AUTOLOGOUS BONE MARROW TRANSPLANTATION

ESSAY
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BY

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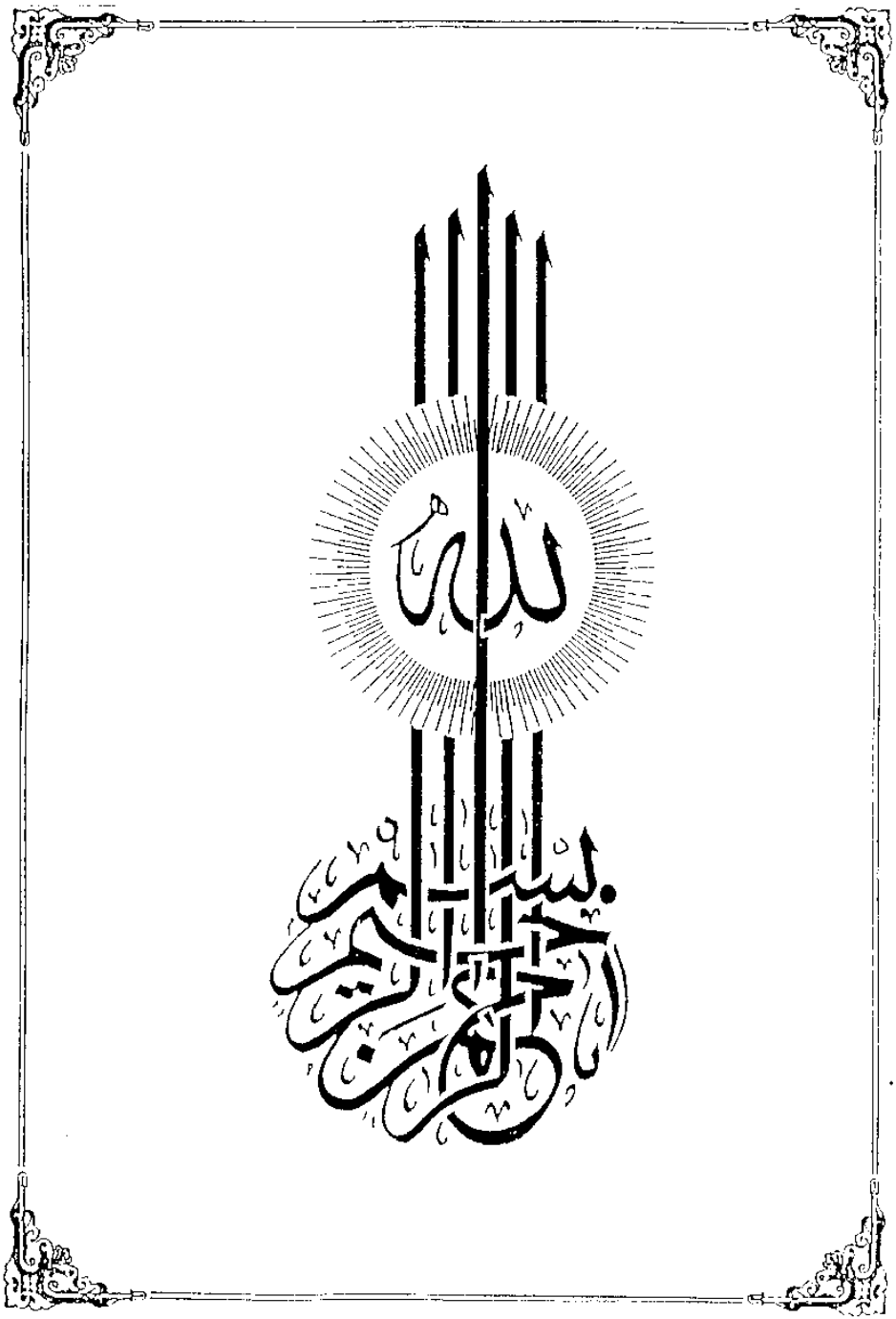
بسم الله الرحمن الرحيم

« قالوا سبحانك لا علم لنا إلا ما علمتنا
إنك أنت العليم الحكيم »

صدق الله العظيم
سورة البقرة ، الآية ٣٢



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LIST OF ABBREVIATIONS

ABMT : Autologous Bone Marrow Transplantation.
AILD : Angio-Immunoblastic Lymphadenopathy.
AL : Acute Leukemia.
ALL : Acute Lymphoblastic Leukemia.
AML : Acute Myeloblastic Leukemia.
AMML : Acute Myelomonocytic Leukemia.
ANLL : Acute Non-Lymphoblastic Leukemia.
APBSC : Autologous Peripheral Blood Stem Cell Transfusion
ARDS : Adult Respiratory Distress Syndrome.
ASTA-Z-7557: Mefosfamide.
BEAM : BCNU, Etoposide, Aracytine and Melphalan.
BEE : Basal Energy Expenditure.
BFU-E : Burst Forming Units.
BL : Burkitt's lymphoma.
BM : Bone Marrow.
BMT : Bone Marrow Transplantation.
Br-Ob : Bronchiolitis Oblitrans.
BW : Body Weight.
CEAC : Carmustin, Etoposide, Cytartine and Cyclophosphamide.
CGL : Chronic Granulocytic Leukemia.
CFU-C : Colony Forming Unit Cells.
CFU-GM : Colony Forming Unit Granulocyte Macrophage.
CMI : Cell Mediated Immunity
CML : Chronic Myeloid Leukemia.
CMV : Cytomegalovirus
CPDA : Citrate-Phosphate Dextrose Adenine.
CR : Complete Remission.
CSF : Colony Stimulating Factor.
CY : Cyclophosphamide.

DAH : Diffuse Alveolar Hemorrhage.
DFS : Disease Free Survival.
DLIF : Digoxine Like Immunoreactive Factor.
DMSO : Dimethyl Sulphoxide.
EBMT : European Bone Marrow Transplant.
EBV : Epstein-Barr Virus.
EN : Esthesioneuroblastoma.
EPO : Erythropoitein.
FCM : Flow Cytometry.
GM-CFC : Granulocyte-Macrophage Colony Forming Cells.
GVHD : Graft Versus Host Disease.
GVL : Graft-versus Leukemia.
Hb : Haemoglobin.
4-HC : 4 Hydroxyperoxycyclophosphamide.
HC : Haemorrhagic Cystitis.
HD : Hodgkin's Disease.
HEPA : High Efficiency Particular Air.
HSV : Herpes Simplex Virus.
HUS : Haemolytic Uremic syndrome.
IL : Interleukin.
IIP : Idiopathic Interstitial Pneumonitis.
IP : Interstitial Pneumonitis.
IV : Intravenous.
IVGTT : Intravenous Glucose Tolarence Test.
LDH : Lactate Dehydrogenase Enzyme.
LPRT : Laser Photoradiation Therapy.
LTMC : Long Term Marrow Culture.
MM : Multiple Myeloma.
MoAb : Monoclonal Antibody.
MRD : Minimal Residual Disease.
N_2 : Nitrogen.
NCI : National Cancer Institute.
PC : Pneumocytis Carnii.

Ph^1 : Philadelphia Chromosome.
PBMC : Peripheral Blood Mononuclear Cells.
RBC : Red Blood Cell.
RhGM-CSF : Recombinant Human Granulocyte Monocyte-Colony Stimulating Factor.
RIL : Recombinant Interleukin.
RMS : Rhabdomyosarcoma.
RSV : Respiratory Simplex virus.
SCCL : Small Cell Carcinoma of Lung.
SNUC : Sinonasal Undifferntiated Carcinoma.
T_3 : Tri-iodothyronine.
TBI : Total Body Irradiation
TC : Technetium.
Thiolepa : N,N', N'' Triethylenethiophosphoramide.
TPN : Total Parenteral Nutrition.
VOD : Venoocclusive Disease.
VP 16-213 : Etoposide.
VZV : Varicella-Zoster virus.
WBC : White Blood Cells

Introduction

and Aim of Work

INTRODUCTION AND AIM OF WORK

Autologous bone marrow transplantation (ABMT) means collection and cryopreservation of the patient own bone marrow (BM), for later reinfusion after giving a conditioning regimen that consists of myeloablative doses of chemotherapy with or without irradiation. ABMT is used for treating certain malignant diseases and allows for greater tumor cell kill, if dose-response to therapy exists for that tumor **(Cho and Blume, 1991)**.

The first trial of ABMT in man has been reported in 1959 **(Mc Govern et al., 1959)**. However, all attempts at human ABMT in the early 1960s were defeated by the lack of information about the technical aspects of the procedure. In the mid 1970s, the therapeutic potential of ABMT was reidentified and ABMT was employed as an alternative to allogeneic BMT in patients who lack HLA-identical siblings **(Mangoni et al., 1987)**. Recently, however, most trials consider ABMT as the therapy of choice, due to the greater toxicity, the higher procedure-related mortality and the limited age range of allogeneic BMT **(Goldstone and Linch, 1992)**. Moreover, ABMT has demonstrated high efficacy, with a percentage of complete response similar to those obtained with allogeneic graft **(Chopra et al., 1991a)**.

ABMT is now successfully applied for patients with many hematological malignancies, including acute lymphoblastic leukaemia **(Blaise et al.,1990)**, acute myeloblastic leukaemia **(Chopra et al.,1991b)**, acute monoblastic leukaemia **(Rossetti et al., 1991)**, chronic leukaemia **(Champlin, 1990)**, malignant lymphoma **(Goldstone and linch, 1992)** and multiple myeloma **(Attal et al., 1991)**, as well as, solid tumors **(Yaniv et al., 1990)**.

A major theoretical limitation of ABMT, especially for the treatment of hematological malignancies, is the probability that remission BM may contain clonogenic malignant stem cells capable of reestablishing the malignant process in the patient. Thus, a number of purging techniques have been developed that attempt to remove such residual cells from the BM inoculum **(Goldstone and Linch, 1992; Uckun et al., 1992)**.

Aim Of Work:

This study aims at reviewing ABMT as regards to:

1- Indication of ABMT in various hematological disorders.
2- Techniques of BM collection and processing.
3- Marrow purging techniques.
4- Marrow cryopreservation techniques.
5- Post-transplant care.
6- Complications of ABMT.

Review of Literature

Definition and Historical Aspects

AUTOLOGOUS BONE MARROW TRANSPLANTATION (ABMT)

DEFINITION

Transplantation of tissues from one individual to another was described in ancient mythology and has remained a focus of more modern science-fiction, but only recently has the reality of organ transplantation become a standard component of medical practice. In theory, transplantation of a viable functioning organ to an affected individual could ameliorate his or her clinical condition. Such organs could potentially be obtained from living human donors or cadavers, from other species, or from biotechnical engineering laboratories synthetically creating "artificial" organs. Conceptually, the ready availability of organ transplantation techniques could be highly therapeutic for the majority of serious medical problems other than those causing simultaneous system failure **(Sondel, 1989).**

Bone marrow transplantation (BMT) refers to intravenous infusion of hematopoietic progenitor cells to reestablish hematopoiesis after an otherwise fatal bone marrow insult. The patient's own bone marrow is destroyed by high doses of chemotherapy with or without total body irradiation (TBI) that is given to eradicate a malignant lesion (the most common situation) **(Armitage, 1992).**