SOME HAEMATOLOGICAL ASPECTS OF CHRONIC RENAL FAILURE

THESIS

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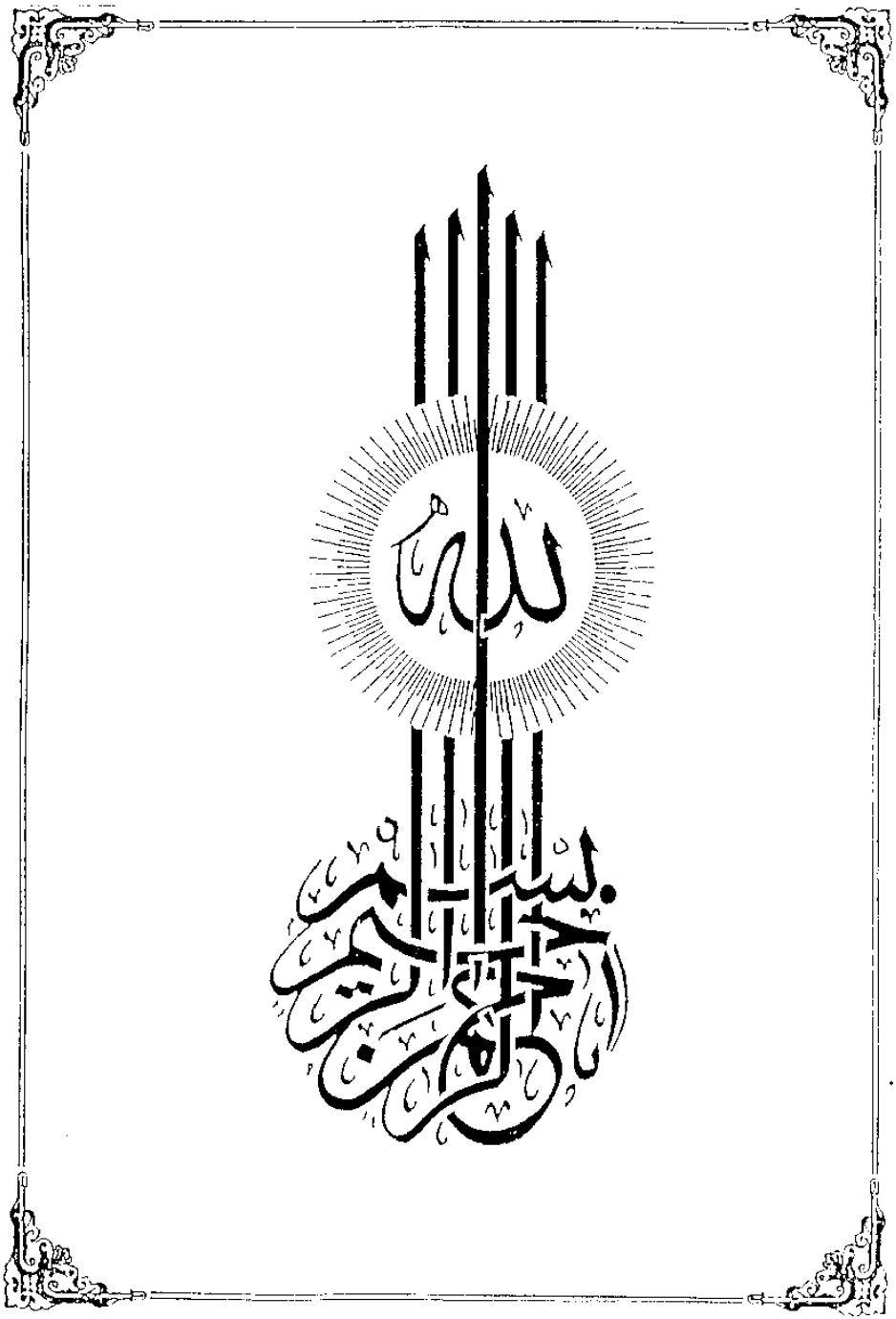

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An association between anaemia and renal failure has been recognised since 1836. Many alterations may occur during the course of chronic renal failure. The major factor in this anaemia is the inability of the bone marrow to produce enough red blood cells, yet bone marrow cellularity in chronic renal failure has not been adequately studied.

Accumulation of some trace metals such as arsenic, aluminium may be of importance for the development of this anaemia.

Predisposition to increased risk of infection may play a role, but the defect is not well understood.

Moreover, with the introduction of haemodialysis, other factors to be recognised may contribute to anaemia such as deficiency of water soluble vitamins, blood loss, uraemic toxin, ... etc.

Inspite of the improvement of erythropoiesis with regular haemodialysis, anaemia continues to be a major problem and incompletely understood.

Thus, the purpose of this study is to review some haematological aspects of chronic renal failure. The effect of regular haemodialysis on the cause and course of this anaemia will be stressed upon. Additionally, the diagnostic significance of bone marrow aspiration and biopsy in such patients will be discussed.

BIOCHEMICAL FEATURES

OF

CHRONIC RENAL FAILURE

Chronic renal failure consists of a persistant impairment of both glomerular and tubular function. The condition is of such severity that the kidneys are no longer able to keep the internal environment normal. Among its outstanding peculiarities is that the biochemical changes do not cause any symptoms while, most of the clinical abnormalities have an unknown biochemical cause (Wardener, 1967).

BIOCHEMICAL FEATURES OF CHRONIC RENAL FAILURE:

I. Urea and Creatinine:

The rise of blood urea is due to diminished glomerular filtration rate, urea itself is not responsible for any of the symptoms of renal failure. It has been shown that uraemic patients can be greatly improved by the use of artificial kidney without changing the level of blood urea (Wardener, 1967).

Renal tubular secretion of creatinine increases in renal failure, so making a small change in the relationship between creatinine clearance and the true glomerular filtration rate, but not in that between creatinine clearance and serum creatinine provided that creatinine production is unchanged (Morgan, 1983).

The rise in plasma creatinine is not thought to produce any symptoms. The importance of the rise in plasma creatinine is that in advanced renal failure, it is a far better guide to the extent of accumulation of protein metabolites than is the level of blood urea. Plasma creatinine of 20 mg/100ml, the patient is likely to die within few days from gastrointestinal haemorrhage, haemorrhagic pericarditis or some other calamitous complications (Wardener, 1967).

II. **Sodium and Potassium Metabolism:**

Abnormalities of electrolyte balance are unusual until the final stage of chronic renal failure. As the nephron diminishes, each remaining nephron reabsorbs lesser salts and secretes more potassium, nevertheless, patients with chronic renal failure are progressively less able to adjust the sudden changes in sodium and potassium intake.

In chronic renal failure, if sodium intake remains constant, fractional excretion by remaining nephrons must increase greatly in order to maintain sodium balance, but the exact mechanism involved is incompletely understood (Bricker, 1982). Minor degree of sodium overload contribute to the hypertension that

affect about 80% of patients with CRF. In general, the adaptive increase of sodium excretion is so successful that severe overload and oedema are unusual until the late stage. Paradoxically, sodium depletion is sometimes a risk in renal failure (Polak, 1971).

Reduction of sodium excretion in response to reduced intake which may take several days in normal person, is slower in CRF. Patients are therefore susceptible to volume depletion, particularly when intercurrent illness promotes gastrointestinal loss (Danovitch et al., 1977).

Water excretion is linked to sodium excretion, but an important additional factor, thirst, regulates body water through its effect on drinking (Morgan, 1983).

Tubular diluting capacity is normal, but on the other hand, urinary concentration capacity is depressed out of proportion to changes in solute load. This is probably because nephron loss prevents the maintenance of normal medullary osmotic gradient (Morgan, 1983). When renal mass is reduced oliguria results, water overload and hyponatraemia may occur.

quantity of acid produced which is about 1 mEq/Kg/day (Brenner and Stein, 1981). This is due to reduced ability to excrete ammonia which is caused by diminished numbers of nephrons and reduced titratable acid excretion due to diminished excretion of buffer phosphaste, which is mainly due to diminished intake of phosphate (Wardener, 1967).

The ability to acidify the urine in response to a standard rise in plasma hydrogen ion concentration is below normal, this is due to the nephrons impaired ability to reabsorb bicarbonate (Wardener, 1967).

IV. **Calcium and Phosphate Metabolism**:

A decline in renal function regardless of etiology is associated with abnormalities in calcium and phosphorus metabolism and the hormones that regulate the concentration of these minerals in body fluids.

One of the first abnormalities in minerals metabolism to be detected in CRF is a rise in plasma parathyroid hormone (PTH), which can be detected at a glomerular filtration rate (GFR) of 30 to 50 ml/min (Slatopolsky and Bricker, 1973).

Osteodystrophy caused by hyperparathyroidism is a universal feature of CRF (Katz et al., 1969). In fact PTH has been identified as uraemic toxin (Massry, 1977) as many of disabling syndrome of CRF may be related to it.

V. **Magnesium (Mg^{++}):**

Plasma magnesium and magnesium balance are normal in CRF whatever the creatinine balance. There is reduced alimentary absorption and urinary excretion of Mg^{++} due to reduced intake, increased anorexia, and medical advice to eat less protein (Wardener, 1967).

Azotaemia and uraemia:

Azotaemia means elevation of blood urea nitrogen. On the other hand uraemia refers to a syndrome complex that results from or is associated with retention of nitrogenous metabolites related to renal failure. In the later case, there is decrease in GFR with maximal tubular reabsorption of reabsorbable urea in contrast to non reabsorbable creatinine. This lead to retention of urea that is disproportionate to creatinine retention (normal ratio in plasma is 10%), Golden and Maher, (1977).

ANAEMIA

OF

CHRONIC RENAL FAILURE

ANAEMIA OF CHRONIC RENAL FAILURE

It is hypoproliferative anaemia with generally normocytic red cells and is seen invariably when patients with chronic renal failure become symptomatic to uraemia and require haemodialysis or peritoneal dialysis (Eschbach and Adamson, 1985)

The association of anaemia with the kidney failure is important because this organ is responsible for both sensing oxygen availability to tissue and for releasing erythropoietin into the circulation (Adamson, 1968). In general, the extent of renal insufficiency in patients with chronic renal failure is correlated directly with the severity of anaemia (McGonigle et al., 1084).

MECHANISM OF ANAEMIA IN CHRONIC RENAL FAILURE:

The major mechanisms that have been recognized to contribute to the anaemia in CRF are:

I. **Decreased Erythropoietin (EPO) Production:**

It has been known for twenty years that serum levels of EPO in patients with CRF are below those of comparable anaemic patients with normal renal function (Adamson et al., 1968). What was not appreciated initially is that a number of patients with CRF have