HUMORAL IMMUNE RESPONSE

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Humoral immune response

- Type of adaptive immune response mediated by antibodies
- Antibodies are produced by plasma cells derived from B lymphocytes
- Humoral immunity is the principal defense mechanism against extracellular microbes and their toxins

Phases of humoral immune responses

- Antigen recognition
- Activation of B lymphocytes
- Communication
- Battle (effector functions)
- Memory

Antigen recognition

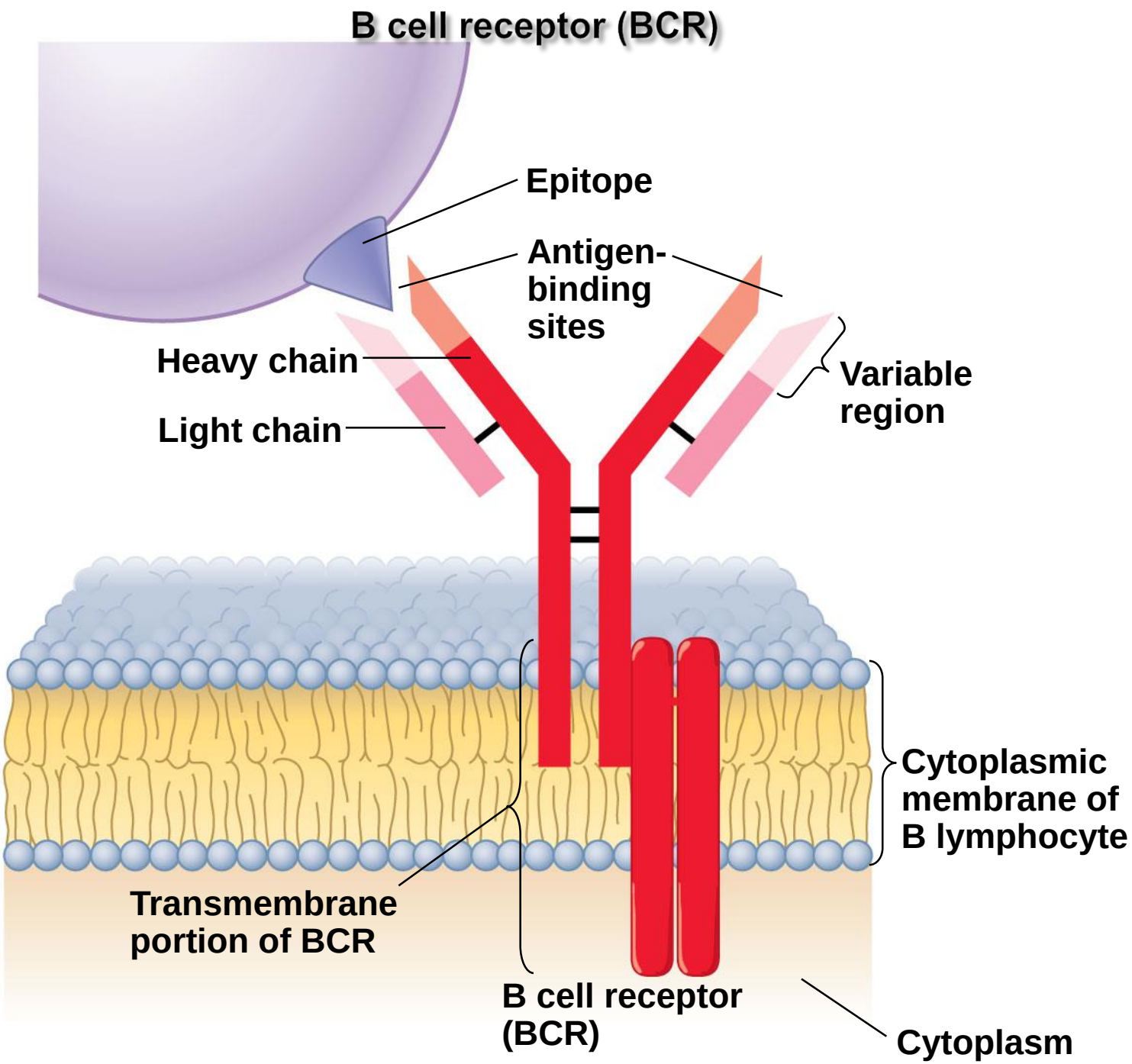
- B cells express two classes of antibodies, IgM and IgD that function as the receptor for antigens (B cell Receptor / BCR)

B Cells

- Arise, mature - BM
- Primarily in - spleen, lymph nodes, and MALT
- Small percentage - circulates
- Major function - secretion of antibodies

B cell receptor (BCR)

- One B cell - multiple copies of same BCR
- Variable regions - antigen-binding sites
- Recognizes only one epitope
- Able to recognize millions of different epitopes



Phases of humoral immune responses

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Activation of B lymphocytes

- Activation of B lymphocytes - proliferation of antigen-specific cells (Clonal expansion)
- B cells differentiate into effector cells (plasma cells) that actively secrete antibodies
- Some B cells undergo class switching or affinity maturation
- Some B cells become memory cells

Humoral Immune Response

Two types

- T-independent humoral immunity
- T-dependent humoral immunity

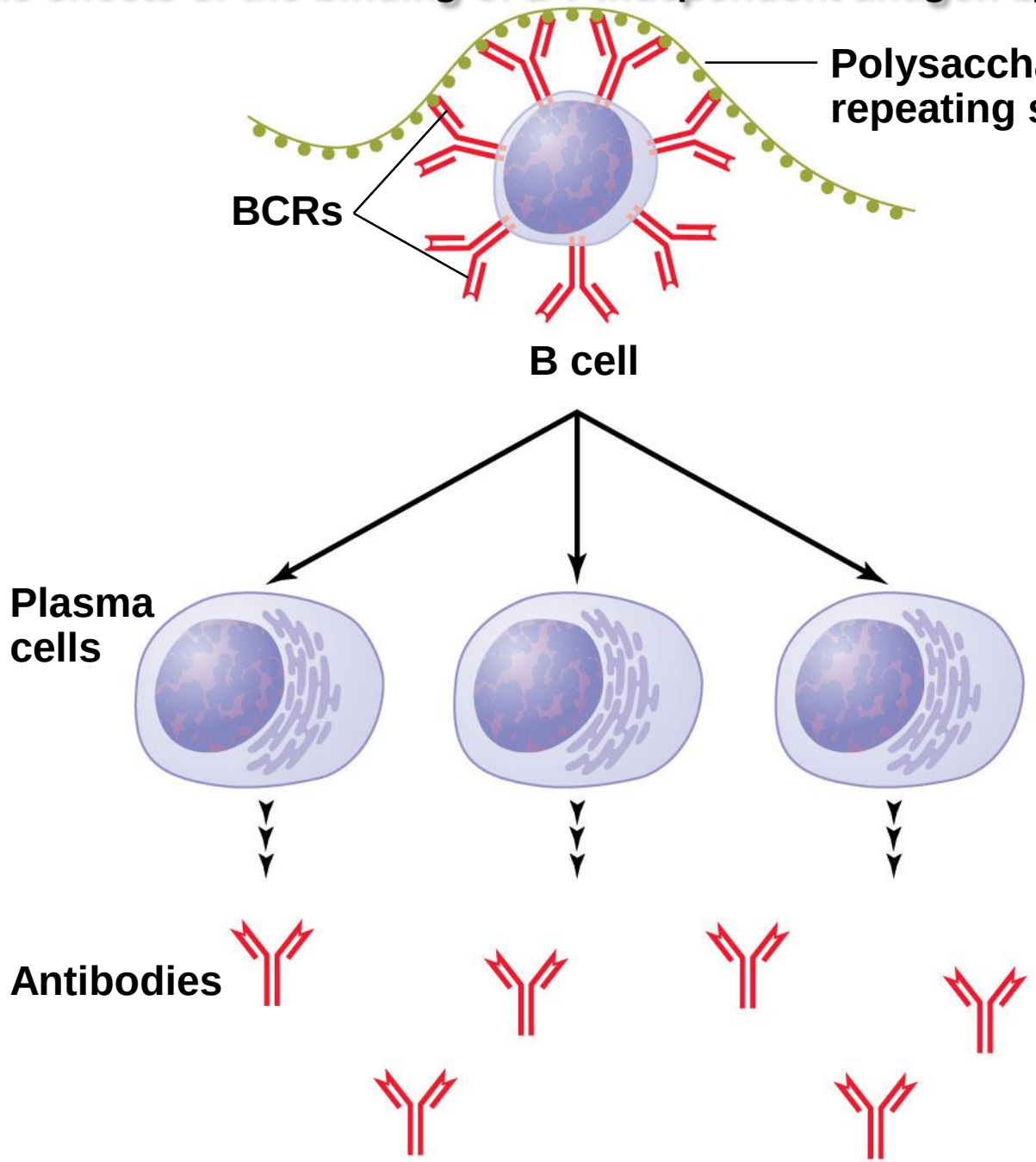
T-independent humoral immunity

- T cells - not always involved in B cell response

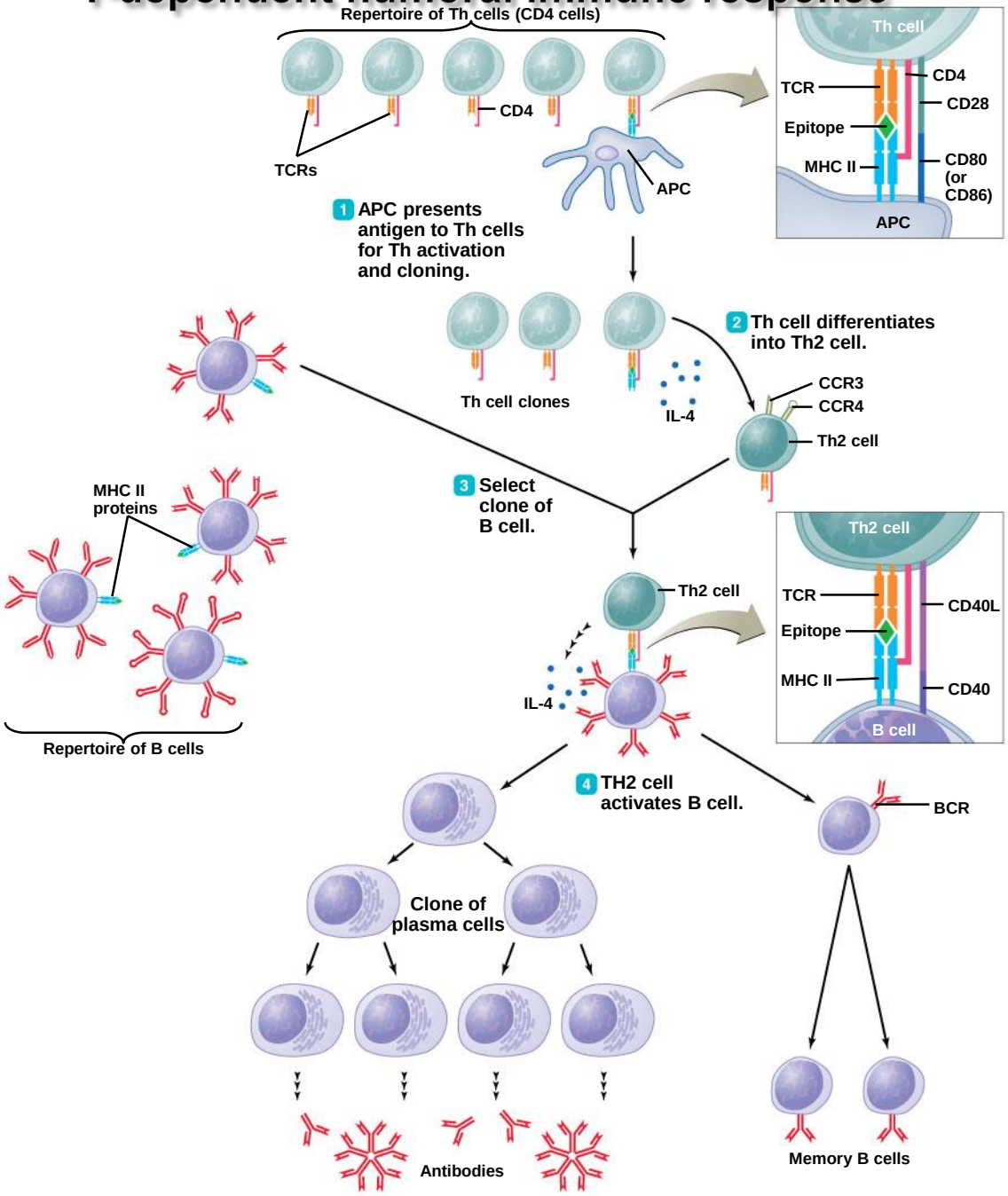
- B cells can respond independently to polysaccharides (capsules); LPS

- Response is not strong, especially in young children

The effects of the binding of a T-independent antigen by a B cell



T-dependent humoral immune response



Phases of humoral immune responses

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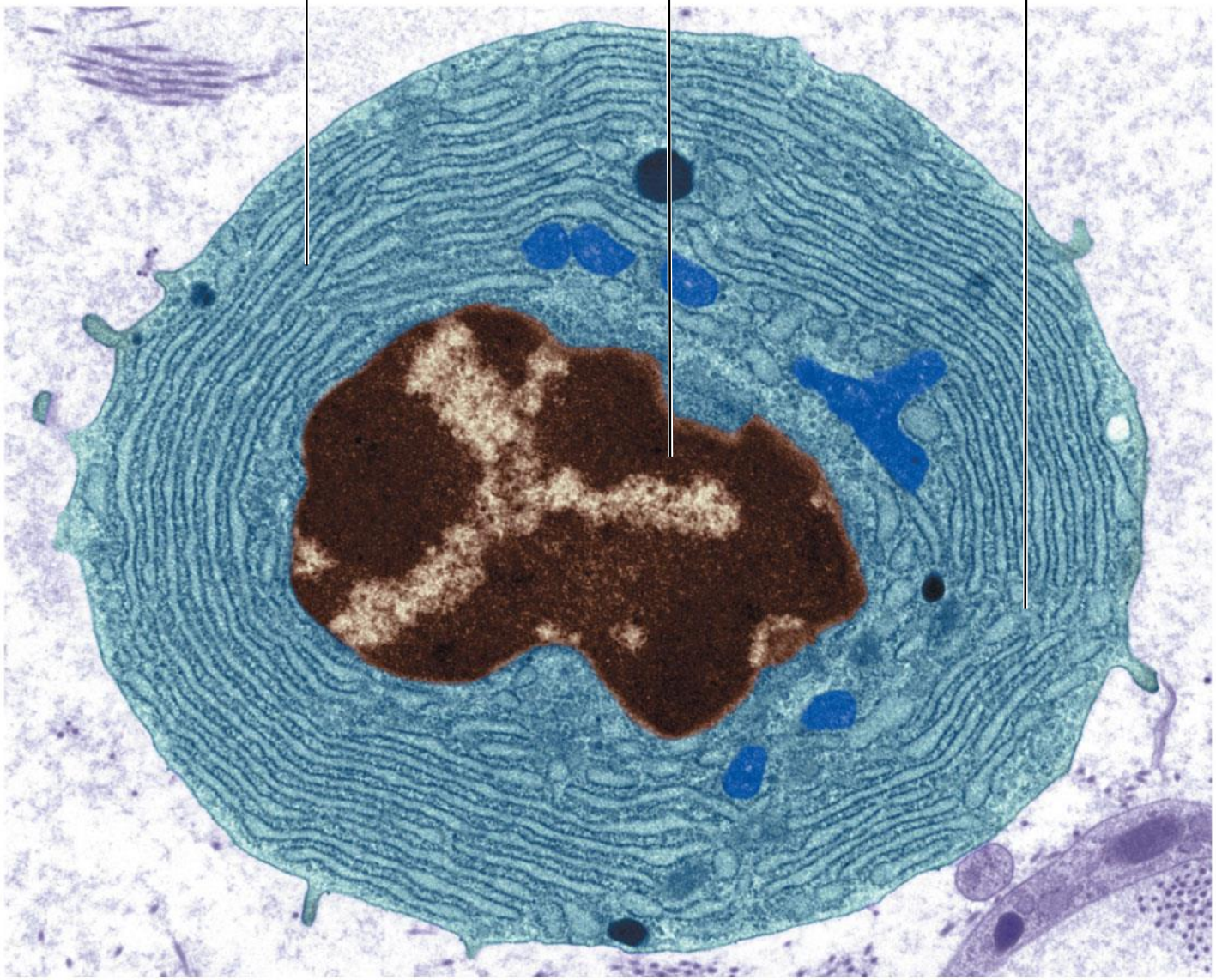
Plasma Cells

- Secretes only antibody molecules complementary to the specific antigenic determinant
- Short-lived
- Die within a few days of activation

A plasma cell



Phases of humoral immune responses

- Antigen recognition
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- Memory

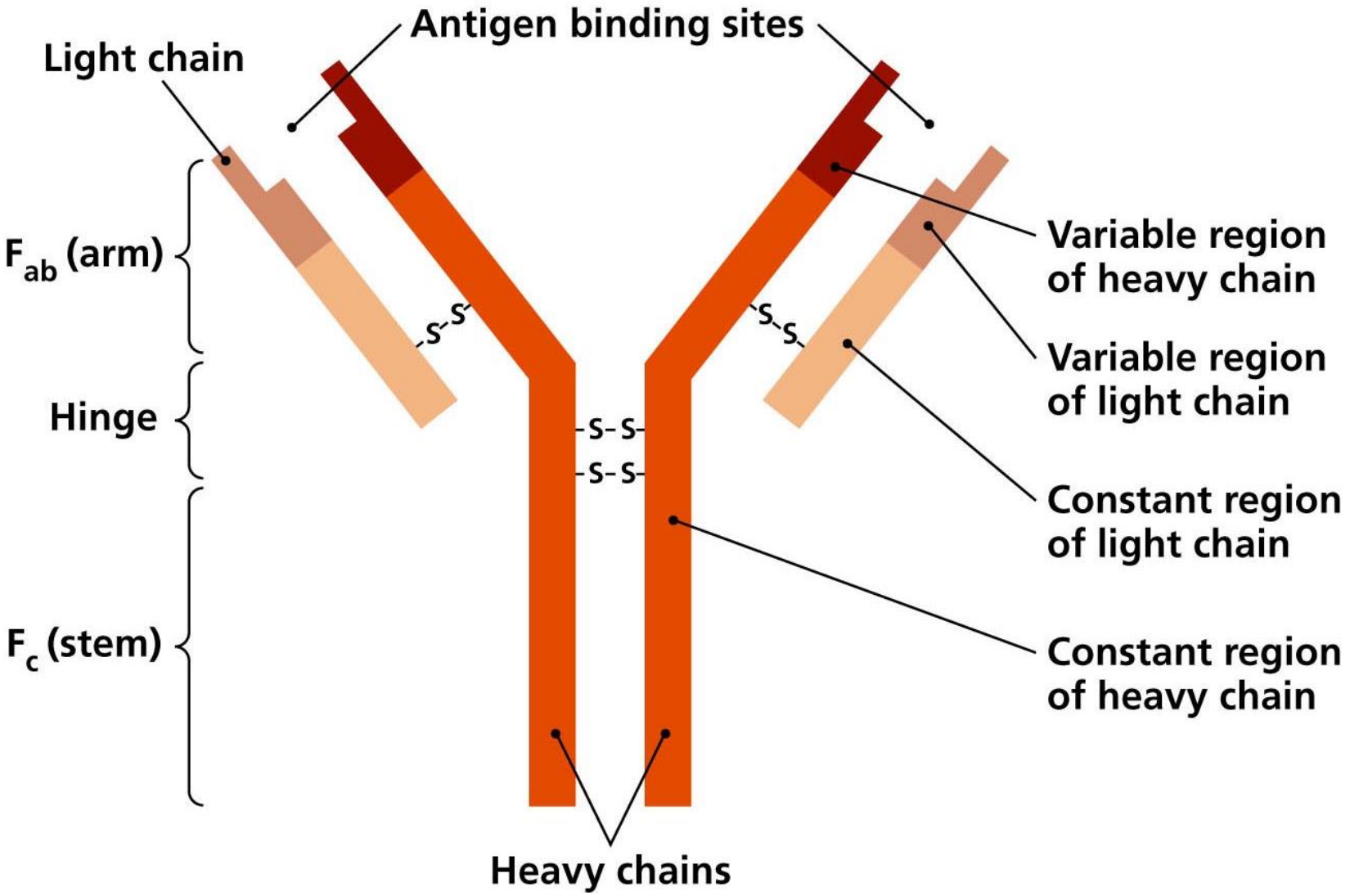
Memory B Cells

- Produced by B cell proliferation
- Long-lived cells
- Divide only a few times and then persist in lymphoid tissue
- Do not secrete antibodies
- Have BCRs complementary to the antigenic determinant
- Initiate antibody production if antigen is encountered again

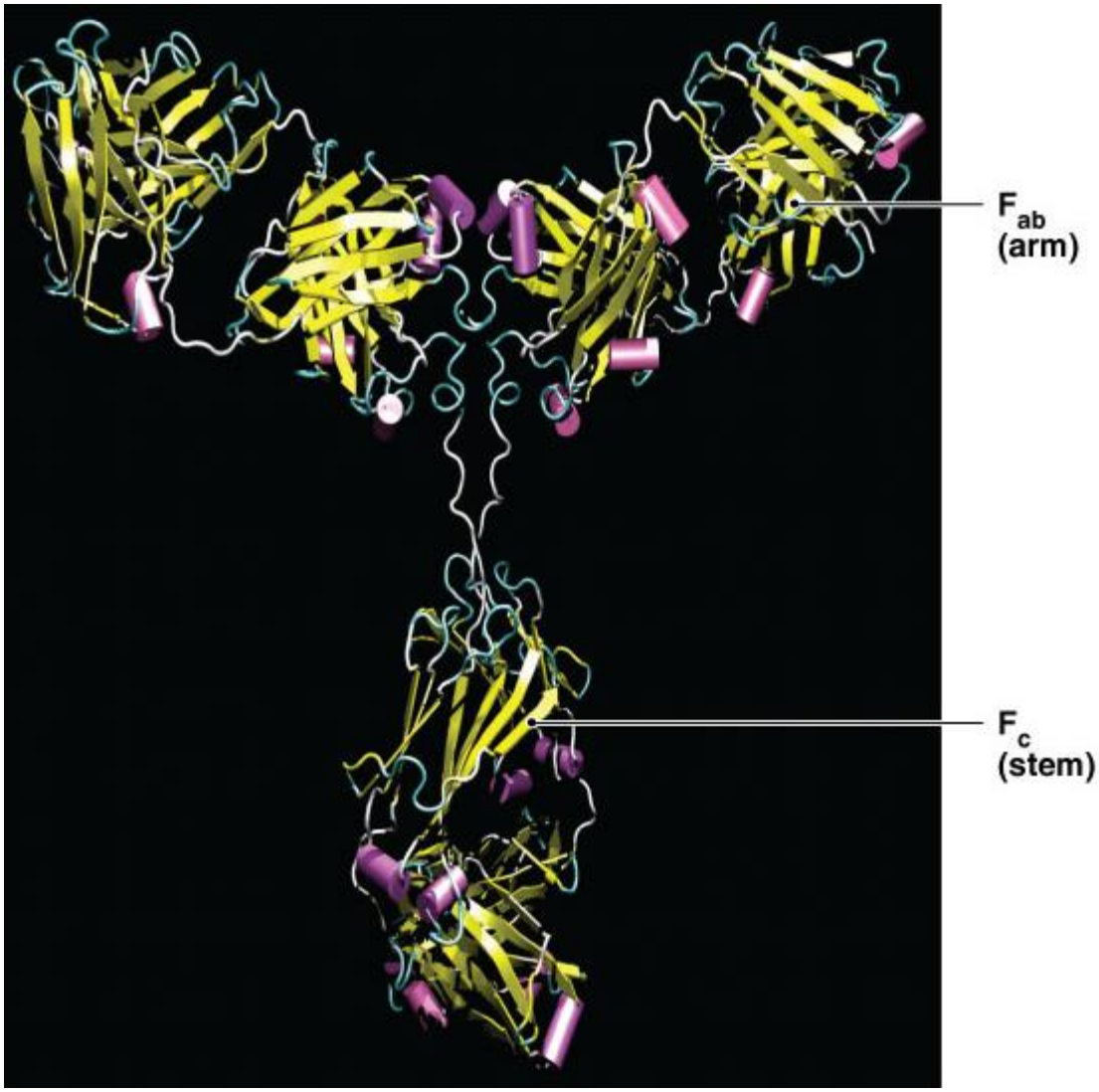
HUMORAL IMMUNE RESPONSE

Activation Phase

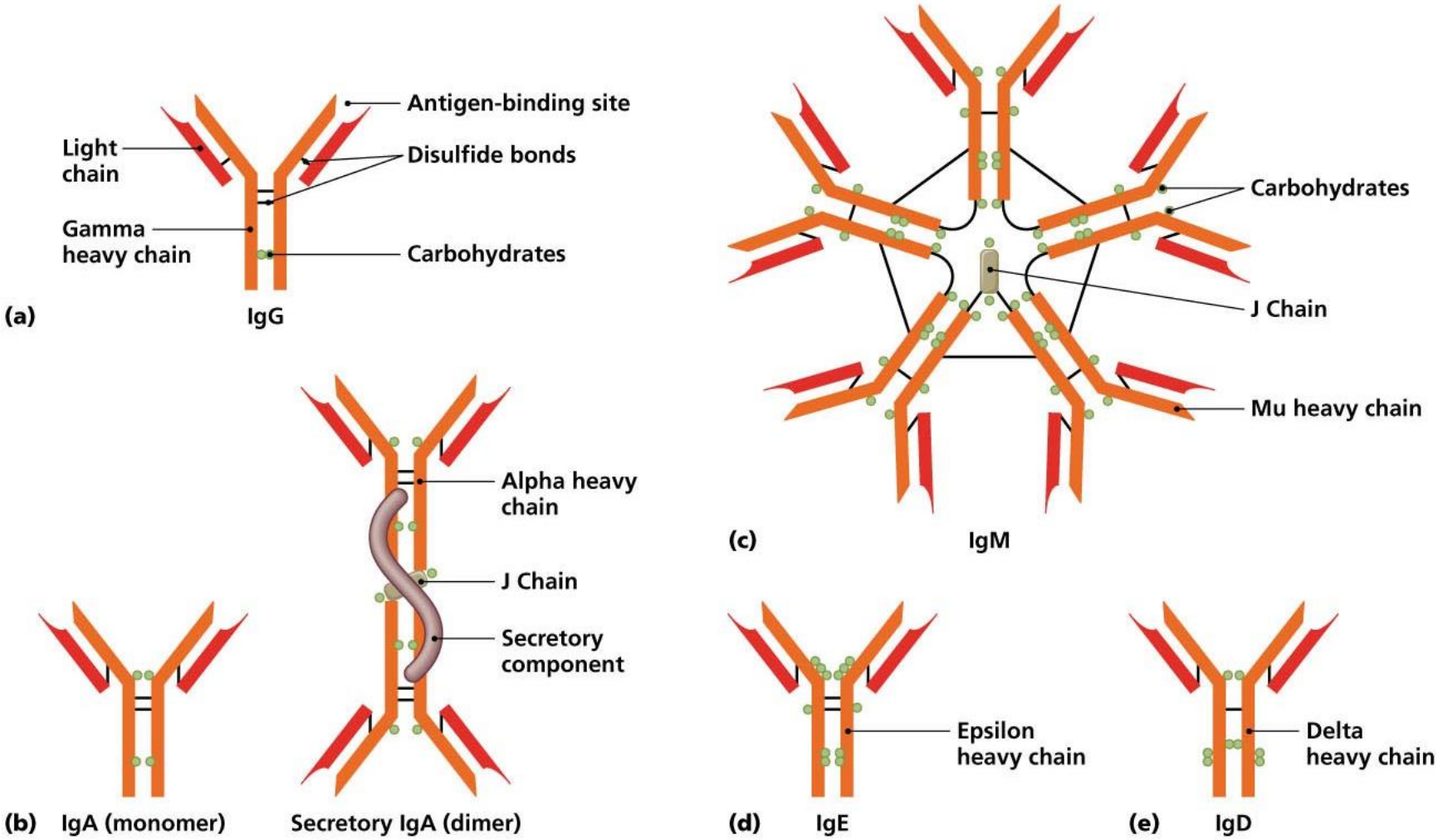
Antibody Structure



- Variable region binds to a different antigens
- Constant regions fall into five classes


F_{ab}
(arm)
F_c
(stem)

Classes of Antibodies



Classes of antibodies

- Class depends on

  type of antigen

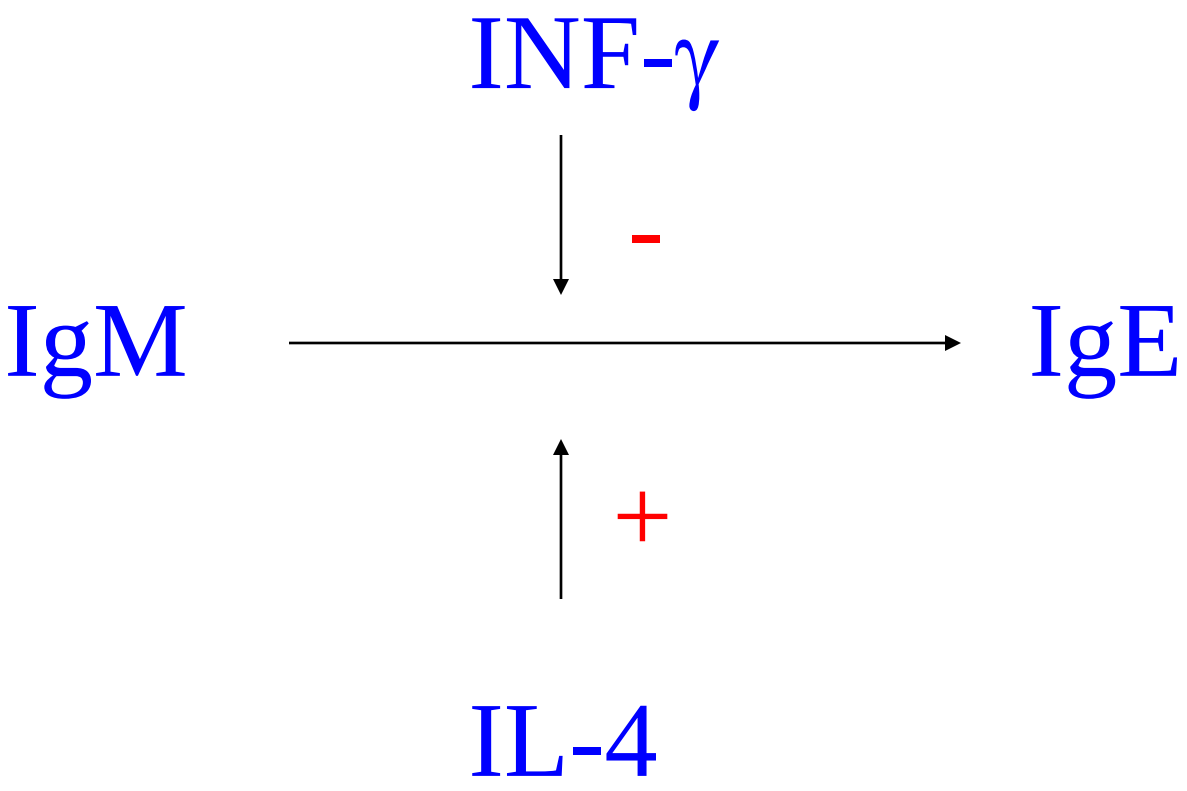
  portal of entry

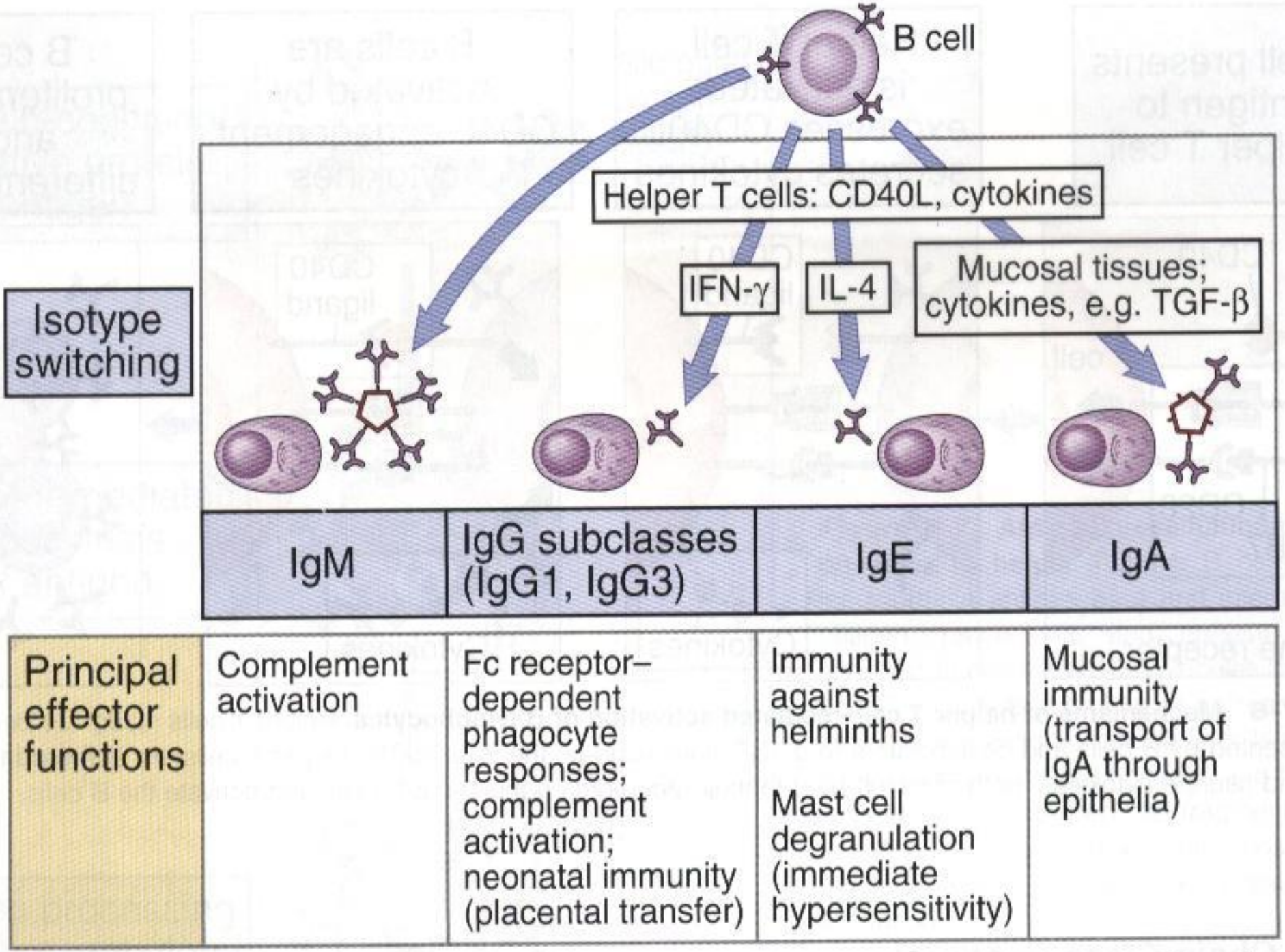
  antibody function needed

- Five different classes of antibodies present

Class switching

The process of making B cells to produce different heavy chain class.





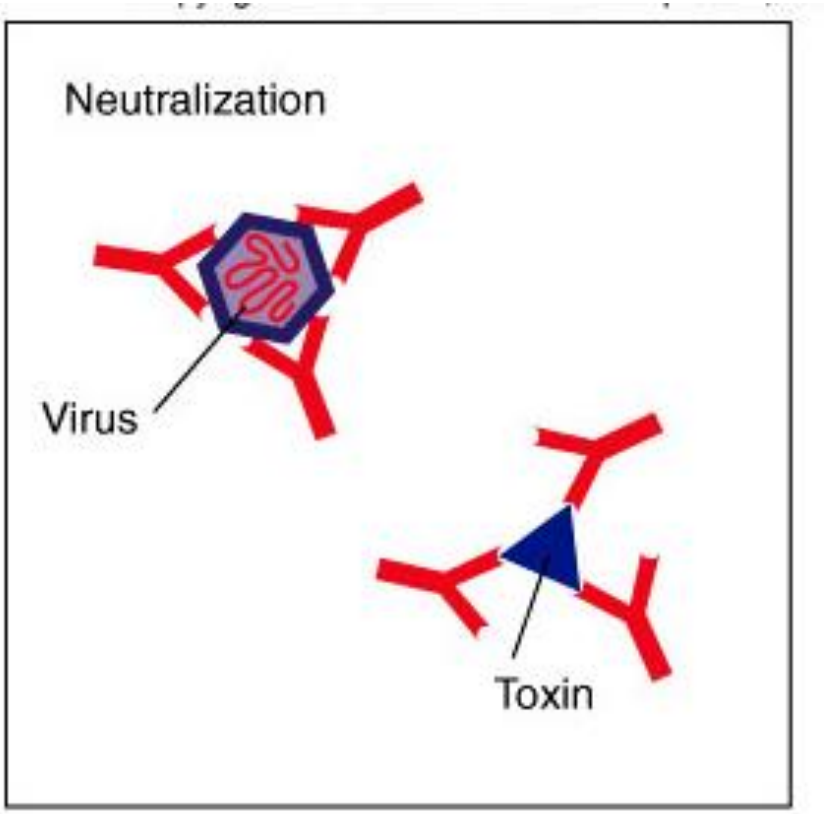
Heavy-chain class (isotype) switching. Antigen-stimulated B lymphocytes may differentiate

Affinity maturation

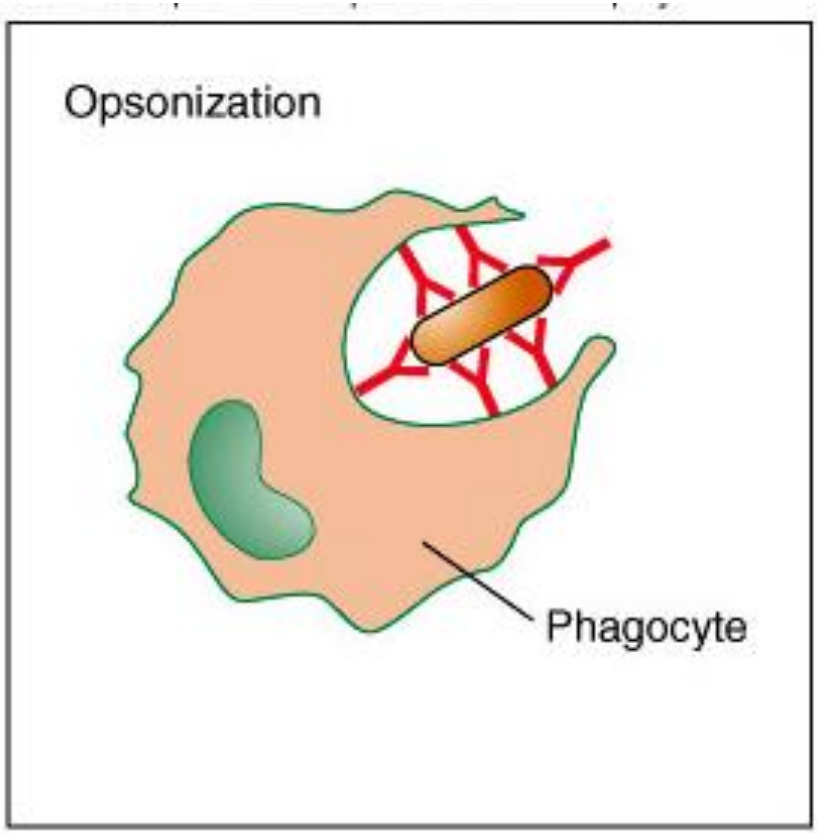
- The process that leads to increased affinity of antibodies for a protein antigen as a humoral response progresses.

Functions of Antibodies

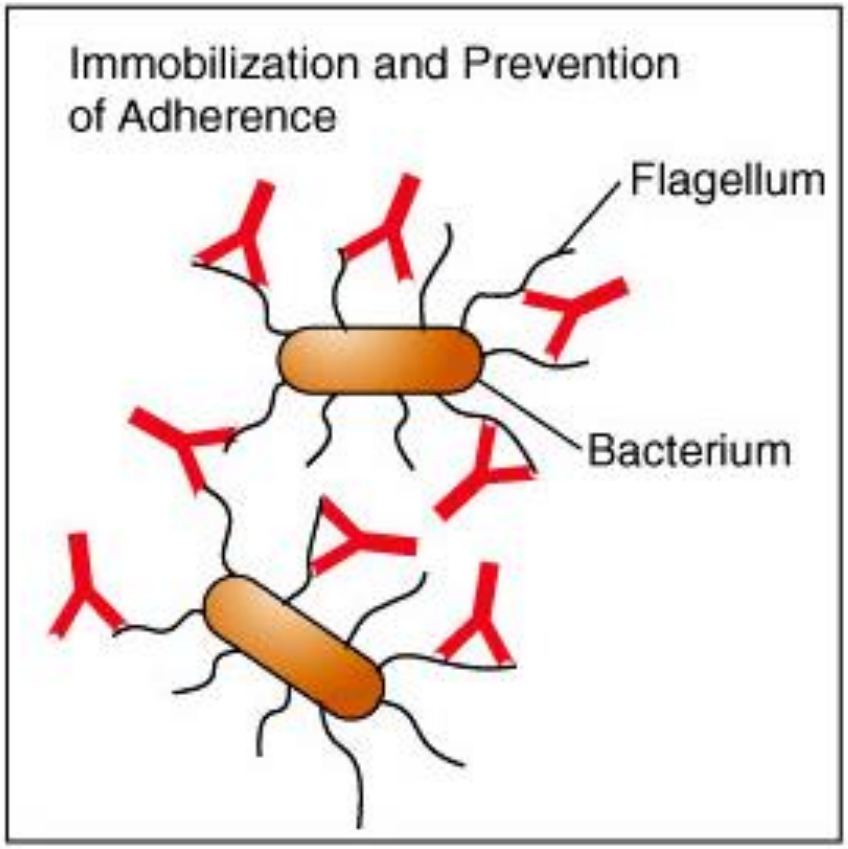
Neutralization



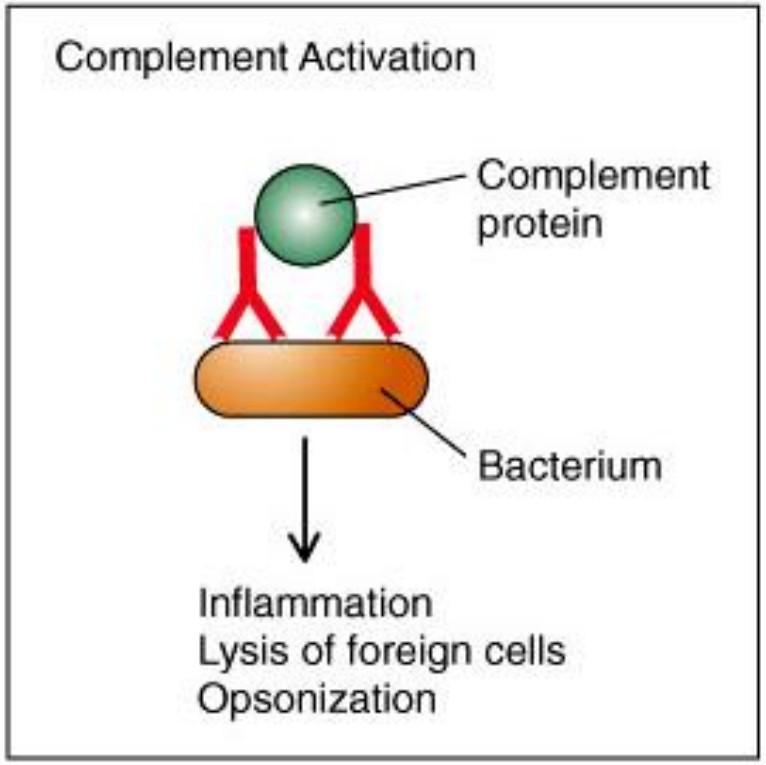
Opsonization



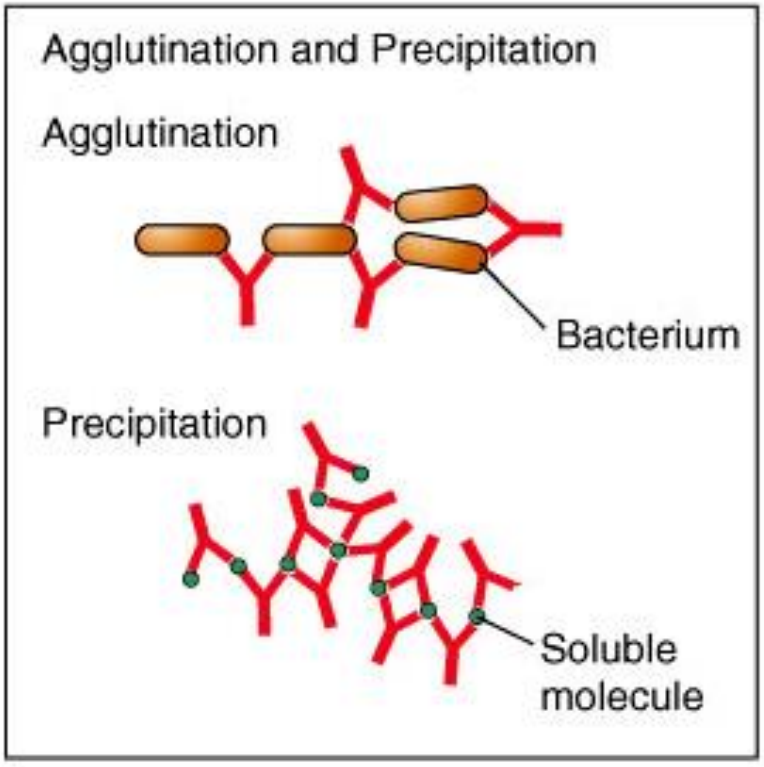
Immobilization and prevention of adherence



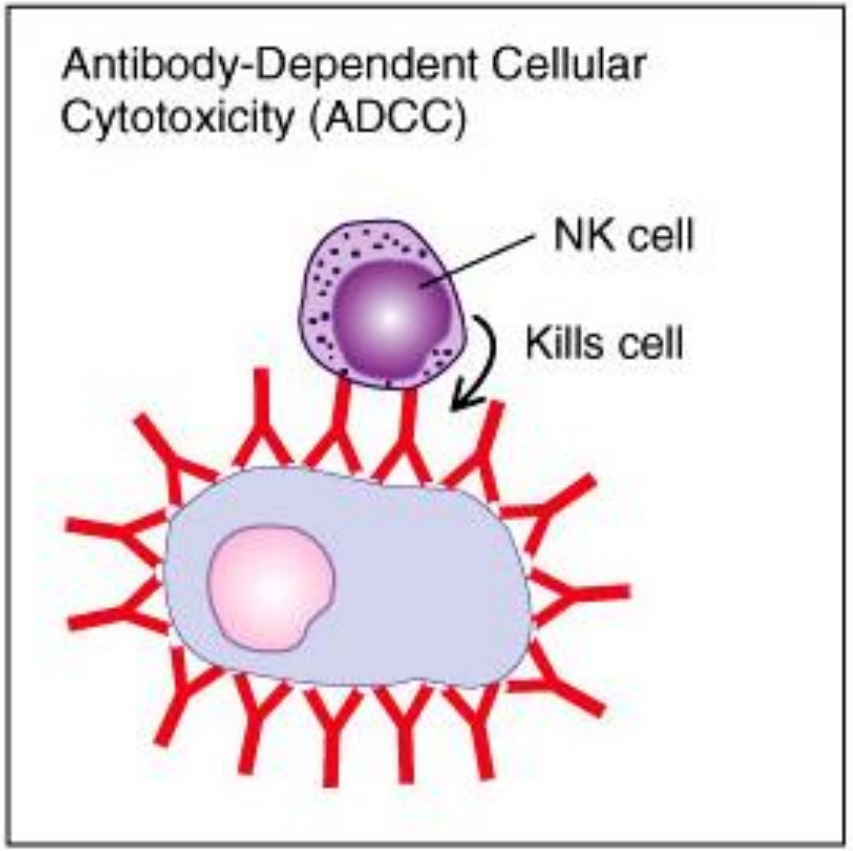
Complement activation and inflammation



Agglutination



Antibody-dependent cellular cytotoxicity (ADCC)



Effector functions

- IgA – Mucosal immunity
- IgG – Transplacental immunity

  Complement cascade activation

  Opsonization

  Neutralization of toxins

  Antibody dependent cytotoxicity
- IgM – Complement cascade activation

  Neutralization of toxins

- IgE–involved in response to parasitic infections and allergies

- IgD– exact function is not known

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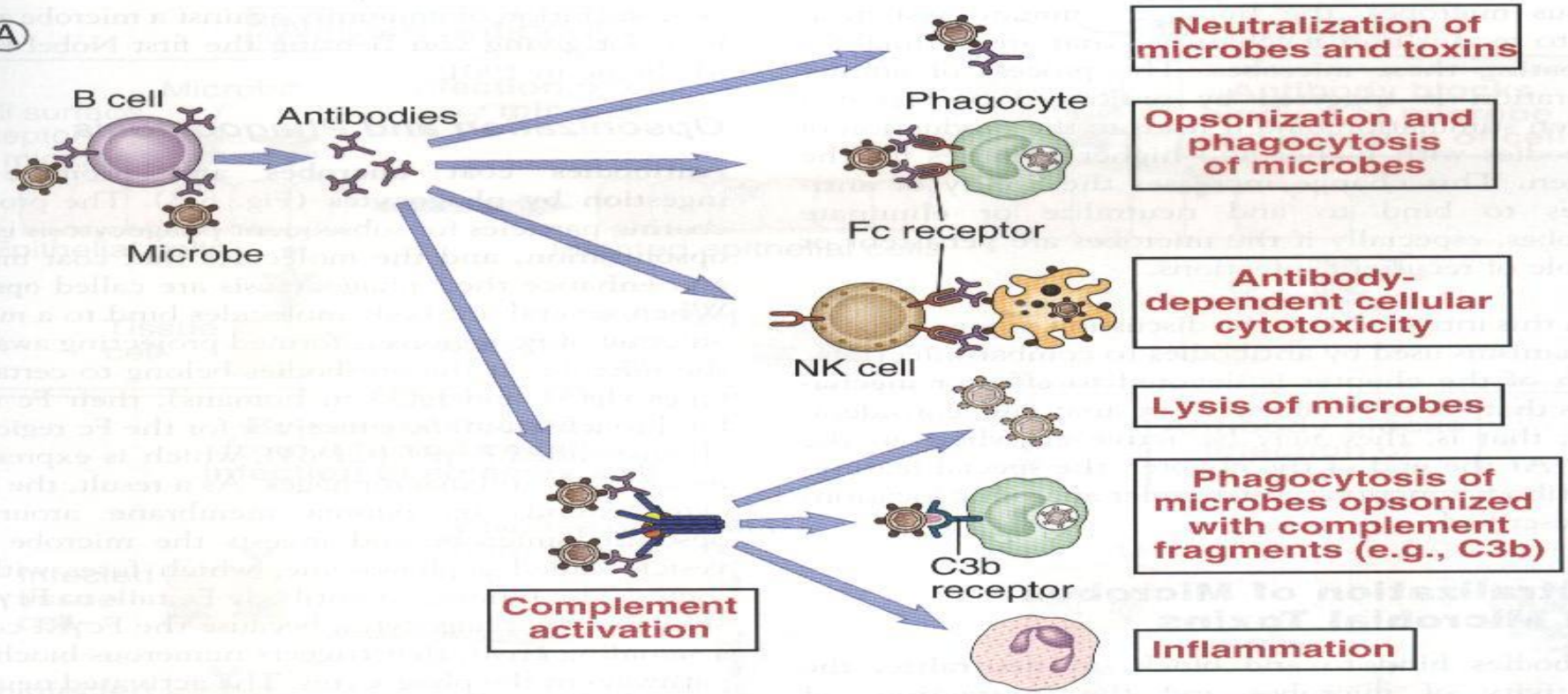

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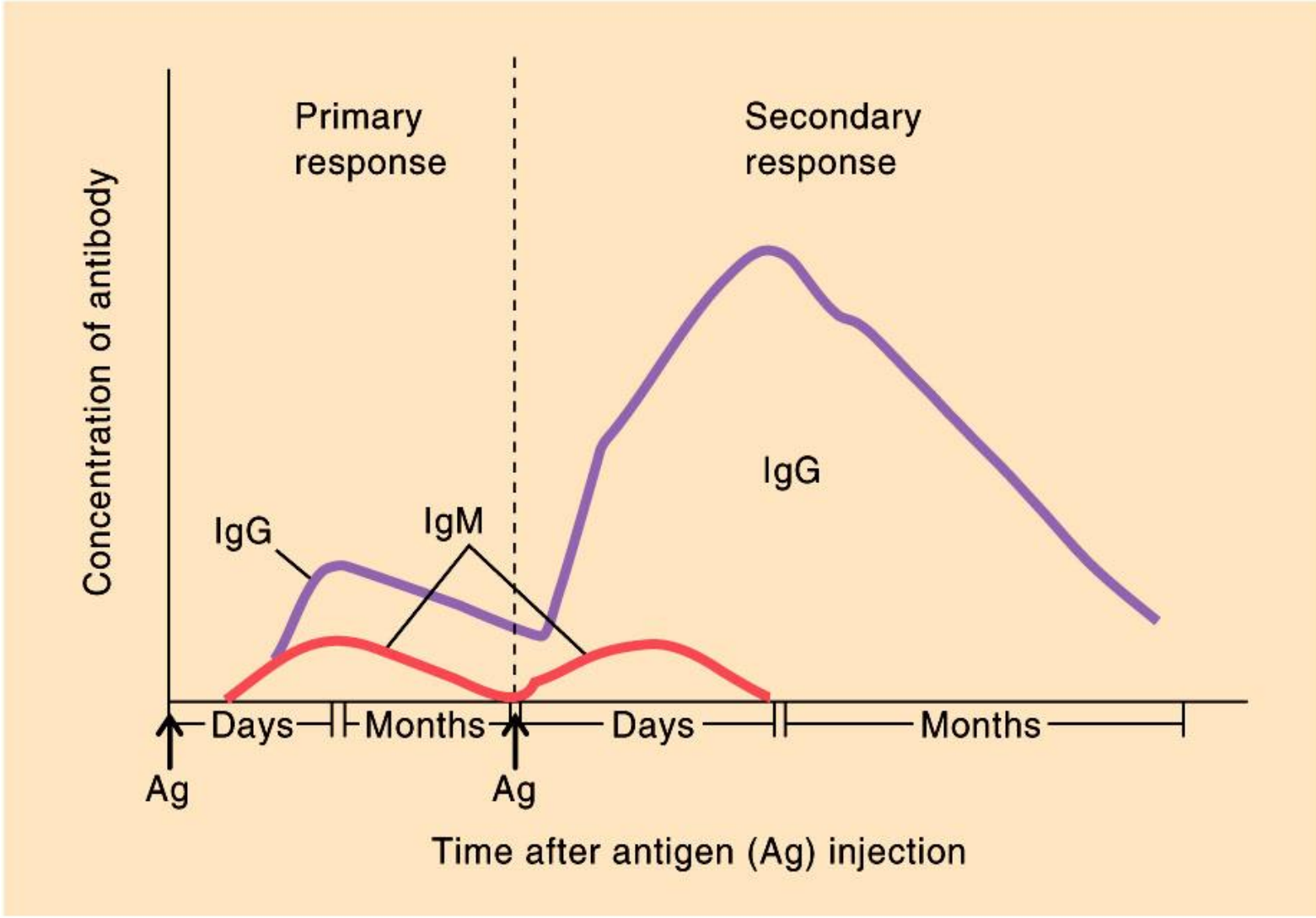
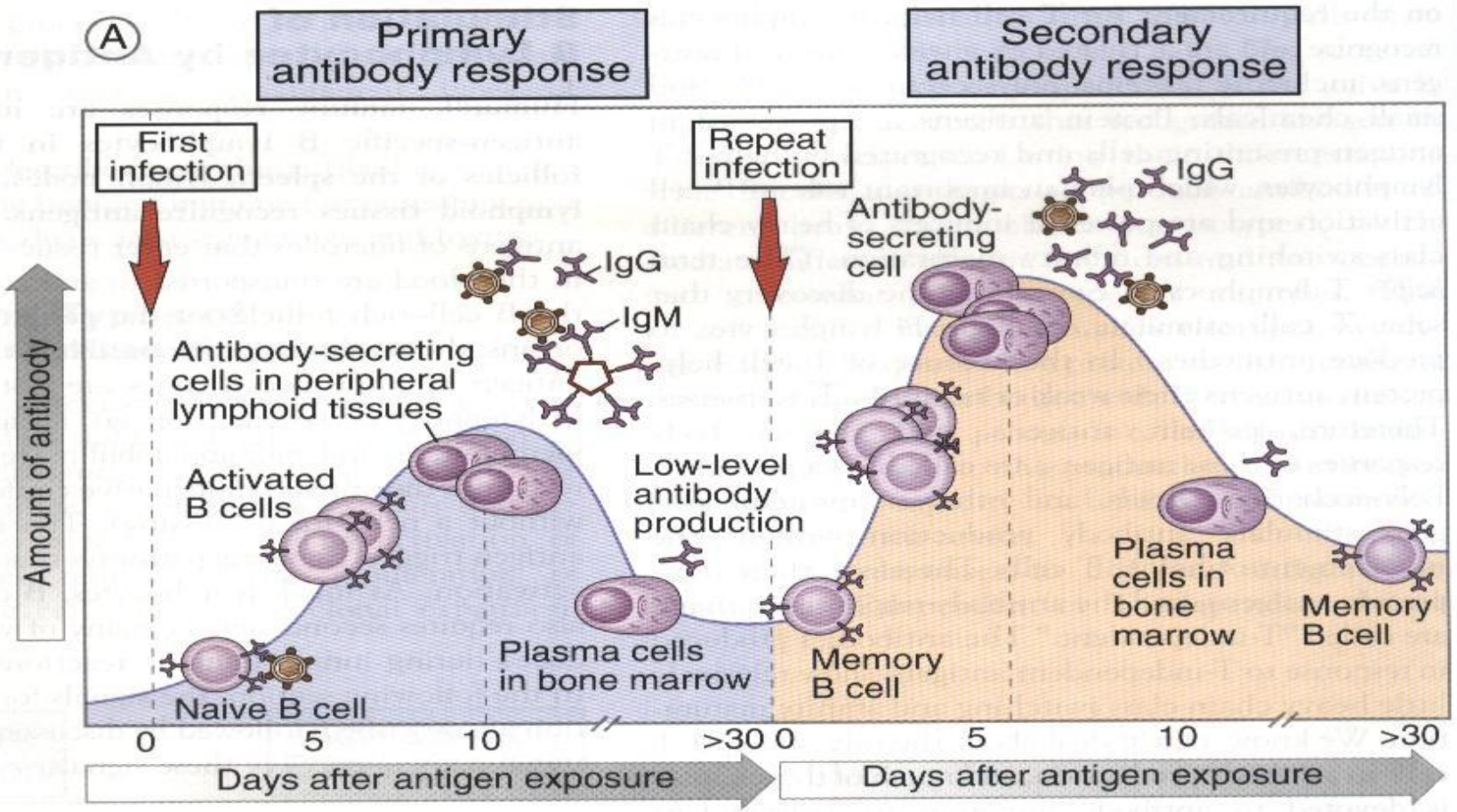
Antibody isotype	Isotype specific effector functions
IgG	Neutralization of microbes and toxins Opsonization of antigens for phagocytosis by macrophages and neutrophils Activation of the classical pathway of complement Antibody-dependent cellular cytotoxicity mediated by NK cells Neonatal immunity: transfer of maternal antibody across placenta and gut Feedback inhibition of B cell activation
IgM	Activation of the classical pathway of complement
IgA	Mucosal immunity: secretion of IgA into lumens of gastrointestinal and respiratory tracts, neutralization of microbes and toxins
IgE	Antibody-dependent cellular cytotoxicity mediated by eosinophils Mast cell degranulation (immediate hypersensitivity reactions)

Types of immune response

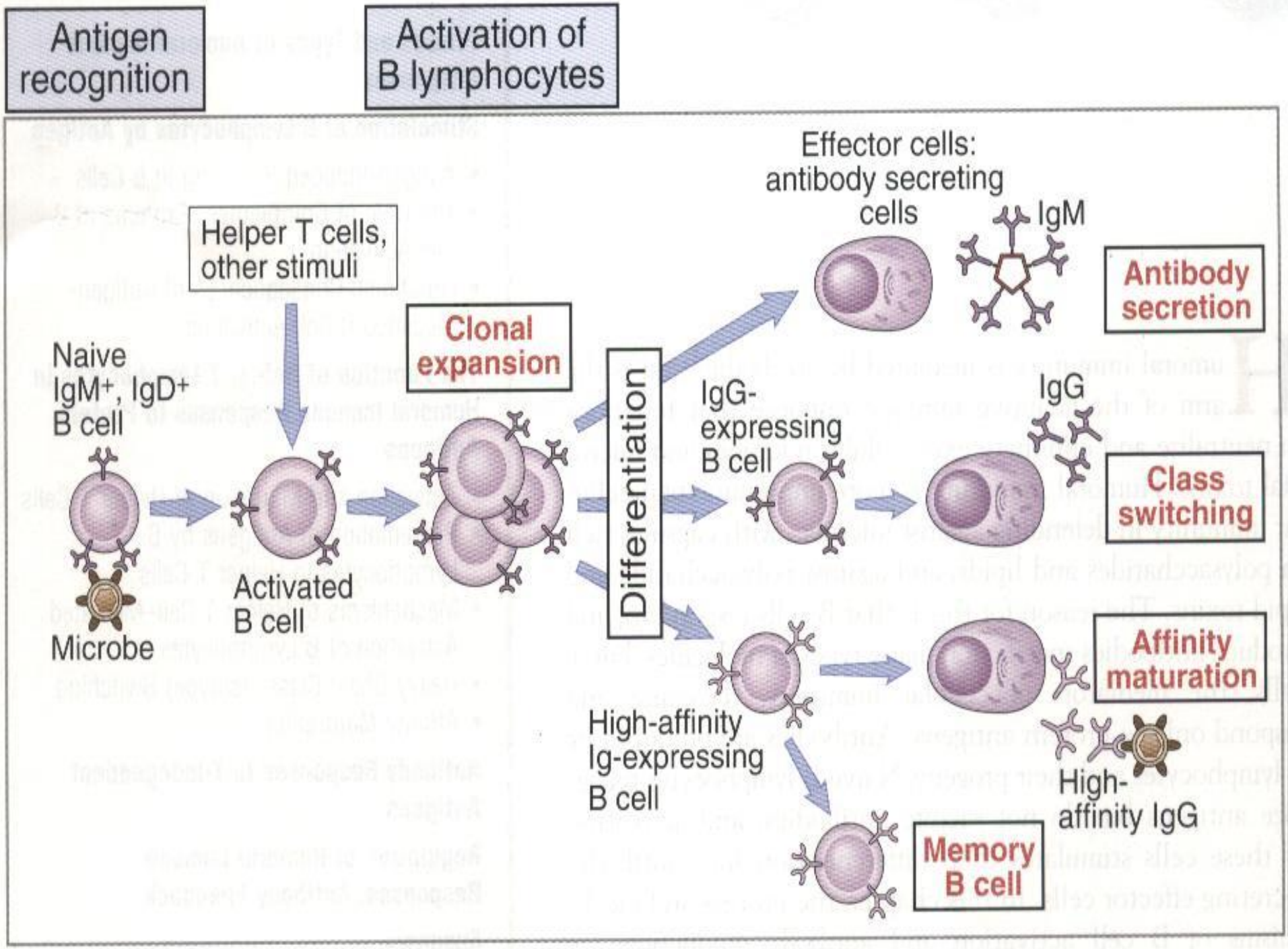
- Primary (first exposure)
  - Mainly IgM
  - IgG is present
- Secondary (subsequent exposure)
  - Mainly IgG





B

	Primary response	Secondary response
Lag after immunization	Usually 5-10 days	Usually 1-3 days
Peak response	Smaller	Larger
Antibody isotype	Usually IgM>IgG	Relative increase in IgG and, under certain situations, in IgA or IgE (heavy chain class switching)
Antibody affinity	Lower average affinity, more variable	Higher average affinity (affinity maturation)


Antigen recognition
Activation of B lymphocytes
Effector cells: antibody secreting cells
IgM
Antibody secretion
Helper T cells, other stimuli
Clonal expansion
Naive IgM+, IgD+ B cell
Differentiation
IgG-expressing B cell
IgG
Class switching
Activated B cell
Microbe
Affinity maturation
High-affinity Ig-expressing B cell
High-affinity IgG
Memory B cell