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Enzymes Degrading Adenine, Nucleotides in Erythrocytes of Patients with Chronic Renal Failure

Thesis

Submitted in Partial Fulfillment of the Requirements
for the Master Degree in Internal Medicine

By

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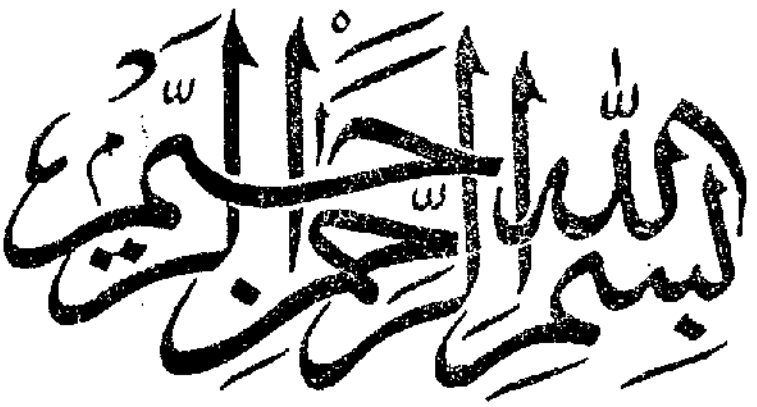
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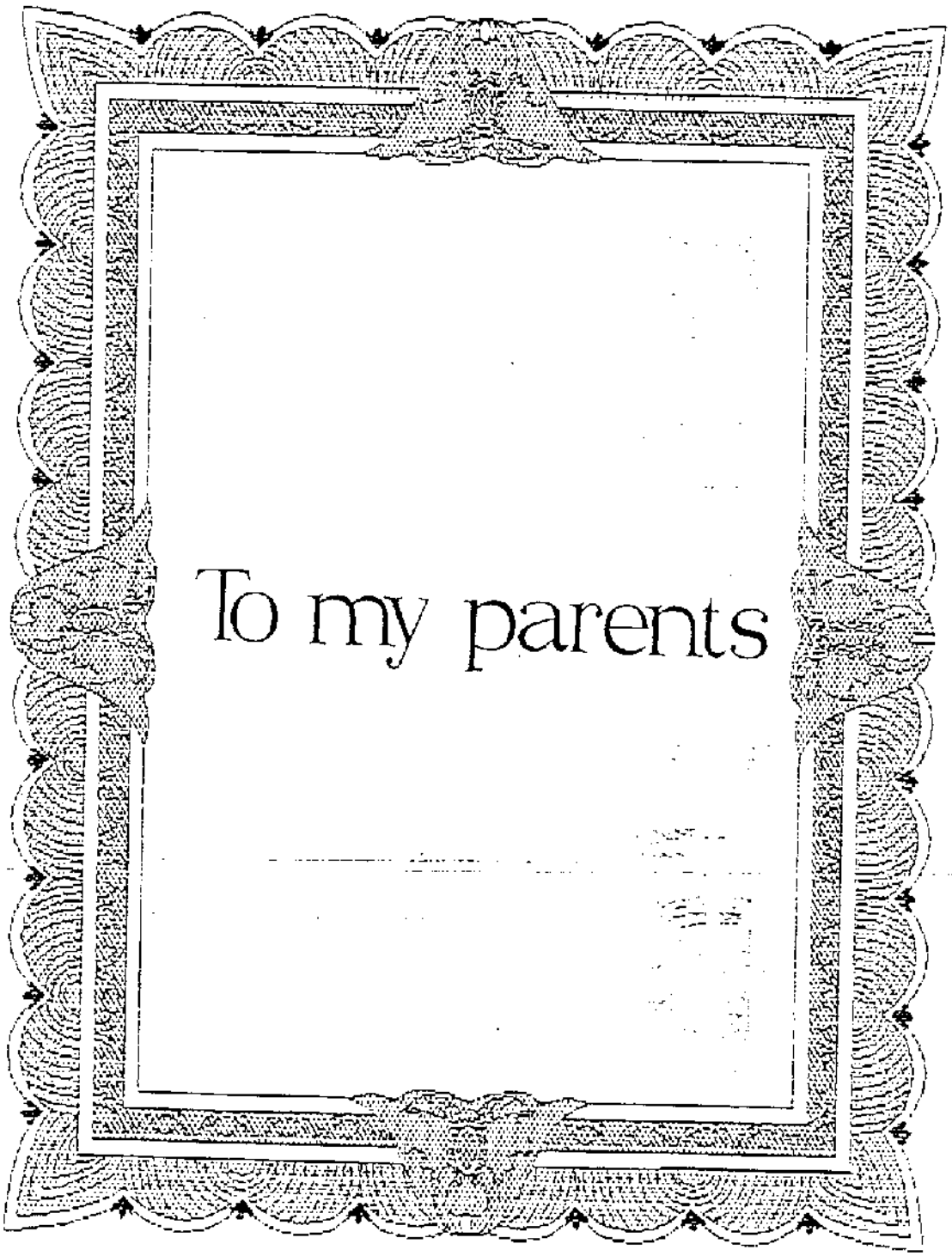
To my parents

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INTRODUCTION AND AIM OF WORK

Chronic renal failure is a syndrome which develops as a consequence of persisting and progressive loss of nephron function and is due to the resultant impairment of renal excretory, metabolic, endocrinal and homeostatic functions (Edwards and Bouchier, 1991).

Patients with chronic renal failure are now frequently encountered among the attendants of Internal Medicine Clinics. Besides its various widespread deleterious effects, the syndrome is accompanied by marked disturbances in immunological functions. To some extent, the nature of these abnormalities depends on the cause of the renal failure and its duration. While treatment of the renal failure with dialysis may slowly ameliorate some of the immunological abnormalities, others may not improve because of the widely variable conditions under which the clinical studies of immune disturbances in renal failure have been conducted besides the compounding effects of malnutrition, vitamin deficiency, drug therapy and dialysis (Glassback and Massry, 1989). Therefore, a consistent and uniform picture of disordered state of immunity in uraemia could not be obtained.

The disturbed immunity in uraemia involves both cellular and humoral immunity. Despite the manifest effects on humoral immunity exhibited by decreased levels of immunoglobulins, disturbances in cell mediated immunity are consistently marked and usually dominate the picture in uraemia (Glassock and Massry, 1989).

Atrophy of lymphoid tissues together with lymphocyte depletion of cortical areas and germinal centers and impairment of cell-mediated immune response are observed in uraemic patients (Glassock and Massry, 1987).

In recent years, the role of the 2 enzymes; adenosine deaminase and 5'-nucleotidase in immune status has been extensively studied. Specifically, most patients with adenosine deaminase (ADA) deficiency show immunodeficiencies of both cell mediated (T-cell) and humoral immunity (Kredich and Hershfiel, 1989).

This enzyme which is widely distributed in mammalian cells, with the highest activity being reported in lymphoid organs (Seegmiller et al., 1980), plays an important role in removing adenosine and deoxyadenosine and their metabolites that are potentially toxic to cells, particularly those of the immune system (Martin and Gelfand, 1981).

The studies conducted on adenosine deaminase and 5'-nucleotidase in uraemic patients are very limited. Thus, Mansell et al. (1982) reported significantly decreased activity levels of ADA and 5'-nucleotidase in lymphocytes of patients with chronic renal failure. According to these investigators, these changes are associated with the immunological incompetence in renal failure.

In contrast to lymphocytes, Mansell et al. (1981) have shown that severe renal failure is associated with alterations in the levels of purine nucleotides and significant increases in the mean activities of some of the enzymes concerned with their metabolism, especially ADA and 5'-nucleotidase.

In a recent study, Smolenski and Marlewski (1989) studied the degradation of adenine nucleotides in the erythrocytes of patients with chronic renal failure. These investigators observed that in erythrocytes of chronic renal failure, the AMP-deaminase pathway is nine times higher while 5'-nucleotidase pathway operates at less than twice as high velocity as compared to erythrocytes of healthy subjects. However, further studies are required to clarify this point.

The immune changes accompanying uraemia are still of obscure aetiology. However, uraemic toxins, urea, creatinine together with nutritional deficiencies of zinc and pyridoxal phosphate have all been incriminated as participating factors. up till now, no complete studies correlating all these incriminated factors, with ADA and 5'-nucleotidase and immunoglobulins in plasma and erythrocytes of patients with chronic renal failure could be traced in literature, which is the main aim of the present study. Besides the effects of dialysis on these biochemical variables were evaluated.

REVIEW OF LITERATURE