

# Erythropoietin: Genetics, Control, Action and Clinical Applications



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

By

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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                            |
| CoCl    | 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   |
| MnCl        | Manganese chloride   |
| mRNA        | Messenger ribonucleic acid   |
| NiCl        | 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<br>stimulating factor            |
| r-Hu GM-CSF | Recombinant human granulocytic macrophage<br>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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## **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 erythropoietin in the therapy of different types of anemia will also be reviewed.

## I-INTRODUCTION

## I- INTRODUCTION

Normal erythropoiesis is regulated and maintained by a glycoprotein hormone, erythropoietin (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. Conversely, 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