Immunity against Bacteria

By

Lecture 13

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Introduction

- Mechanisms of protection from bacteria depend on their structure and pathogenicity.
- **There are four main types of bacterial cell wall:**
- • Gram-positive bacteria;
- • Gram-negative bacteria;
- • mycobacteria;
- • spirochetes.
- Bacterial structures trigger protective **innate immune responses** and guide the development of **adaptive immunity.**

Variation of bacterial pathogenicity

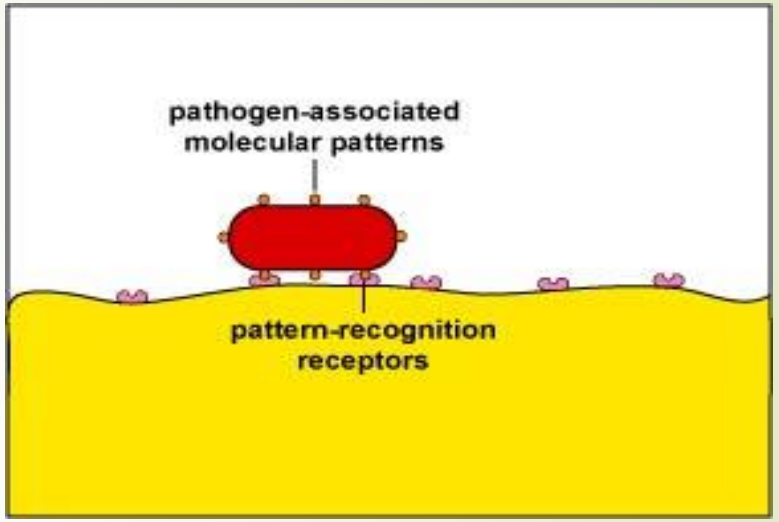
- The bacteria may be:
- • **toxicity without invasiveness**;
- • **invasiveness without toxicity**
- most bacteria are intermediate between these
- *Corynebacterium diphtheriae* and *Vibrio cholerae* are examples of organisms that are **toxic, but not invasive.**
- The immunity of toxic bacteria by **neutralizing antibody to the toxin.**
- The immunity of invasive bacteria **requires killing of the bacteria** themselves

Innate immunity to bacteria

- Intact skin is impenetrable barrier to most bacteria
- fatty acids produced by the skin are toxic to many organisms
- Epithelial surfaces are cleansed by ciliary action in the trachea or by flushing of the urinary tract.
- Many bacteria are destroyed by acidic pH in the stomach and vagina
- Commensals normal flora can limit pathogen invasion through the production of antibacterial proteins **(colicins)**
- When the normal flora are disturbed by antibiotics, infections by *Candida* spp. or *Clostridium difficile* can occur
- Mostly Gram-negative, bacteria are directly killed by complement.

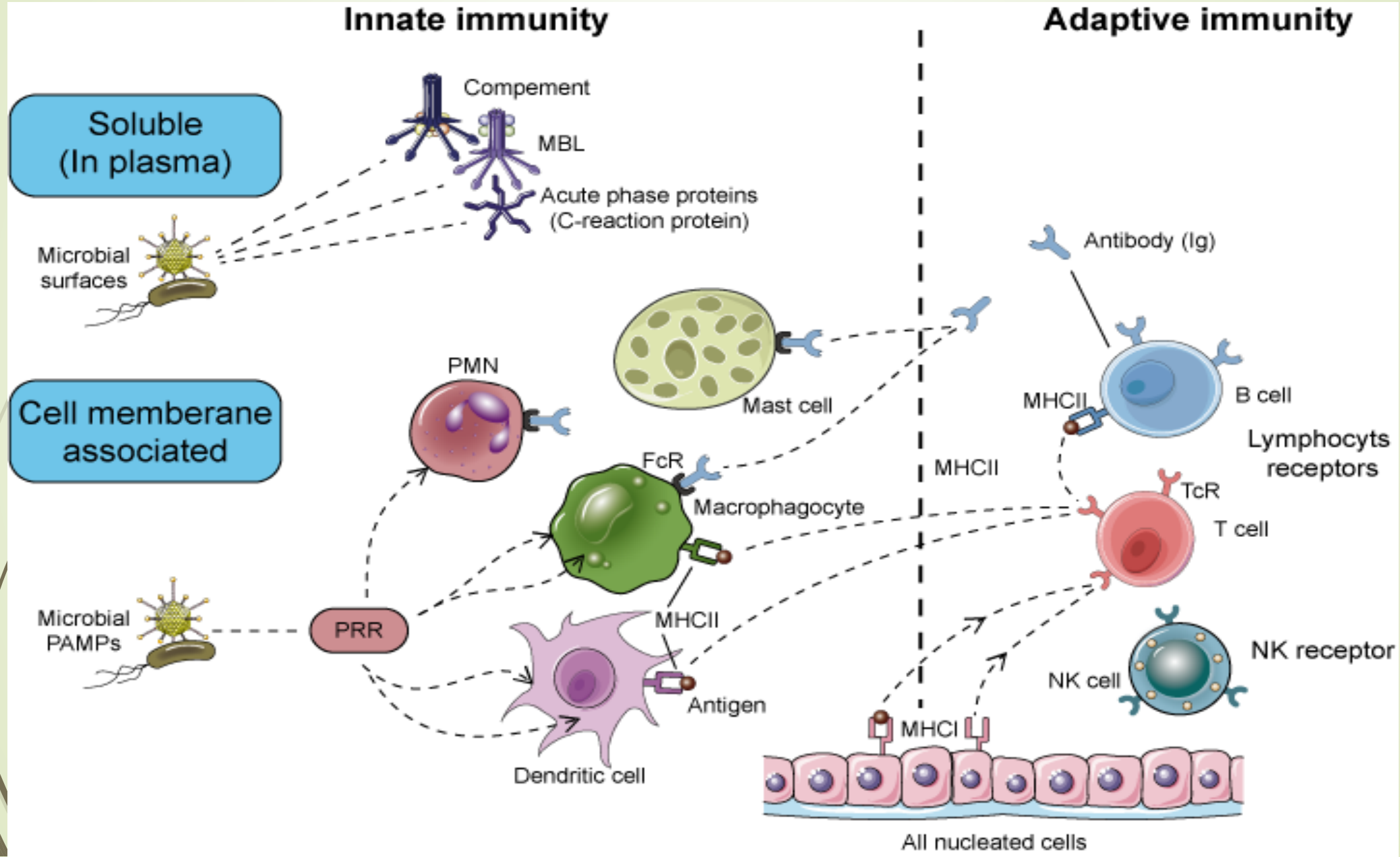
Bacterial PAMPs activate cells via Toll-like receptors

- The bacterial components ‘pathogen-associated
- molecular patterns’ (PAMPs) are recognized by innate immune response



- Many bacterial PAMPs activate cells via Toll-like receptors (TLRs)
- The most prominent TLRs involved in recognition of bacterial components are TLR1, 2, 4, 5, 6, and 9
- TLRs are expressed on phagocytes, dendritic cells, and epithelial cells at sites of bacterial entry to host

Bacterial (PAMPs) recognition and innate immunity

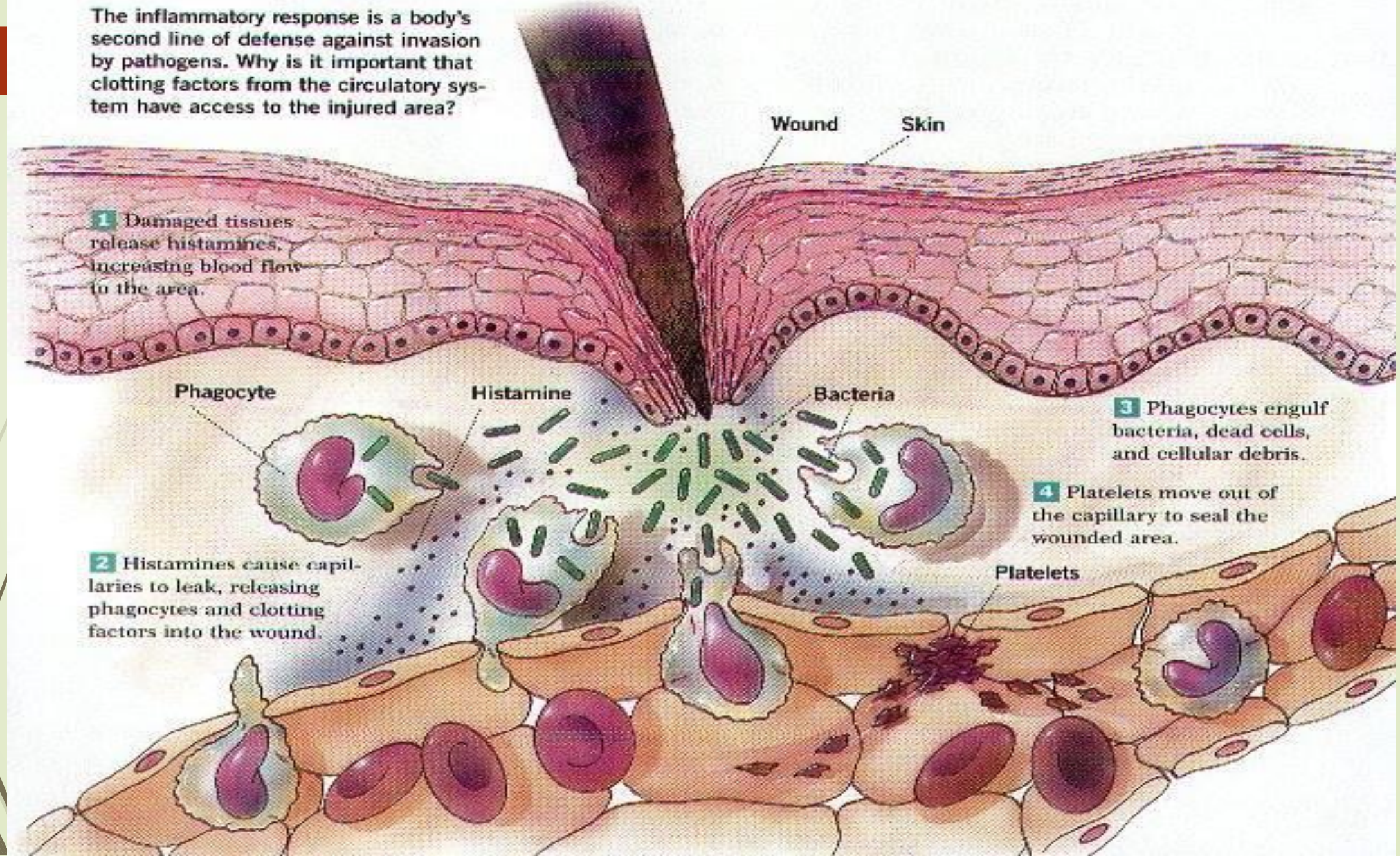


Innate immunity to bacterial structures

- **LPS** of gram-negative bacteria is activator of **innate immunity** in such as interleukin-1 **(IL-1), IL-6**, and tumor necrosis factor **(TNF),** leading to **severe shock.**
- **Peptidoglycans** and **lipoteichoic acids** of gram+ bacteria are activators of **innate immunity**
- Capsular polysaccharides are not potent activators of inflammation
- Outer lipid bilayer **activate complement** via the **alternative pathway**

Steps of the Inflammatory Response

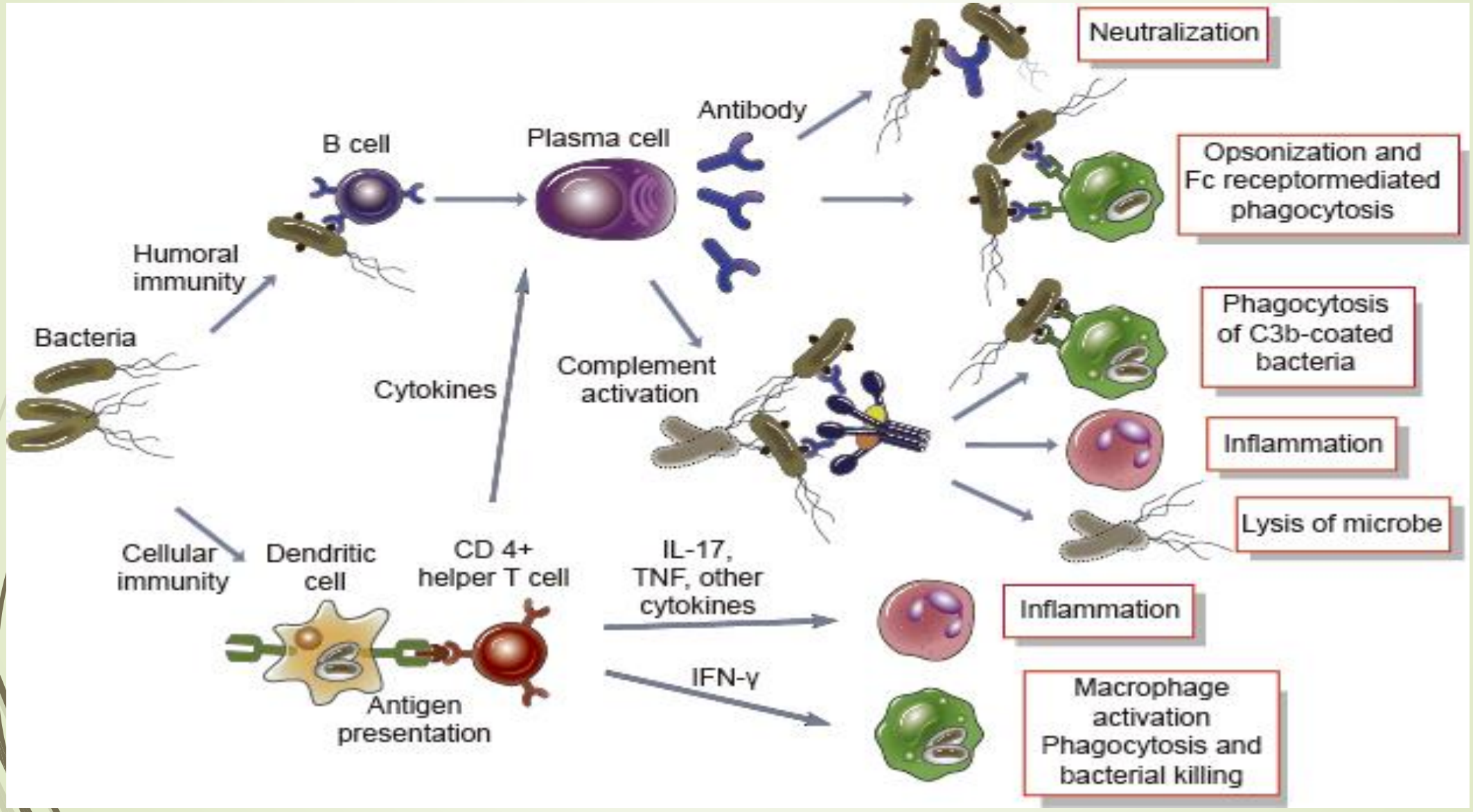
The inflammatory response is a body's second line of defense against invasion by pathogens. Why is it important that clotting factors from the circulatory system have access to the injured area?



Adaptive immunity to bacteria

- Ultimately most bacteria are killed by **phagocytes Macrophage, neutrophils** enhanced by chemotaxis.
- Optimal activation of macrophages is dependent on TH1 CD4 T cells which produce **IFN-γ** during the adaptive immune response.
- TH1 T cells provide both IFNγ for macrophage activation and B cell help to produce IgG subclasses for opsonization of bacteria
- If intracellular pathogens are not quickly eliminated, the Persistent macrophage recruitment and activation can result in **granuloma formation**.

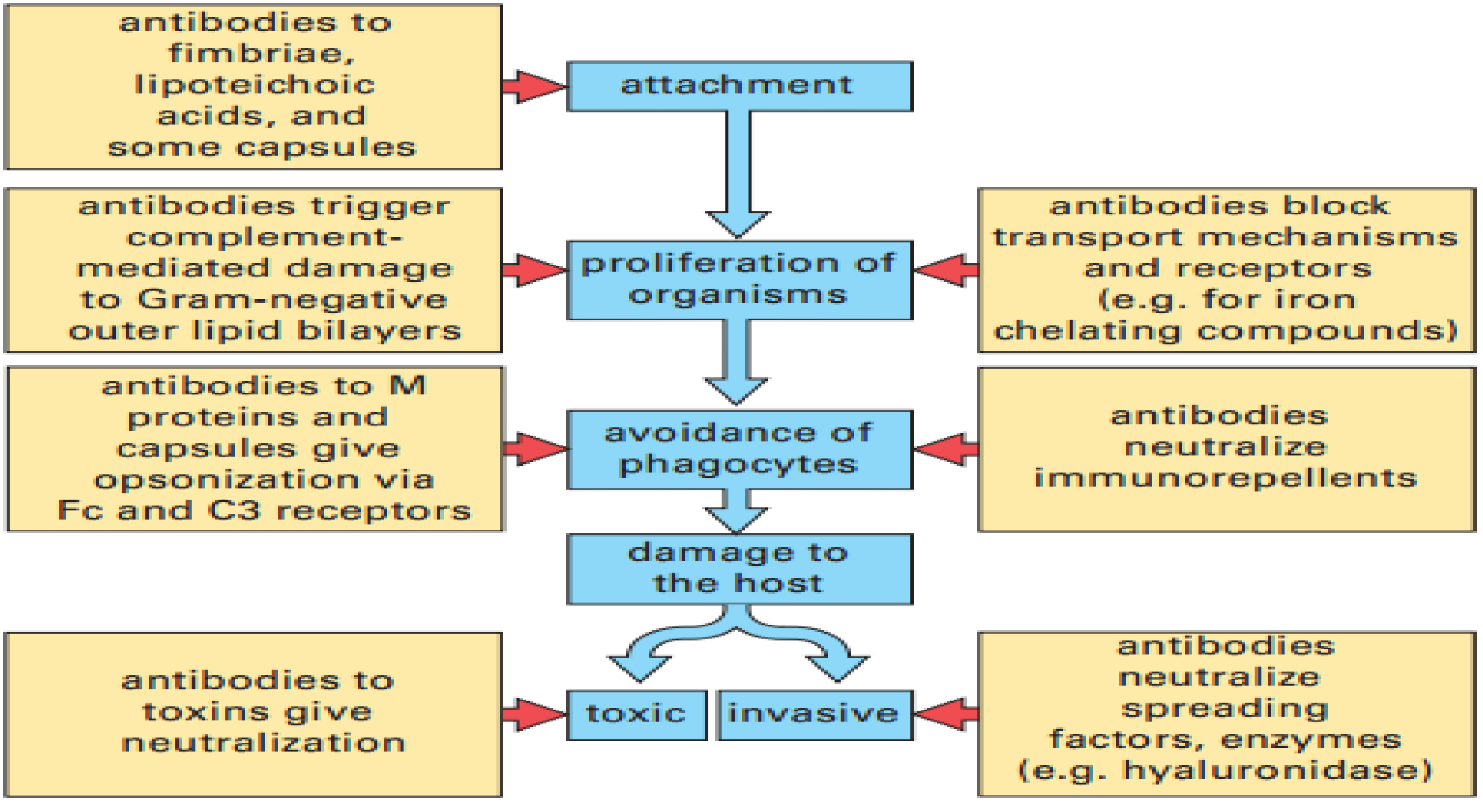
Humeral and cellular immunity



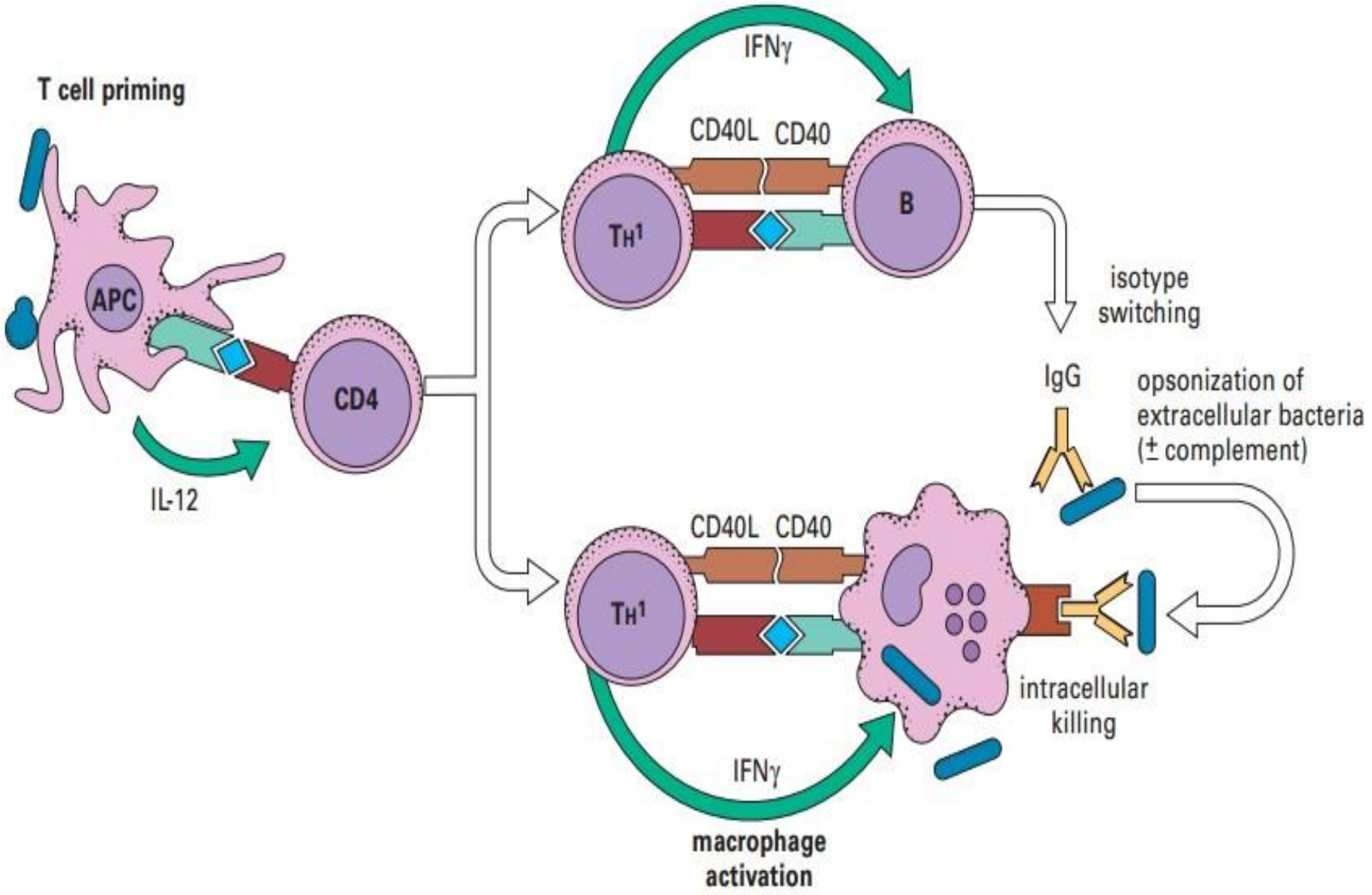
Antibody and bacteria

- Neutralizes diphtheria toxin by blocking the attachment to its target cells
- Interfere with motility by binding to flagellae
- Secretory IgA stop bacteria binding to epithelial cells
- Block functional requirements of bacteria such as binding of iron-chelating compounds
- An important role of antibody in targeting of complement
- The most efficient complement-fixing antibodies in humans are IgM, then IgG3

The antibacterial roles of antibody



Overview of CD4⁺ T cell-mediated immunity to bacteria and fungi



Bacterial evasions of immune defences

- Antiphagocytic machanisms: toxins, capsular polysaccharides
- Inhibition of the complement system: *Str. pyogenes, E. coli, N. meningitidis*
- Antigenic variations: *Borrelia recurrentis*
- Proteases lysing IgA - *Neisseria, Haemophilus*
- Sequestration in avascular regions- *Salmonella typhi* in the gall bladder and urinary tract
- Intracellular parasitism

Immunity in some important bacterial infections

infection	pathogenesis	major defense mechanisms
Corynebacterium diphtheriae	non-invasive pharyngitis – toxin	neutralizing antibody
Vibrio cholerae	non-invasive enteritis – toxin	neutralizing and adhesion-blocking antibodies
Neisseria meningitidis (Gram-negative)	nasopharynx →bacteremia →meningitis →endotoxemia	killed by antibody and lytic complement; opsonized and phagocytosed
Staphylococcus aureus (Gram-positive)	locally invasive and toxic in skin, etc.	osponized by antibody and complement; killed by phagocytes
Mycobacterium tuberculosis	invasive, evokes immunopathology	macrophage activation by cytokines from T cells, CTLs
Mycobacterium leprae	invasive, space-occupying and/or immunopathology	

Thank you