Immunity

Avian Physiology
Immunity

Definition

• The Latin term “IMMUNIS” means EXEMPT, referring to protection against foreign agents.

• The ability to remember a previous encounter with a foreign substance.
The Immune System is the Third Line of Defense Against Infection

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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
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
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.
Antibodies are Produced by B Lymphocytes
Antibody Structure
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
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
Clonal Selection of B Cells is Caused by Antigenic Stimulation
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
• Polyclonal antibodies
ANTIBODIES

POLYCLONAL.

Derived from different B Lymphocytes cell lines

Batch to Batch variation affecting Ab reactivity & titre

NOT Powerful tools for clinical diagnostic tests

MONOCLONAL.

Derived from a single B cell clone

mAb offer Reproducible, Predictable & Potentially inexhaustible supply of Ab with exquisite specificity

Enable the development of secure immunoassay systems.
Cell-mediated immunity

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

Antigens that stimulate this response are mainly *intracellular*.

Requires constant presence of antigen to remain effective.

Unlike humoral immunity, cell mediated immunity is not transferred to the fetus.
Cell Mediated Immunity

Cellular Components of Immunity:

– T cells are key cellular component of immunity.

– T cells have an antigen receptor that recognizes and reacts to a specific antigen (T cell receptor).

– T cell receptor only recognize antigens combined with major histocompatibility (MHC) proteins on the surface of cells.
  
  • MHC Class I: Found on all cells.
  • MHC Class II: Found on phagocytes.

– Clonal selection increases number of T cells.
Cell Mediated Immunity

Types of T cells:

1. **T Helper (T<sub>H</sub>) Cells**: Central role in immune response.

2. **Cytotoxic T (T<sub>c</sub>) Cells**: Destroy target cells.

3. **Delayed Hypersensitivity T (T<sub>D</sub>) Cells**: Mostly T helper and a few cytotoxic T cells that are involved in some allergic reactions (poison ivy) and rejection of transplanted tissue.

3. **T Suppressor (T<sub>s</sub>) Cells**: May shut down immune response.
T Cells Only Recognize Antigen Associated with MHC Molecules on Cell Surfaces

(a) Antigen-presenting cell (an infected cell)
- Class I MHC molecule
- Antigen fragment
- T-cell receptor
- Cytotoxic T cell (T<sub>C</sub>)

(b) Antigen-presenting cell (a macrophage)
- Class II MHC molecule
- Antigen fragment
- T-cell receptor
- Helper T cell (T<sub>H</sub>)
Central Role of Helper T Cells

Interleukin-2 and other cytokines activate $T_H$ cells, $T_C$ cells, and $B$ cells.

Cell-mediated immunity (attack on infected cells)

Humoral immunity (secretion of antibodies by plasma cells)
Cytotoxic T Cells Lyse Infected Cells

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1. Antibody Production:

T-Dependent Antigens:
- Antibody production requires assistance from T helper cells.
- A macrophage cells ingest antigen and presents it to $T_H$ cell.
- $T_H$ cell stimulates B cells specific for antigen to become plasma cells.
- Antigens are mainly proteins on viruses, bacteria, foreign red blood cells, and hapten-carrier molecules.

T-Independent Antigens:
- Antibody production does not require assistance from T cells.
- Antigens are mainly polysaccharides or lipopolysaccharides with repeating subunits (bacterial capsules).
- Weaker immune response than for T-dependent antigens.
Relationship Between Cell-Mediated and Humoral Immunity

2. Antibody Dependent Cell Mediated Cytotoxicity

- Target cell is covered with antibodies, leaving Fc portion sticking outwards.
- Natural killer and other nonspecific cells that have receptors for Fc region are stimulated to kill targeted cells.
- Target organism is lysed by substances secreted by attacking cells.
- Used to destroy large organisms that cannot be phagocytosed.
Humoral Response to T Dependent Antigens

1. Bacterium with T-dependent antigens
   - Class II MHC protein
   - Macrophage (will become antigen-presenting cell)

2. Bacterial antigen fragments presented by class II MHC proteins

3. CD4 Helper T cell
   - T-cell receptor

4. IL-2 and other cytokines
   - Activated helper T cell
   - Antigen fragment
   - Class II MHC protein

5. Clone of memory B cells
   - Clone of plasma cells
   - Secreted antibodies
http://faculty.evansville.edu/md7/bact02/specificimmuno/SpecificDefenses_files/SpecificDefenses.ppt#50
Clonal Selection of B Cells is Caused by Antigenic Stimulation

- Antigen receptor
- Antigens
- Variety of B cells
- Cell proliferation
- Clone of plasma cells
- Clone of memory cells

Antibodies secreted into circulation
Antibodies are Proteins that Recognize Specific Antigens
Consequences of Antibody Binding

- **Agglutination**: Enhances phagocytosis and reduces number of infectious units to be dealt with.
- **Opsonization**: Coating antigen with antibody enhances phagocytosis.
- **Neutralization**: Blocks adhesion of bacteria and viruses to mucosa.
- **Activation of complement**: Cell lysis
  - Complement
  - Bacterium
  - Lysis
- **Inflammation**: Disruption of cell by complement/reactive protein attracts phagocytic and other defensive immune system cells
  - Blood vessel
  - Infecting cell
  - Macrophage
- **Neutralization**: Blocks active site of toxin
  - Virus
  - Bacterium
  - Toxin
- **Antibody-dependent cell-mediated cytotoxicity**: Antibodies attached to target cell cause destruction by non-specific immune system cells

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Destruction of Large Parasites by ADCC

- Macrophage
- Cytokines and lytic enzymes
- Perforin and lytic enzymes
- Eosinophil
- Extracellular damage
- Fc region
- Large parasite

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Consequences of Antibody Binding

Binding of antibodies to antigens inactivates antigens by:

- Neutralization (blocks viral binding sites; coats bacteria and/or opsonization)
  - Virus
  - Bacterium

- Agglutination of antigen-bearing particles, such as microbes
  - Bacteria

- Precipitation of soluble antigens
  - Soluble antigens

- Complement fixation (activation of complement)
  - Foreign cell
  - Complement
  - Lesion

Enhances:
- Phagocytosis
  - Macrophage

Leads to:
- Cell lysis