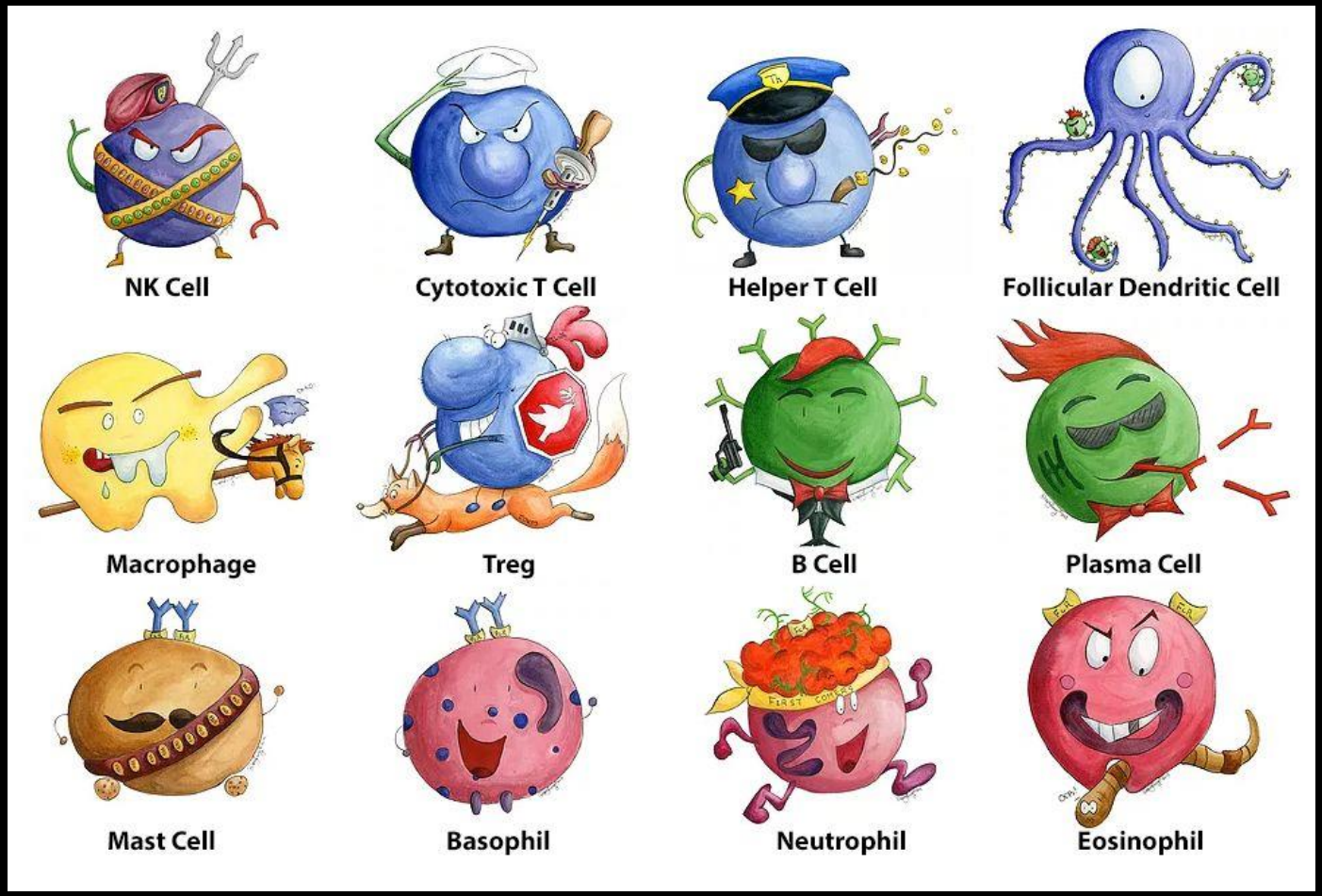
Science of Living System: BS20001

Host Defense and Prevention of Diseases



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Human Diseases

1. Infections (caused by bacteria, virus, fungi etc)
2. Autoimmune diseases (Failure of our immune system in recognition of self vs non-self)
3. Immunodeficiency (lack/defect in immune system)
4. Cancers (several known and unknown reasons)

Immunology: The Beginning

Edward Jenner: father of Immunology

- In 15th century dried crusts from small pox were either inhaled or inserted into small cuts in the skin (**Variolation**).

- In 1796, **Edward Jenner** demonstrated that inoculation with cow-pox protects against small pox, a lethal disease at that time. A process he termed **Vaccination**

- **Louis Pasteur**'s hypothesis: Weakened or attenuated strain could be administered to protect from that specific strain causing disease - **Vaccine**

The Immune System: Body's Defense Mechanism

- The main objective is to seek, identify and kill invaders

- A complex system that encompasses every organ and compartment of the body
- Highly adaptable (can act against pathogens ranging from ~ 30nm to ~100 cm)
- Distinguishes between **self and foreign** and mount response to only foreign while preserving self ('us' vs 'them')

Challenges of the Immune System

- **Pathogen-induced diseases:**

Major groups of human pathogens	Specific examples	Disease
Viruses	*Poliovirus*	Poliomyelitis (Polio)
	Variola Virus	Smallpox
	Human Immunodeficiency Virus	AIDS
	Rubeola Virus	Measles
Fungi	*Candida albicans*	Candidiasis (Thrush)
	Tinea corporis	Ringworm
	Cryptococcus neoformans	Cryptococcal meningitis
Parasites	*Plasmodium species*	Malaria
	Leishmania major	Leishmaniasis
	Entamoeba histolytica	Amoebic colitis
Bacteria	*Mycobacterium tuberculosis*	Tuberculosis
	Bordetella pertussis	Whooping cough (pertussis)
	Vibrio cholerae	Cholera
	Borrelia burgdorferi	Lyme disease

- **Autoimmune diseases:** When self is attacked by the immune system
- **Cancer:** Failure of Immune system to attack defective cells
- **Immune deficiency:** A component of immune system is absent/defective

Our immune system generates almost infinite variety of cells and substances

Foreign Recognition

Effector Response

- To eliminate or neutralize foreign particle

- when a person becomes infected by a disease, the body builds immunity against the disease (**natural**)
- a person can build a resistance to a disease following vaccination (**artificial**)
- when an infant receives mother's antibodies (**natural**)
- when a person receives antibodies (gamma globulin injection), say after a snake bite (**artificial**)

Memory

- Upon second exposure produces enhanced response

- **Active immunity**: Immunity that will generate **long** term memory
- **Passive immunity**: Immunity that will generate **short** term memory

The immune system

A functional system – **NOT** an organ system:

A very complex system that includes:

- Skin – physical barrier
- Lining of mucus membranes – physical barrier
- Secretions – tears, mucus etc **-** antimicrobial
- Blood cells and vasculature – White blood cells (WBCs)
- Bone marrow—source of Hematopoietic Stem Cell (HSC)
- Lymphatic system and lymphoid organs
- Most tissues – have resident immune cells

Distribution of the Immune System

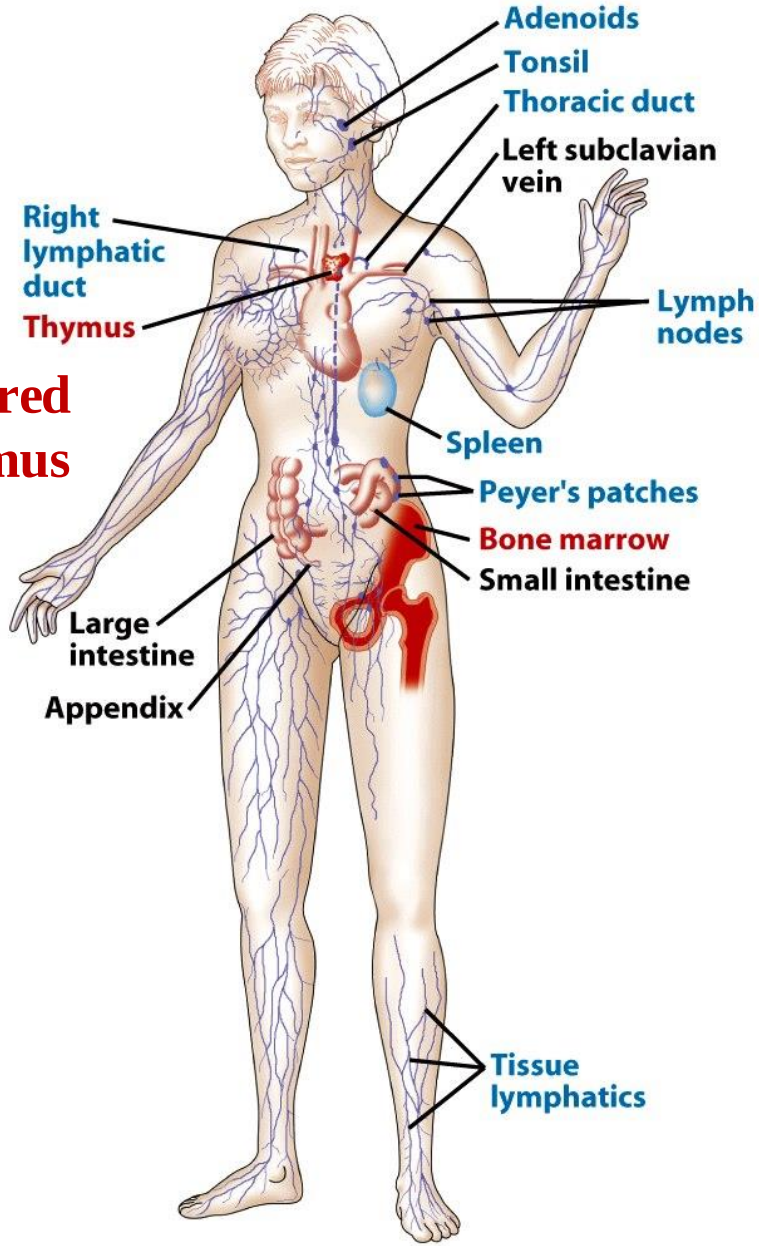


Figure 2-11
Kuby IMMUNOLOGY, Sixth Edition

T cells are matured in the thymus

Red: Primary lymphoid organs
Blue: Secondary lymphoid organs

The **bone marrow** contains **blood-forming Stem cells,** and **makes B cells, innate cells, and all other blood cell types**

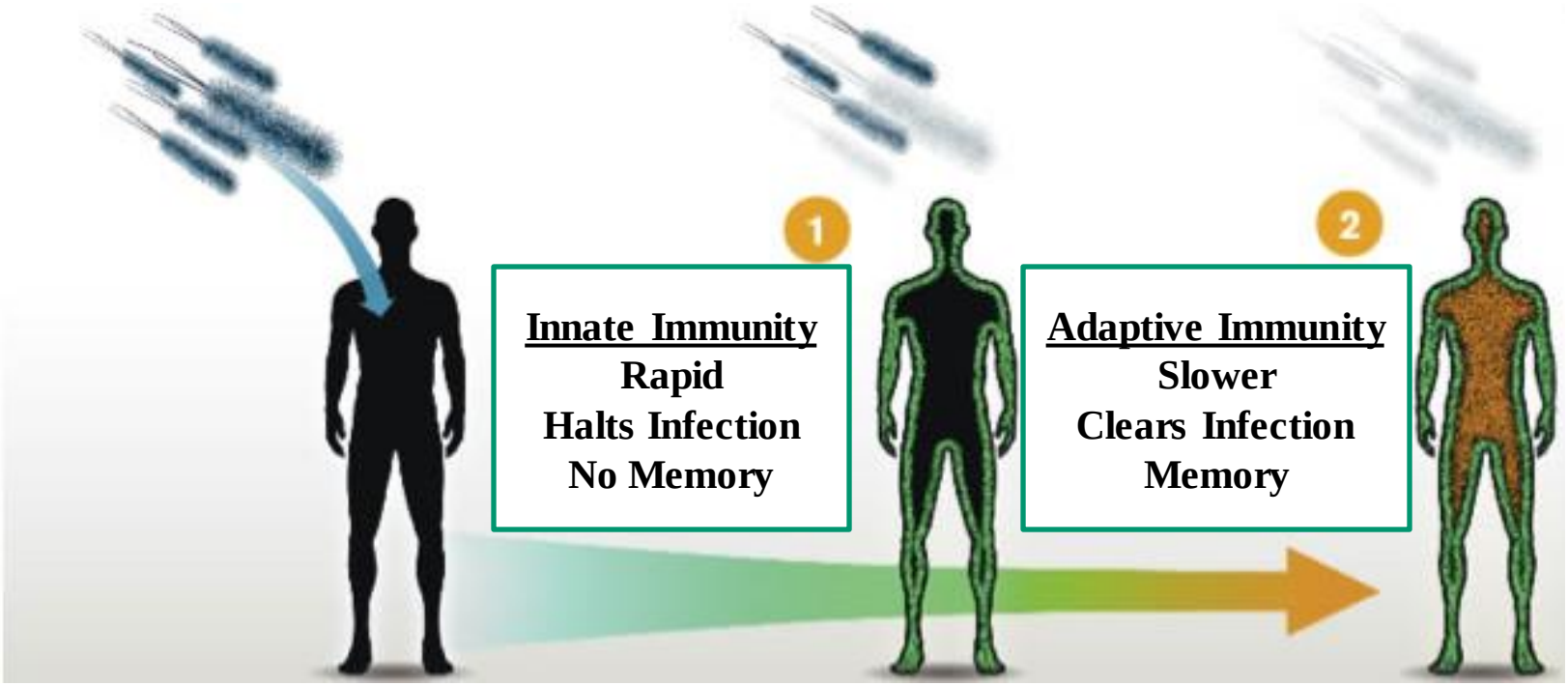
Two modes of immunity

In response to pathogens, vertebrate immune systems use two interconnected systems:

Innate immunity: inborn

Adaptive immunity: acquired during the life-span

Innate vs Adaptive Immunity



First insights into mechanisms of immunity

Elie Metchnikoff

Emil von Behring

S. Kitasato

- **1880's-** Metchnikoff discovered *phagocytic cells* that ingest microbes and particles-
  - **cells confer immunity**
- **1890-** von Behring and Kitasato discovered blood sera could transfer immunity-
  - **liquid of blood confer immunity**

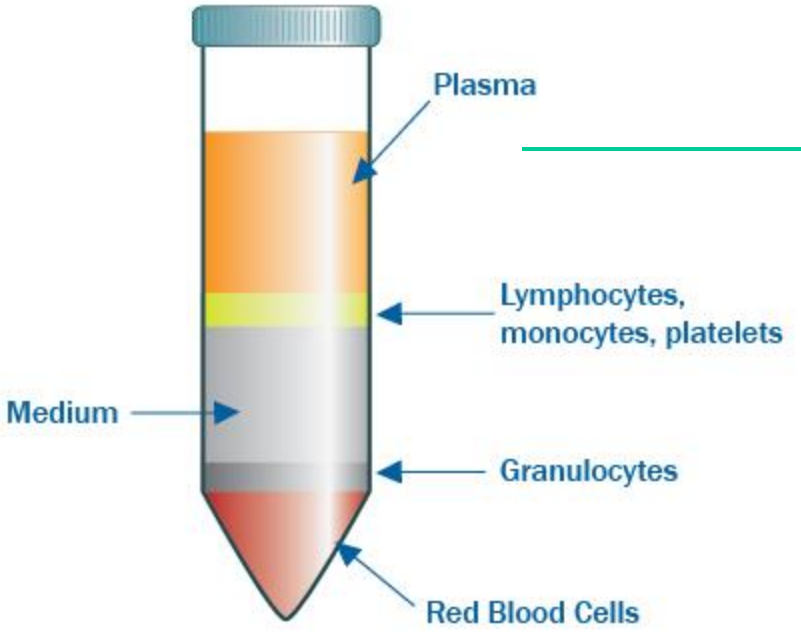
❖ **What confers immunity…**

➢ **cells or serum?**

Components of immune system in Blood

Centrifugation of blood

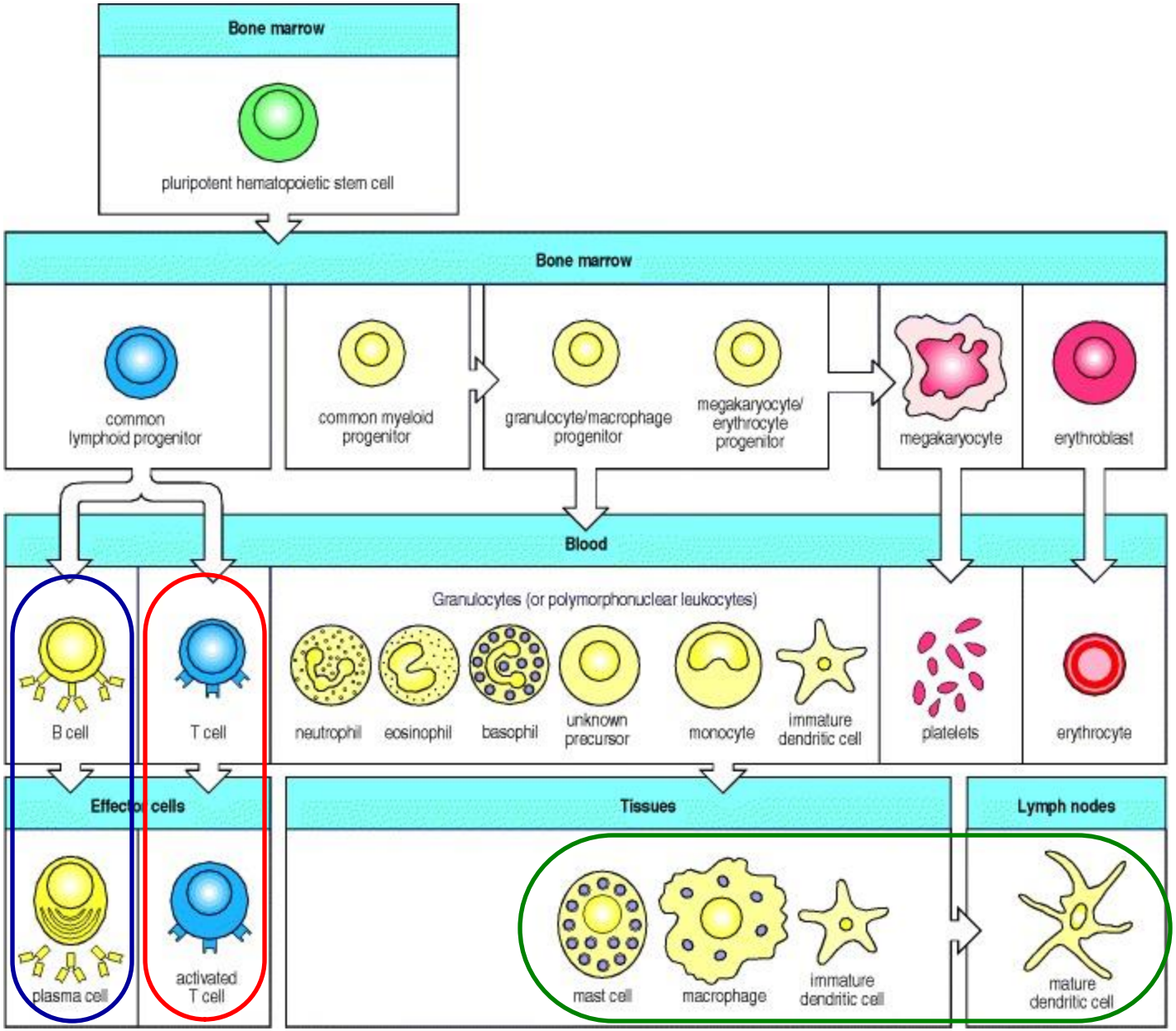
Immune component



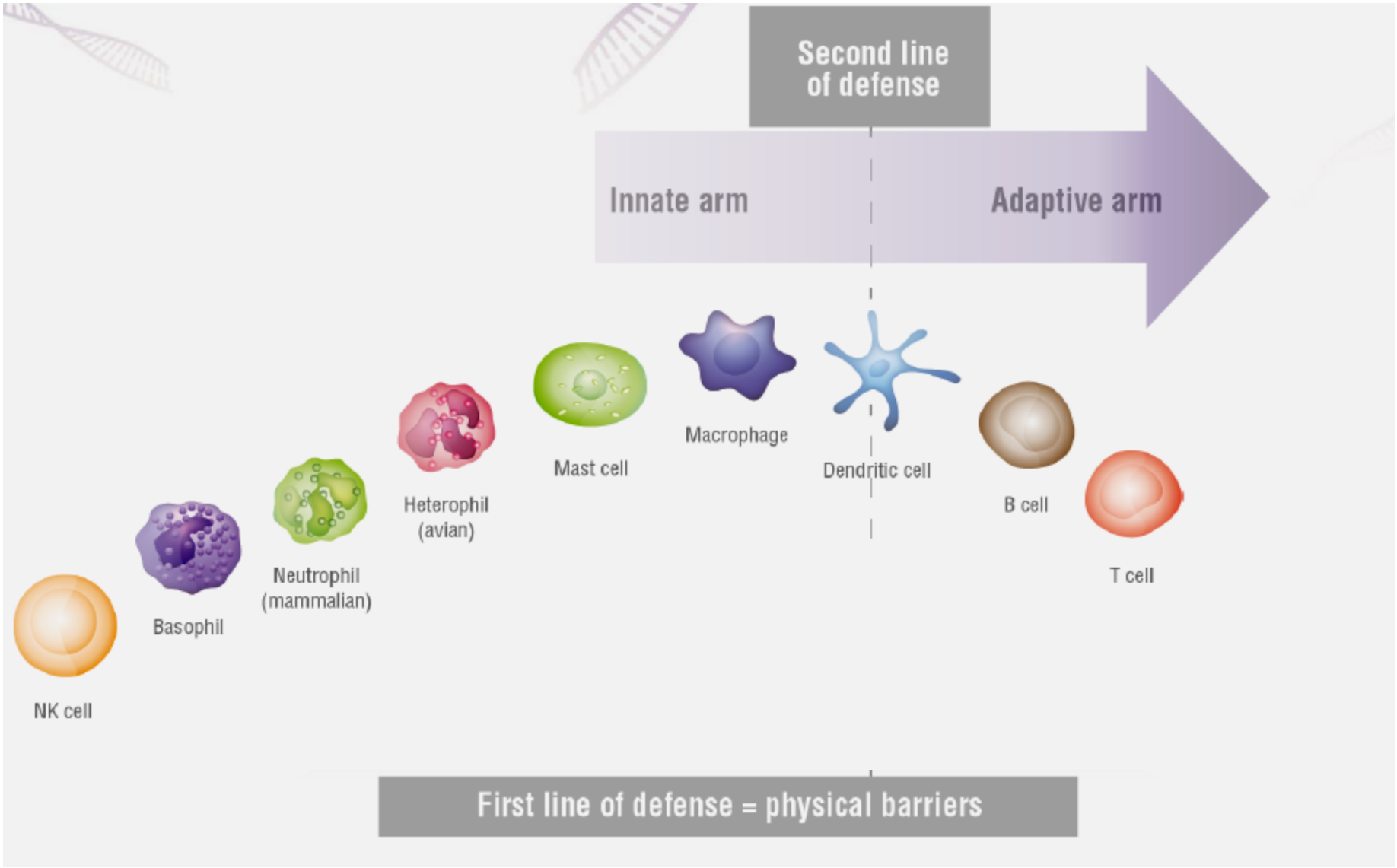
Antibodies and others

WBCs

Blood cell types and their origin



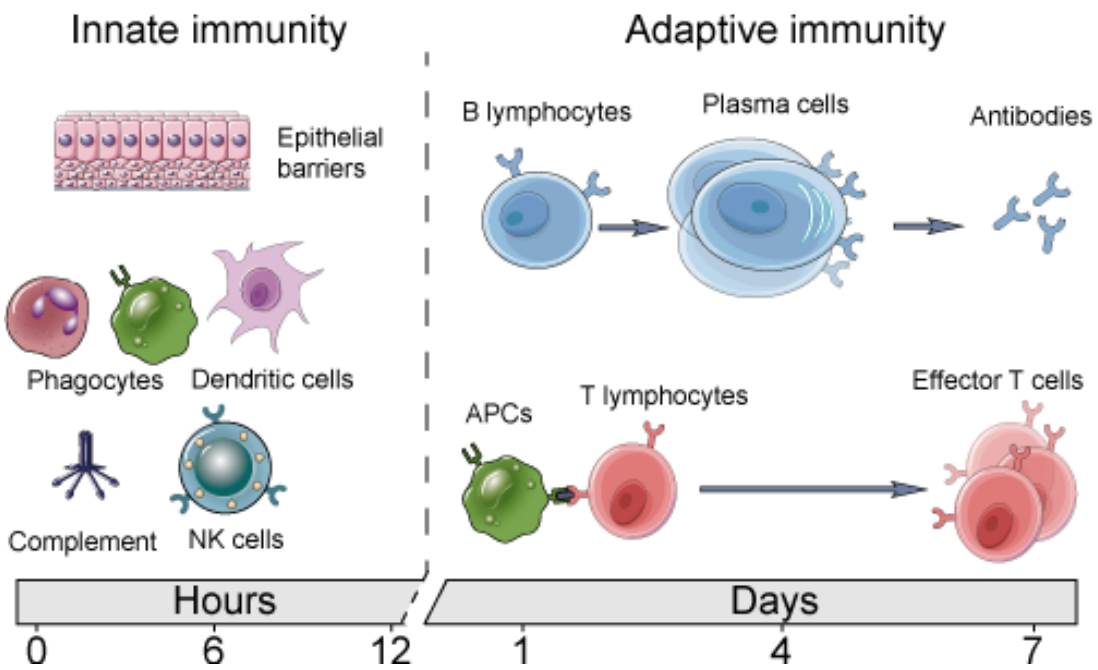
Immune system defends against infection



Innate vs **Adaptive :** Differences at a glance

	Innate	Adaptive
Response time	Minutes to hours	Days
Specificity	Limited and fixed	Highly diverse; adapts to improve during the course of immune response
Response to repeat infection	Same each time	More rapid and effective with each subsequent exposure
Major components	Barriers (e.g., skin); phagocytes; pattern recognition molecules	T and B lymphocytes; antigen-specific receptors; antibodies

Table 1-4
Kuby Immunology, Seventh Edition

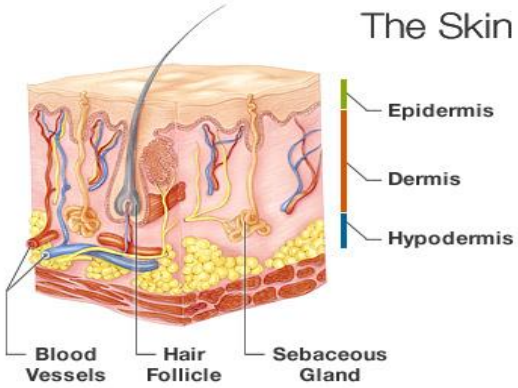


Innate immune system

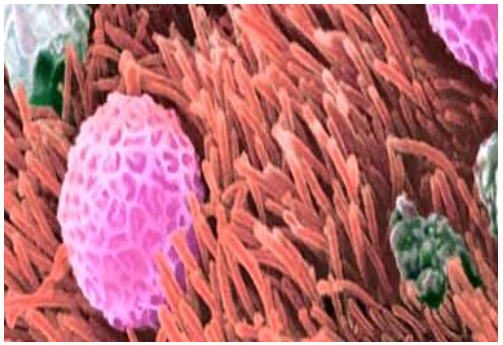
http://sciencebyadam.blogspot.in/

Mechanical Factors

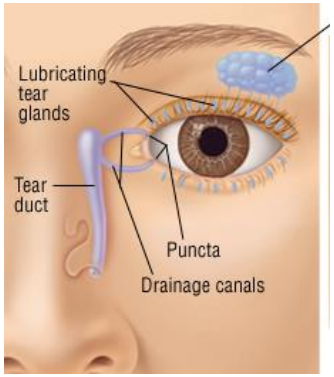
- Skin



- Mucous



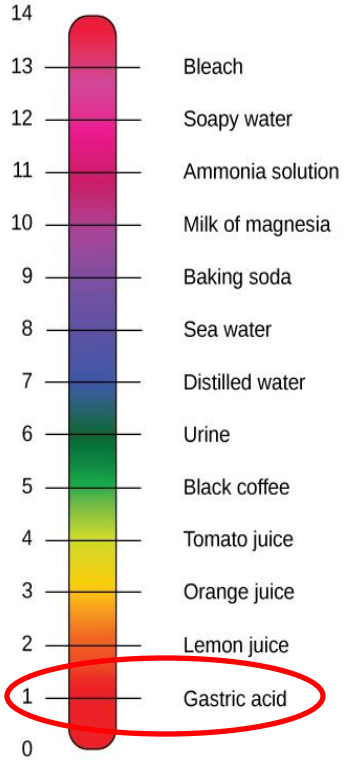
- Flushing action of saliva, tear, urine



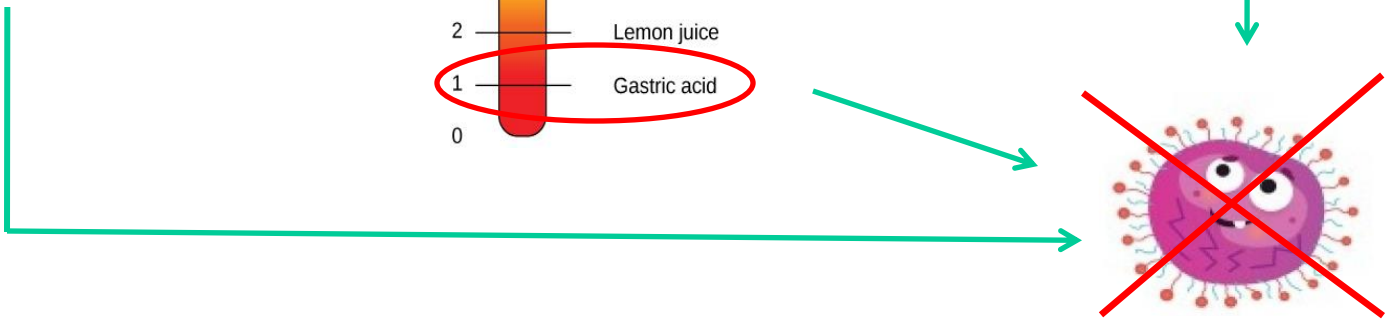
Chemical factors

Antimicrobial Peptides in sweat

HCl in stomach

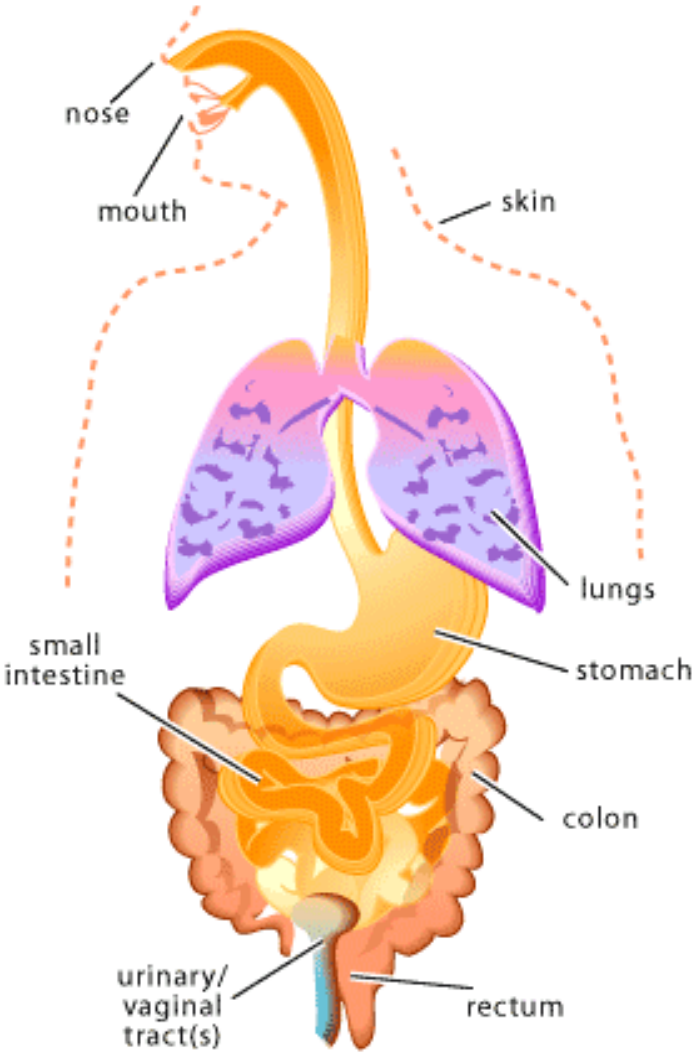


Lysozyme in tears /saliva



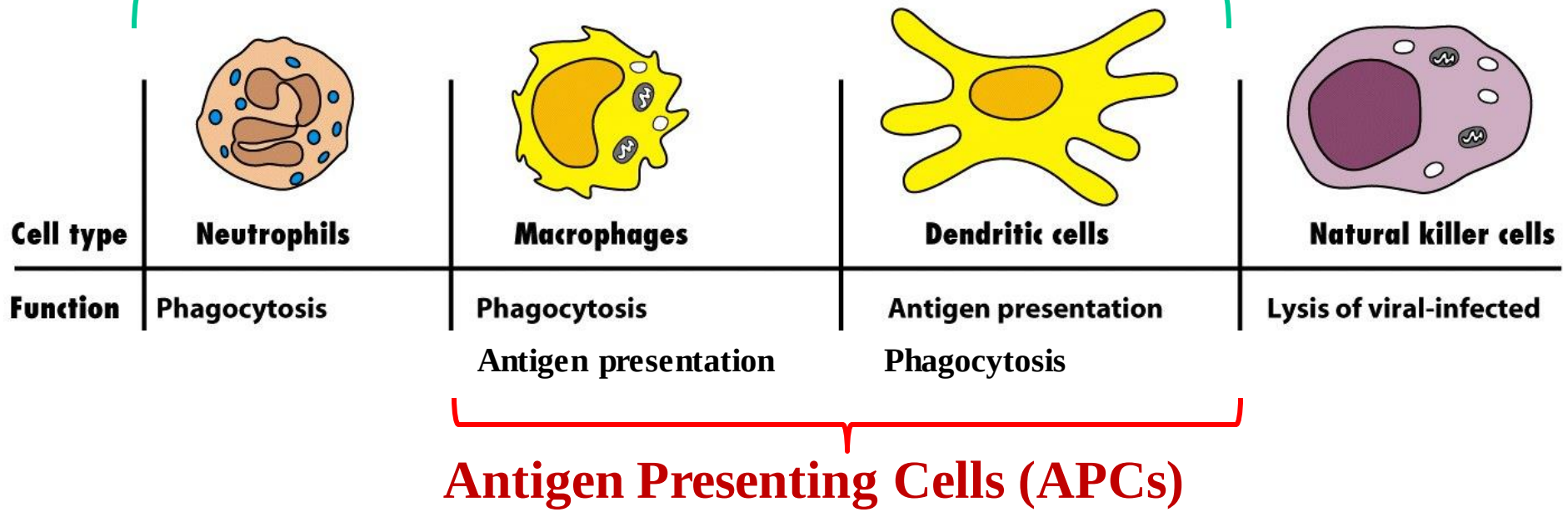
Biological factors

- Symbiotic (commensal) **microbial flora**:
  - microbes in many parts of the body
  - > 1000 species of bacteria
  - competes with pathogens for nutrients and space



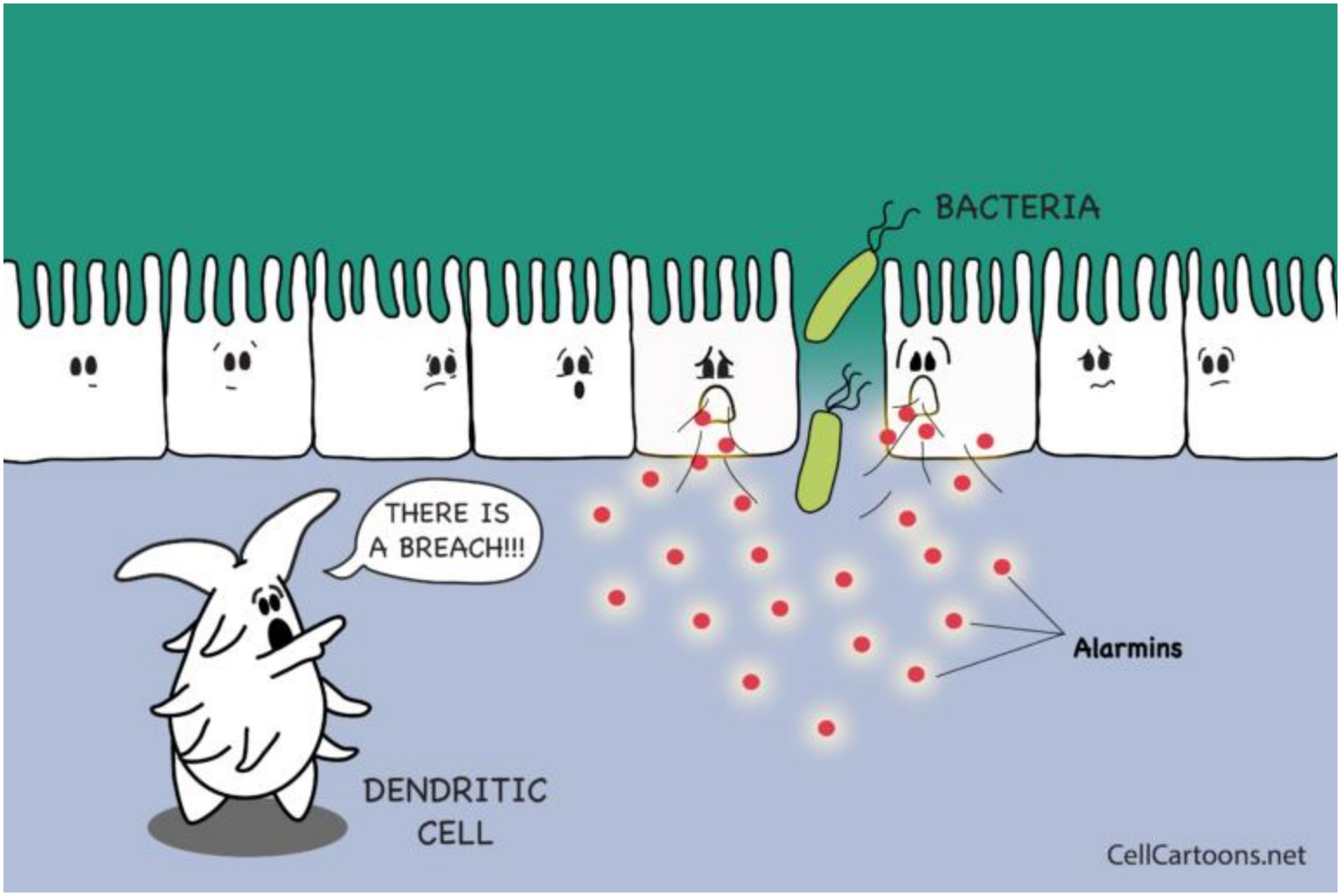
The Major Cells of Innate Immunity

Big eaters/Always hungry

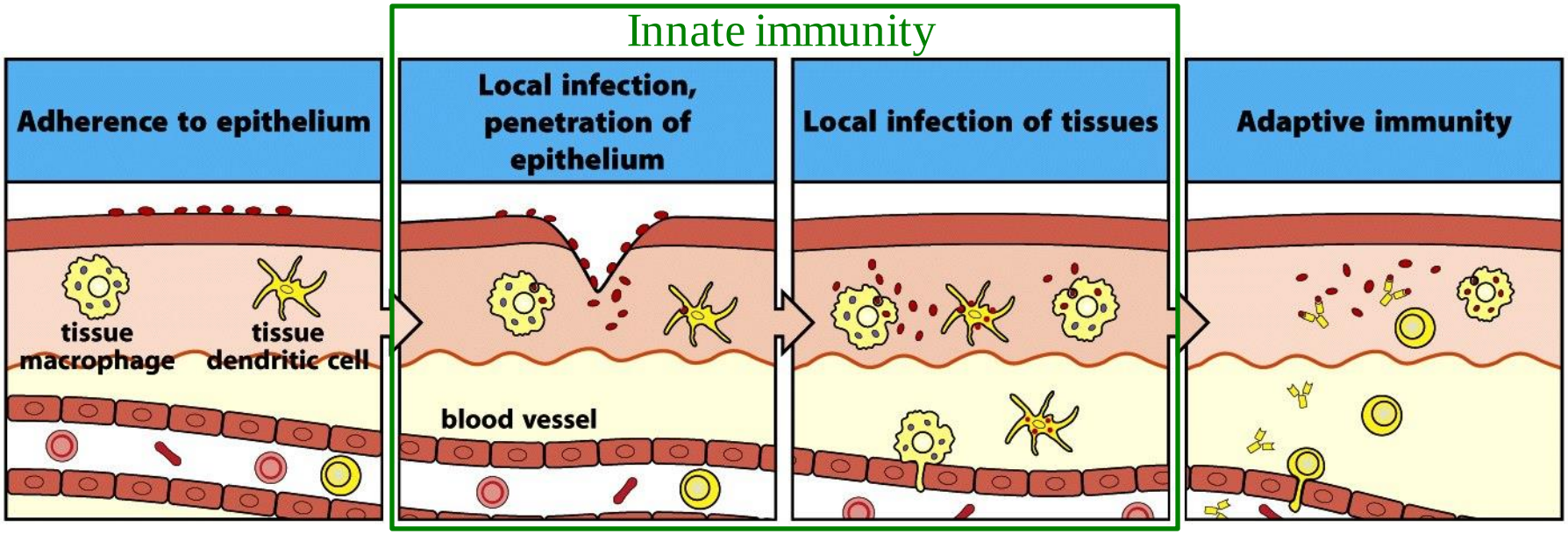


Antigen Presenting Cells (APCs)

- Proteins eaten by APCs are broken down to small pieces (peptides), which are loaded on special receptors (MHCs) and transported to the cell surface. Peptides loaded MHC complex can be recognized by T cells and that interaction can lead to adaptive immune response.


BACTERIA
THERE IS A BREACH!!!
Alarmins
DENDRITIC CELL
CellCartoons.net

Epithelial Barriers: what happens after a breach?



Janeway 7th edition

Epithelial Barriers: what happens after a breach?

Inflammatory response: A fundamental type of response by the body to injury/localize infection is characterized by the classical signs of :

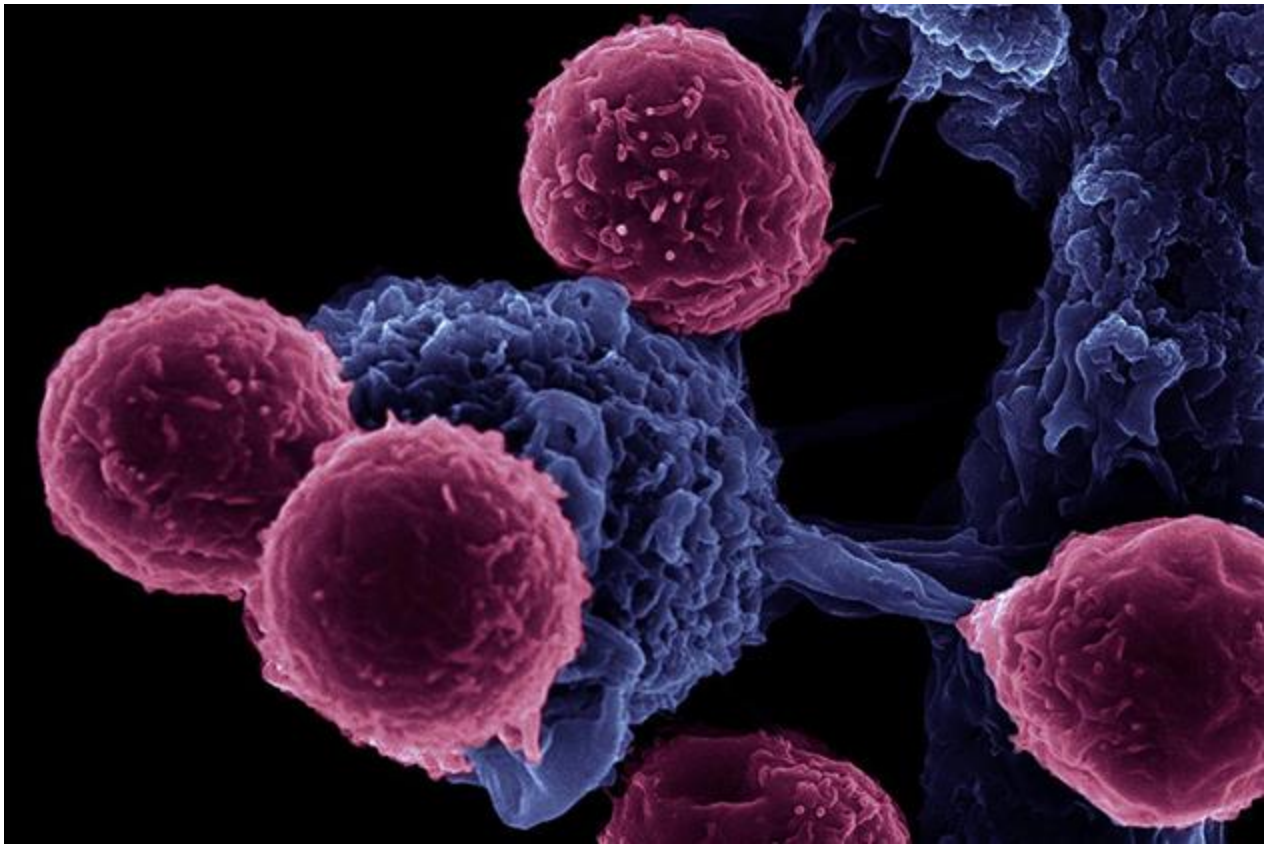
1. Vasodilation → Increase in blood volume in the area → **Heat and Redness**

2. Vascular permeability increases → Leakage of fluid from blood vessel → **Swelling, Pain**

Inflammation: Heat, Redness, Swelling, Pain

WBCs enter the tissue from the local blood vessels and halts or clears the potential threat

Components and Mechanisms of the **Adaptive Immune Response**

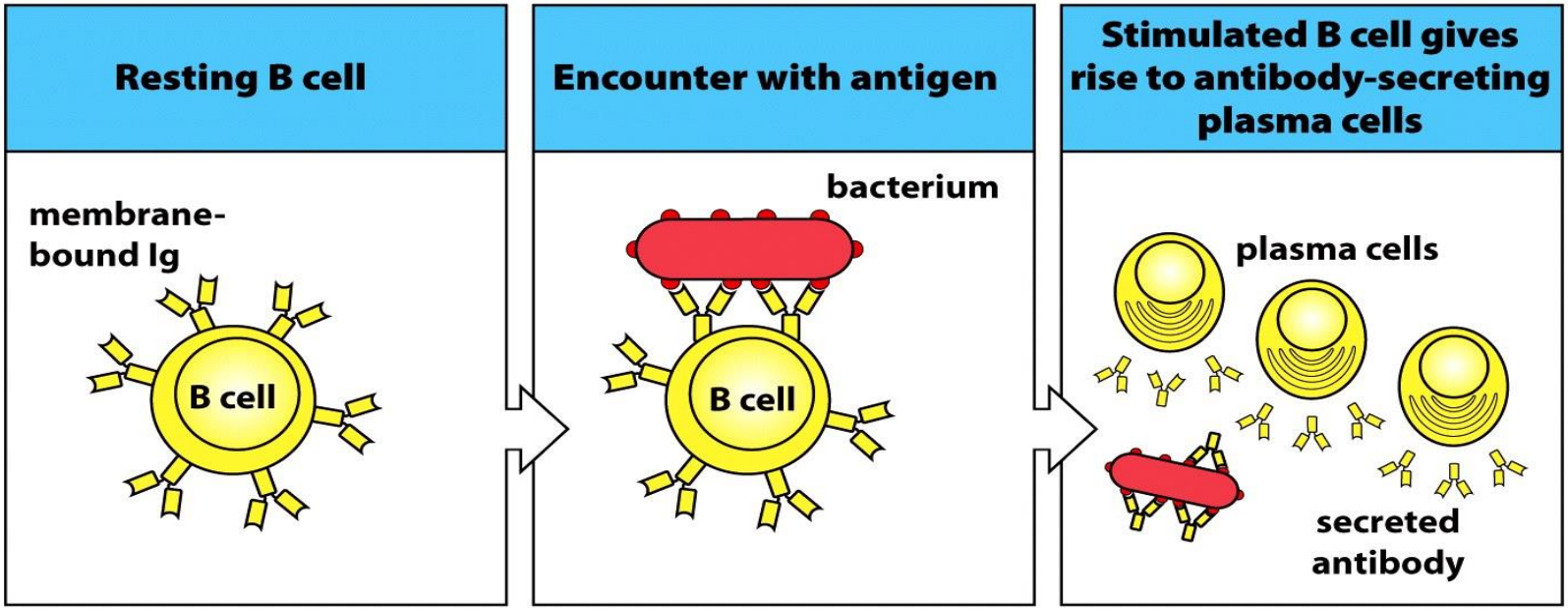


An image of immune cell communication, showing dendritic cells interacting with T cells, taken using an FEI microscope, magnification 16,000x. (Rita Serda/FEI Image)

Adaptive Immunity: Our most powerful defense

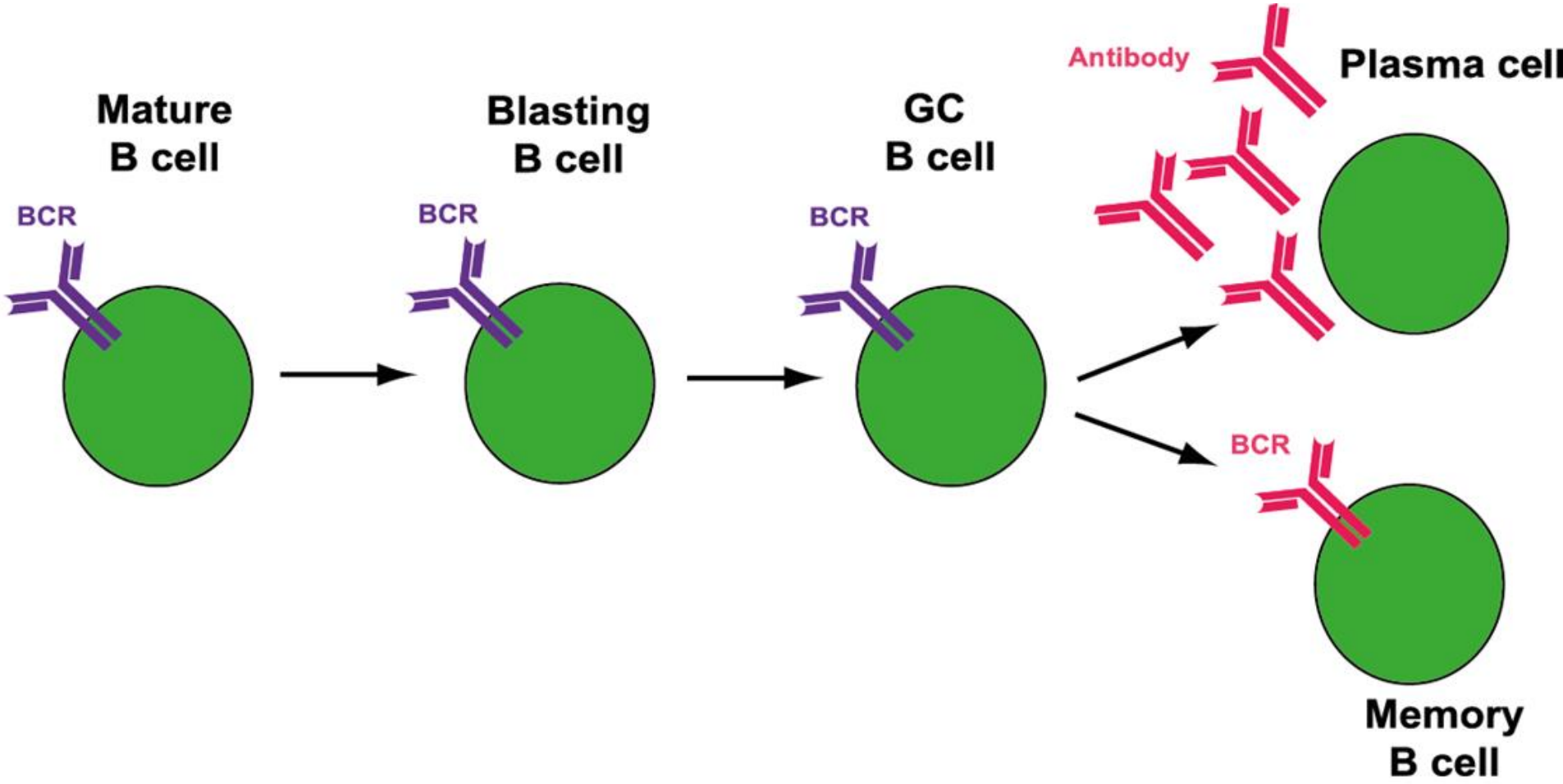
- More **tuned** to subtle molecular differences
- Takes more **time** to develop; antigen specific
- Gradual resolution of infection is outcome; depends on **B and T cells**
- Able to better **recognize**, **eliminate**, & **remember** the invading pathogen
- Development is dependent upon earlier innate pathways
- Adaptive immunity provides a second & **more comprehensive** line of defense based on the struggles of innate immunity

Activation of B Cell and Production of Antibody

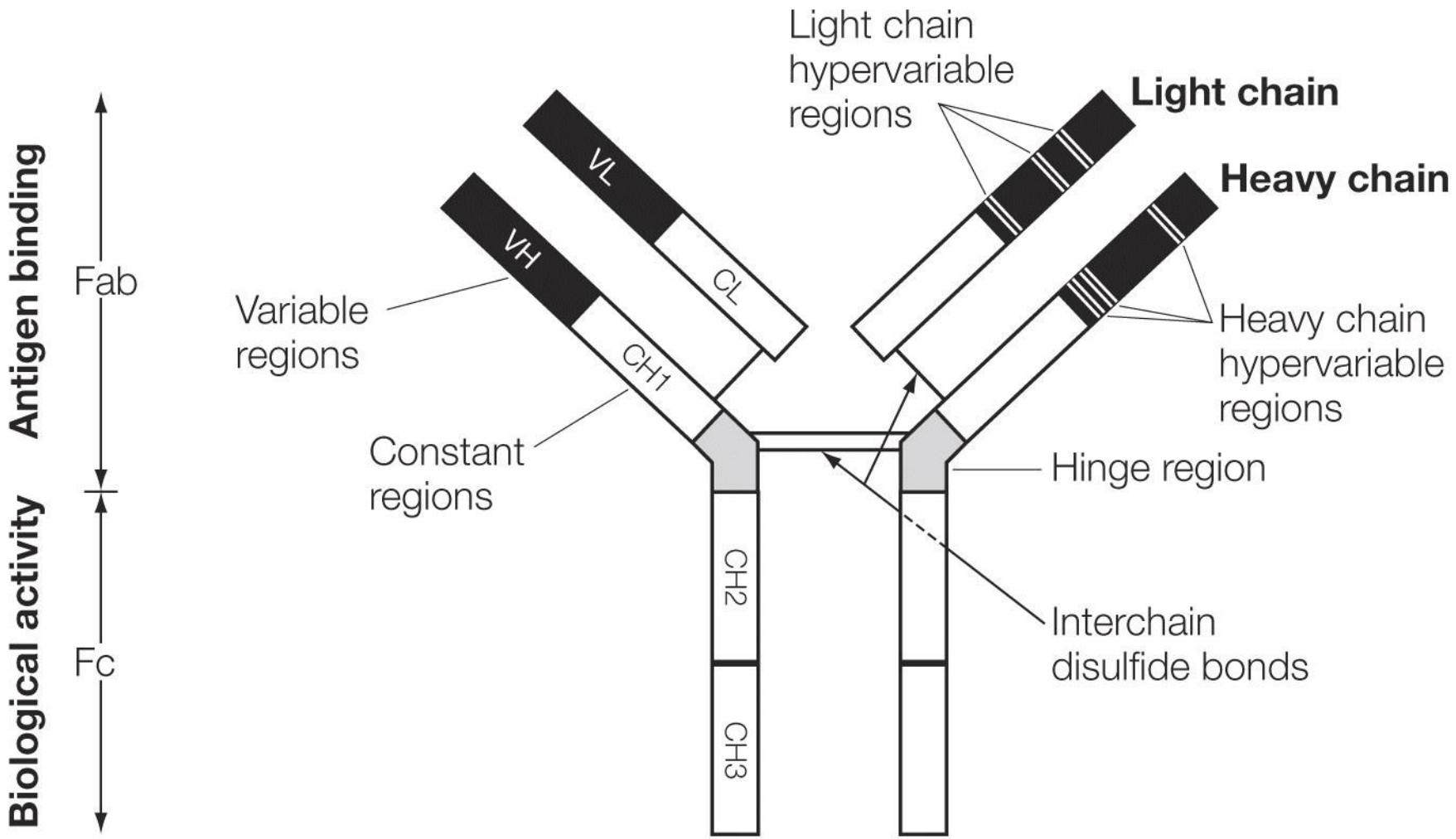


1. Each B cell can recognize only one antigen
2. That B cell gets activated and differentiated into numerous plasma cells
3. All of these plasma cells produce same antibody in a very efficient manner
4. These antibodies are then utilized in the clearing of initial antigen/antigen providing microorganisms, which was initially detected by B cell

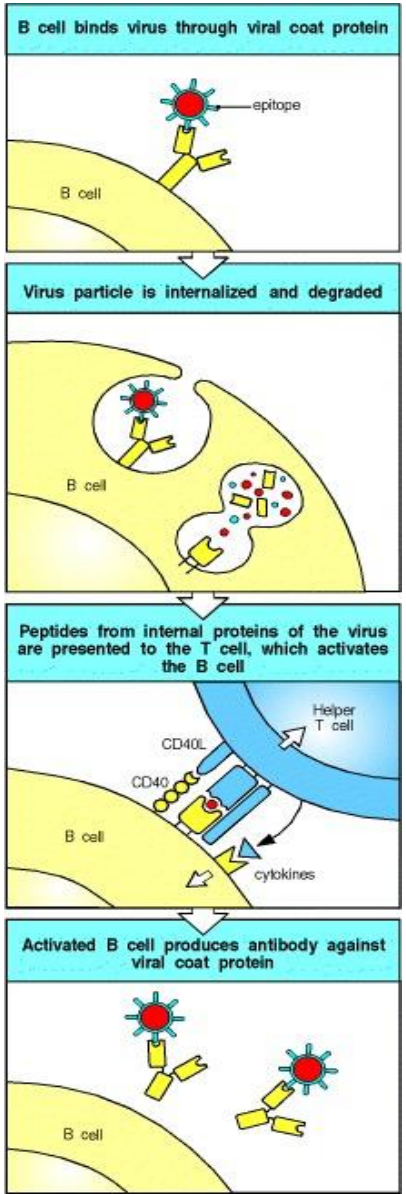
B cell differentiation after activation



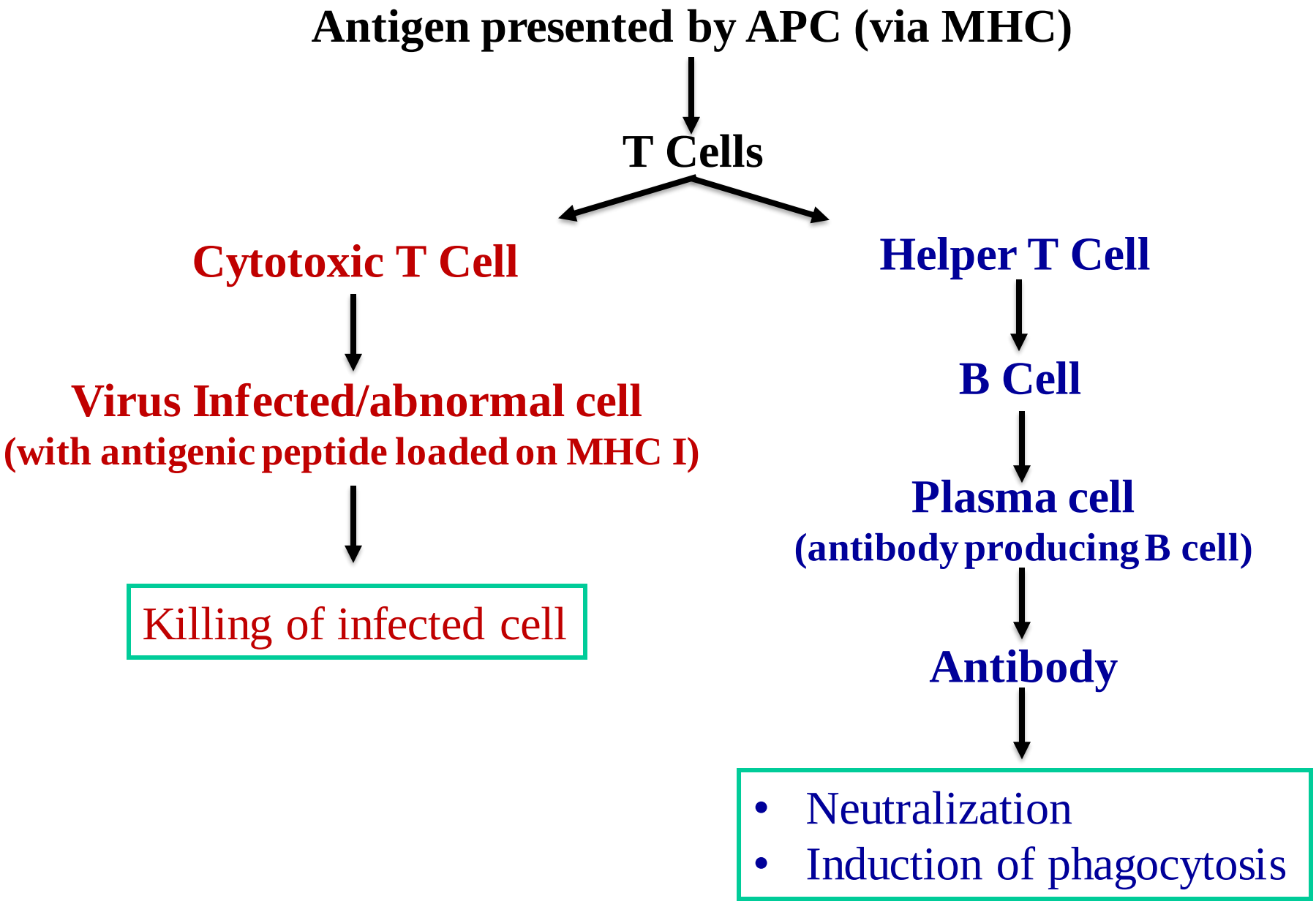
Structure of an Antibody molecule



B cells and T cells must recognize epitopes of the same molecular complex in order to interact



Adaptive Immune Response: Role of T cells



‘Professional’ Antigen Presenting Cells (APCs)

express both MHC class I and class II molecules

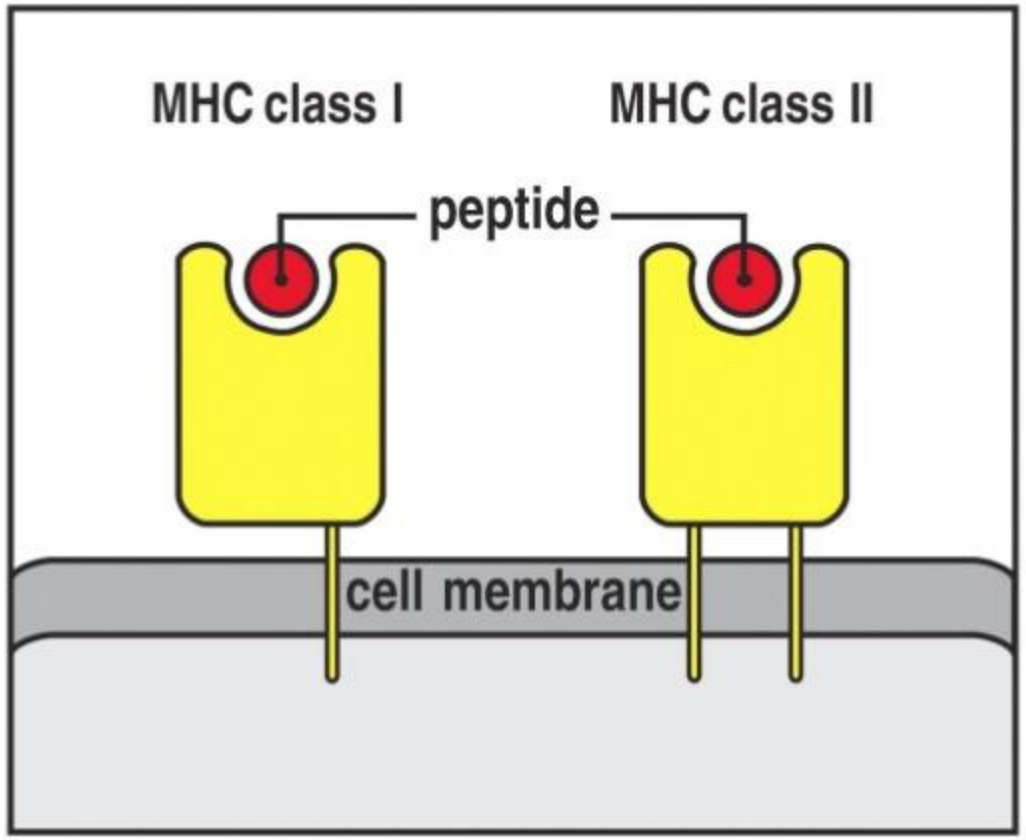


Figure 1-27 Immunobiology, 6/e. (© Garland Science 2005)

Examples of APCs:

1) Dendritic cells
2) Macrophages
3) B cells

Adaptive Immune Response: Key Points

- Initiated by innate system
- Diverse set of **receptors**
- Recognizes **pathogen-specific epitopes** (immune specificity)
- Immune **memory**

Innate vs **Adaptive**

Timeline after infection

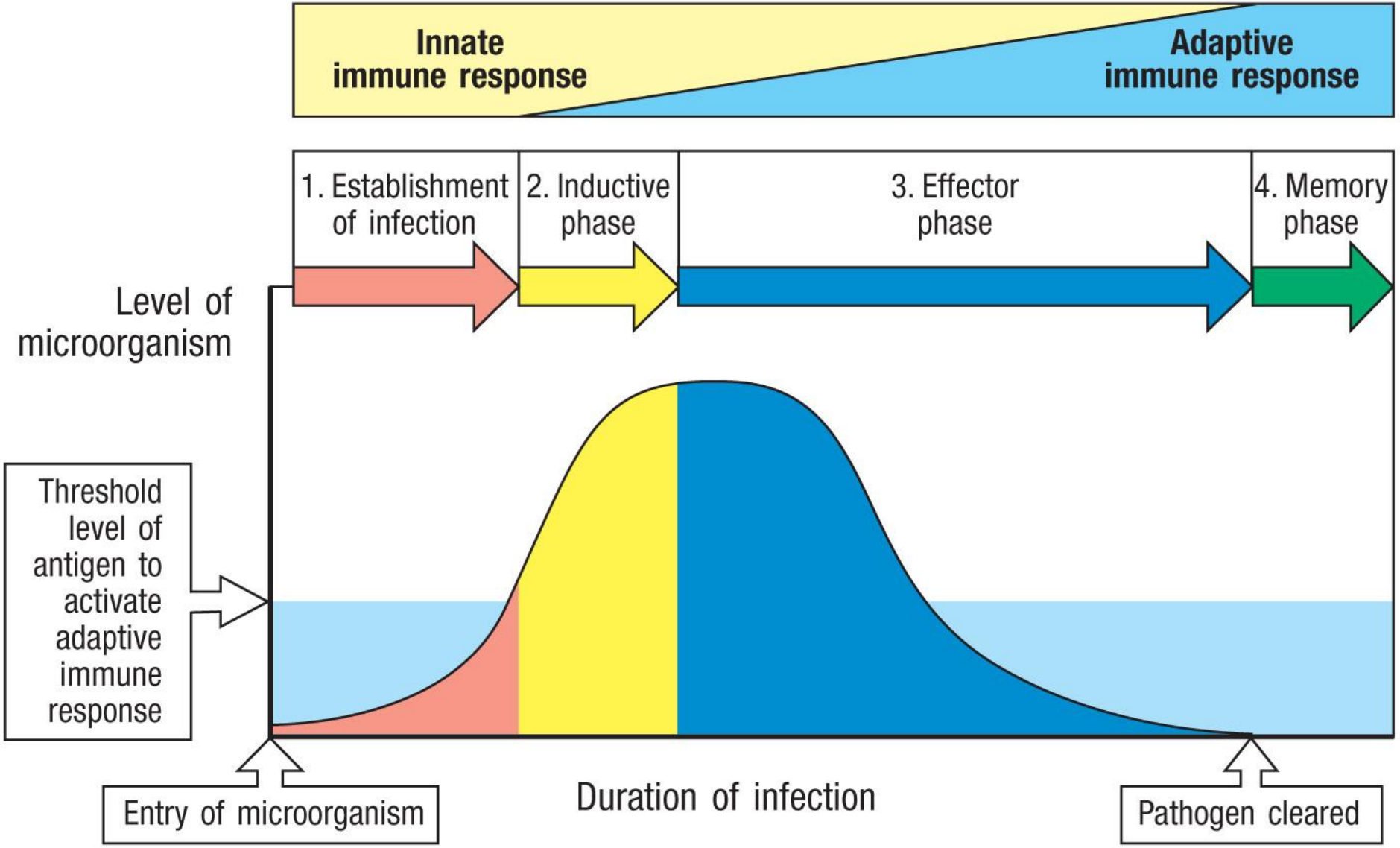


Figure 11.1 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

Innate vs **Adaptive**

Which immunity confers more protection?

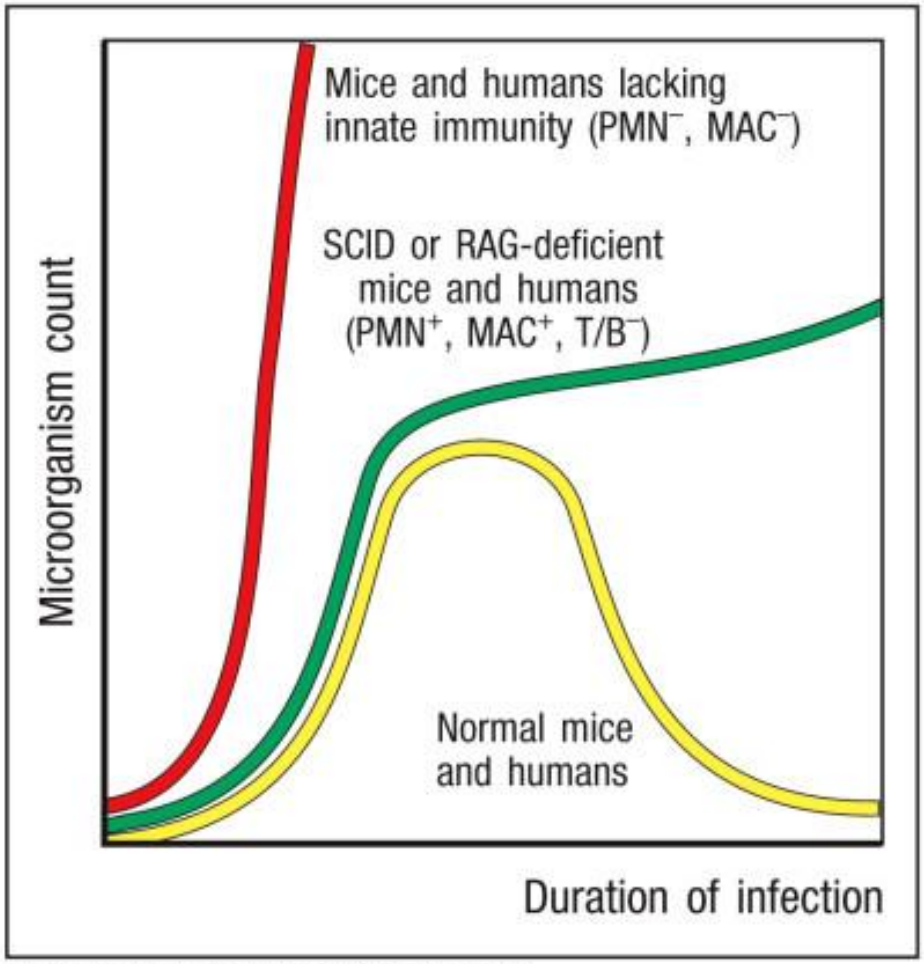


Figure 11.4 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

- Losing the Innate arm of the immune system results in more disastrous outcome than losing the acquired arm

Vaccination (Immunization)

http://www.who.int/campaigns/

Drug vs Vaccine

- **Concept of Drug**
  - Kill invaders or foreign pathogens
  - Inhibit the growth of pathogens

- **Concept of Vaccine**
  - Train immune system to face various existing disease causing agents
  - Generate memory against specific pathogens

Vaccination: an ongoing global effort

- Vaccination has yielded some of the most successful stories in alleviating worldwide mortality rates
- The last case of naturally acquired case of small pox was reported in 1977
- Consequence of eradication: universal vaccination not required
- Most vaccine carry slight risk to the person vaccinated
- In many cases every person do not need to be immunized to protect most of the population
- **Herd immunity**: if a critical mass of people acquire protective immunity they can serve as buffer for the rest

Immunological Memory & Vaccination

- **Natural infections:**

  1st infection → memory → 2nd infection

  slow response — *fast response*

  pathogens multiply — *pathogens disposed*

  Symptoms/disease — *no disease*

- **Vaccination → memory → natural infections**

  no disease — *fast response*

  pathogens disposed

  no disease

Vaccination protects us from infection by inducing the adaptive immune response, bypassing the need for a natural infection

References

- Janeway’s Immunobiology
- Kuby’s Immunology

https://www.youtube.com/watch?v=zQGOcOUBi6s

Assessing a vaccine that targets the SARS-CoV-2 coronavirus