

# **Anesthesia for Patients Undergoing Bone Marrow Transplantation**

## **Essay**

Submitted for Partial Fulfillement  
of Master Degree in Anesthesiology

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## Anaesthesia for patient undergoing bone marrow transplantation

التخدير لمرضى زرع النخاع العظمى

رسالة

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بكالوريوس الطب والجراحة

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## List of Abbreviations

- **AA** : Aplastic Anemia.
- **ALL** : Acute Lymphatic Leukemia.
- **ANC** : Absolute Neutrophil Count.
- **ATG** : Anti Thymocyte Globulin.
- **BFU-E** : Bursa Forming Unit Erythroid.
- **CFU-E** : Colony Forming Unit Erythroid
- **CFU-G/M** : Colony Forming Unit  
Granulocyte/macrophage.
- **CLL** : Chronic Lymphatic Leukemia.
- **CML** : Chronic Myeloid Leukemia.
- **CMV** : Cytomegalovirus.
- **DMSCO** : Dimethyl Sulfoxide.
- **FTT** : Failure To Thrive.
- **G-CSF** : Granulocyte Colony Stimulating Factor.
- **GVHD** : Graft Versus Host Disease.
- **GVL** : Graft Versus Leukaemic Effect.
- **HD** : Hodgkins Disease.
- **HDCT** : High Dose Cytoreductive Therapy.
- **HIV** : Human Immunodeficiency Virus.
- **HLA** : Human Leukocyte Antigen.
- **HSCs** : Hematopoeitic Stem Cells.

- **HSV** : Herpes Simplex Virus.
- **PBSCs** : Peripheral Blood Stem Cells.
- **PRBCS** : Packed Red Blood Cells.
- **MM** : Multiple Myeloma.
- **NHD** : Non Hodgkins Disease.
- **NSAIDS** : Non Steroidal Anti-Inflammatory Drugs.
- **OPM** : oropharyngeal mucositis.
- **SIADH** : Syndrome of Inappropriate Anti  
Diuretic Secretion.
- **TBI** : Total Body Irradiation.
- **VOD** : Veno-occlusive Disease.



# Introduction

## **Introduction**

The earliest attempts to use bone marrow therapeutically appear to have been made by Borow-Sequard and A'drosonaval in 1891. They administered marrow by mouth in cases characterized by defective blood formation, notably in leukemia. However, it was found that the only value of this marrow extract lay in its minerals content, and quite clearly minerals are more easily obtained in other way. **(Wintrobe and Champlin, 2000)**

In 1937, Schertzenmayer appears to have been the first to administer bone marrow cells by a technique which could permit the cells to survive in the recipient. He used intramuscular injection of freshly aspirated autologous or allogenic bone marrow in treatment of anemic patients.

In 1939 injection of bone marrow cells into the medullary cavity was used in the treatment of leukemia. Subsequent work has shown that most of the injected material passed into the general circulation and that intramedullary injection has no advantages over the-intravenous route. However, this route of marrow administration was ignored in the next years, and the intramedullary injections was used in reports which antedate the fundamental radiation protections and marrow transplantation studies of Jacobson, Simmonds, Lorenz and others .**(Wintrobe and Champlin, 2000)**

After the conclusion of world war II, there was great concern about the biologic effects of irradiation and a number of experimental studies were directed towards the question of how to protect against lethal irradiation effects on bone marrow. **(Thomas, 1999)**

It was **demonstrated** that mice could be protected against otherwise lethal total body irradiation (TBI) by shielding the spleen or by an intravenous infusion of bone marrow.

At first it was thought that this protective effect was due to humoral factor but by 1956, several laboratories using a variety of blood genetic markers demonstrated that the protective effect against lethal irradiation was due to colonization of the recipient marrow by donor cells. **(Thomas, 1999)**

In 1957 Thomas and his colleagues showed that large amounts of marrow could be infused intravenously with safety and described a transient marrow graft in man. They also provided estimates of the number of marrow cells needed and pointed out the potential applications of marrow grafting to irradiation accident victims, to the therapy total body irradiation (TBI) of leukemia and to the therapy of patients with immunologic deficiency disorders. In 1959, scientists attempted the dramatic treatment by marrow transplantation, of six human victims of an irradiation accident, four survived. **(Thomas, 1999)**

The next decade was one of frustration and disappointment. Most marrow grafts were carried out in terminally ill patients who did not live long enough for a graft to be evaluated. With the exception of a few identical twin transplants these grafts were unsuccessful and the few successful allogenic grafts were followed by a lethal immunologic reaction of the graft against the host. The development of knowledge" of histocompatibility typing and supportive measures for patients with no marrow functions has renewed interest in the subject of marrow transplantation. **(Thomas, 1999)**

Many basic research laboratories using mice and dogs provided essential informations about transplantation immunology and the role of histocompatibiluy factors in determining the outcome of marrow transplantation. The first successful case of marrow transplantation from a human leukocyte antigen (HLA) identical sibling into a patient with an inherited

immunologic deficiency was reported in 1968 (**Thomas, 1999**).

In the past few years the chances of successfully using autologous marrow transplants in cancers that may involve the marrow itself have been dramatically improved with the development of strategies for eradicating contaminating malignant cells from the autologous marrow inoculum. (**Wintrobe and Champlin, 2000**)

# Bone Marrow Stem Cells

# BONE MARROW STEM CELLS

## Embryological Origin of Blood Cells

In human embryo, clusters of stems cells, called 'blood islands', appear in the yolk sac in the third week of fetal development. At about the third month of embryogenesis, some of these cells migrate to the liver, which then becomes the chief site of blood cell formation until shortly, before birth, (the spleen, lymph nodes, and thymus make a small contribution during the last two trimesters.).

At the beginning of the fourth month of development, hematopoiesis commences in the bone marrow. At birth, all the marrow throughout the skeleton is active. And is virtually the sole source of blood cells. **(Wintrobe and Champlin, 2000)**

In the full-term infant, hepatic hematopoiesis may persist in widely scattered small foci, which become inactive soon after birth. Up to the age of puberty, all the marrow throughout the skeleton is red and hematopoietically active. Usually by 18 years of age only the vertebrae, ribs, sternum, skull, pelvis, and proximal epiphyseal regions of the humerus and femur retain the marrow, the remainder becoming yellow, fatty, and inactive. Thus, in adults, only about one-half of the marrow space is active in-hematopoiesis. **(Wintrobe and Champlin, 2000)**

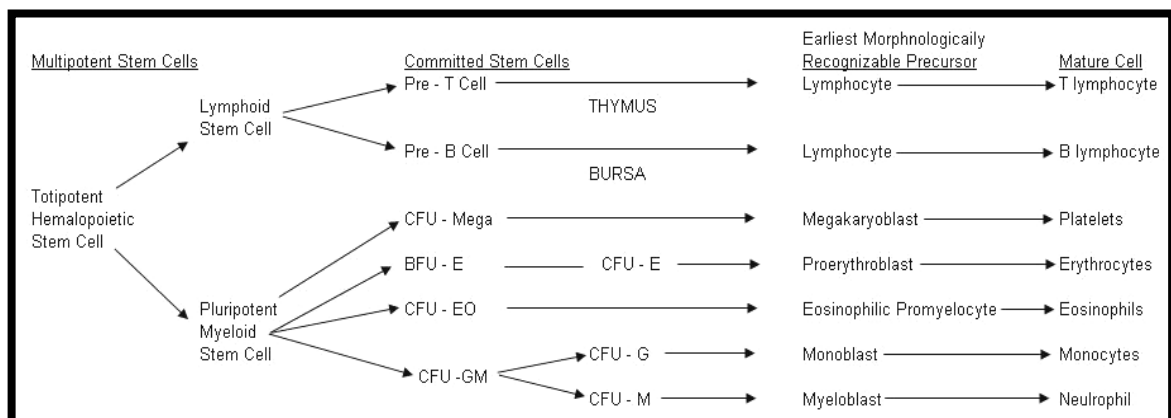
By the time of birth, the bone marrow is virtually the sole source of all forms of blood cells and a major source of lymphocyte precursors.

In the premature infant, foci of hematopoiesis are frequently evident in the liver, rarely in the spleen, lymph

nodes, or thymus, but significant postembryonic extramedullary hematopoiesis is abnormal in the full-term infants. With an increased demand for blood cells in the adult, the fatty marrow may become transformed to red, active marrow and this is accompanied by increased productive activity throughout the marrow. (Wintrobe and Champlin, 2000)

## Origin and Differentiation of Hematopoietic Stem Cells

There is no doubt that the formed elements of blood—erythrocytes, granulocytes, monocytes platelets, and lymphocytes have common origin totipotent hematopoietic stem cells (Figure 2). This common precursor then gives rise to lymphoid stem cells and the pluripotent myeloid stem cells, which are committed to produce lymphocytes and the myeloid cells, respectively.



**Figure 1: Differentiation of hematopoietic cells.**  
(Wintrobe et al., 2000)