

### 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:**

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
- 4) Named according to their tissues location

eolar 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

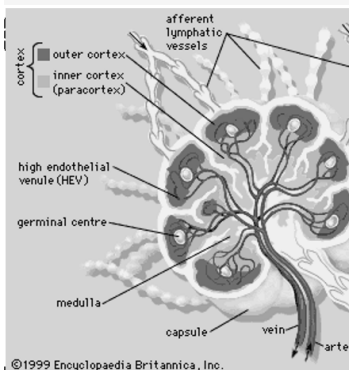
### B-lymphocytes

- 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

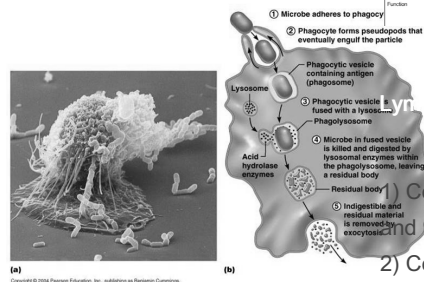
### Accessory cells – 2 types

|                               |                                                                                                       |
|-------------------------------|-------------------------------------------------------------------------------------------------------|
| Inter-<br>digitating<br>cells | Mediate T cell<br>activation and differ-<br>entiation. Found in<br>periphery and<br>lymphatic tissues |
|-------------------------------|-------------------------------------------------------------------------------------------------------|

### Dendritic Cells (cont)

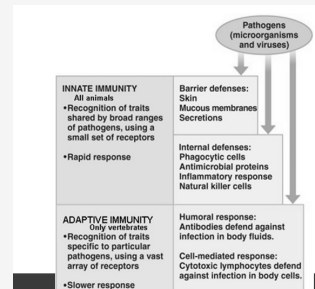
Follicular dendritic cells  
Unrelated to the above. Mediate B cell activation and differentiation.  
Restricted to lymphatic tissues.

### Phagocytosis



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### Inflammation accompanies an immune response



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

### The 5 Immunoglobulin (Ig) Classes

|                                       | IgM monomer                                                                  | IgG monomer                                                                                    | Secretory IgA dimer                           | IgE monomer                      | IgD monomer      |
|---------------------------------------|------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|-----------------------------------------------|----------------------------------|------------------|
| Heavy chains                          | $\mu$                                                                        | $\gamma$                                                                                       | $\alpha$                                      | $\epsilon$                       | $\delta$         |
| Number of antigen-binding sites       | 10                                                                           | 2                                                                                              | 4                                             | 2                                | 2                |
| Molecular weight (Daltons)            | 900,000                                                                      | 150,000                                                                                        | 380,000                                       | 200,000                          | 180,000          |
| Percentage of total antibody in serum | 6%                                                                           | 80%                                                                                            | 10%                                           | 0.0001%                          | 1%               |
| Crosses placenta                      | no                                                                           | yes                                                                                            | no                                            | no                               | no               |
| Fixes complement                      | yes                                                                          | yes                                                                                            | no                                            | no                               | no               |
| It binds to                           | phagocytes                                                                   | Most types of antibody                                                                         | Secreted into mucus, tears, saliva, colostrum | Attract cells and kill parasites | It cell receptor |
| Function                              | Most antibody of primary response, best at killing bacteria, but not viruses | Most abundant antibody in circulation, most effective against bacteria, viruses, and parasites | Secreted into mucus, tears, saliva, colostrum | Attract cells and kill parasites | It 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

