THE ENHANCED SUSCEPTIBILITY TO INFECTION IN RENAL FAILURE

THESIS

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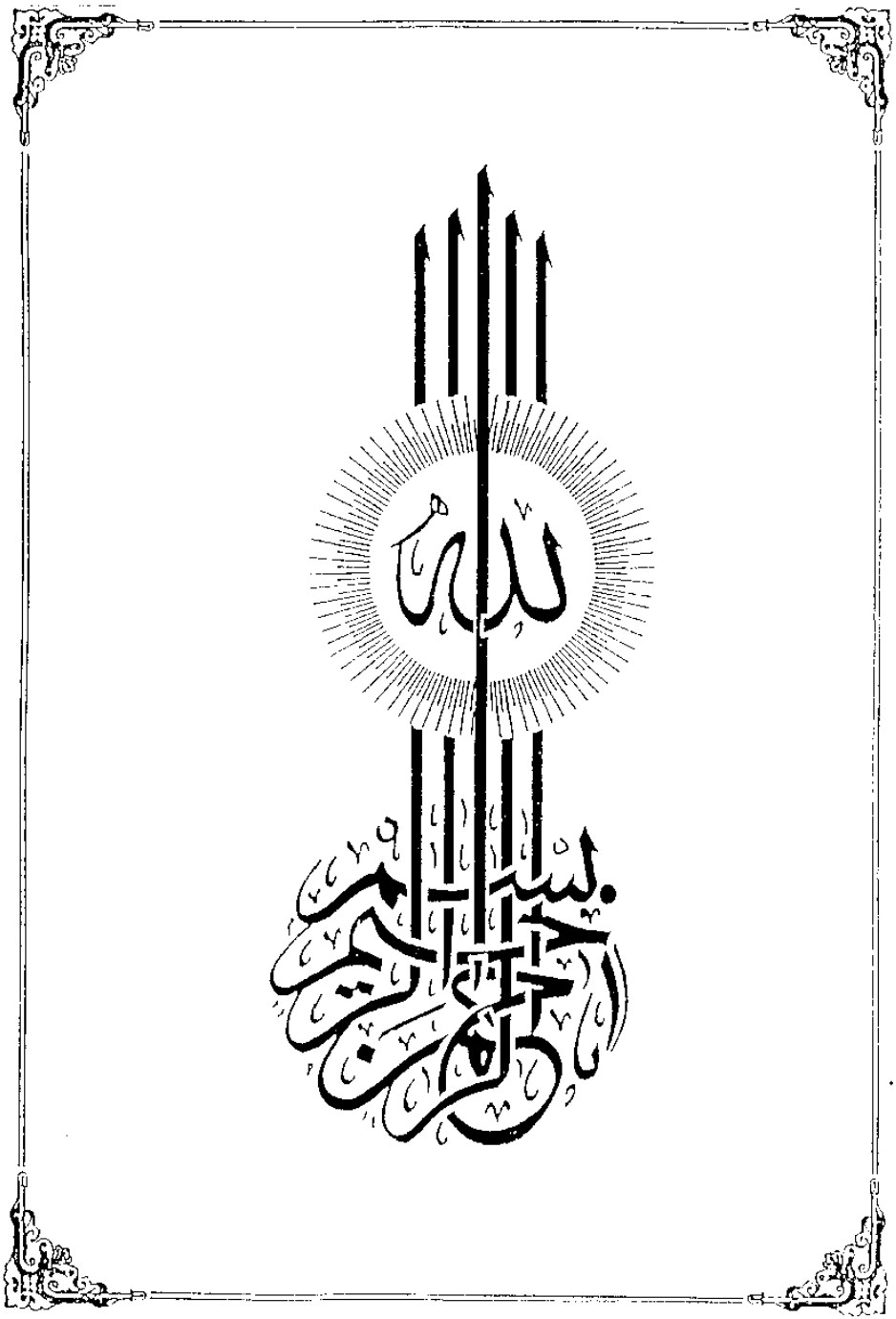

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Dr. SALAH OMAR

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INTRODUCTION

I N T R O D U C T I O N

Merrill (1968), Montogomerie, Kalmanson and Guze (1968), reported that infection is a serious problem in patients with both acute and chronic renal failure. Schleiner and Maher (1961), reported that the major cause of mortality is superimposed intercurrent infection. Infections complicate 30 - 70% of all cases of acute renal failure (Anderson and Schrier, 1980).

Balch (1956), found a significant infection present in 20 out of the 24 oliguric patients studied, but also in 8 out of the 13 non-oliguric patients in post-traumatic renal failure.

Montogomerie et al (1968), reported that of all deaths from chronic glomerulonephritis studied by Allwal, two thirds had severe infection in the terminal part of their illness.

Infection was also reported to account for 25% of all mortality in chronic dialysed uraemic patients (Brenner and Lazarus, 1980).

Siriwatratananonta, Sinsakul, Stern and Salvin (1978), found that 8 out of the 16 uraemic patients studied had higher incidence of infection.

The most common infections in such conditions reported by Maher et al are pyelonephritis, bacterial pneumonia and septicaemia; one half have bacterial pneumonia (as cited by Montogomerie et al, 1968, and Stanly Shaldon, 1963).

Pulmonary infections developed in 41 out of 81 (51%) patients with chronic renal failure at Wadsworth Hospital (Montogomerie et al, 1968).

From the previous reports, an increased susceptibility to infection in renal failure, has been noticed. The possible factors for this may be defects in immune host status, phagocytic function of polymorphs, disruption of mucosal barriers, protein calorie malnutrition, and the use of immunosuppressive drugs and carticosteroids in renal transplanted patients or some renal diseases (Brenner and Lazarus).

It is therefore urgent to define possible defects in the host defence mechanisms in patients with renal insuffeciency such knowledge is the basis for a therapeutic approach to decrease the individual patient's disposition towards infection, since it converts stable renal deficiency to overt acute renal failure and leads to progressive loss of nephron mass.

REVIEW OF LITERATURE

Physiology Of Host Resistance

1- Mechanical Barriers and Body Secretions

The first barrier that most microbes encounter against their successful invasion is the intact skin or mucous membranes.

Skin is the most resistant barrier because of its horny layer. In addition, lactic acid and other unstatured fatty acids with a distinct antibacterial action are secreted from the sebaceous glands. Statured fatty acids are present in the skin secretions and are distinctly fungistatic (Barrett, 1974).

The damp surface of the mucous membrane of the respiratory tract acts as a trapping mechanism, and together with the action of the cilia, sweeps away foreign particulate material (Green, 1968).

Lower in the digestive system, the microorganisms encounter the tremendous acidity of the stomach. Only aciduric organisms or those embedded deeply in food particles, can escape the protein-precipitating capacity of this acidity. Little is known about any protective functions other than the slight acidity, lysozyme content and flushing action of urine, all of which help to cleanse the urinary system (Barrett, 1974).

Bactericidal substances of tissues and body fluids

Lysozyme

It is a bactericidal mucolytic enzyme first found in tears by Sir Alexander Fleming in 1922. Combination of lysozyme with bacteria is followed by hydrolytic digestion of the bacterial cell wall. In strict biochemical terms, lysozyme is a muramidase and cleaves the beta 1 - 4 glycoside bond that unites N-acetyl glucosamine and muramic acid. Lysozyme is synthesized in the parotid glands, in the mucosa of the respiratory, gastrointestinal tracts and on the spleen lymph nodes and mononuclear phagocytes (Weir, 1979, Barrett, 1974, Weissman & Duker, 1970, and Richards, 1976).

Basic Polypeptides

Basic polyamines, polypeptides or proteins display antibacterial activity. Histones, protamines, spermine and spermidine are examples; these function by combining electrostatically with negatively charged bacterial cells and altering in some way the vital cellular functions of the bacteria.

Lactenin from milk, haematin and mesohaematin from erythrocytes are bactericidal.

Several glycoproteins of serum, of which transferrin and α_1 glycoprotein are examples, inhibit attachment of viruses to susceptible cells and aid in termination of virus infections (Barrett, 1974).

2- Phagocytesis

Phagocytic system consists of sessile mononuclear cells, circulating polymorphnuclear leucocytes and mononuclear leucocytes. Phagocytic leucocytes develop from pluripotent stem cells in the bone marrow. They circulate in the blood stream for a short time (4 - 10 hours).

Of 5000 to 10,000 white blood corpuscles 60 - 70% are neutrophils. Neutrophils contain primary granules which contain peroxidase and several digestive enzymes and secondary granules contain the microbicidal protein lactoferrin (Barrett, 1978).

Macrophages of the body originate from common bone marrow precursors which migrate through the blood as monocytes and tissues such as lungs (alveolar macrophages), liver (kupffer cells) and spleen constitute the mononuclear phagocytic system.

Macrophages secrete several products, of which are :

- Enzymes such as lysozymes, neutral proteases such as plasminogen activator, collagenase, elastase, estrase and acid hydrolase.
- Proteins such as C_2 , C_4 , C_5 and pyrogens.
- Factors such macrophage chemotactic stimulating factor and granulocyte chemotactic stimulating factor (Gordon and Cohen, 1976).

The Process of Phagocytesis

Chemotaxis

It means mobilization of the cells into an area of inflammation. The chemotactic chamber is composed of two compartments, one compartment contains the cells to be analysed for their chemotactic mobility and the other a substance with potential chemotactic activity (Barrett, 1978).

Humoral Aspects of Chemotaxis

Complement activation by microorganisms generate C_{3a} and C_{5a} from C_3 and C_5 by activating the incompletely defined alternative pathway or properdin system. Non-specific proteases released from bacteria or damaged tissue can attack C_3 and C_5 directly to yield C_{3a} and C_{5a} (Stossel, 1974; Craddock, James and Jacob, 1977).

Human plasma kallikrin has been shown to directly and selectively attract human neutrophils. Hagman factor fragments were chemotactic alone (Kaplan, 1972).

Synderman and Mergenhagen (1976), reviewed that chemotactic lymphokine for monocytes released from lymphocytes and amino-acids of newly synthesized bacterial proteins are chemotactic for leucocytes and monocytes.

MacClotchey (1974), showed that prostaglandin PGE_2 can affect monocyte chemotaxis (as cited by Synderman et al, 1976).