BLOOD CYTOLOGY IN RHEUMATIC DISEASES

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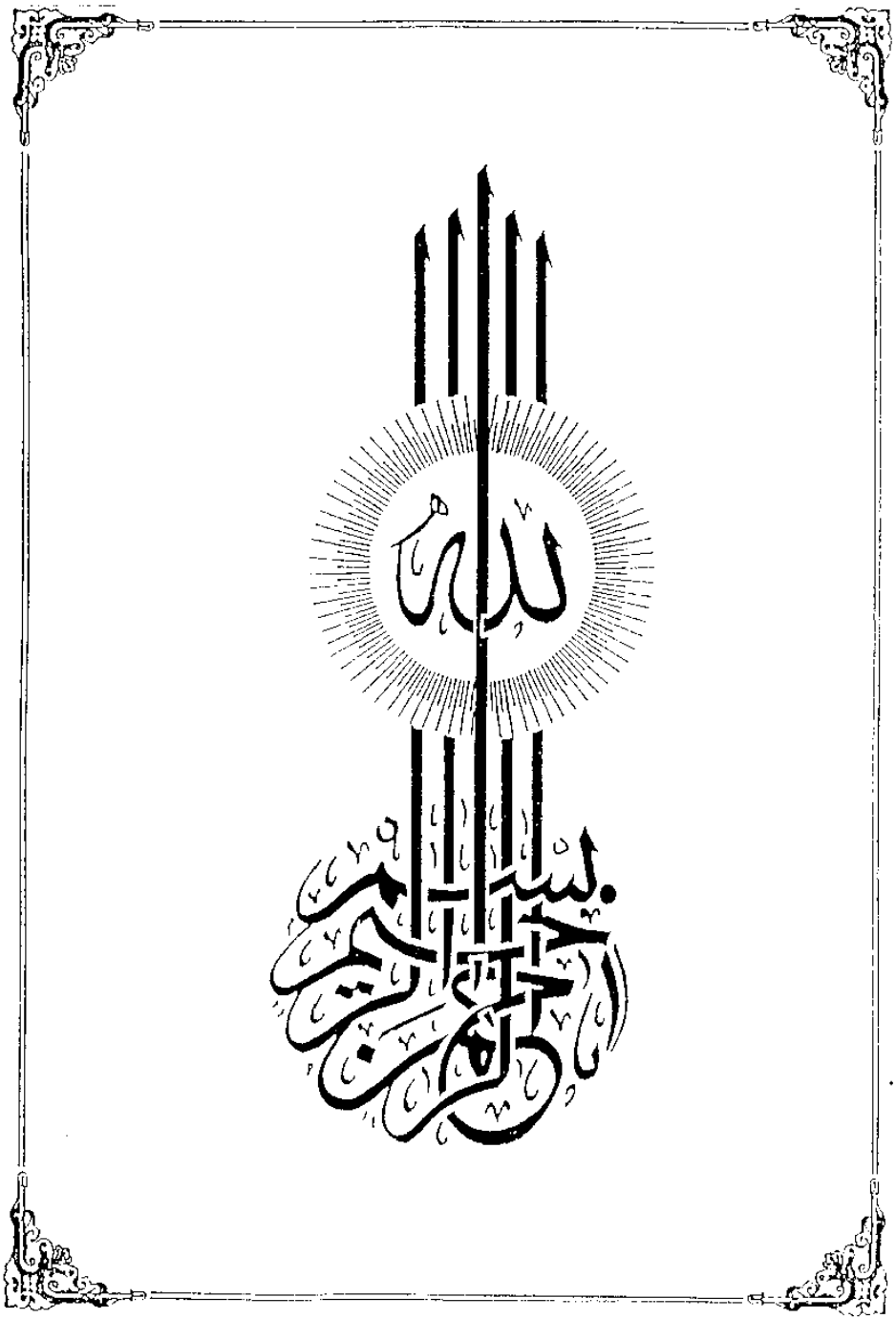

C O N T E N T S

INTRODUCTION

Rheumatic diseases are defined as a heterogenous group of chronic systemic diseases and disorders commonly affecting the locomotor system, although joints appear to be the main site of symptoms, the arthritis is only one component of a constitutional illness of considerable complexity.

These disorders comprise numerous derangements of the musculo-skeletal, articular (joints), and locomotor (movement) systems, with special referance to joint disease (Scot, 1980).

These disorders are wide-world distribution. In the United States, according to the survay by the national center for health statistics, the relative incidence of rheumatoid arthritis was about 3.6 millions and more recent estimates bring the figure closer to 5 millions (Gifford, 1973).

The disease was thought to be rare in tropical and subtropical countries, but now it has been described in several African populations .

The incidence of these diseases rises with the adaptation of a more sophisticated life style (Carsondick, 1983) so it constitutes an ongrowing problem through the future years.

El-Rawi, (1977), stated that RA occurs about 1 % among adults in Iraq and it is of a mild form and less destructive than in European countries. In Egypt, the pattern of this disease is milder than that seen in Western

parts of the world with less systemic involvement as well as severe joint damage (El-Badrawy, 1979).

The underlying causes of these diseases cannot be determined in most instances, they have in common wide-spread immunologic and inflammatory alterations of C.T. but, the offending agent causing inflammation of these diseases is unknown. The inflammatory reaction causes pain and limitation of function of joints and leads to the destruction of skeletal and extra skeletal tissues.

Many of the major rheumatic diseases are auto-immune in nature and this is the most accepted theory due to the presence of seriological changes always seen in these patients (Fye & Sacke, 1982).

Among the different pathogenic theories for these diseases, that it is related to viral infection, but this was found to be hypothetical except for association of poly-arteritis nodosa with hepatitis B-virus (Gocke, et al., 1970).

As the real pathogenic mechanism of these diseases is not reached uptill now, it was difficult to classify them. The preliminary proposal of the Glossary Committe of the American Rheumatism Association classifies the rheumatic diseases as:

I Defuse C.T. diseases.

II Arthritis associated with spondylitis.

III Degenerative joint disease (Oesteoarthritis, Oesteoarthrosis).

IV Artheritis tenosynovitis, and brusitis associated with infectious agents.

V Metabolic endocrine diseases associated with rheumatic states.

VI Neoplasms.

VII Neuropathic diseases.

VIII Bone and cartilage disorders associated with articular manifestations.

IX Non articular rheumatism.

X Miscellaneous disorders

(Gerald et al.,1983)

These headings include a wide variaties of differently named rheumatic diseases which are shared nearly in the same clinically manifested symptoms and signs.

These diseases usually presented with constitutional symptoms in the form of fever, weight loss, headache, malaise or leathergy either early in the disease or during its activity, as well as the affection of C.T. in the joint itself, synovial membrane, articular cartilage and the joint capsule which causes the arthretic pain. The affection of C.T. around the joint and near muscles and tendons are considered to be periarthritis .

The extra-articular manifestations of different rheumatic diseases are not specific for diagnosis.

The skin manifestations in RA appear as rheumatoid nodules. In S.L.E., the skin shows erythematous areas of certain distribution. The increased deposits of collagen fibers in skin is seen in PSS (Scleroderma).

The vasculitis occurs in polyarterits nodosa and necrotizing arteritis, Rheumatoid arteritis may produce skin necrosis and ulceration while in SLE vascuitic lisions appear on extensor surface of the fore-arm. At the same time in hypersensitivity vasculitis, palpable purpura or heamorrhagic infarcts seen in legs.

Raynoud's phenomenon, which occurs in 90 % of patients with S.L.E (Martin & Ephiraim, 1985) is also one of the manifestations of M.C.T.D and it is also found in 20 % of patients with Sjogren's syndrome (Fye & Sackenc,1982).

The affection of C.T. of the salivary and lacrimal glands that is characteristic of Sjogrens, is also seen in patients with S.L.E. whom developed also sicca syndrome and accompanies some of rheumatoid arthretic patients.

Pleurisy in S.L.E. and pericarditis or endocarditis in RA. are different forms of polyserositis seen in different rheumatic diseases.

The overlapping manifestations of all the rheumatic diseases makes the clinical diagnosis somewhat difficult and the rheumatologist really is in need of further investigation.

Blood examination is one of the earliest and widely used investigation for rheumatologists.

Golding, (1982) considered that the blood count, HB, W.B.C.(total and differential) and blood film should be done in all patients with suspected inflammatory polyar thritis, as the anaemia is considered to be probably the

commonest systemic manifestation of R.A (Jeffrey, 1953) and it was found to be more common than the reduction of W.B.C.count in S.L.E.So Hb determination is important in arthretic patients.

Leucocytosis is seen in rheumatic fever, polyarteritis, septic arthritis and occasionally seen in rheumatoid arthritis. Patients treated with gold shows eosinophilia. Thrombocytopenia occasionally seen in S.L.E patients.

These blood changes are still not known to be either a part of the disease activity itself, caused by the same pathological mechanism, occurs as a complication of the chronic disease or as a result of the long use of drugs.

Studying these changes may be helpfull in diognosis or used as an index of disease activity or in the assessement of patient during treatment.

The aim of this work is to review the different changes of blood cells (red blood cells, W.B.C.and platelets) in different rheumatic diseases, in order to select the most characteristic changes and studing their value as a diagnostic and prognostic aid.

NORMAL HEAMATOPOIESIS AND PERIPHERAL BLOOD CELLS

Heamatopoiesis

Blood cells are formed in the red bone marrow, it is limitted in adults to the marrow in the axial skeleton and the proximal portions of the long bones of the extremities.

The main activity of the marrow is the formation of blood cells.

1) Erythropoiesis - the formation of erythrocytes.

2) Granulopoiesis - the formation of granulocytes.

3) Thrombopoiesis - the formation of plateletes.

Each of these have specific control mechanism and kinetics.

In a bone marrow smear, the immediate proginators of erythrocytes are the erythroblasts and normoblasts. Those of granulocytes are the myloblasts and mylocytes and of plateletes are megakaryocytes. These cells can be readily recognised morphologically.

The more primitive cells are the pleuripotential stem cells or "precursor cells" which are cells with little or no self- replicating capacity, but are sensetive to specific regulatory factors and capable of differentiating into one cell line only, as the erythropoietin-sensetive cells which give rise to the erythroid series.

These stem cells and the factors affecting their differentiation are responsible for maintaining constant number and proportions of peripheral blood cells. When there is increased demand of one type of cells, the

appropriate cellular increase promptly occurs in the marrow.

The formation of colonies is supported by growth factors termed colony-stimulating factors (CSFS) that are released by a variaty of blood and tissue cells. (Yokota et al., 1984).

Like other physiologic processes in many organ systems efficient hemopoises probably requires the interaction among many types of cells such as fibroblasts, macrophages, endothelial cells and T-cells (Schickwann et al., 1986).

Erythropoiesis :

The increased demand for RBC is met by increased activity of nucleated precursors capable of division, a process that takes several days.

The erythroid cells in the marrow are the basophilic pro-erythroblasts (pro-normoblasts) which are the most immature cells of the series, then the basophilic normoblasts, the polychromatic normoblasts then the reticulocytes which is the most immature form of the non-nucleated red blood cells.

An adequate supply of stem cells sensetive to influences ordering their maturation, an adequate supply of materials necessay for normal growth of the red cells with the existance of normal regulatory mechanisms are important factors for maintaining normal erythropoiesis. Also the circulating erythrocytes must not suffer such a

degree of premature destruction that the blood forming tissues are unable to maintain normal numbers of cells in the circulation. Recently Schickwann, et al., (1986) stated that it seams that stromal fibroblasts, together with erythropoietin and serum proteins could fulfill the minimal requirements for the development of erythroid burst colonies.

Erythropoitin is of most important influence at several stages of red cell formation, the major site of action of erythropoietin is not definitly determined either on the pluripotential stem cells, committed stem cells or the erythropoietic progenitor cells.

Recently Junko, et al. (1986) suggested that interlukon-3 (IL-3) maintains the growth of the progenitor cells, which could differentiates into erythroid cells, while erythropoietin facilitated the terminal differentiation and amplification of erythroid cells, although it did not sustain the growth of multipotential stem cells.

The important organ involved in the production of erythropoietin is the kidney, which then act on a serum substance found in alpha 2 globulin fraction to become active.

Hypoxia is a fundamental stimulus of Erythrocyte Stimulating Factor formation. The hormone is also found in serum of aneamic patients. There are some endocrinal influances on erythropoiesis as the anderogenes,

oesterogens, adrenocortical steroids, thyroid H. and pituitary Hs.

Iron, vitamin B12 and folic acid are the essential materials required for RBC formation. Cobalt is known to increase erythropoieses, as it helps erythropoietin release.

The marrow can increase its effective erythropoiesis to about six times the normal and its total erythropoiesis (effective and ineffective) to eight or ten times normal (Thampson,1977).

Granulopoiesis :

The myeloid series begins with the myloblast, promylocyte, mylocyte (with specific granules in their cytoplasm, neutrophilic, eosinophilic and basophilic) meta-mylocyte, band form and segmented cells (polymorpho-nuclear leukocytes).

Monocytes and monoblasts are found in normal marrow. The monoblasts cannot be distinguished from myloblasts. Lymphocytes, plasma cells, reticulum cells which may be macrophages are also seen among marrow cells.

It can be said that granulopoiesis is a cell renewal system, and cell production equals cell death. Little is known about the stem cell, which has to increase its rate of cell production on demand.

The maturation of myloid cells is characterized by progressive condensation of the nucleus with appearance of granules in the cytoplasm. With complete maturation, the