

Key Terms:

Immunology: Study of immunity (the response of the immune system to infection)

Immunity: Ability of the host to protect itself against foreign organisms

Immune response: A reaction of the body in response to the presence of a foreign substance (i.e. antigens)

Antigens: Molecules from a pathogen or foreign organism that provoke a specific immune response

Spleen

1) Mounting immune response to antigens in blood stream

2) Large, ovoid organ situated high in left abdominal cavity

3) Surrounded by a capsule that extends a number of projections (trabeculae) into interior to form a compartmentalised structure

4) Two types of compartments: red pulp and white pulp, which are separated by a diffuse marginal zone

Cellular basis of immunity

1) Immune cells:

1. Mononuclear phagocytes: Monocytes and Macrophages

2. Dendritic cells: Langerhans, Interdigitating and Follicular

3. Granulocytes: neutrophils, eosinophils, basophils – help fight off infection

4. Lymphocytes: B and T cells, NK cells

Primary Lymphoid Organs

1) Immature lymphocytes generated in haematopoiesis mature and become committed to a particular antigenic specificity within the primary lymphoid organs

2) **Bone marrow:** supports the maturation of all erythroid and myeloid cells in humans and mice, the maturation of B lymphocytes

Primary Lymphoid Organs (cont)

3) **Thymus:** unlike B lymphocytes, T lymphocytes do not complete their maturation in the bone marrow. T lymphocyte precursors need to leave the bone marrow and travel to the unique microenvironments provided by the other primary lymphoid organ, thymus, in order to develop into functional cells

Eosinophils

- 1) Comprise about 1-3% of total WBCs
- 2) Bi-lobed nucleus and acidophilic granules
- 3) Granules contain major basic protein
- 4) Produced by haematopoiesis in the bone marrow and migrating into the tissues
- 5) Mobile and phagocytotic
- 6) Mediate anti-parasitic response and type I hypersensitivity reactions (allergy)

Basophils

- 1) Comprise less than 1% of total WBCs
- 2) Single lobed nucleus and heavily granulated cytoplasm
- 3) Non-phagocytic
- 4) Support mast cell function in tissues, mediate Type I hypersensitivity reactions
- 5) **Mast cells** – cytoplasmic granules that contains histamine, play an important role in allergic response

T-lymphocytes

- 1) Morphologically identical to B cells
- 2) Produced in bone marrow and mature in thymus
- 3) Mediated cell-mediated arm of adaptive response
- 4) Several sub-population exist: T helper cells (CD4), cytotoxic T cells (CD8) and Natural killer T cells (NKTs)
- 5) B and T cells form memory cells

Homeostasis and the Immune system

1) Pathogens invade organisms because they are seeking: Source of food

Protection

Site for reproduction

2) Defense systems are evolved to get rid of the invading organisms

1. Mononuclear phagocytes

Monocytes and Macrophages

- 1) Long lived phagocytic cells
- 2) Key initiators of inflammation
- 3) Involved in phagocytosis or intracellular killing of microorganisms
- 4) Can initiate an adaptive response
- 5) Found in blood (monocytes) and tissues (macrophages)



Secondary Lymphoid Organs

- 1) Located along vessels of lymphatic system
- 2) Distributed throughout the body and share some anatomical features
- 3) Some lymphoid tissues in the lung and lamina propria of intestinal wall consists of diffuse collections of lymphocytes and macrophages
- 4) Other lymphoid tissue is organised into structures called lymphoid follicles, which consist of aggregates of lymphoid and non lymphoid cells surrounded by a network of draining lymphatic capillaries
- 5) Lymphoid organs are connected to each other and to infected tissues by blood and lymphatics

Macrophages

- 1) Terminally differentiated, long-lived monocytes residing in tissues
- 2) Like monocytes, macrophages are motile and highly adherent upon phagocytic activity

Macrophages (cont)

- 3) Serve different functions in different tissues
 - Phagocytosis, Adaptive immunity, Muscle regeneration, Limb regeneration, Wound healing, Iron homeostasis – maintain constant concentrations of iron in the brain internal environment
- 4) Named according to their tissues location

alveolar macrophages – lung
 Histocytes - connective tissues
 Kupffer cells – liver
 Mesangial cells – kidney
 Microglial cells – brain
 Osteoclasts - bone

Natural Killer cells

- 1) Larger rim of cytoplasm
- 2) Cytotoxic cells that kill tumour and virus infected cells
- 3) Constitute 5-10% of lymphocytes
- 4) Do not have membrane receptors for antigen but has NK cell receptors
- 5) Kill by releasing small cytoplasmic granule of proteins (perforin and granzyme) -> cause host cells to die by apoptosis

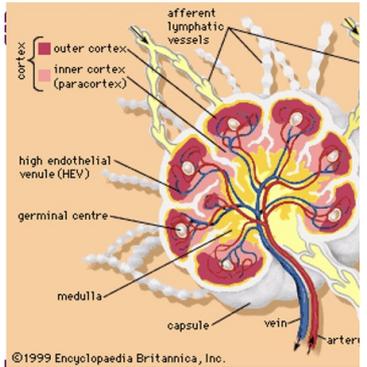
B-lymphocytes

- 1) Small cells, thin rim of cytoplasm
- 2) Mature in bone marrow
- 3) Differentiate into plasma cells to secrete antibodies
- 4) Mediate humoral arm of adaptive immune response
- 5) B cells interact with T-helper cells which proliferate and switch to different sub-populations
- 6) Plasma cells are terminally differentiated cells, many die in 1 or 2 weeks

Humoral Mediated Immunity

- 1) **Cytokines** – glycoproteins that co-ordinate immune response (interleukins, growth factors)
- 2) **Antimicrobial peptides** - broad-spectrum anti-infectives against wide ranges of bacteria
- 3) **Complement** – approx. 30 when activated promote bacterial cytolysis, phagocytosis and inflammation
- 4) **Acute phase proteins** - contribute to acute response to infection by binding pathogens such as bacteria and facilitating complement activation

Lymph cell



Lymphatic System

- 1) Immune system consists of immune cells that continuously circulate between blood and lymphoid organs
- 2) Lymphatic system consists of lymphoid tissues and organs and circulating clear fluid called lymph
- 3) Site of initiation of adaptive immune response

Neutrophils

- Most abundant myeloid cell type, comprising 40-70% of total WBCs
- Multilobed nucleus and a granulated cytoplasm
- Produced by haematopoiesis in the bone marrow that are released into the peripheral blood and circulate for 7-10 hours before migrating into the tissues, where they have a life span of only a few days

Neutrophils (cont)

- Mobile and highly phagocytic
- 1) Major role in anti-bacterial response: ingest, kill, digest microbial pathogens
- 2) Contain multiple antimicrobial agents, such as lysozyme (peptidoglycan degradation), hydrogen peroxide and lactoferrin (iron chelator)
- 3) Neutrophils dying at the site of infection contribute to the formation of the whitish exudate called Pus

Dendritic Cells

- 1) Arises from hematopoietic stem cells via different pathways and in different locations
- 2) **Antigen presenting cells:** Acquire antigen by phagocytosis and display them to T cells
- 3) **Langerhans cells:** immature cells primarily found in skin and mucosal tissues

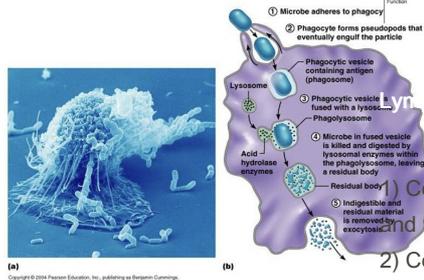
Accessory cells – 2 types

- | | |
|-----------------------|---|
| Interdigitating cells | Mediate T cell activation and differentiation. Found in periphery and lymphatic tissues |
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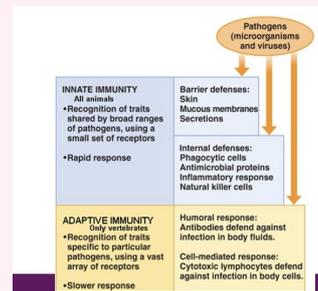
Dendritic Cells (cont)

- | | |
|----------------------------|---|
| Follicular dendritic cells | Unrelated to the above. Mediate B cell activation and differentiation. Restricted to lymphatic tissues. |
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Phagocytosis



Inflammation accompanies an immune response



Our immune response includes **innate and adaptive** responses

The 5 Immunoglobulin (Ig) Classes

	IgG antibody	IgM antibody	Secretory IgA dimer	IgE antibody	IgD antibody
Heavy chains	γ	μ	α	ε	δ
Number of antigen binding sites	10	10	10	10	10
Molecular weight (kDa)	150,000	900,000	380,000	250,000	180,000
Percentage of total antibody in serum	80%	10%	10%	0.0001%	1%
Classed placenta	no	yes	no	no	no
Fixes complement	yes	yes	no	no	no
Fixes to	phagocytes			mast cells and basophils	B cell receptor
Function	Main antibody of primary responses; long-lived; one of four in mucosal immune system	First antibody to appear in response	Secreted into mucus, tears, saliva, colostrum	Antibody of allergic and autoimmune activity	B cell receptor

Lymphocytes

- 1) Constitutes 20-40% of WBCs and 99% of cells in lymph
- 2) Continually circulate in the blood and lymph and are capable of migrating into tissue space and lymphoid organs
- 3) Subdivided into 3 classes
 - (a) B-lymphocytes
 - (b) T-lymphocytes
 - (c) Natural killer cells (NK cells)

Granulocytes

- 1) Contain cytoplasmic granules
- 2) Also called polymorphonuclear leukocytes (PMN, PML, PMNL)
- 3) Produced via granulopoiesis in bone marrow
- 4) Based on cellular morphology, cytoplasmic staining characteristics, granulocytes are classified as
 - (a) Neutrophils
 - (b) Eosinophils
 - (c) Basophils

Lymphatic Continued

- 4) Lymphoid organs are either primary (central) or secondary (peripheral)
- 5) **Primary lymphoid organs:** Major sites of lymphocyte development i.e. thymus and BM
- 6) **Secondary lymphoid organs:** Spleen, lymph nodes, mucosal-associated lymphoid tissues (MALT) including tonsils and Peyer's patches

Monocytes

- 1) Comprise up to 10% of circulating WBCs
- 2) Motile and highly adherent upon phagocytic activity
- 3) During haematopoiesis in the bone marrow, monocyte progenitor cells differentiate into promonocytes, which leave the bone marrow and enter the blood, where they further differentiate into mature monocytes
- 4) Monocytes circulate in the bloodstream for about 8 hours, during which they enlarge; then migrate into the tissues and differentiate into macrophages and dendritic cells (Antigen presenting cells)

Lymph node

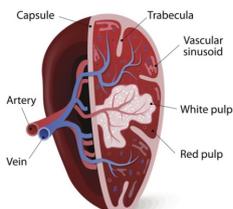
- 1) Sites where immune responses are mounted to antigens in lymph
- 2) Encapsulated bean shaped structures containing a reticular network packed with lymphocytes, macrophages, and dendritic cells
- 3) First organised lymphoid structure to encounter antigens that enter tissue spaces

Effector mechanism

- 1) Processes by which pathogens are destroyed and cleared from the body
- 2) Can be both cell-mediated and humoral in origin
- 3) Cell-mediated – effector function is performed by a cell e.g. cytotoxic T cells (Tc), phagocyte, natural killer (NK) cell
- 4) Humoral – effector function is mediated by soluble molecules e.g. complement, antibodies

Spleen Anatomy

SPLEEN ANATOMY



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