Innate Immunity

① Present from birth

② Non-specific

③ Forms no memory

④ Initial and subsequent response same

⑤ Rapid onset : acts ēin minutes

⑥ Responds to universal microbial patters eg: PAMP

⑦ Cell component:
- Neutrophil
- Eosinophil
- Basophil, Mast cell
- Macrophage
- Dendritic cell
- NK cell
- LAK cell

⑧ Humoral component:
- Complement
- cytokines

Adaptive Immunity

① Acquired after birth upon exposure to Antigen

② highly Specific

③ Forms immunological memory

④ Response improve upon repeated exposure (Primary and Secondary immune response)

⑤ Slow onset : requires several days before becoming effective

⑥ Diversity: Can respond to millons of different antigens

⑦ Cell component:
- B lymphocyte
- T lymphocyte
- Macrophage
- Dendritic cell
- NK cell
- LAK cell
- Eosinophil

⑧ Humoral component:
- Antibody
- Complement
- Cytokine

Traits	Active immunity	passive immunity
1. Active participation by host	Yes	No
2. **Onset of action**	Immunity starts to develop after a considerable latent period	Starts immediately
3. **Duration of action**	Long Lasting	short (short life of these antibodies)
4. **Immunological memory**	Present	Absent
5. **Secondary immune response**	Occurs	Not Occurs
6. Risk of hypersensitivity	No risk of type I and type III hypersensitivity	There is risk of type I and type III hypersensitivity
Natural	After clinical & sub-clinical infection E.g hepatitis A virus infection	Transfer of maternal antibody to fetus through placenta to infants by breast milk
Arificial	Different types of vaccines e.g bacterial viral & live attenuated vaccines and toxoids etc	Antisera & antitoxins e.g TIG (tetanus ig) ATS (anti-tetanius serum) ADS (anti-diphtheria

Characteristics of active and passive immunity

	Mediators	Advantages	Disadvantages
Active Immunity	Antibody and T cells	Long duration (years)	Slow onset
Passive Immunity	Antibody only	Immediate availability	Short duration (months)

Important Features of the Primary and Secondary Antibody Response

Feature	Primary Response	Secondary Response
Lag period before antibodies detected	7–10 days	3-5 days
Main antibody type produced	IgM	IgG
Amount of antibody produced	Relatively small	Relatively large
Duration of antibody response	Short	Long
Affinity maturation occurs	No	Yes
Dependent on T cell	T cell dependent or independent	T cell dependent

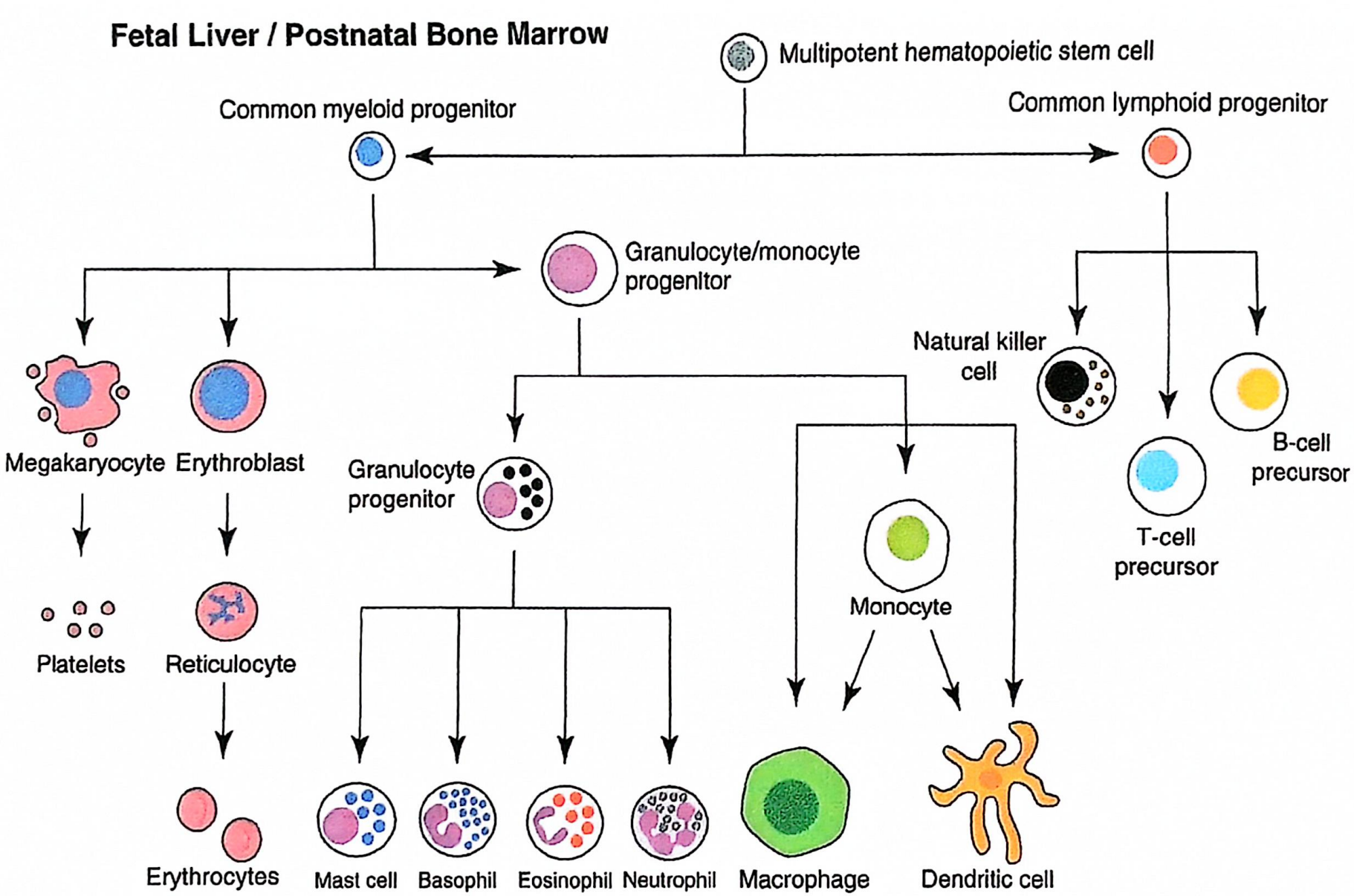


FIGURE 58–1 Origin of hematopoietic cells. Stem cells in the bone marrow (or fetal liver) are the precursors of all blood cells. Stem cells differentiate into myeloid or lymphoid progenitor cells. The myeloid cells are the source of platelets, erythrocytes, granulocytes, macrophages, and dendritic cells. Monocytes are a special type of myeloid cell that can differentiate into macrophages or dendritic cells when needed. The lymphoid cells are the source of T lymphocytes, B lymphocytes, and natural killer cells. The development of lymphocytes is covered in detail in Chapter 59.

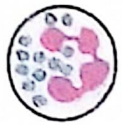
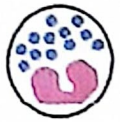
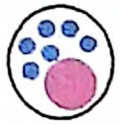
		Characteristics	Key Functions	Interaction with Adaptive Immunity
Macrophage		Large phagocytes, located in all tissues, class II MHC expression	Engulfs and kills many classes of microbes, removal of debris, tissue repair	Possess surface IgG receptors that facilitate phagocytosis (opsonization), activated by IFN-γ, TNF-α from T cells. Professional APC expressing class II MHC
Dendritic cell		Sentinel cells with long branches; reside in epithelial barriers and secondary lymphoid organs, class II MHC expression	Antigen uptake and presentation including cross-presentation	Professional APC expressing class II MHC, responsible for priming of naive T cells
Neutrophil		Most common leukocyte in blood, first responder in inflamed or necrotic tissue	Engulfs and kills bacteria and fungi, digests cellular debris	Attracted into tissues by chemokines, which are increased by T cell-derived IL-17
Eosinophil		Eosinophili granules contain major basic protein; recruited into inflamed tissue by eotaxin	Granule proteins are toxic to cells; involved in asthma and allergic diseases, and protective against invasive helminth infections	Surface IgE receptors; maturation and survival supported by IL-5 from T cells
Basophil		Present at low frequency in the blood	Release histamine, proteases, chemokines, and cytokines; contribute to allergic disease and anaphylaxis	IgE receptors hold IgE molecules that survey for antigen
Mast cell		Distributed throughout the tissues around the vasculature		

TABLE 58–4 Important Features of Natural Killer (NK) Cells

I. Nature of NK Cells

- Large granular lymphocytes
- Lack T-cell receptor, CD3 proteins, and surface IgM and IgD
- *Thymus not required for development*
- Normal numbers in severe combined immunodeficiency disease (SCID) patients
- Activity not enhanced by prior exposure
- Have no memory

II. Function of NK Cells

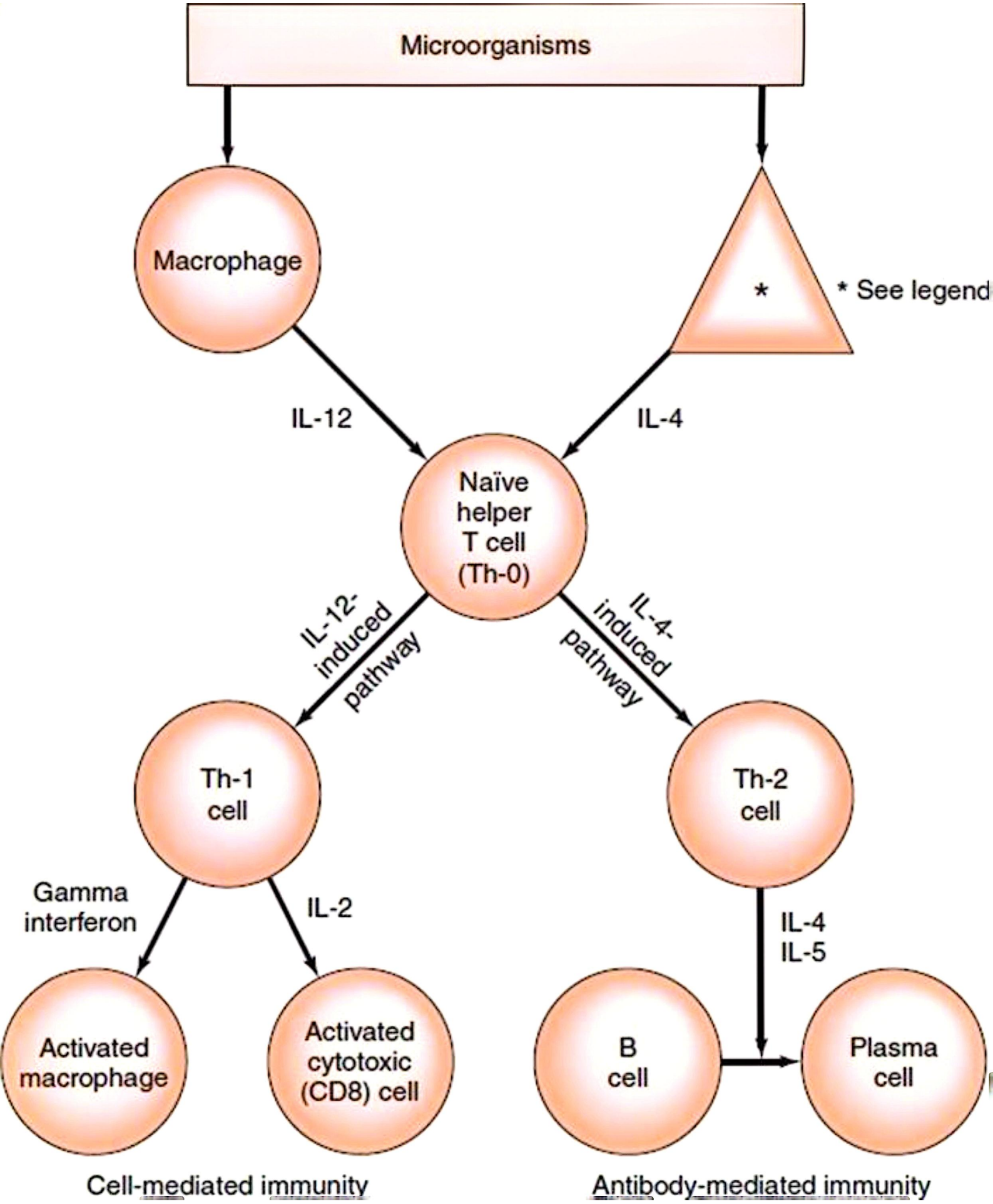
- Recognize virus-infected cells by detecting lack of class I MHC proteins on the surface of the infected cells
- Kill virus-infected cells and cancer cells using perforin and granzyme
- Killing is nonspecific and is not dependent on foreign antigen presentation by class I or II MHC proteins
- Produce gamma interferon that activates macrophages to kill ingested bacteria

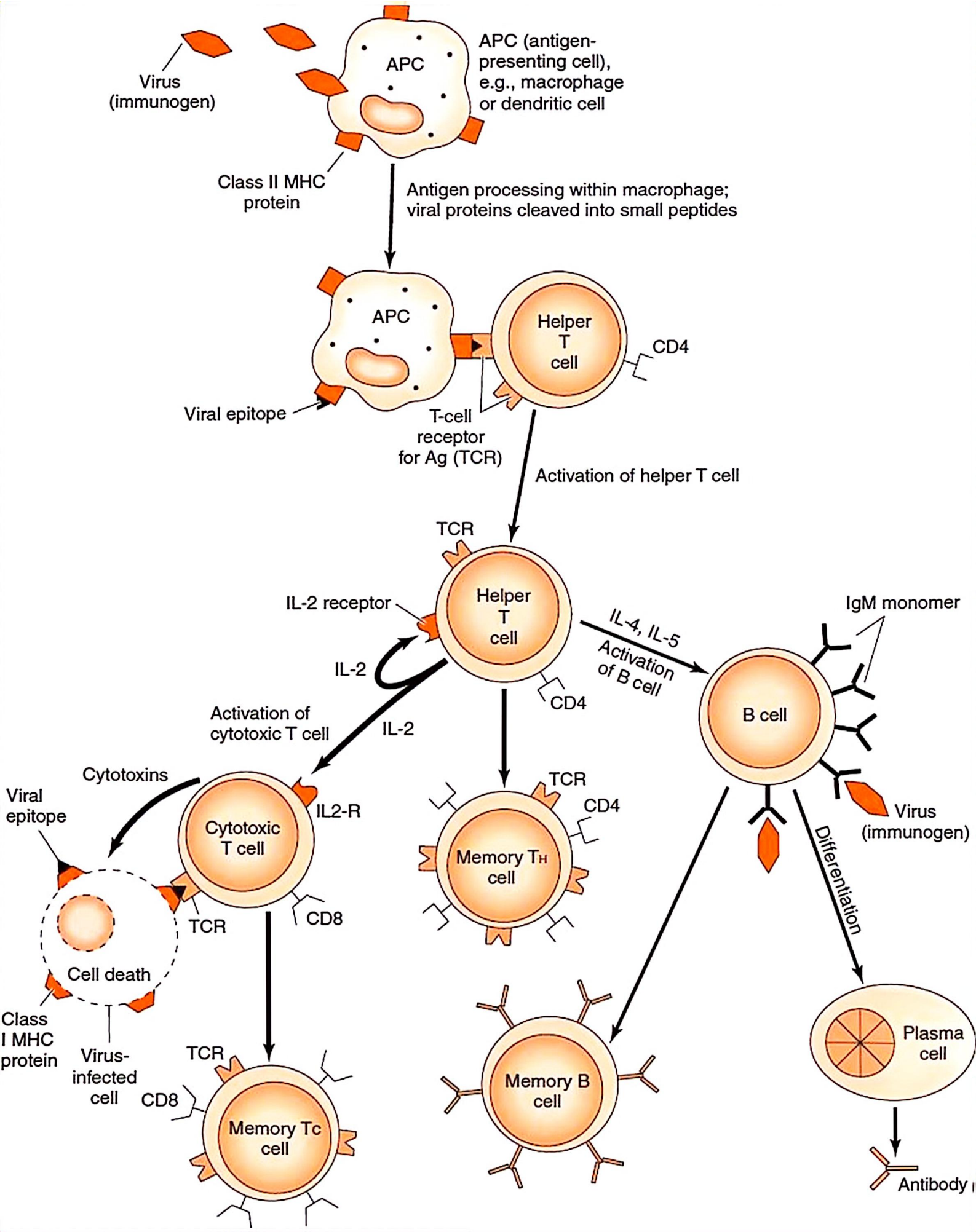
Ig = immunoglobulin; MHC = major histocompatibility complex.

TABLE 59–1 Comparison of T Cells and B Cells

Feature	T Cells	B Cells
Antigen receptors on surface	Yes	Yes
Antigen receptor recognizes only processed peptides in association with MHC protein	Yes	No
Antigen receptor recognizes whole, unprocessed proteins and has no requirement for presentation by MHC protein	No	Yes
IgM on surface	No	Yes
CD3 proteins on surface	Yes	No
Clonal expansion after contact with specific antigen	Yes	Yes
Immunoglobulin synthesis	No	Yes
Regulator of antibody synthesis	Yes	No
IL-2, IL-4, IL-5, and gamma interferon synthesis	Yes	No
Effector of cell-mediated immunity	Yes	No
Maturation in thymus	Yes	No
Maturation in bone marrow	No	Yes

IgM = immunoglobulin M; IL = interleukin; MHC = major histocompatibility complex.


Microorganisms
Macrophage
*
* See legend
IL-12
IL-4
Naïve helper T cell (Th-0)
IL-12-induced pathway
IL-4-induced pathway
Th-1 cell
Th-2 cell
Gamma interferon
IL-2
IL-4
IL-5
Activated macrophage
Activated cytotoxic (CD8) cell
B cell
Plasma cell
Cell-mediated immunity
Antibody-mediated immunity


Virus
(immunogen)
APC
APC (antigen-presenting cell), e.g., macrophage or dendritic cell
Class II MHC protein
Antigen processing within macrophage; viral proteins cleaved into small peptides
APC
Helper T cell
CD4
Viral epitope
T-cell receptor for Ag (TCR)
Activation of helper T cell
TCR
Helper T cell
IL-2 receptor
IL-2
CD4
IL-4, IL-5
Activation of B cell
IgM monomer
B cell
Activation of cytotoxic T cell
IL-2
Cytotoxins
Viral epitope
Cytotoxic T cell
IL2-R
TCR
CD8
Cell death
Class I MHC protein
Virus-infected cell
TCR
CD4
Memory TH cell
Virus (immunogen)
Differentiation
TCR
CD8
Memory Tc cell
Memory B cell
Plasma cell
Antibody

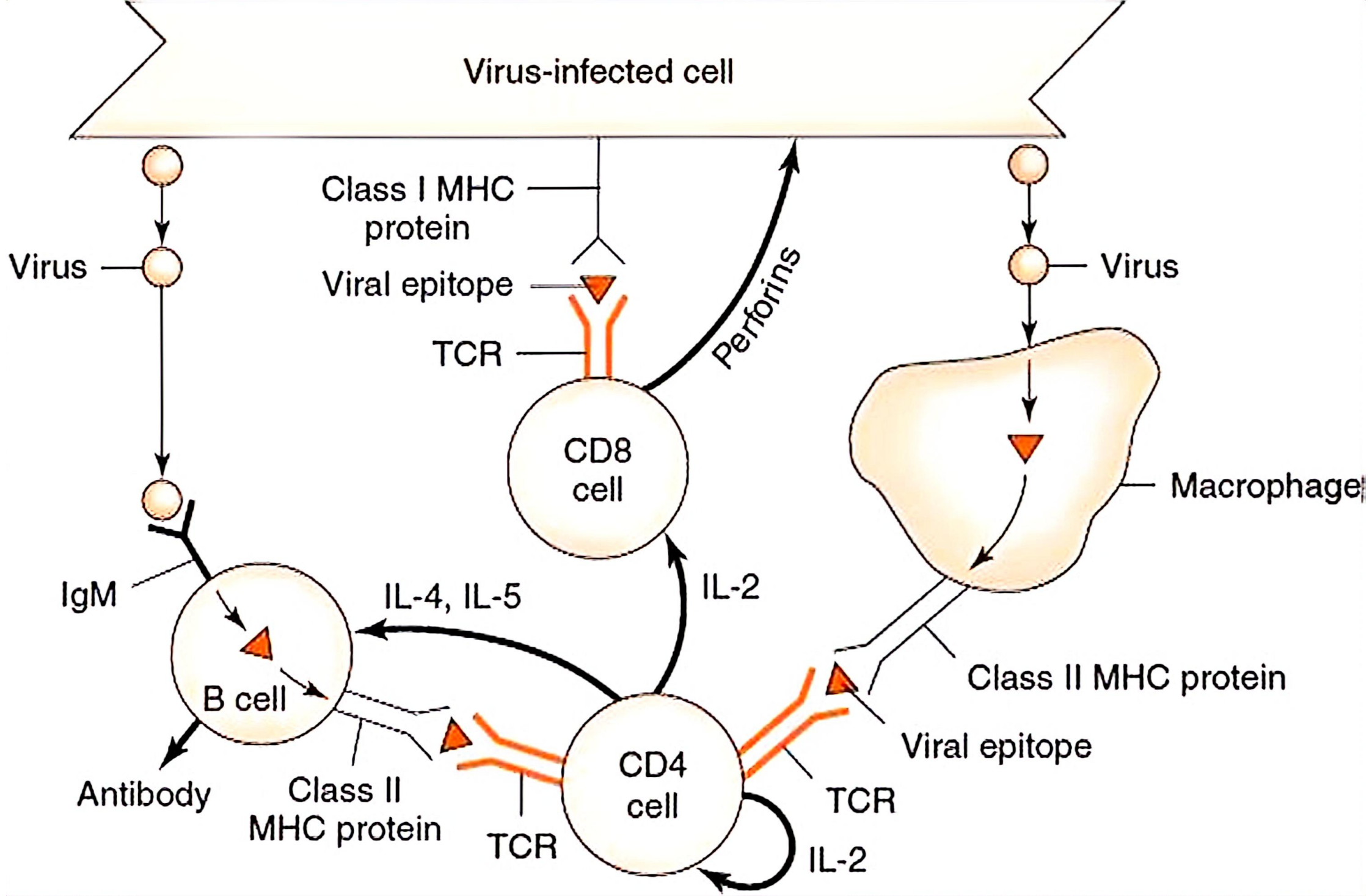

Virus-infected cell
Class I MHC protein
Viral epitope
TCR
Perforins
Virus
Virus
CD8 cell
Macrophage
IgM
IL-4, IL-5
IL-2
B cell
Class II MHC protein
Viral epitope
Antibody
Class II MHC protein
TCR
CD4 cell
TCR
IL-2

TABLE 61–1 Important Functions of Immunoglobulins

Immunoglobulin	Major Functions
IgG	Main antibody in the secondary response. Opsonizes bacteria, making them easier to phagocytize. Fixes complement, which enhances bacterial killing. Neutralizes bacterial toxins and viruses. Crosses the placenta.
IgA	Secretory IgA prevents attachment of bacteria and viruses to mucous membranes. Does not fix complement.
IgM	Produced in the primary response to an antigen. Fixes complement. Does not cross the placenta. Antigen receptor on the surface of B cells.
IgD	Uncertain. Found on the surface of many B cells as well as in serum.
IgE	Mediates immediate hypersensitivity by causing release of contents from the granules of mast cells and basophils upon exposure to antigen (allergen). Defends against worm infections by causing release of enzymes from eosinophils. Does not fix complement. Important host defense against tissue-invasive helminth infections.

TABLE 61–2 Properties of Human Immunoglobulins

Property	IgG	IgA	IgM	IgD	IgE
Percentage of total immunoglobulin in serum (approximate)	75	15	9	0.2	0.004
Serum concentration (mg/dL) (approximate)	1000	200	120	3	0.05
Sedimentation coefficient	7S	7S or 11S[1]	19S	7S	8S
Molecular weight (×1000)	150	170 or 400[1]	900	180	190
Structure	Monomer	Monomer or dimer	Monomer or pentamer	Monomer	Monomer
H chain symbol	γ	α	μ	δ	ε
Complement fixation	++	–	++	–	–
Transplacental passage	++	–	–	–	–
Mediation of allergic responses	–	–	–	–	++
Found in secretions	–	++	–		
Opsonization	++	–	–[2]	–	–
Antigen receptor on B cell	–	–	++	?	–
Polymeric form contains J chain	–	++	++	–	–

[1]The 11S form is found in secretions (e.g., saliva, milk, and tears) and fluids of the respiratory, intestinal, and genital tracts.

[2]IgM opsonizes indirectly by activating complement. This produces C3b, which is an opsonin.

Example of Type-2 Hypersensitivity:

1. **Blood transfusion reactions.** (Immunologically mediated).
2. **Rhesus incompatibility.**Erythroblastosisfetalis (Haemolytic disease of the newborn)
3. **Autoimmune haemolytic anaemia:** Mycoplasma pneumonia infection can induce IgG autoantibodies that cross react with red-cell antigens, resulting in autoimmune haemolyticanaemia.
4. **Idiopathic thrombocytopenic purpura**. Autoantibodies against platelets.
5. **Autoimmune agranulocytosis.** Autoantibodies are against the white cell
6. **Pernicious anaemia.** Antibodies against intrinsic factor and gastric parletal cells.
7. **Vasculitis.** Antineutrophil cytoplasmic autoantibodies (ANCA)
8. **Thrombotic phenomenon.** Antiphospholipid antibodies.
9. **Type II drug reactions:** Drugs which are haptens couple with cell surface proteins and act as antigens which sensitize the individual:

i) Haemolyticanaemia may occur with administration of penicillin, phenacetin and chlorpromazine,
ii) Agranulocytosis associated with amidopyrine or quinidine.
iii) Thrombocytopenic purpura by quinine.

10. **Graves diseases**
11. **Myasthenia Gravis**
12. **Rheumatic fever:** Antibodies against the M proteins of certain strain Streptococcus pyogenes cross-react with tissue glycoproteins in the heart, joints and other tissues. Autoimmune disorder.
13. **Good pasture's syndrome.** Antibody to type IV collagen in basement membrane of glomeruli in kidneys and lung alveoli.
14. **Pemphigus vulgaris.** Antibodies against desmosomes. An autoimmune disorder
15. **Insulin resistance Diabetes Mellitus**

Example of Type-III Hypersensitivity:

1. **Serum sickness:** Fever, urticaria, arthralgia, lymphadenopathy, spleenomegaly, and eosinophilia a few days to 2 weeks after injection of the foreign serum (thymoglobulin, diphtheria antitoxin, ATS etc) or drugs (more common) such as penicillin. e.g., Rheumatoid arthritis, Immune complex glomerulonephritis.
2. **Arthus reaction**: Hypersensitivity pneumonitis (allergic alveolitis) such as farmer's lung, cheese-workers lung, woodworker's lung, & wheat-millers lung. Erythema nodosumleprosum.

Examples:

A. Systemic (Circulating) Immune complex Disease:

1. Serum Sickness.
2. Immune complex glomerulonephritis, e.g., Post Streptococcal glomerulonephritis, AGN
3. Systemic lupus erythematosus
4. Rheumatoid arthritis
5. Immune complex Vasculitis, e.g., Polyarteritis nodosa.
6. Haemorrhagic shock syndrome of dengue.
7. Drugs. e.g. Penicillin (hapten)
8. Cryoglobulinemia
9. Reactive arthritis

B. Local Immune Complex Diseases.

1. Arthus Reaction
2. Extrinsic allergic alveolitis.
3. Erythema nodosumleprosum

Type-IV Hypersensitivity:

Cells involved: Lymphocyte and monocyte-macrophage series. (CD4+, CD8+ & Macrophage, Mainly CD4+ cell)

Example of Type-IV Hypersensitivity:

1. Granulomatous inflammation (e.g., sarcoidosis)
2. Tuberculin test (Mantoux test)
3. Lepromin test
4. Contact dermatitis
5. Graft rejection.
6. GVHD
7. Tumor immunity
8. Type I Diabetes Mellitus
9. Hasimoto's Thyroiditis
10. Erythema Multiforme,
11. Stevens-Johnson Syndrome
12. Toxic Epidermal Necrolysis
13. Psoriasis
14. Inflammatory bowel disease
15. Multiple sclerosis