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

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

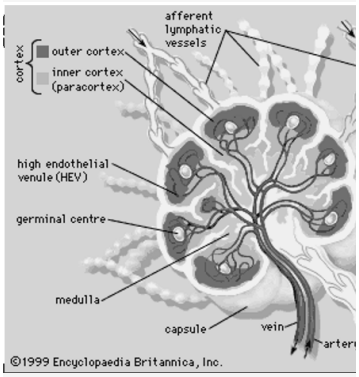
1) **Cytokines** – glycoproteins that co-ordinate immune response (interleukins, growth factors)

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

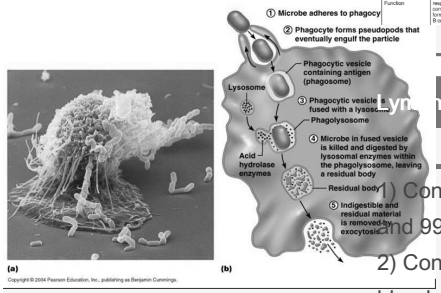
Accessory cells – 2 types

Interdigitating dendritic cells	Mediate T cell activation and differentiation. Found in periphery and lymphatic tissues

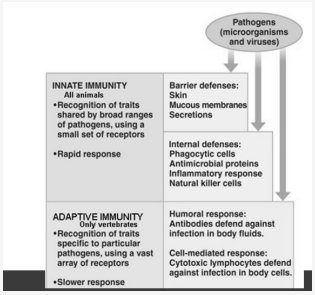
Dendritic Cells (cont)

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

Phagocytosis



Inflammation accompanies an immune response



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

The 5 Immunoglobulin (Ig) Classes

The Five Immunoglobulin (Ig) Classes

	IgM pentamer	IgG monomer	Secretory IgA dimer	IgE monomer	IgD monomer
Heavy chains	μ	γ	α	ε	δ
Number of antigen binding sites	10	2	4	2	2
Molecular weight (Daltons)	900,000	150,000	385,000	200,000	180,000
Percentage of total antibody in serum	0%	80%	13%	0.002%	1%
Crosses placenta	no	yes	no	no	no
Fixes complement	yes	yes	no	no	no
Fc binds to		phagocytes		mast cells and basophils	
Function	Main antibody of primary responses, best at fixing complement; the monomer form of IgM serves as the B cell receptor	Main blood antibody of secondary responses; neutralizes toxins, opsonization	Secreted into mucus, tears, saliva, colostrum	Antibody of allergy and antiparasitic 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