

Reconstitution of the immune system after Bone Marrow Transplantation (BMT)

*Essay Submitted for
The Partial Fulfillment of Master Degree in
Clinical and Chemical Pathology*

by

Nevine Hafez Helmy

M.B.B.CH

Under supervision of

Prof.Dr.Laila El-Shawarby

Professor of Clinical and Chemical Pathology Department
Ain Shams University

Assist. Prof. Dr. Manal Zaghloul

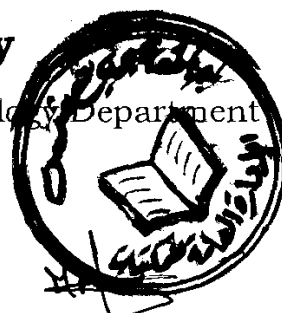
Assistant Professor of Clinical and Chemical Pathology
Department
Ain Shams University

Dr. Hossam Fahmy

Lecturer of Clinical and Chemical Pathology Department
Ain Shams University

*Faculty of Medicine
Ain Shams University*

1999





Acknowledgment

First of all, thanks to God. I wish to express my thanks and gratitude to Prof. Dr. Laila El-Shawarby, Professor of Clinical Pathology, Ain Shams University, for her constructive criticism, valuable comments and kind advice.

My deepest thanks and special regards are due to Dr. Manal Zaghloul, Assistant Professor of Clinical Pathology, Ain Shams University, for her generous help and continuous encouragement. She provided me with valuable comments and enthusiastically revised the essay.

I am profoundly grateful to Dr Hossam Fahmy, Lecturer of Clinical Pathology, Ain Shams University, for his devotion, all the time and effort he sacrificed and the valuable friendship he offered me in order to start and complete this work.

Last, but not least, no words could even express my deepest gratitude to every member of my family. Their favour is unforgettable.

CONTENTS

	<i>Page</i>
List of Abbreviations	<i>i</i>
List of Tables	<i>iv</i>
Introduction	<i>1</i>
Aim of The Work.	<i>3</i>
Review	<i>4</i>
Chapter I (Types and technique).	<i>4</i>
*Historical perspective.	<i>4</i>
*Types of BMT.	<i>7</i>
*Sources of Stem cells.	<i>10</i>
*In utero transplantation of stem cells.	<i>13</i>
*Technology of BMT.	<i>14</i>
*Conditioning programs.	<i>19</i>
*Procedure.	<i>22</i>
*Engraftment.	<i>28</i>
Chapter II (Indications of BMT).	<i>29</i>
I-Malignant indications.	<i>29</i>
a-Acute leukemia	<i>29</i>
b-Myeloproliferative diseases.	<i>35</i>
c-Lymphoproliferative leukemia	<i>38</i>

d-Lymphomas	39
e-Others	41
f-Solid tumors	43
II-Non malignant indications	45
a-Haematological	45
b-Immunological	49
c-Storage diseases	51
d-Radiation accidents	52
e-Systemic AL Amyloidosis	52
Chapter III (Complications of BMT).	54
a-Complications related to grafts	54
b-Infections	60
c-Organ complications	63
d-Haematological complications	66
e-Neurological complications	71
f-Malignancies	73
g-Others	74
Chapter IV (Immune reconstitution after BMT)	75
a-Introduction	75
b-T-cell reconstitution	78
c-B-cell reconstitution	87
d-Neutrophil reconstitution	91

e-Natural killer cell reconstitution	94
f-Monocyte reconstitution.	96
g-Immune deficiency, immunization and immunotherapy	98
Conclusions	102
Summary	103
References	108
Arabic Summary	1

LIST OF ABBREVIATIONS

4-HC:	4 Hydroxy-cyclophosphamide.
ABMT:	Autologous bone marrow transplantation.
ADCC:	Antibody dependant cellular cytotoxicity.
ADP:	Adenosine diphosphate.
AML:	Acute myeloid leukemia.
ANLL:	Acute non lymphoblastic leukemia.
ARN:	Antibody reactive with neutrophil.
BLCL:	B-lymphoblastoid cell lines.
BMT:	Bone marrow transplantation.
CBT:	Cord blood transplantation.
CD:	Cluster of differentiation.
CDR ₃ :	Third complementarity determining region.
CFU-GM:	Colony forming unit-granulocyte macrophage.
CGVHD	Chronic graft versus host disease.
CLL:	Chronic lymphocytic leukemia.
CLS:	Capillary leak syndrome.
CML:	Chronic myeloid leukemia.
CMV:	Cytomegalovirus.
CTLP:	Cytotoxic T-lymphocyte precursors.
Cy:	Cyclophosphomide.
DLI:	Donor leucocyte infusion.
DNA:	Deoxyribonucleic acid.
EBV:	Epstein Bar virus.
EFS:	Event free survival.
FA:	Fanconi anaemia.
FLT:	Fetal liver transplantation.
G-CSF:	Granulocyte-colony stimulating factor.
G-CSF:	Granulocyte colony stimulating factor.
GF:	Growth factor.

GM-CSF:	Granulocyte Macrophage-colony stimulating factor.
GVL:	Graft versus leukemia.
HB:	Hepatitis B.
HCL:	Hairy cell leukemia.
HGF:	Haemopoietic growth factor.
H-IgG:	Homogenous-Immunoglobulin G.
HLA:	Human leucocytic antigen.
HPC:	Haematopoietic progenitor cells.
HSCs:	Haemopoietic stem cells.
HTLP:	Helper T-lymphocyte precursors.
IFN- α :	Interferon- α .
IG:	Immunoglobulin.
ITP:	Idiopathic thrombocytopenic purpura.
IVIG.	Intravenous immunoglobulins.
LAK:	Lymphocyte activated killer cells.
LONIPC:	Late onset non infectious pulmonary complications.
MAb:	Monoclonal Antibody.
MDS:	Myelodysplastic syndrome.
mHag:	Minor histocompatibility antigen.
MHC:	Major histocompatibility complex.
MNC:	Mononuclear cells.
MODs:	Multiple organ dysfunction.
NHL:	Non Hodgkin lymphoma.
NK:	Nature killer cells.
PBSCT:	Peripheral blood stem cell transplantation.
PHA:	Phytohaemagglutinin.
PMNcs.	Polymorphonuclear cells.
PNH:	Paroxysmal Nocturnal Haemoglobinuria.
PT-LPDs:	Post transplantation lymphoproliferative diseases.

rhG-CSF:	Recombinant human granulocyte colony stimulating factor.
rh-GM-CSF:	Recombinant human granulocyte macrophage-colony stimulating factor.
SCID:	Severe combined immunodeficiency.
SQ-PCR:	Semi quantitative-polymerase chain reaction.
TBI:	Total body irradiation.
TCR:	T cell receptor.
TEN:	Toxic epidermal necrosis.
TH:	T-helper.
TLC:	Total leucocytic count.
TNF:	Tumour necrosis factor.
t-PA:	Tissue plasminogen activator.
VLA:	Very late activation.
VOD:	Veno-occlusive disease.
VZV:	Varicella Zoster virus.
WAS:	Wiskott-Aldrich syndrome.
WBC:	White blood cells.

LIST OF TABLES

Table (1)	The three principal phases of bone marrow transplantation.....	20
Table (2)	Clinical grading of acute GVHD.....	56

