Erythropoietin: Genetics, Control, Action and Clinical Applications



Review of Literature Submitted for Partial Fulfillment of Master Degree in Clinical Pathology

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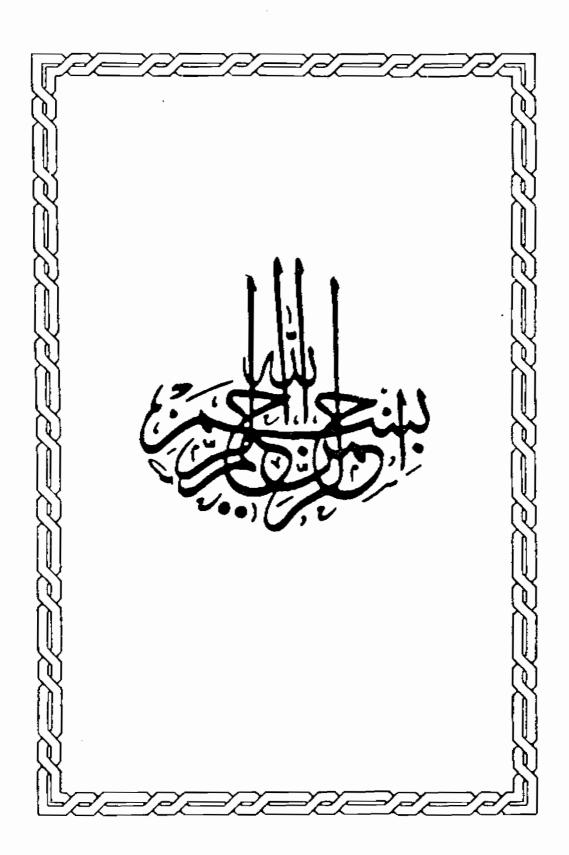
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List of Abbreviations

BFU-E Burst forming unit- erythroid

bp Base pair

cAMP Cyclic adenosine monophosphate

CAPD Chronic ambulatory peritoneal dialysis

cDNA Complementary deoxyribonucleic acid

CsA Cyclosporine

CFU-E Colony forming unit -erythroid

CFU-GM Granulocytic macrophage colony forming unit

CFU-MK Megakaryocytic colony forming unit

CFU-S Colony forming unit- spleen

CoCI Cobalt chloride

EPO Erythropoietin

FPG Fluorochrome- photolysis-Giemsa

FSH Follicle stimulating hormone

5-FU 5 fluorouracil

FVA Friend virus that produces anemia

GVHD Graft versus host disease

hG-CSF Human granulocyte colony stimulating factor

hGM-CSF Human granulocyte macrophage colony stimulating factor

HPLC High pressure liquid chromatography

IGF-I Insulin like growth factor

IL Interleukin

IRMA Immunoradiometric assay

I-rEPO Radioactive labelled erythropoietin

Kb Kilobase

LH

Leutinizing hormone

MDS

Myelodysplastic syndrome

MnCI

Manganese chloride

mRNA

Messenger ribonucleic acid

NiCI

Nickel chloride

PGE

Prostaglandin E

PRCA

Pure red cell aplasia

RA

Rheumatoid arthritis

r-HuEPO

Recombinant human erythropoietin

r-Hu GCSF

Recombinant human granulocytic colony

stimulating factor

r-Hu GM-CSF Recombinant human granulocytic macrophage

colony stimulating factor

RIA

Radioimmunoassay

SCD

Sickle cell disease

SV

Simian virus

TCA

Trichloroacetic acid

TFR

Transferrin receptor

TNF

Tumor necrosis factor

TSH

Thyroid stimulating hormone

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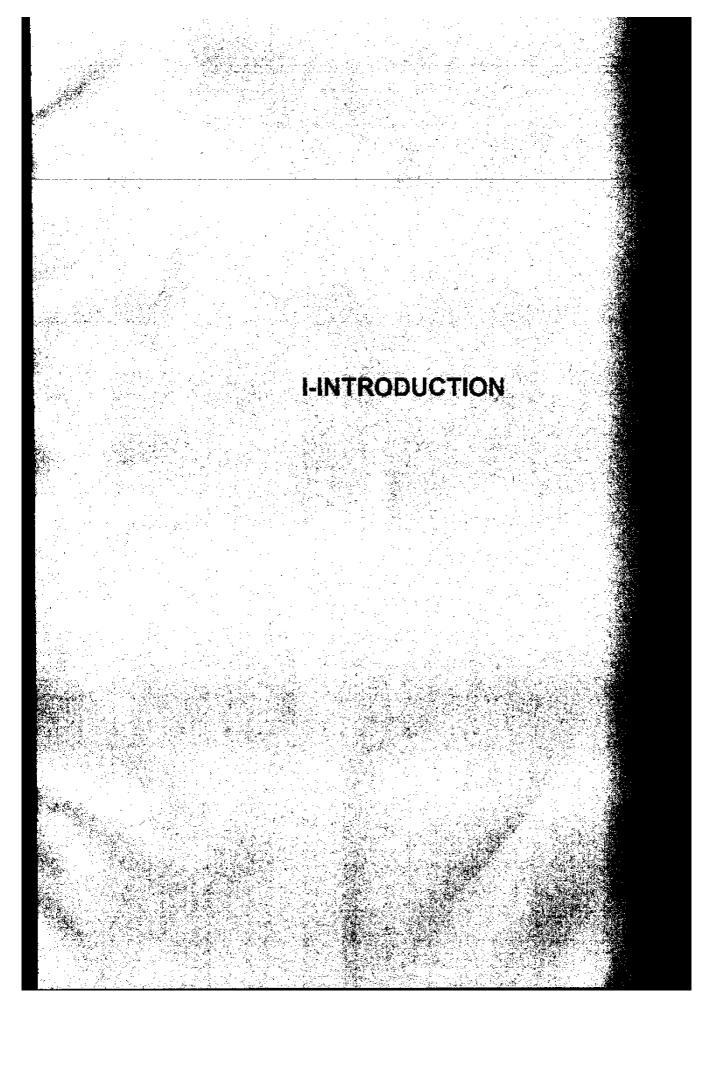
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AIM OF THE WORK

The aim of the work is to review the mode of synthesis, genetics, chemistry, physiology, regulation and clinical applications of erythropoietin.

The use of recombinant human erythropoletic in the therapy of different types of anemia will also be reviewed.



1- INTRODUCTION

Normal erythropolesis is regulated and maintained by a glycoprotein hormone, erythropoletin (EPO) which is synthesized mainly in the kidneys in response to anemia and hypoxia.

Renal synthesis of erythropoietin is regulated by a negative feedback system. Decrease in the concentration of hemoglobin in the blood leads to reduction in the tissue oxygen tension within the kidney. Tissue oxygen tension depends on the relative rates of oxygen supply and demand. Oxygen supply is a complex function of interacting, but semi-independent variables, including blood flow, blood hemoglobin concentration, hemoglobin oxygen saturation and hemoglobin oxygen affinity. Each of these functions may be altered to compensate for a deficiency in one of the others. For example, in severe anemia cardiac output and respiratory rate may increase, and hemoglobin oxygen affinity may be reduced. Conversly, in respiratory insufficiency, secondary polycythemia occurs.

Despite the influence of cardiovascular and respiratory adjustments, tissue oxygen tension decreases roughly in proportion to the degree of anemia. The decrease in the tissue oxygen tension (tissue hypoxia) is sensed by the kidney's oxygen sensor. The kidney responds by increasing erythropoietin.

Red cell progenitors in the bone marrow possess receptors for EPO and are stimulated to proliferate and differentiate. This leads to an increase in the red cell mass (The erythron) and oxygen carrying capacity. The improved tissue