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Lecture title: **Innate (Nonspecific)Immunity**

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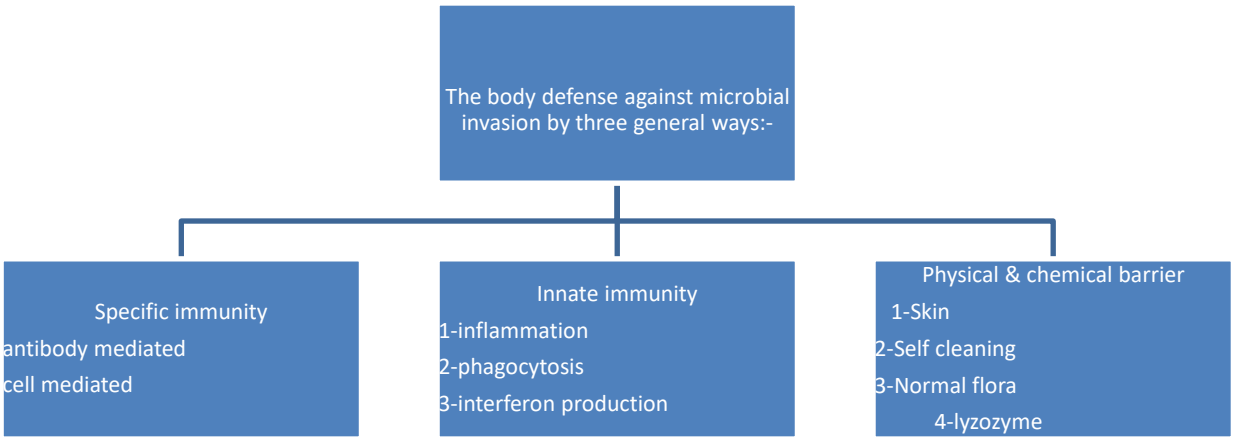
Summary:

1- **Learning what the nonspecific immune system is**
2- **The importance and function of innate immunity**
3- **Pathways of its activation**
4- **The role it plays in the immune defence**
5-

Innate (nonspecific) immunity:



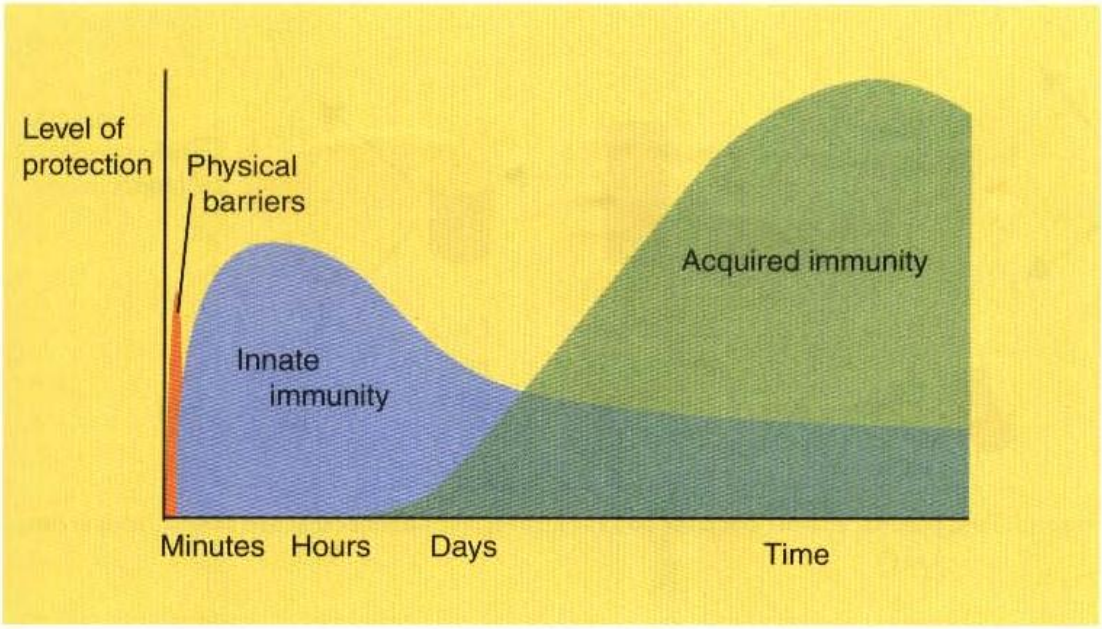
innate immunity: is the defence of the body that is present at birth, it provides a rapid response against disease, it has no specific response or specific recognition of microbes or memory cells.

But it responds rapidly to invaders by detecting them and attempting to eliminate them.

A comparison of innate and acquired immunity:-

TABLE 1-1
A Comparison of Innate and Acquired Immunity

	Innate Immunity	Acquired Immunity
Cells engaged	Macrophages, dendritic cells neutrophils, NK cells	T and B cells
Evolutionary history	Ancient	Recent
Onset	Rapid (min-hr)	Slow (days-weeks)
Specificity	Common microbial structures	Unique antigens



The time course of innate and acquired immunity

Factor their determined the non- specific immunity :-

1- Genetic influence.
2- Difference due to age.
3- Hormonal effect.
4- Interferon.
5- Normal flora.
6- Other effects as:- a- Physical effect → Skin
→ Self-cleaning

b- chemical effect- enzyme.

c- Cellular effect: → Phagocytosis
→ Natural killer cells

Physical effect:

The major physical barrier is:-

1- Skin:- The microbes can not penetrate the intact skin, and continual shedding of the top layer of the skin helps to remove microbes at the surface. dryness of the skin plays a major role in microbial inhibition.
2- Mucous membrane: - which covers the entire gastrointestinal, respiratory, and urogenital tract with Secretions of mucin to form a viscous glycoprotein membrane (mucus membrane) help to inhibit the invasion of many microorganisms

3- Lacrimation: continual washing action from tears helps keep microorganisms from settling on the surface of the eye.
4- Ciliary action:- that removal dust, pollutants and microorganisms to the outside of the trachea.
5- Cough, sneezing, vomiting, diarrhoea, ear wax, also helps to prevent microbes from entering the body.

chemical effect:

1- Skin: Sebaceous glands found in skin produce sebum, which consists of unsaturated fatty acids and prevents the growth of certain pathogenic bacteria and fungi, also lower ph of skin helps to reduce the growth of many microbes.
2- Saliva:- contains lysozymes and has a low pH

Normal flora:-

It is not considered a part of body defence, but flora helps the body to prevent infection by:-

a- Competing with them for nutrients
b- Changing the condition that effect survival of pathogen as pH or oxygen availability (alter of vagina pH by action of *lactobacillus bacteria* prevent infection by *candida*)
c- Produce a substance that is harmful to pathogens.(Bacteriocins produced by *E. coli* prevent Salmonella infection)

Cellular effect:- it consists of

1- **Natural killer cell**
2- **Phagocytosis**
3- **Inflammation**

Natural killer cells (NK cells):-

It's a part of large granular lymphocytes that are found in a normal unsensitized host, have the ability to recognise and kill a wide variety of infected body cells (virus-infected cells) and tumour cells which display abnormal plasma membrane proteins.

NK cells produce a protein which causes cell self-destruction or apoptosis.

Phagocytosis:-

In Greek, it means eating the cells. It's the ability of the cell to eat or engulfment and destroy foreign substance particles or microorganisms

Most cells that eat foreign substances and microorganisms are neutrophils, macrophages and eosinophils. These cells are called **phagocytes**

Most of the material gaining entrance to the skin and mucous membrane is removed by the action of phagocytosis.

Phagocytosis can be divided into several stages

1- Activation
2- Chemotaxis
3- adherence and opsonisation
4- Ingestion and digestion.

A- activation:- although neutrophils are always ready to attack and destroy invading organisms, they can, under some conditions, become activated and degranulate, mount a respiratory burst and release elastase and oxidant material which promotes adhesiveness and attract more neutrophils.

B- Chemotaxis :- directed migration of neutrophils called chemotaxis. bacteria invasion and the resulting tissue damage generating many different attractants. These include peptides like C5a generated from complement, peptides called fibrinopeptide generated from fibrinogen also produce many different chemokines and lipids such as leukotriene B and lysozyme all these attract the phagocytic cells (neutrophils , eosinophil and monocytes).

Chemokines:- a family of proinflammatory and chemotactic cytokines . they regulate emigration of leukocytes from blood into tissue.

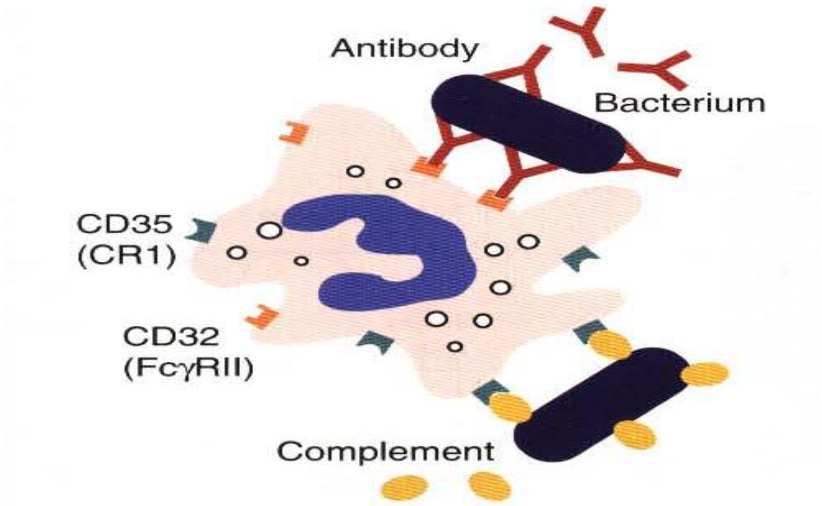
Cytokines :- protein that mediate cellular interaction and regulate cell growth and secretion. So they regulate many aspect of immune system.

C- Adherence and opsonization :-

Opsonins:- molecules that coat bacteria and promote phagocytosis

The opsonin make the bacterial tastier for the neutrophil and is promotion phagocytosis ethier by specific in conjunction with complement (mannose binding protien+ complement) or by antibodies and this process called opsonization .

process also include antibody receptor mediated phagocytosis (type I phagocytosis) involves the use of specific antibody receptors in neutrophils or the complements mediated phagocytosis(type II phagocytosis) process include complement C3b with its receptor in neutrophils .



D- Ingestion :- as neutrophil crawl towards a chemotactic source. a pseudopod advances first ,the cytoplasm of neutrophil contain filament on network of protein called actin and myosin when neutrophil meet bacteria it is pseudopod flows over and around it. Then binding occur between opsonin on the organism and receptors on the neutrophil these binding enables cup like pseudopode to cover the particles and drown it into cytoplasm as cytoplasm engulfs and becomes enclosed in a vacuole called phagosome.

E- Destruction or Digestion :- destruction of the ingested bacterium occurs through two important processes

1- involve the generation of potent oxidants (respiratory burst)

2- release of lytic enzyme and antimicrobial peptide from intracellular granules .

Respiratory Burst (oxidative brust):-

Its an increase in enzymatic activity during digestion in phagocytes involoving increase oxygen consumption 100 fold by neutroplilsand these lead to activation of several oxidation / catalyzation process ending by production of toxic oxygen product (superoxide ridecles “O2”, nitric oxide “NO”, hydrogen peroxide” H2O2”, hypochlorous acid “HOCl”).Which is have antibacterial activity.

Lysozyme:-

It destroys bacterial peptidoglycan in the bacterial cell wall, especially in Gram-positive bacteria, leading to the destruction of the cell wall. It is found in all body fluids except cerebrospinal fluid, sweat and urine and is found in high concentration in saliva, tears, and nasal secretions.

An enzyme found in high concentration in neutrophil granules accumulates in the area of acute inflammation (site of bacterial invasion).

Lysozymes also act as potent opsonins, binding to the bacterial surface and facilitating phagocytosis in the absence of specific antibody.

Lectins:-

These are a group of proteins that bind to the carbohydrate of the bacterial cell wall and play a role in the activation of the complement system, also promoting phagocytosis of invading microorganisms ex:-

a- mannose binding lectin(MBL):-has multiple binding carbohydrate sites found in serum and binds to oligosaccharides, and it promotes opsonisation.

b- C-reactive proteins and serum amyloid: they are called acute phase proteins found in blood in an inactivated state and become activated when inflammation occurs.

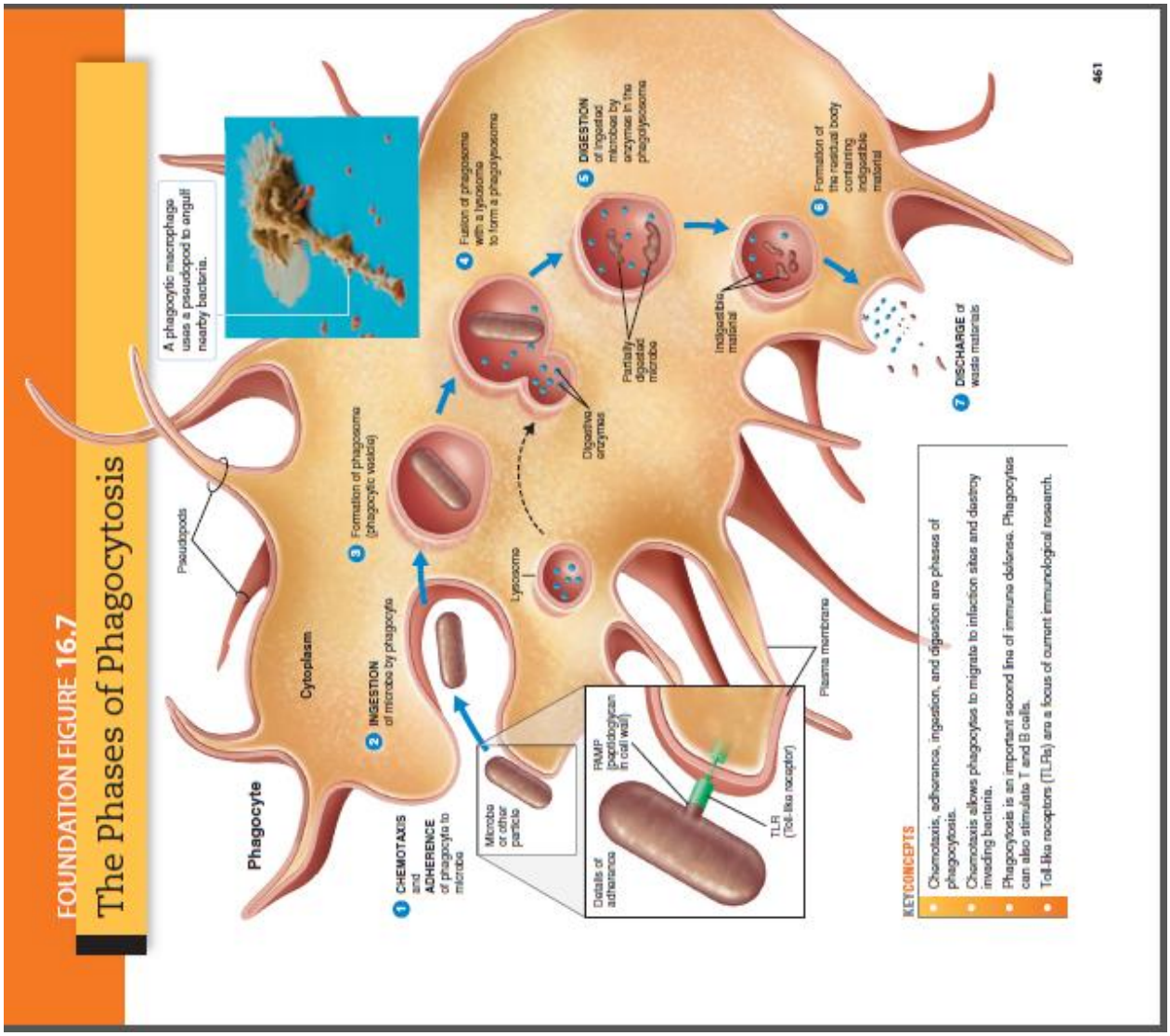
They promote complement activation and stimulate and augment the activity of macrophages, monocytes, neutrophils, and Natural killer cells.

c- Iron binding protein:- a large group of proteins which serve for the removal of iron from the site of bacterial invasion, as a result low iron concentration and preventing bacterial growth.

Ex: lactopherrin ⟶ mammary gland

Haptoglobin ⟶ liver

Transferrin ⟶ liver



Interferon:-

It types of cytokines that can interfere with virus replication and play a role in the regulation of the immune response.

It consists of glycoprotein and has a nonspecific, broad-spectrum antiviral effect on viruses. Interferon is present in birds, reptiles, fish and large animals and has three main types: α, β, and ω. A and β They are secreted from leukocytes, then bind to

an individual's cells and inhibit viral replication within them. It also helps in activation of natural killer cells and phagocytes.