

Immunodeficiencies and diseases related to it.

Introduction - Our immune system called internal defence system is powered with two important processes

- (1) To recognize 'self' from 'non self' foreign antigens or proteins or pathogens
- (2), consequently to kill them

our defence mechanisms has three strategic operative lines

- (1) first line of defence mediated by natural immunity by phagocytosis and other methods.
- (2) Second line of defence mediated by humoral immunity involving B cells and
- (3) Third line of defence mediated by cellular or cell mediated immunity accomplished by T cells.

The deficiency or failure of any of the above three lines of defence mechanisms leads to several immunodeficiency diseases. For eg B cell deficient person frequently suffers from bacterial infection and T cell deficient person from viral infection. The immunodeficiency diseases may be inherited or may be because of combined immune deficiencies of several immune components. The immunodeficiency disease may be due to secondary immunodeficiency involving environment, pollutants or parasitic infections. The immunodeficiency disease may also be acquired called as acquired immunodeficiency syndrome. (AIDS)

Types of immunodeficiency diseases - Immunodeficiency diseases are divided into following types

- ②
- (1) Primary immunodeficiency disease.
 - (2) Combined immunodeficiency and severe combined immunodeficiency diseases.
 - (3) Secondary immunodeficiency diseases and
 - (4) Acquired immunodeficiency (diseases (AIDS))
- I Primary immunodeficiency Diseases.

The primary immunodeficiency diseases are all inherited diseases reported as genetic diseases associated with natural, humoral and cellular immunity affecting all three lines of defence mechanisms. These immunodeficiency diseases affect the ~~organ~~ man and animals both. The inherited defects pertain to

- (i) Natural immunity diseases
- (ii) Stem cell deficiency diseases
- (iii) B cell deficiency diseases
- (iv) T cell deficiency diseases.

(I) Natural immunity diseases—

In natural immunity system, skin serves as strong anatomical barrier for entry of various viruses, bacteria and ~~Eukaryotic~~ Eukaryotic parasites. In first line of defence the killing of pathogen is effected by various immune components such as monocytes, neutrophils (microphages / macrophages), free radicals and various proteolytic enzymes. The inherited defects in any of above components lead to uncontrolled viral or bacterial infections causing following diseases—

Neutropenia - Neutropenia is caused by deficiency of neutrophils or polymorpho nuclear leukocytes. Neutrophils internalize and kill invading organisms by phagocytosis especially bacteria. Deficiency or absence of neutrophils causes frequent bacterial infection. Neutrophils contain primary azuro granules, defensins (bacteriocidal) myeloperoxidase and Cathepsin-4, which phagocytose bacteria. The neutrophil deficient person frequently suffer from streptococous and micrococous infection.

② / chronic granulomatous disease (CGD) - This disease usually occurs in children who get recurrent infection of *Staphylococcus aureus*, *Salmonella*, *Pseudomonas* and *Aspergillus*. These infections cause pneumonia, dermatitis, osteomyelitis and sepsis respectively. The granulomatous changes consist of necrosis in the central area of tissues surrounded by thick layer of inflammatory cells which are referred as granuloma.

In above disease the polymorphonuclear leukocytes and monocytes fail to produce reactive oxygen intermediates (ROI) due to genetic defect. They fail to produce NADPH respiratory burst as the enzyme cytochrome B558 oxidase is not synthesized and activation by phagocytosis. Enzyme Cyt B558 oxidase is membrane bound present on the surface of neutrophil and monocytes. This is due to defect in gene located on X chromosome in male but in girls the second X chromosome

ensures normal gene function. As soon as any bacteria enter the host, there is immediate increase of hexose monophosphate NADPH shunt in monocytes and neutrophils, which cause electrons to pass FAD containing flavoprotein. Then electrons move to cyt B558 oxidase that reduces molecular oxygen forming superoxide anion. Superoxide anions react with superoxide dismutase forming H_2O_2 which is a strong bactericidal which kills bacteria. Because of genetic defect the cyt B558 oxidase enzyme is not synthesized and hence no generation of H_2O_2 takes place. Enzyme B558 oxidase has two polypeptide chains of 92 KDa and 25 KDa. In X linked male children above enzymes are not produced in some cases mutation occurs and only a weak 92 bp polypeptide chain is synthesized. Most common pathogens associated with above diseases are Staphylococcus, Aspergillus, Candida albicans etc. Some catalase positive bacteria survive by destroying H_2O_2 . Although the neutrophils takes up catalase positive Staphylococci in presence of complement and some antibodies but fail to kill bacteria

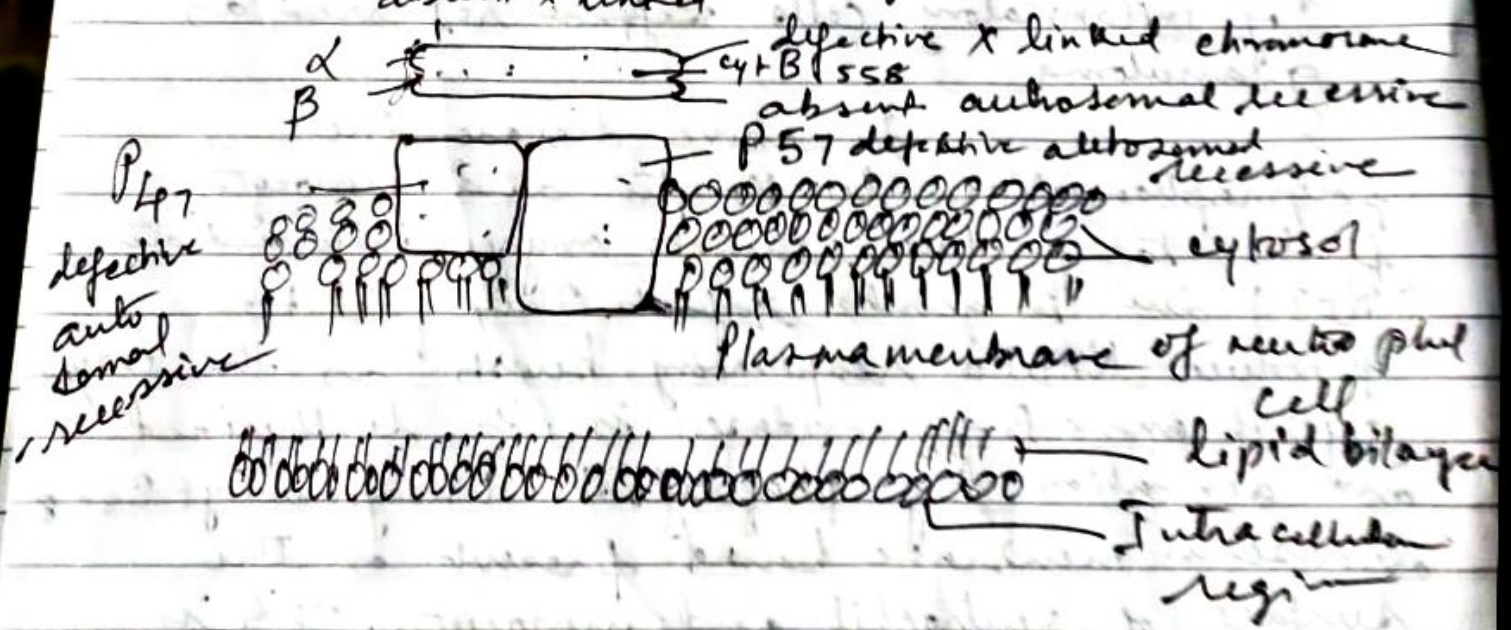


Fig. NADPH oxidase structure showing genetic defect in neutrophil. To be contd. Dr. Bibhokantra Dept of Zoology