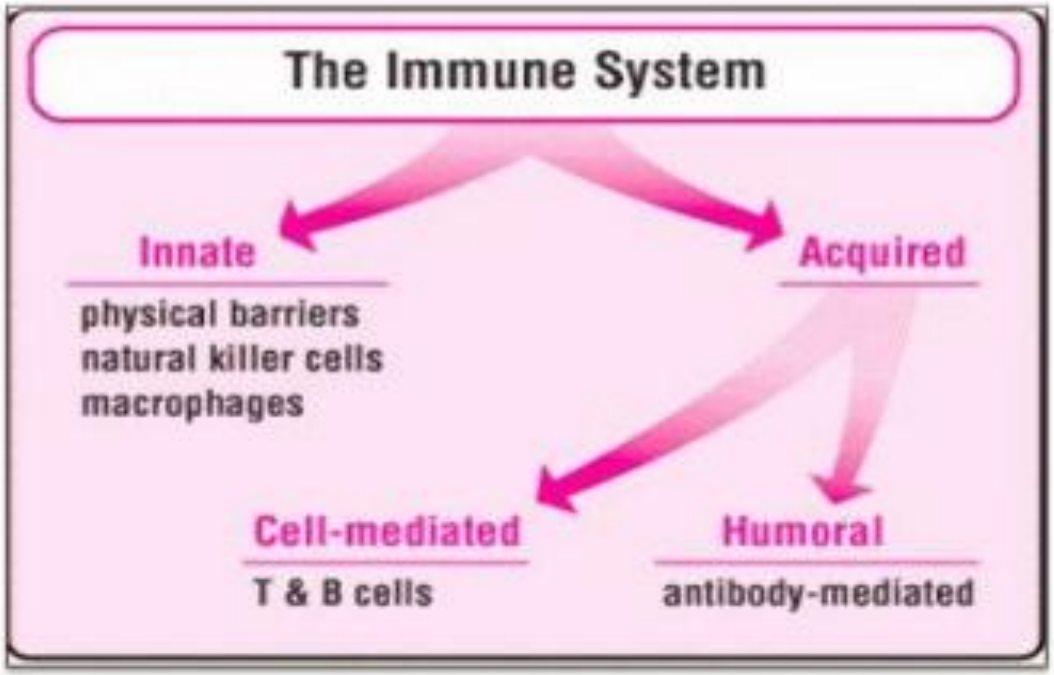
IMMUNOTOXICITY

Immunotoxicology refers to the effects of toxicants on the immune system.

To understand how toxicants can affect the immune system, it is necessary to have a general idea of immune system functions.

If the immune system is defined as mechanisms preventing or decreasing the impact of foreign bodies on organismic function, then plants also have an immune system, although it is usually considered to be a specific property of animals.

- **immunity** is the state of having sufficient biological defense to avoid infections, disease, or other unwanted biological invasion.



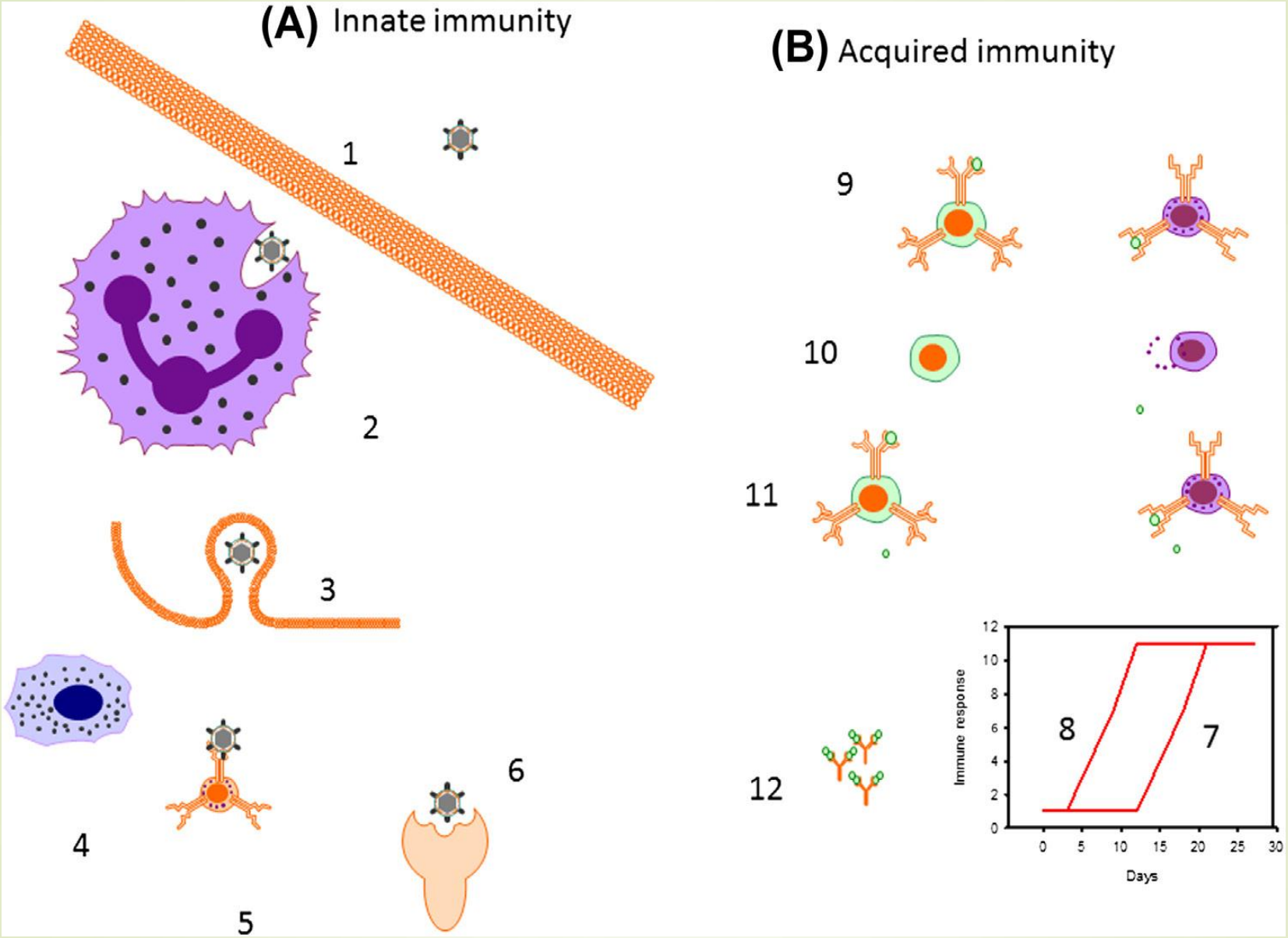


FIGURE The basic principles of the immune system in animals. Immunity consists of (A) innate

Figure: The basic principles of the immune system in animals.

Immunity consists of

(A) Innate immunity
(B) acquired immunity, which is known certainly to exist only in vertebrates.

Innate immunity is a property of the organism, and is not altered during its lifetime. Thus, the responses are similar in one-day-old and one-year-old animals.

Innate immunity consists of

- a barrier function: foreign particles are prevented from entering the body by barriers such as the skin.
- If a particle enters the animal, it can be phagocytosed and broken down by phagocytosing cells.
- The invading particle can also be rendered inactive by encapsulation or broken down by the action of natural killer cells.

(5) or proteins that break down foreign bodies (6).

These proteins do not change in the lifetime of the organism.

The inflammatory reaction, typically involving mast cells (4) and histamine release, is another aspect of innate immunity.

In acquired immunity, the second exposure to a pathogen is followed by a faster immune response (8) than the first exposure (7).

The immune response typically involves two types of lymphocytes,

- B-lymphocytes
- T-lymphocytes

(9) and humoral antibodies (12) secreted by these cells.

The diversity of antibodies can be huge as a result of different combinations of subunits making up the antibody.

In acquired immunity, a portion of cells, after the initial exposure to a pathogen, produce "**memory cells"** (10), which enable rapid response to a new exposure to a pathogen by helping a new population of specific pathogenresponsive cells (11) to be formed.

Immunotoxicological research addresses the question of how toxicants affect any aspect of the above.

Immunotoxicity

- Interaction of the Xenobiotics on immune system

  (Xenobiotic - A chemical that is foreign to the biosphere i.e. is not produced by a natural biological or abiotic source)

- Inhibit or depress immune function
  - Immunosuppression - Susceptibility to bacterial, viral and parasitic infection
  - Damage to primary and secondary lymphoid organs
- Elicitation of an immune response –

  Hypersensitivity & Autoimmune disease.

- ✓The immune system represents the interface between an individual's health and the pathogens present in its environment.

- ✓The immune system is exquisitely sensitive for assessing the toxic effects of chemicals of environmental concern.

Xenobiotics that elicit Immune Reactions

- Polyisocyanates - Toluene diisocyanate
- Acid Anhydrides - Trimellitic anhydride
- Metals & Metal Salts - Pt, Co, Ni, Cr
- Drugs – Penicillin
- Pesticides – Carbamates
- Polycyclic aromatic hydrocarbons & halogenated aromatic hydrocarbons – PCBs & PBBs
- Benzene
- Dibenzodioxin (TCDD – dioxin)
- Organophosphorous compounds, ozone, metals, organotin, cyclophosphamide

(Zeeman and Brindley, 1981; Dunier and Siwicki, 1993; Anderson and Zeeman, 1995; Luebke *et al*., 1997; Zelikoff *et al*., 2000; Bols *et al*., 2001; Rice, 2001; Burnett, 2005; Carlson and Zelikoff, 2008)

AQUATIC TOXICOLOGY

- Dissolved metals – minute amounts in the aquatic environment
- Through industry may be transported, concentrated, changed into other forms and are reintroduced into the aquatic system as contaminations.
- Fish are a fairly inexpensive protein-rich food that constitutes the sole protein source for many people. Unfortunately they are frequently exposed to many pollutants in the aquatic environment.
- Fish and their immune system may also represent an important scientific tool in the monitoring of environmental quality, particularly immunotoxic environmental pollution

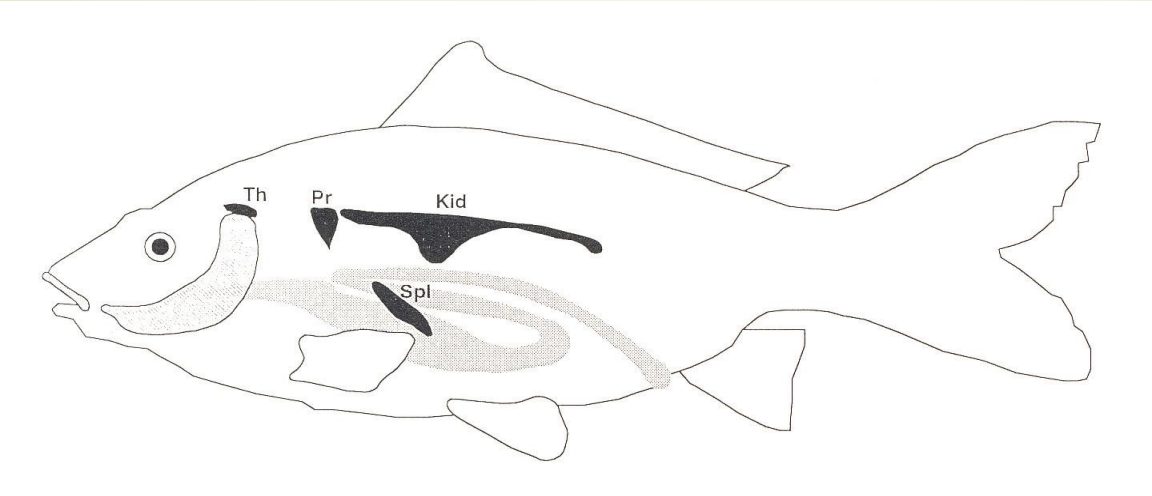
FISH IMMUNE SYSTEM

Fish are the first group of vertebrate animals with both innate and adaptive immune responses.

The immune system of fishes can be subdivided into broadly three categories which differ in the speed and specificity of response

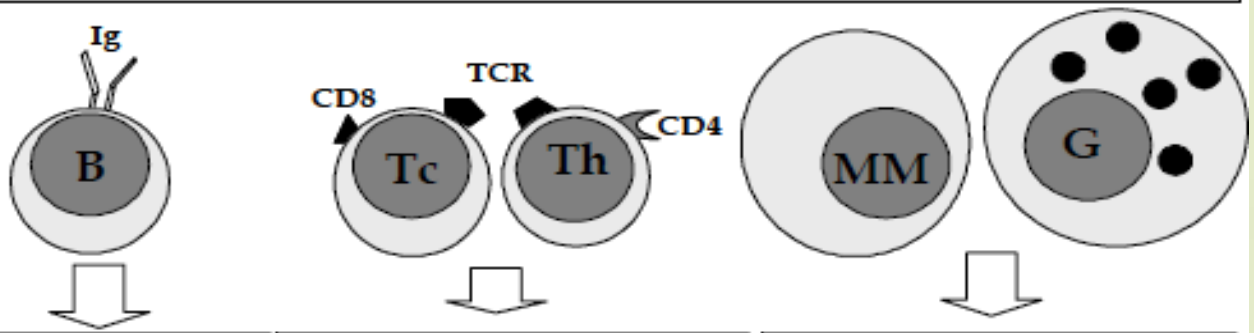
1. First line of defence is external barriers separating the fish from its environment, i.e., the epithelia of skin, gills and alimentary canal
2. Inside the fish, the second immune category is formed by the innate immune system which enables a rapid response to invading pathogens.
3. The third line of immune defense is the adaptive or acquired immune system, a set of humoral and cellular components that enable a pathogen-specific response. Adaptive immune system of fish usually shows a rather slow response to infective pathogens, taking weeks instead of days as in mammals.

The immune system of teleost fishes



Humoral immunity (serum, mucus)	Cellular immunity (kidney, spleen, thymus, blood, peritoneum)

Antibodies
Complement
Lysozyme
Lectins
C-reactive protein
Interferons
Transferrin
Anti-proteases
Proteases
Eicosanoids
Cytokines



Circulating antibodies Antibody-forming cells Proliferation	Specific cytotoxicity Proliferation	Phagocytosis Respiratory burst Antigen presentation

Cytotoxic activity (NCCs, NK, Tc), circulating leucocytes, infiltration, distribution, gene expression, cytokines…..

The immune system of teleost fishes…

- The immune tissues are quite different since fish lack the bone marrow and lymphatic nodules.
- Pronephros (anterior/head-kidney) is the main lympho-haematopoietic tissue
- Thymus is the main tissue for T cells development and maturation.
- Spleen is the main secondary lymphoid tissue
- Other important site for the immune response is the mucosal associated-lymphoid tissue (MALT) – skin, gills and gut.
- The non-specific immune parameters are useful to determine the health status of fish and to evaluate the immunomodulatory substances for fish farming as markers for pollution and diseases resistances.

The immune system of teleost fishes…

- The humoral immune response is a compilation of proteins and glycoproteins
- The complement system, in plasma and mucus, shows classical, alternative and lectin activation pathways
- An important bacteriolytic enzyme is the lysozyme, mainly found in eggs, mucus, plasma and leucocytes
- There are also other innate immune factors such as acute phase proteins (C-reactive protein CRP), antimicrobial peptides, interferon (IFN), lectins, proteases, protease inhibitors or eicosanoids
- Ig are the major component of the adaptive humoral immune response.
- Fish have only one immunoglobulin isoform, the IgM - tetrameric instead of pentameric as it occurs in mammals.
- WBCs are functional equivalent to lymphocytes, granulocytes, macrophages and NK cells.
- Fish macrophages secrete a wide range of biologically active molecules including reactive oxygen species (ROS) including superoxide anion (O_{2-}) hydrogen peroxide (H_2O_2) and hypochlorous acid (HOCl) etc., which are involved in the bactericidal activity, during a phenomenon termed the respiratory burst (Secombes 1990).

Implications

- Assessment of the hazard of immunotoxic chemicals not only focus on the relationship between chemical exposure and the immune system, but it needs to take into consideration the complex functional properties and the ecological context of the immune system.

- The results of this study would emphasize the importance of integration of immunological assays into environmental monitoring with reference to industrial effluents.

- The immunotoxicity of industrial effluents may influence the ability of fish to defend against infectious diseases.