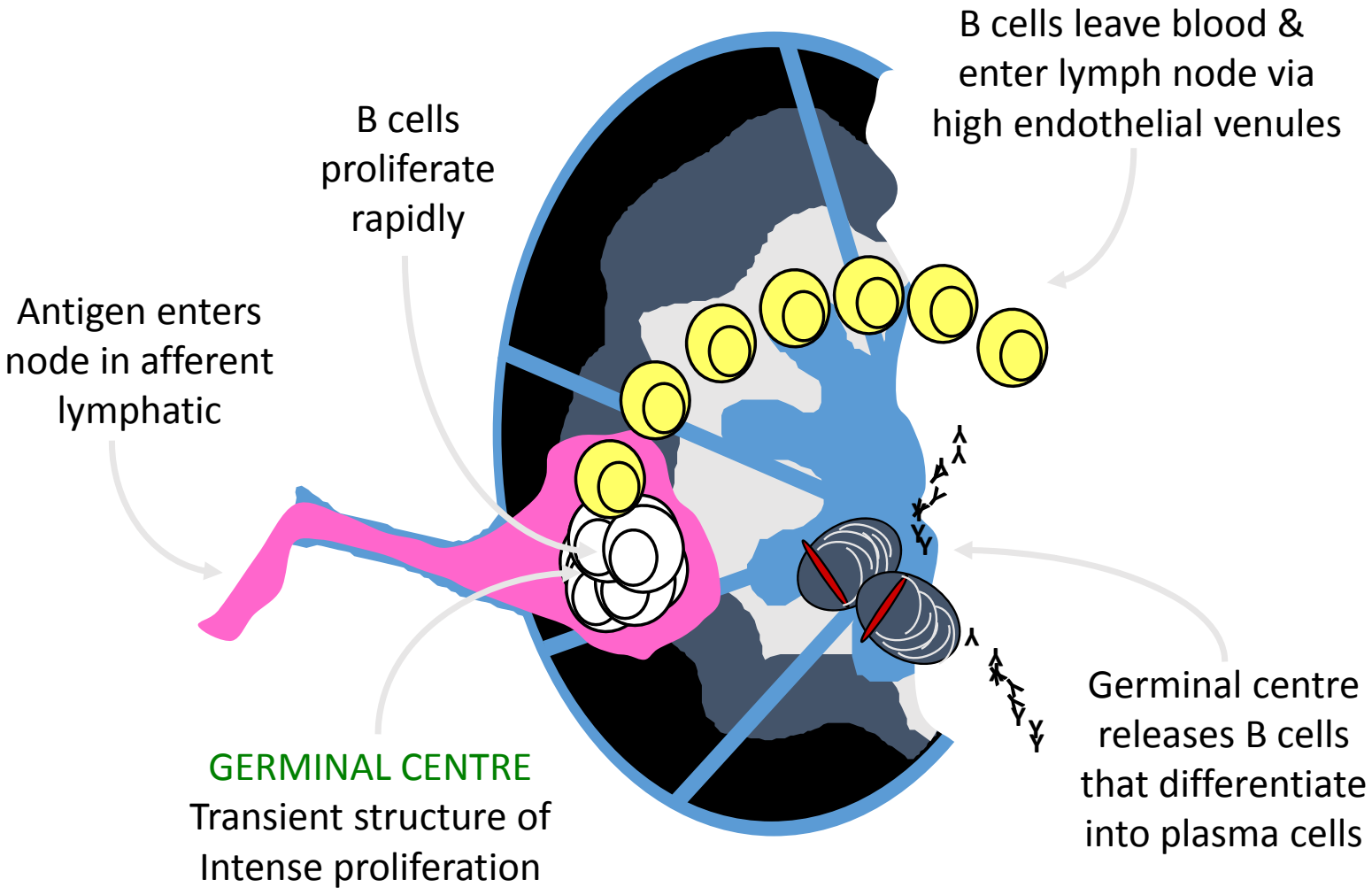
1. B lymphocytes recognize specific antigens
   - proliferate and differentiate into Ab-secreting plasma cells
2. Abs bind to specific Ags on microbes; destroy microbes
3. Some B lymphocytes evolve into memory cells



# Recirculating B cells pass through lymphoid organs



# Recirculating B cells are trapped by foreign antigens in lymphoid organs



# Summary (1)

**Innate immunity**

- relies on mechanisms already existing before microbe infects host
- is the first line of defense
- has no memory for subsequent exposure
- relies on non specific mechanisms

# Summary (2)

**Adaptive immunity**

- develops following entry of microbe
- comes into action after innate immunity fails to get rid of microbe
- has memory to deal with subsequent exposure
- happens through specific cells
  - T cells (cell mediated)
  - B cells (antibody mediated)

# Summary (3)

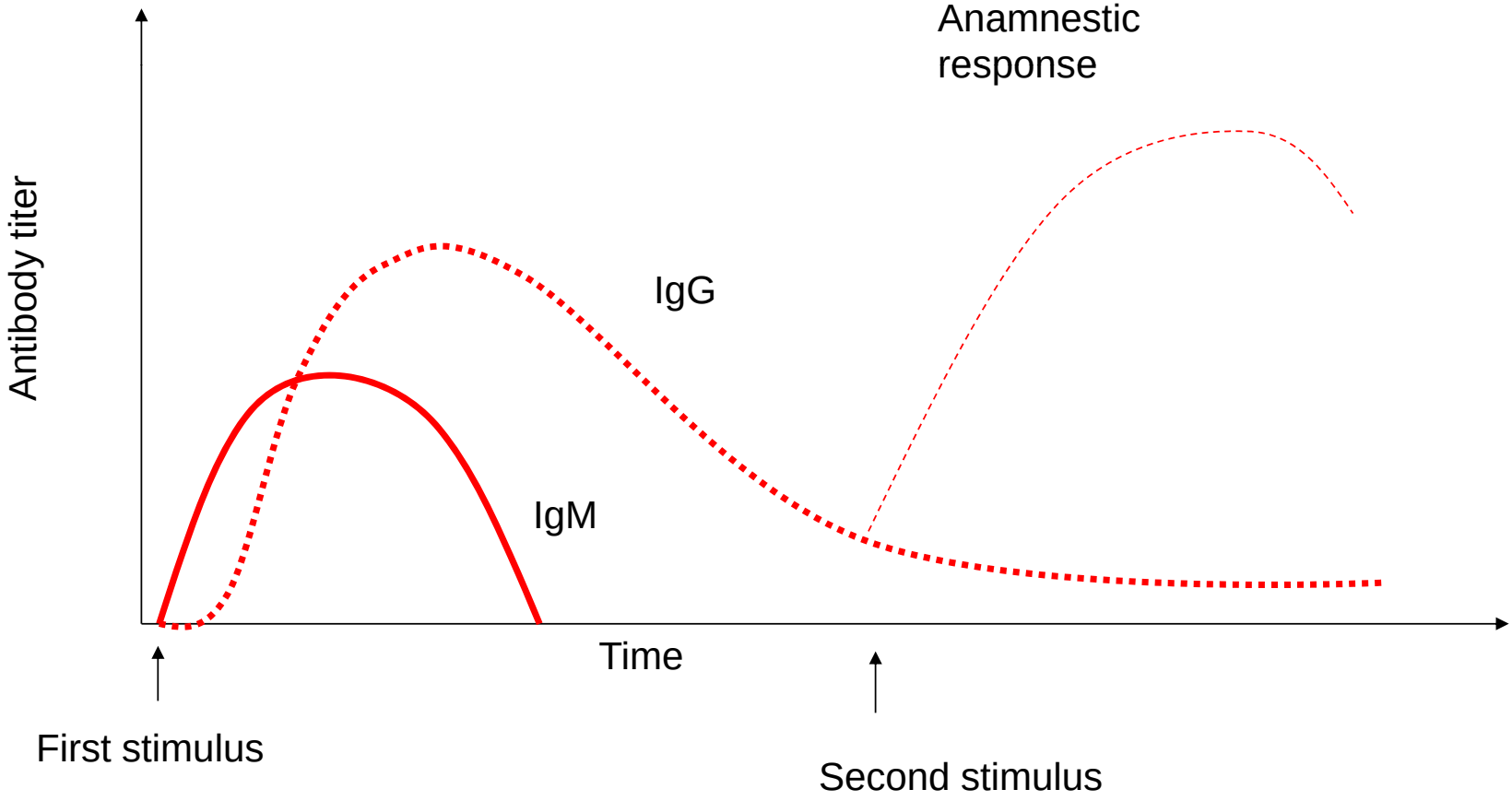
**Primary immune response**

- short lasting
- smaller in magnitude

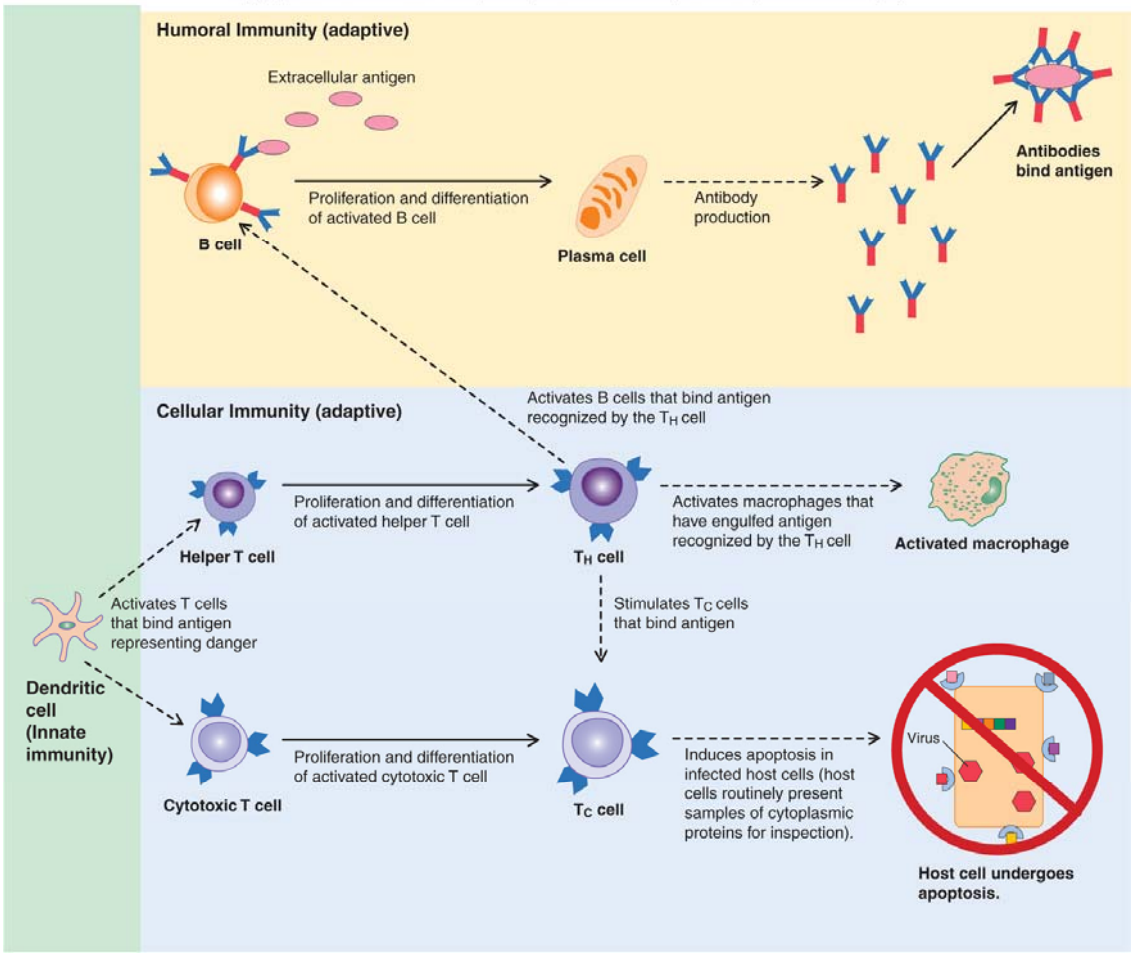
**Secondary immune response**

- longer in duration
- larger in magnitude
- develope ‘memory cells’ following primary response

# IgM – IgG sequential response



# Summary of Adaptive Immune Response



# What is a Vaccine?

- Biological preparation that improves immunity to a particular disease
- Contains antigen(s) that resembles a pathogen
- Stimulates immune system to recognise antigen as foreign,

  destroy it, and "remember" it
- Pathogens later encountered cause memory response

# Types of vaccines

| | Live Attenuated vaccines | Inactivated vaccines | Toxoids | Cellular fraction vaccines | Recombinant vaccines |
|---|---|---|---|---|---|
| | •BCG<br>•Typhoid oral<br>•Oral polio<br>•Yellow fever<br>•Measles<br>•Mumps<br>•Rubella<br>•Intranasal Influenza | •Typhoid<br>•Cholera<br>•Pertussis<br>•Plague<br>•Rabies<br>•IPV<br>•Influenza<br>•Japanese encephalitis | •Diphtheria<br>•Tetanus | •Meningococcal polysaccharide vaccine<br>•Pneumococcal polysaccharide vaccine<br>•Hepatitis B polypeptide vaccine | •Hepatitis B vaccine |

**Live attenuated pathogens**

MMR, BCG, Cholera

**Inactivated pathogens**

IPV, Pertussis

**Subunit / Peptide components**

HepB (Hepatitis B surface antigen)

Influenza (purified HA & NA antigens)

**Conjugate (polysaccharides joined to protein carrier)**

HiB , PCV,  MenB, C, ACWY

**Toxoids**

Diphtheria, tetanus

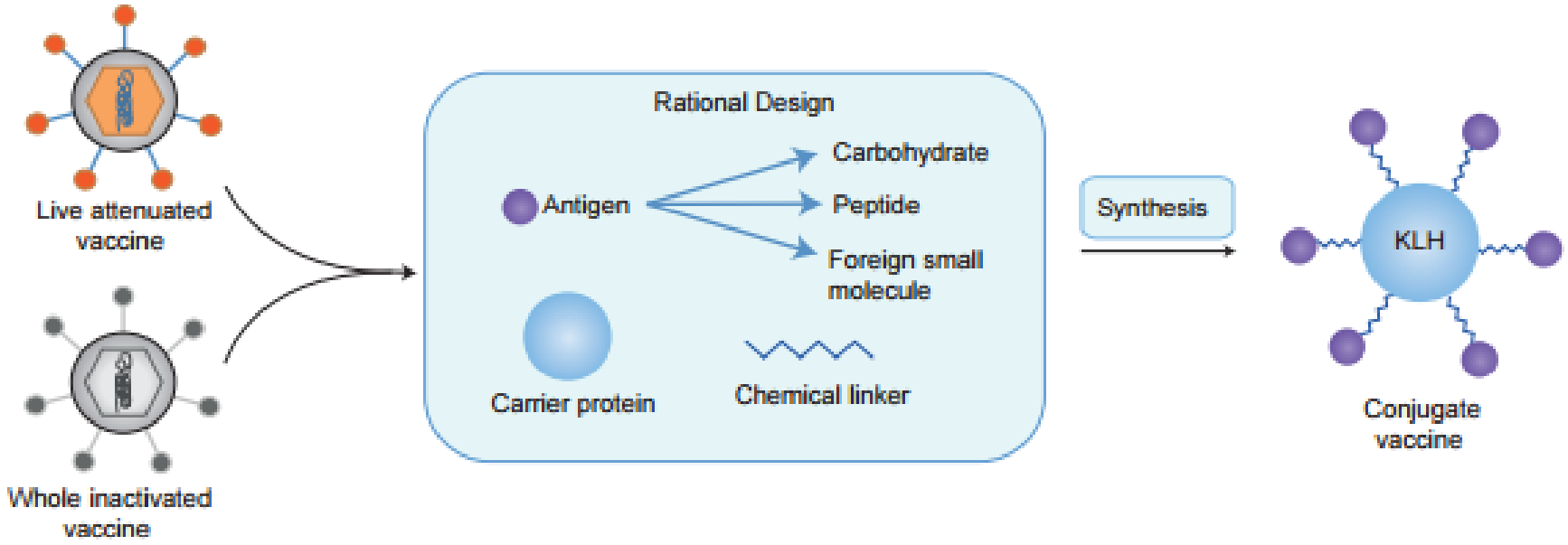


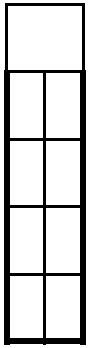

**Figure 1 | Modular approach to rationally designed synthetic vaccines.** The empirical nature of traditional vaccine development, which relies on the use of live attenuated or whole inactivated viruses, is being replaced by a more sophisticated molecular approach that harnesses computational design and advanced synthetic techniques to create well-defined conjugate vaccines.

# Pros and Cons of Different Types of Vaccines

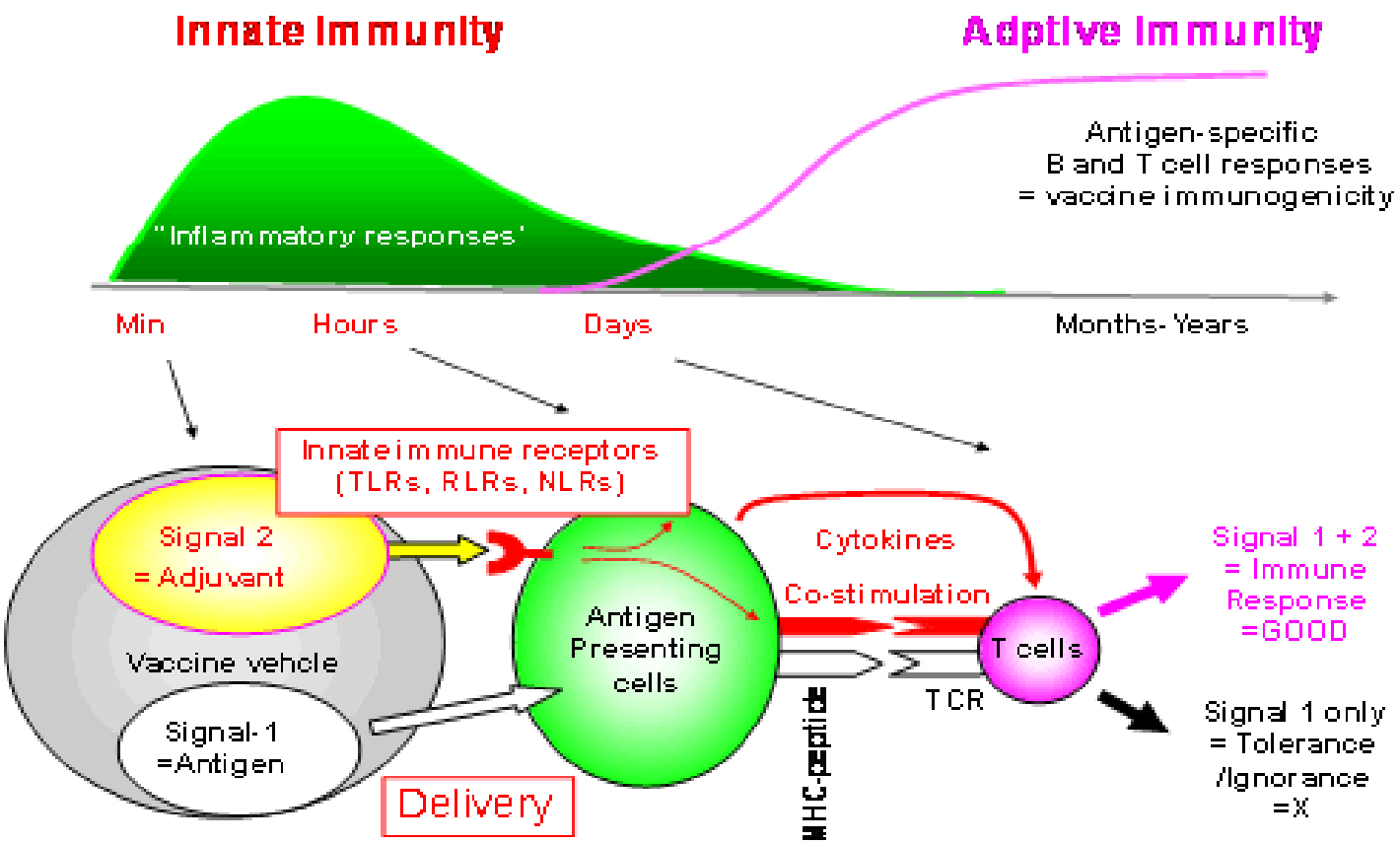
**Live attenuated** pros: better immune response
cons: reversion - oral polio
infection in immunodeficient
less stable

**Inactivated** pros: may be safer; more stable than live
cons: weaker immune response; boosters
contaminants

**Molecular components** pros: no living pathogen present
very stable
fewer side effects
cons: fewer epitopes
weaker immune response



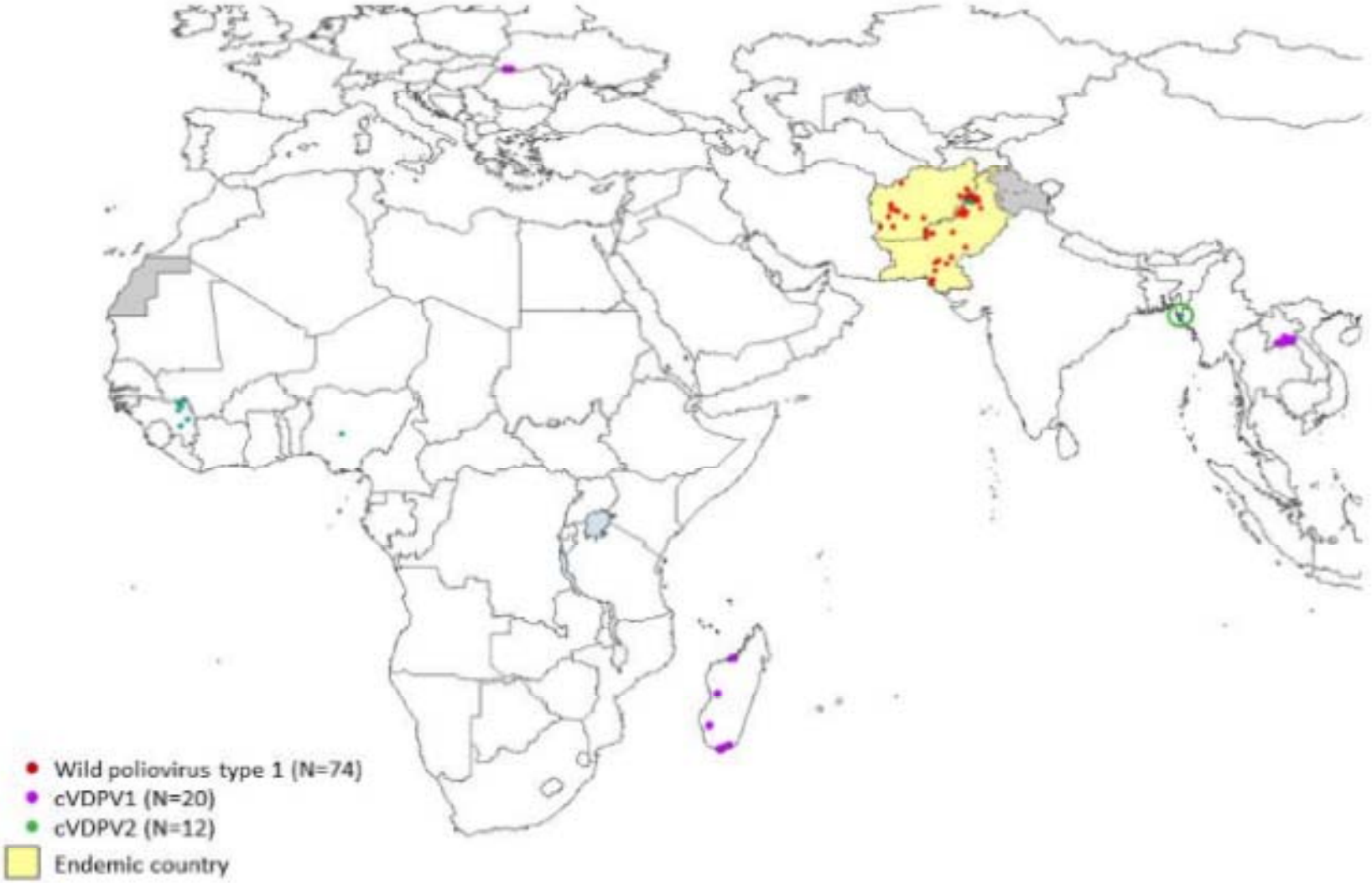
# Innate control of vaccine immunogenicity



# Reported Cases of VPDs, Europe

| | 1980 | 2000 | 2011 | 2012 | 2013 |
|---|---|---|---|---|---|
| Diphtheria | 608 | 1,585 | 33 | 32 | 32 |
| Measles | 851,849 | 37,421 | 37,073 | 26,982 | 25,375 |
| Mumps | No data | 243,344 | 27,448 | 38,141 | 35,075 |
| Pertussis | 90,546 | 53,675 | 34,432 | 56,941 | 27,824 |
| Polio | 549 | 0 | 0 | 0 | 0 |
| Rubella | No data | 621,039 | 9,672 | 30,509 | 39,614 |
| Rubella (CRS) | No data | 48 | 7 | 60 | 50 |
| Tetanus | 1,715 | 412 | 197 | 194 | 93 |

# Wild Poliovirus & cVDPV Cases[1], 2015
## 01 January – 31 December




[1]Excludes viruses detected from environmental surveillance.

POLIO TYPE

WPV & cVDPV

SURVEILLANCE

- ☐ ADEQUATE STOOL COLLECTION (Rolling 12 Month Period)
- ☐ NONPOLIO ACUTE FLACCID PARALYSIS (Rolling 12 Month Period)
- ☐ ENVIRONMENTAL (Rolling 6 Month Period)

**YEAR-TO-DATE 2016**

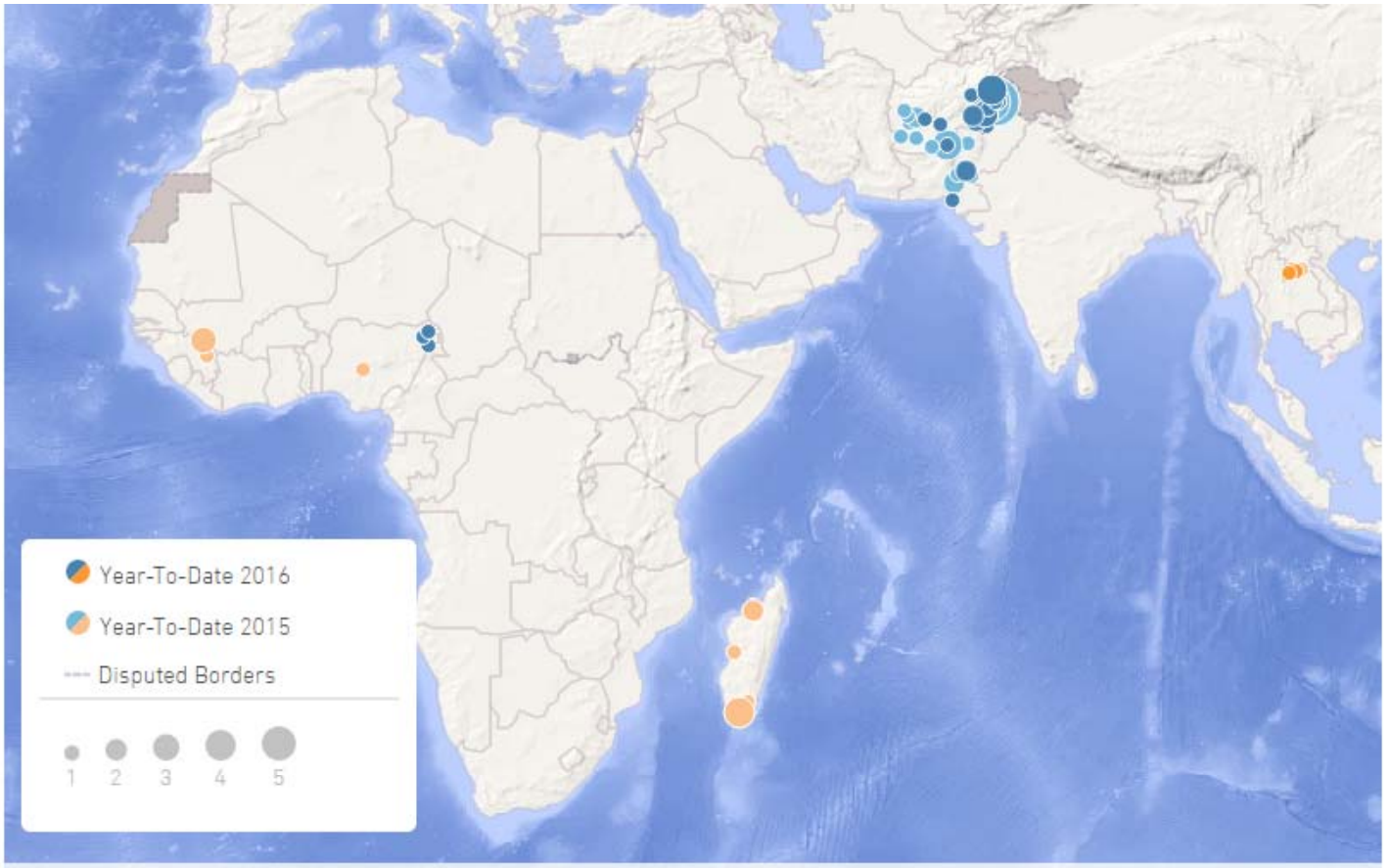
Jan 1 - Oct 10, 2016

**26** WPV **3** cVDPV

**YEAR-TO-DATE 2015**

Jan 1 - Oct 10, 2015

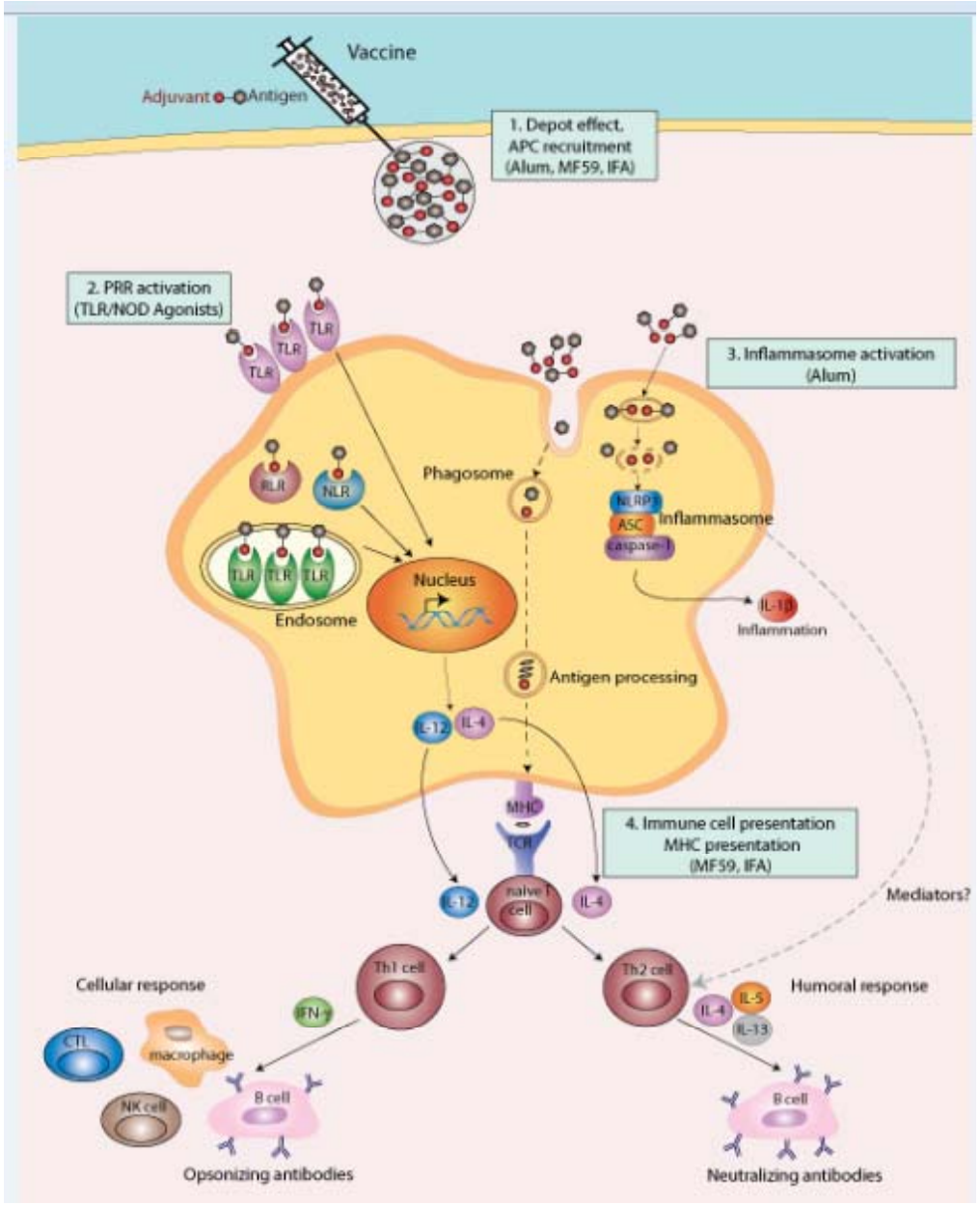
**48** WPV **20** cVPDV






World Health Organization

# How Vaccines Work



# Primary and Memory Response