Reticuloendothelial System

Avian Physiology
Reticuloendothelial System (RES)

• First-line of defense against infections from disease causing agents like:
  – Bacteria
  – Viruses
  – Parasites

• Part of Circulatory System because components come from tissues that make blood cells.
Reticuloendothelial System (RES)
2 Major Functions

• Phagocytosis
  – Removal and destruction of invaders

• Immunity
  – Formation of products that prevent reoccurrence of infection
    • Antibodies
    • Cytokines
    • Etc.
Reticuloendothelial System (RES) Composition

• 3 Cell types
  – Blood Leukocytes
  – Stationary Macrophages
  – Wandering Macrophages
Macrophages
Stationary

- Derived from circulatory monocytes

- Stationary macrophages
  - Remain at their site of action by sticking to inner surface of blood vessels
  - Snatch and eat (phagocytosis) foreign particles as they pass by
  - Include Kupffer cells of the liver, spleen, bone, adrenal, and renal
Macrophages
Wandering

• In all tissues, but most occur in:
  – lymph glands
  – Body cavities
  – Connective tissue
  – Nerve tissue
• Never re-enter circulation
• Live 20-30 days
• Patrol the tissue and phagocytize
Macrophage

1. Macrophage moving toward bacteria.

2. Bacteria being engulfed.

3. Bacteria contained within a vesicle.

4. Lysosome fusing with a vesicle and releasing phagocytic enzymes.

5. Bacteria being destroyed and digested.

6. Undigested remains of bacteria.

- Pseudopod
- Nucleolus
- Nucleus
- Mitochondrion
- Ribosomes
- Lysosome
- Endoplasmic reticulum
- Golgi apparatus
- Bacterium
- Long, thin pseudopod

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Leukocytes
Properties

• Margination
  – Ability to lineup along the inner walls of capillaries

• Diapedesis
  – Leaving the circulatory system
  – After margination, pseudopods (false feet) of leukocyte extend through pores in capillary wall and then entire cell enters tissue.
Diapedesis
Phagocyte Properties

• Ameboid Movement
  – How they move to site of infection
  – Extend pseudopod and follow it.
  – Travel at 40µm/min or 3 times length/min
  – At this point they are called phagocytes
Phagocyte Properties

- Chemotaxis
  - Injured cells or bacteria secrete substances that attract or repel phagocytes.

- Positive chemotaxis = attract
  - Usually injured tissue

- Negative chemotaxis = repel
  - Usually bacteria
Phagocyte Properties

• Phagocytosis:
  – The body’s major defense against infection

  – Vacuolization
    • When a foreign particle (cell) is engulfed by a phagocyte
Phagocyte
Properties
Vacuolization

• Part of the cell membrane surrounds the invader
• Acidic substances (↓ pH) are then secreted into the vacuole to kill the invader
  – Lactic acid
  – Lysozyme
• Next digestive enzymes digest the killed invader and it is used as food by the cell.
Phagocyte Properties

• How do phagocytes recognize a foreign cell?
  – Body cells have “self” markers
    • Cell surface proteins
  – Also antibodies and antibody like substances attach to foreign cells
    • Inactivates, kills, and/or marks invaders for destruction by phagocytes.
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Inflammation

- Recognized by early Greeks
- Defined as changes in tissue in response to injury.
- Greek signs of inflammation:
  - Heat
  - Pain
  - Swelling
  - Redness
Inflammation

Events

• 1. Injury
• 2. Clotting
• 3. Extracellular Edema (swelling)
• 4. Browny Edema
• 5. 1st WBC Event – Monocytic
• 6. 2nd WBC Event - Granulocytic
• 7. 3rd WBC Event - Lymphocytic
• 8. Pus Formation
• 9. Scar Formation
Inflammation
Events

• Cells release chemotaxins and necrosins.
  – ↑ permeability of cells in injured area
  – Fluids leak into extracellular space
• Fluids Clot because of fibrinogen
• **Extracellular edema** = initial swelling
• A fibrin net is created around the clotted area resulting in **Browny Edema**
  – Only small molecules, electrolytes and leukocytes (diapedesis) can penetrate net
Clotting Proteins and Clotting

- Clotting should not occur unless injury

- Initiated by **Prothrombin activating factors**, i.e., **Thromboplastin**

- Factors that cause release of thromboplastin:
  - **Extrinsic Factors** = external trauma that damages vessels
  - **Intrinsic Factors** = damage of blood cells

- Fast uncontrolled once started
Clotting Proteins and Clotting

• Cascade:

\[ \downarrow \text{Prothrombin activating factors} \]

Prothrombin \(\Rightarrow\) Thrombin
(an \(\alpha\) globulin)

\[ \downarrow \]

Fibrinogen \(\Rightarrow\) \(\Rightarrow\) Fibrin threads

+ \(\text{Ca}^{++}\)

+ fibrin stabilizing factor =

Polymerization and clotting
Inflammation
3 major leukocytic events

• 1\textsuperscript{st} WBC event is Monocytic

• Monocytes 1\textsuperscript{st} to leave circulation to become macrophages.

• Monocytes are the most active and efficient of WBC.
Inflammation
3 major leukocytic events

• 2\textsuperscript{nd} WBC event is Granulocytic

• Heterophils main one entering inflammed area for most infections

• With round worm infection, eosinophils are the main ones entering
Inflammation
3 major leukocytic events

• 3rd WBC event is Lymphocytic
• Lymphocytes enter
  – They are poor phagocytes.
  – But they are in great number.
• Lymphocytes can “REMEMBER”
• They can pass their “MEMORY” on down to their progeny cells genetically.

• This memory results in IMMUNITY
Inflammation
Final Events

• Pus formation:
  – 1st sign of healing
  – Cellular debri from battling infection
  – Cavity formed within fibrin net fills with pus and PRESSURE
  – Once pressure is excessive, wound can rupture.

• Scar formation:
  – Formed by connective tissue to repair damage from infection.
Immunity

Avian Physiology
Immunity
Definition

• The ability to remember a previous encounter with a foreign substance.
Immunity
2 Limbs (divisions)

• Humoral Immunity
  – Ability to produce **antibodies** that are specific for one or a few extremely similar **antigens**.

• Cell-mediated Immunity
  – Protection by cells that produce **cytokines**
    • Some kill cells
    • Some stimulate antibody producing cells
    • Some kill viruses
History of knowledge of immune functioning

- In 1950s - know that animals produce specific antibodies than bind to specific proteins (antigens) - basis of vaccination.

- Role of thymus (McFarland Burnett) - no thymus in mice - wasting and lymphopenia (reduced numbers of blood lymphocytes).

- Role of Bursa of Fabricius in chicken - Bruce Glick (MSU). Bursectomy - antibody production greatly reduced/lack of immune competence.
History II

• Dr. Good at the Mayo - children without thymus - wasting.
  – Postulated that thymus in mammals - the functional equivalent of the bursa in chickens.
• Dr. Max Cooper - thymectomized and bursectomized chickens (ablation approach)
  – Thymectomized chickens - normal antibodies’
  – Bursectomized chickens - greatly reduced antibody production

⇒⇒⇒ Concept of humoral and cell mediated immune responses
Concept of humoral and cell mediated immune responses

• Bursa produces B cells or B lymphocytes.
• B cells are influenced by bursal environment.
• Leave bursa and ultimately become antibody producing cells.
• Thymus produces T cells or T lymphocytes - responsible for cell mediated immunity.
• Bursa and thymus are the PRIMARY IMMUNE TISSUES.
Definitions

• Antigen - binds to an antibody in a specific manner, foreign to the body.
• Immunogen - provokes an antibody response
• Antibody - binds to an antigen
• Antisera - Sera containing specific antibodies
• Monoclonal antibody - Molecular identical antibodies that are derived from only one clone of cells and recognizes only one antigen or antigenic site.
Humoral immunity

• Foreign protein(s) result in slow development of antibodies in the circulation.
• Primary humoral immune response
  – After challenge
  – 2-3 day little or no antibodies detected = Lag phase
  – 6-8 days peak antibody conc. = Exponential phase
  – 14-21 days after challenge - no antibodies detected - degradation phase.
Humoral immunity

- Primary humoral immune response

![Diagram showing the stages of an immune response: LAG, LOG, PLATEAU, DECLINE. The graph plots Ab Titer against Days After Immunization, with Ag (antigen) induction leading to an exponential rise followed by a plateau and decline.]
Humoral immunity II

- Secondary (Anamnestic) humoral immune response
  - After a second challenge
  - 2 days Very high antibody concentrations
  - 4 days peak antibody conc. (2x as many as in primary response)
  - 14-21 days after challenge - high conc. antibodies.
- NOTE - rapid and very large response
Humoral immunity II

- Secondary (Anamnestic) humoral immune response
Humoral immunity II

- Secondary antibody immune response
  - High concs. of antibodies capable of inactivating large numbers of bacteria
  - Immunological memory
  - Basis of vaccination
Immunological memory

• During primary immunological response - those B - lymphocytes capable of producing antibodies that bind to the antigen present in secondary immune tissues (spleen, lymph nodes, Harderian glands, Peyer’s patches, Merkel’s diverticulum) start to divide.

• Two populations:
  – Enlarge to become Plasma Cells actively producing antibodies (primary response)
  – Memory Cells - Continue to divide and aren’t active until secondary response
Concept

• Foreign and self
  – Normally **only** foreign proteins provoke an antibody or other immune response

• One specific antibody from one clone of plasma cells (from a single B-cells)

• Different clones produce different antibodies to different sites on the surface of the foreign protein

• Monoclonal antibody

• Autoimmune diseases
Cell-mediated immunity

• T-cells from thymus but migrate out
• Produce cytokine called lymphokines (>30)
  – Interleukins
  – Interferons
  – Macrophage-activating factors
• T-cells and lymphokines
  – Kill viruses, tumor cells, reject foreign tissue,
  – Help lymphocytes recognize antigens, inhibit some lymphocytes and activate macrophage