

RESISTANCE TO PARASITIC DISEASES

I. Introduction

- When 2 organisms live in intimate association, each **responds** to the presence and activities of the other;
- This is especially true of the host-parasite relationship.
- ❖ **Hosts respond** to the presence of nonself material (*i.e.*, parasite) in **two ways**:
 - 1st there are **non-specific responses**. The host is able to differentiate “self” from “nonself”, but these responses are not dependent on specific recognition of a nonself molecule. It is the **1st line of defense**.
 - 2nd type of response is a **specific recognition** of foreign or nonself molecules.

II. Nonspecific Responses

- ✓ 1st line of defense against small foreign invaders, be they bacteria or parasitic protists, is **endocytosis**, the process of ingesting particulate bodies;
 - **Endocytosis** is also referred to as:
 - **Phagocytosis** when particulates are ingested, or
 - **Pinocytosis** when liquid is ingested,
 - But, it is often not possible to differentiate between the two, and
 - **Endocytosis** is the preferred term.
- ✓ Several cell types are endocytotic including **monocytes**, **polymorphonuclear leucocytes** (PMNs), **histocytes** in tissues, and **sinus-lining reticuloendothelial cells** in the liver and spleen.
- ✨ The function of endocytosis is to **engulf foreign material** and **digest** it through **lysosomal action**.
- ✨ **Lysosomes** are organelles in phagocytic cells that **release enzymes**, **have a low pH**, and **cause breakdown** of the foreign cell.
- ✨ Endocytosis can occur independently of specific responses, but it is greatly **facilitated** by certain specific responses such as:
 - **opsonizing** antibodies and
 - indirectly by serum proteins called **complement**.
- ♣ If the foreign invader is **small**, it may be surrounded by **endocytic cells** and **immobilized** by the deposition of **collagen** around it.
- ♣ If the invader is **large**, a 2nd type of non-specific reaction takes place – **inflammation**. Inflammation is characterized by **redness, heat, swelling** and **pain**.

- ➡ **Acute inflammation** - the 1st phase, lasts for about 3 days and is characterized by **capillary dilation** leading to **fluid accumulation** or **edema** and an **accumulation of PMNs** (polymorphonuclear leucocytes) in the tissues at the site of the insult.
 - ➡ The 2nd phase, **subacute inflammation**, lasts from 3 days to more than a week and is characterized by the presence of **mononuclear cells** (**monocytes and lymphocytes**) in the perivascular spaces and by **fibrocytes**, which secrete **collagen**. Collagen secretion leads to the production of a **fibrous capsule** commonly known as **scar**.
 - ➡ The 3rd phase is **chronic inflammation**, in which the tissue involved has not only the monocytic cells of the 2nd phase but also **plasma cells** come into the area. Where there is a persistent object such as a schistosome egg or an ascarid larva, a **granuloma** forms. This is an aggregation of **mononuclear cells** surrounded by **fibrous connective tissue** and the **cells** that secrete it. In many instances, these granulomas that form in response to a parasite also contain eosinophils, a subset of PMNs.
-) Another non-specific response to parasites is **abnormal growth** responses. These include:
- **hyperplasia**, in which the parasite stimulates the host to produce an **increased number of cells**; *e.g.*, when the adult liver fluke, *Fasciola hepatica*, reaches a bile duct, it induces the enlargement of the epithelium of the bile ducts. The fluke then grazes on these cells. The liver coccidium, *Eimeria stiedai*, of the domestic rabbit causes an exuberant growth of the bile duct epithelium, which appears microscopically to be much like neoplasia. However, much of the growth of the epithelium is resorbed when the infection is terminated. *Dirofilaria immitis*, the cause of heartworm disease in dogs, produces a soluble substance that causes endothelial proliferation in the lining of blood vessels.
 - **Neoplasia** (loosely, cancer) is also an abnormal growth response and there are a number of examples in which parasites are associated with this response. The larva of the tapeworm *Taenia taeniaformis* develops in the liver of the rat and causes sarcomas of the liver. *Spirocerca lupi* is a nematode located most often in the esophageal region of its definitive host, the dog. It gives rise to sarcomas of the esophagus upon longstanding infection. There is also a correlation between the presence of *Schistosoma mansoni* in the large intestine and the occurrence of colonic carcinoma. Even though these associations are clear, the mechanisms associated with the induction of neoplasia are yet to be elucidated.

III. Specific Responses

- ☉ The surfaces of parasites have characteristic **macromolecules** such as **proteins** and **polysaccharides**, which the **host recognizes as nonself**.
- ☉ In other instances, parasites **excrete or secrete** characteristic large **proteinaceous molecules**.
- ☉ These substances are **referred to as antigens (Ag)**, because they **elicit**:
 - **either a specific immune response through the formation of protein antibodies (Ab) or**
 - **the expansion of specific T-lymphocyte populations through Ag-specific T-cell receptor interactions.**
- ☉ **Antibodies or immunoglobulins (Ig)** are secreted by **B-lymphocytes (plasma cells)** and they **attach to specific sites on the antigen by molecular recognition**.
- ☉ This **attachment usually triggers additional host responses**.
- ☉ There are **5 classes** or isotypes of Ig – IgA, IgD, IgE, IgG and IgM – all of which have **different polypeptide structures and specialized functions**.

- ♠ The basic Ig molecule has a Y-shaped structure with **antigen-binding sites** at the ends of the arms of the Y.
- ♠ **Production and secretion of Igs** is called the ***humoral response***, and is manifested in a number of different ways.
- ☺ Each of the Ig molecules listed here has **particular functions**.

- IgE responses are often **elevated in helminth infections**.
- IgE Abs **bind to mast cells and basophils**;
- the subsequent binding of Ag to cell-bound IgE induces the cells to **release vasoactive substances**, such as **histamines**, which **increase capillary permeability**.
- In addition to being commonly associated with helminth infections, IgE is **most associated with hypersensitivity or allergy**.

- IgM and IgG are often considered to be **most important in protistan infections**, because they **activate the complement system**.
 - This system consists of 9 protein complexes that **combine with many different Ag-IgM or Ag-IgG complexes**.
 - The 1st component of the complement system **binds to Ag-bound IgM or IgG** thereby **initiating a cascade of reactions** involving the components of the complement system.
 - This series of reactions **triggers a number of biological activities**; one of the most important in parasitic infections is the **damage to cell membrane leading to lysis of the cell**.
- ⊕ In addition to the humoral response, the immune system also expresses **cell mediated immunity** (CMI), which classically involves the **T-lymphocytes**.
- ⊕ When bound to Ags, T-lymphocytes release proteinaceous substances called **cytokines**, which, in turn, induce non-specific reactions on other cells often **leading to inflammation** or to the release of other cytokines.
- ⊕ Cytokines may also directly damage parasites.
- Cytokines **that are most relevant to parasitic infections** include those with the following effects:
 1. Migratory-inhibitory factors, which prevent the migration of white blood cells (wbcs).
 2. Macrophage stimulating factors, which enhance the activity of macrophages against cells with the target Ag.
 3. Chemotactic factors, which attract inflammatory cells.
 4. Mitogenic factors, which stimulate the division of lymphocytes.
 5. Cytostatic factors, which delay or stop cell proliferation.
 - ♠ Both B-cells and T-cells originate from **stem cells in the bone marrow**.
 - ♠ The processing of these cells in the **thymus** (T-cells) or in an organ equivalent, the **bursa of birds** (B-cells) determines which of the two immune responses will predominate.
 - ♠ Although **humoral** and **cell-mediated immunity** are spoken of as **two systems**, they are **intertwined** and neither is ever the sole response.
 - ♠ In addition, **nonspecific resistance factors such as inflammation are often critical in both disease and immunity**.

- ✓ In general terms, **macrophages** (endocytotic cells) ingest and process parasite antigens.
- ✓ These processed Ags are then **distributed on the surface of the macrophage** and are said to be “**presented**”.
- ✓ Both B- and T-cells **contact the surface of the macrophage or the parasite directly and are primed against the specific Ag presented.**
- ✓ Both types of lymphocytes are stimulated to divide and then to **produce either Abs or cytokines.**
- ✓ **Ag combines with IgE bound to mast cells and basophils** causing these cells to release pharmacologically active molecules such as **histamine.**
- ✓ The subsequent **increase in capillary permeability** allows lymphocytes and other white cells to **reach the parasite.**
- ✓ T-cells combine with parasite Ags and release cytokines, which may attract more endocytotic cells and keep them there to **release their cytotoxic products and nonspecific inflammation**, which changes the parasite’s immediate environment, often to its disadvantage.