

## 조혈모세포이식은 어디까지 발전했는가?

연세대학교 의과대학 내과학교실

정 준 원

Essentials of Primary Care: 혈액종양

1. 조혈모세포 이식에 대한 **overview**

2. 조혈모세포이식의 **최신 동향**

3. **미래**의 조혈모세포이식에 대한 **전망**

라복 70년, 내과 70년 The Korean Association of Internal Medicine

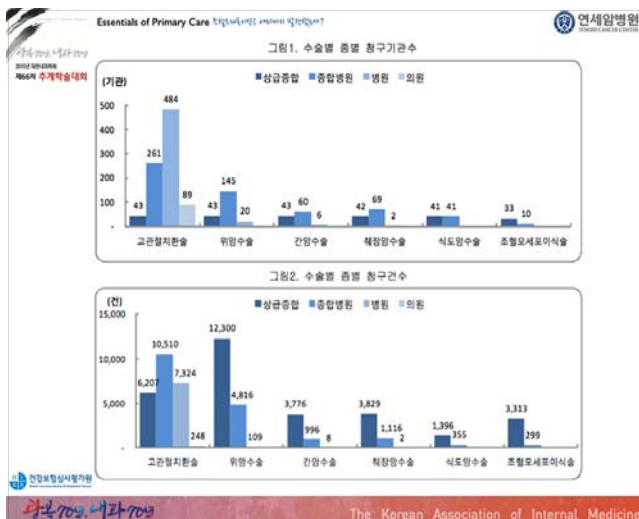
Essentials of Primary Care: 혈액종양

**“Prologue”**

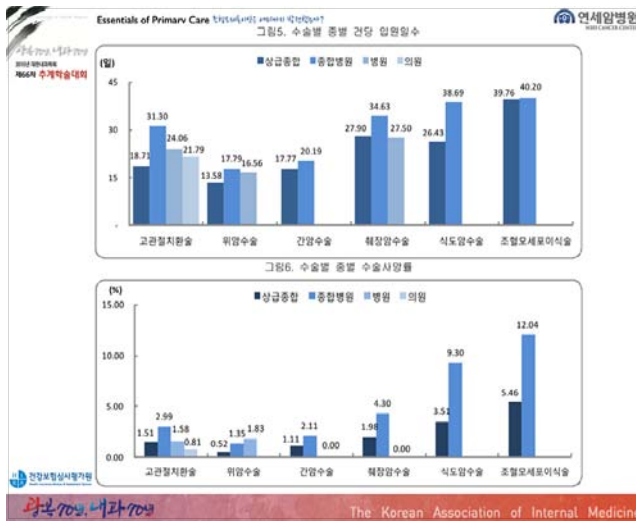
**2014년도 진료량 평가결과 보고서**

HI RA 건강보험심사평가원  
Health Insurance Review & Assessment Service

라복 70년, 내과 70년 The Korean Association of Internal Medicine



— 정준원. 조혈모세포이식은 어디까지 발전했는가? —



Essentials of Primary Care 한국내과진료지침위원회

# I.Lesson from History

대한70년. 내과70년 The Korean Association of Internal Medicine

Essentials of Primary Care 한국내과진료지침위원회

## The Nobel Prize in Physiology or Medicine 1930

### 1901 “ABO”

Karl Landsteiner  
Prize share: 1/1

The Nobel Prize in Physiology or Medicine 1930 was awarded to Karl Landsteiner “for his discovery of human blood groups”.

대한70년. 내과70년 The Korean Association of Internal Medicine

Essentials of Primary Care 한국내과진료지침위원회

## The First failed human marrow infusion

### 1939

**APLASTIC ANEMIA TREATED WITH DAILY TRANSFUSIONS AND INTRAVENOUS MARROW: CASE REPORT \***

By EDWIN E. OSGOOD, M.D., MATTHEW C. ROGUE, M.D., and THOMAS J. MATTHEWS, M.D., Portland, Oregon

This case is of interest for several reasons. The disease is uncommon. This patient received 43 transfusions totaling about 22 liters of blood in 32 days. This prolonged life but produced polycythemia and enlargement of the spleen. Despite the amount of blood transfused the leukocyte and platelet counts remained at a relatively low level. No record was found of so large an amount of blood being given within this space of time.

**CASE REPORT**

A white school girl, 16 years of age, entered Multnomah County Hospital on October 26, 1937, complaining of weakness, pallor, shortness of breath, and bleeding from the gums.

She had flowery anemia of the apex of the right upper lobe since 1935. In 1938 she was treated for pleural effusion. She never had hemoptysis, catarrhs, or tubercle bacilli in the sputum. She was found to be clinically well on examination at regular intervals from 1935 until about September 1937, when she first noticed fatigue on exertion, pallor, and a throbbing sensation in her head. Her physician gave her iron and liver extract and made the blood examinations recorded in table 1. On October 26, she first noticed slight bleeding from a spot on the gum near the left upper molars and black stools. She was sent then into Multnomah County Hospital.

\*Reprinted for publication August 27, 1938, from The Department of Medicine, University of Oregon Medical School, and Multnomah County Hospital, Portland, Ore.

†The information on the illness from 1935 to Oct. 26, 1937, including the information in table 1, was kindly supplied by Dr. Ralph C. Mason of Portland, Oregon.

Ann Intern Med 1939;13:357-367

대한70년. 내과70년 The Korean Association of Internal Medicine

Essentials of Primary Care 한국내과진료지침위원회

1939 The First failed human marrow infusion by Osgood  
1940s~50s Animal experiment by Rekers, Jacobson, Lorenz, Main, Prehn, Ford, etc  
1956 The First successful human marrow grafting

대한70년. 내과70년 The Korean Association of Internal Medicine

Bassett Healthcare Network  
Bassett Medical Center

## The First BMT

### 1956

1930 1990

THE NEW ENGLAND JOURNAL OF MEDICINE

**INTRAVENOUS INFUSION OF BONE MARROW IN PATIENTS RECEIVING RADIATION AND CHEMOTHERAPY\***

E. DONNALL THOMAS, M.D., J. HARRY L. LOCHTE, JR., M.D., J. WAN CHING LI, Ph.D., J. AND JOSEPH W. FERRERA, M.D.†

COOPERSTOWN, NEW YORK, AND BOSTON, MASSACHUSETTS

N Engl J Med 1957;257:491-496

대한70년. 내과70년 The Korean Association of Internal Medicine

Essentials of Primary Care 한국내과사회의 미래를 위한 실천지침서


2015 연세암병원  
연세암학회  
연세암학회  
연세암학회

1958

## The Nobel Prize in Physiology or Medicine 1980

1930 1990 1980

**"HLA"**

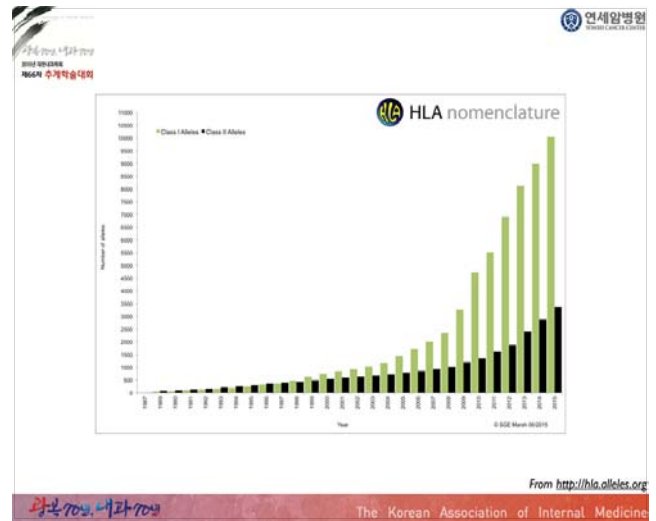


Jean Dausset  
Prize share: 1/3

The Nobel Prize in Physiology or Medicine 1980 was awarded jointly to Baruj Benacerraf, Jean Dausset and George D. Snell "for their discoveries concerning genetically determined structures on the cell surface that regulate immunological reactions".

과학 70년, 내과 70년

The Korean Association of Internal Medicine



Essentials of Primary Care 한국내과사회의 미래를 위한 실천지침서

2015 연세암병원  
연세암학회  
연세암학회  
연세암학회

1968

## The First Successful BMT from matched sibling

IMMUNOLOGICAL RECONSTITUTION OF SEX-LINKED LYMPHOPENIC IMMUNOLOGICAL DEFICIENCY

RICHARD A. GATTI M.D., St. Louis  
RESEARCH FELLOW

HILAIRE J. MEUWISSEN M.D., Nymegen  
RESEARCH FELLOW

HUGH D. ALLEN M.D., Cincinnati  
PEDIATRIC RESIDENT

RICHARD HONG M.D., Illinois  
ASSOCIATE PROFESSOR

ROBERT A. GOOD M.D., Ph.D., Minneapolis  
AMERICAN LEGION MEMORIAL HEART RESEARCH PROFESSOR OF PEDIATRICS AND MICROBIOLOGY

From the Department of Pediatrics and the Pediatric Research Laboratories, University of Minnesota, Minneapolis, Minnesota 55455



TIME  
Toward Control of CANCER  
Immunologist Robert Good

Lancet 1968; 292:1366-1369

과학 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 한국내과사회의 미래를 위한 실천지침서

2015 연세암병원  
연세암학회  
연세암학회  
연세암학회

1972

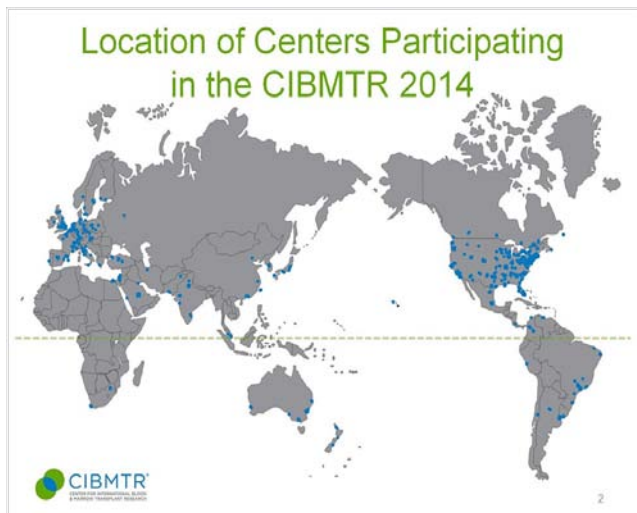
## The International Bone Marrow Transplant Registry



**CIBMTR®**  
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

과학 70년, 내과 70년

The Korean Association of Internal Medicine



Essentials of Primary Care 한국내과사회의 미래를 위한 실천지침서

2015 연세암병원  
연세암학회  
연세암학회  
연세암학회

1973

## The First Successful BMT from Matched Unrelated Donor

### Reconstitution in Severe Combined Immunodeficiency by Transplantation of Marrow from an Unrelated Donor

Richard J. O'Reilly, M.D., Bo Dupont, M.D., Savita Pathwa, M.D., Elena Grimes, M.D., Elizabeth M. Smithwick, M.D., Rajendra Pathwa, M.D., Stanley Schwartz, M.D., John A. Hansen, M.D., Frederick P. Siegal, M.D., Michael Sorell, M.D., Arne Sveigaard, M.D., Casper Jensild, M.D., Mogens Thomsen, M.D., Pier Platz, M.D., Pierre L'Esperance, M.D., and Robert A. Good, M.D., Ph.D.

N Engl J Med 1977; 297:1311-1318 | December 15, 1977 | DOI: 10.1056/NEJM197712152972403

N Engl J Med 1977; 297:1311-1318

### Transplantation of Marrow from an Unrelated Donor to a Patient with Acute Leukemia

John A. Hansen, M.D., Reginald A. Clift, F.I.M.L.S., E. Donnell Thomas, M.D., C. Dean Buckner, M.D., Rainer Storb, M.D., and Eloise R. Giblett, M.D.

N Engl J Med 1980; 303:565-567 | September 4, 1980 | DOI: 10.1056/NEJM198009043031007

N Engl J Med 1980; 303:565-567

과학 70년, 내과 70년

The Korean Association of Internal Medicine

— 정준원. 조혈모세포이식은 어디까지 발전했는가? —

Essentials of Primary Care 진료분야별 1차 진료 지침서

1974

The European Group for Blood & Marrow Transplantation



EBMT  
European Society for Blood and Marrow Transplantation

라온 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진료분야별 1차 진료 지침서

1981

The **First** BMT in KOREA

김길영 · 손영모 · 김홍진 · 김규언 · 김영호 · 송경순  
· 이도형 : 재성분담성 빈혈에 있어서 골수이식의  
실제 이용(抄). 소아과 24(9), 부록 第31次 大韓  
小兒科學會 學術大會抄錄集, p. 14, 1981.

라온 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진료분야별 1차 진료 지침서

1982

The Second BMT in KOREA

大韓血液學會雜誌, 第17卷 第2號 1982年

骨髓移植術에 依한 重症 再生不良性貧血 治驗 1例\*

연세대학교 의과대학  
내과학교실  
고준웅 · 이종화 · 한지숙 · 윤진우  
소아과학교실  
김길영 · 남궁란  
임상병리학교실  
송경순  
아원과학교실  
오홍근

라온 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진료분야별 1차 진료 지침서

1983

The First **Allogeneic** BMT in KOREA

대한내과학회잡지 1 제21권 제4호

실험적 동종 골수이식 및 임상에서의 응용\*

가톨릭대학교 의과학교실  
김관형 · 한지화 · 박종필 · 박진일\*\*  
김원일 · 김춘주 · 김동진  
가톨릭대학 임상병리학교실  
정인숙 · 김병기  
가톨릭대학 방사선학교실  
윤세철  
가톨릭대학 이기종학교실  
한준 · 이종훈

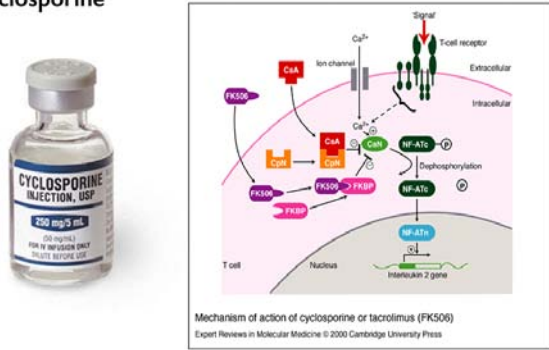
라온 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진료분야별 1차 진료 지침서

1983

Cyclosporine



Mechanism of action of cyclosporine or tacrolimus (FK506)  
Expert Reviews in Molecular Medicine © 2000 Cambridge University Press

라온 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진료분야별 1차 진료 지침서

1986

The National Donor Marrow Program



라온 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진단·치료·예방을 위한 필수지식

1988

### The Bone Marrow Donors Worldwide

**BONE MARROW DONORS WORLDWIDE**

MILLION

과학 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진단·치료·예방을 위한 필수지식

1990

### FK506

Mechanism of action of cyclosporine or tacrolimus (FK506)  
Expert Reviews in Molecular Medicine © 2000 Cambridge University Press

과학 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진단·치료·예방을 위한 필수지식

1992

### The First BM & Kidney Transplant from Non-Human Primate

Dr. Thomas Starzl

과학 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진단·치료·예방을 위한 필수지식

1994

### The Korea Marrow Donor Program

한국 조혈모세포은행협회  
Korea Marrow Donor Program

과학 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진단·치료·예방을 위한 필수지식

1995

### Mycophenolate Mofetil

Mechanism of action of mycophenolate mofetil  
Expert Reviews in Molecular Medicine © 2000 Cambridge University Press

과학 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진단·치료·예방을 위한 필수지식

1996

### The Korean Society of Blood & Marrow Transplantation

대한조혈모세포이식학회

과학 70년, 내과 70년

The Korean Association of Internal Medicine


— 정준원. 조혈모세포이식은 어디까지 발전했는가? —

Essentials of Primary Care 진료분야별 1차 진료의 중요성

연세암병원  
YONSEI CANCER CENTER

1998

2010 연세암  
2010 연세암  
2010 연세암  
2010 연세암



**RAPID COMMUNICATION**

**Nonmyeloablative Stem Cell Transplantation and Cell Therapy as an Alternative to Conventional Bone Marrow Transplantation With Lethal Cytoabduction for the Treatment of Malignant and Nonmalignant Hematologic Diseases**

By Shimon Slavin, Arnon Nagler, Ella Naparstek, Yossi Kapelushnik, Memet Aker, Gabriel Cividalli, Gabor Varadi, Mark Kirschbaum, Aliza Ackerstein, Simcha Samuel, Avraham Amar, Chaim Brautbar, Ofira Ben-Tal, Amiram Eldor, and Pouven Or

*Blood* 1998; 91:756-763

**RAPID COMMUNICATION**

**Donor Leukocyte Transfusions for Treatment of Recurrent Chronic Myelogenous Leukemia in Marrow Transplant Patients**

By H.J. Kolb, J. Mittermüller, Ch. Clemm, E. Holler, G. Ledderose, G. Brehm, M. Heim, and W. Wilmanns

*Blood* 1990; 76:2462-2465

과목 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진료분야별 1차 진료의 중요성

연세암병원  
YONSEI CANCER CENTER

**I. Lesson from History**

**HSCT is**

**Medical Monument,**

**Accompany with Immunology,**

**Act of Challenge, Love and Charity**

과목 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진료분야별 1차 진료의 중요성

연세암병원  
YONSEI CANCER CENTER

**2. Lesson from Trends**

과목 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진료분야별 1차 진료의 중요성

연세암병원  
YONSEI CANCER CENTER

**HSCT**

1	2	3	4
Pre-HSCT Preparation	Conditioning	Transplant	Post-HSCT Management

과목 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진료분야별 1차 진료의 중요성

연세암병원  
YONSEI CANCER CENTER

**HSCT**

	Auto	Allo	Recipient
Pre-HSCT Preparation	Evaluation Mobilization Cryopreservation	Evaluation	
		Selection Evaluation	Donor

과목 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진료분야별 1차 진료의 중요성

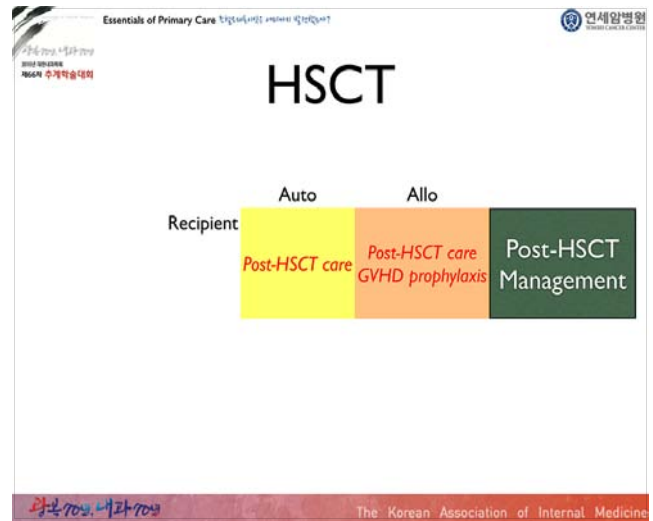
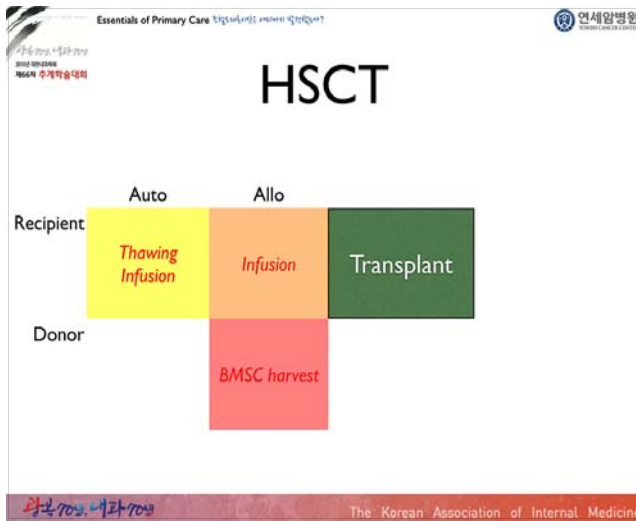
연세암병원  
YONSEI CANCER CENTER

**HSCT**

	Auto	Allo	Recipient
Conditioning	Conditioning	Myeloablative Reduced Intensity Non-Myeloablative	
		PBSC Mobilization	Donor

과목 70년, 내과 70년

The Korean Association of Internal Medicine



Essentials of Primary Care 진료순환의료기초지식

연세암병원  
YONSEI CANCER CENTER

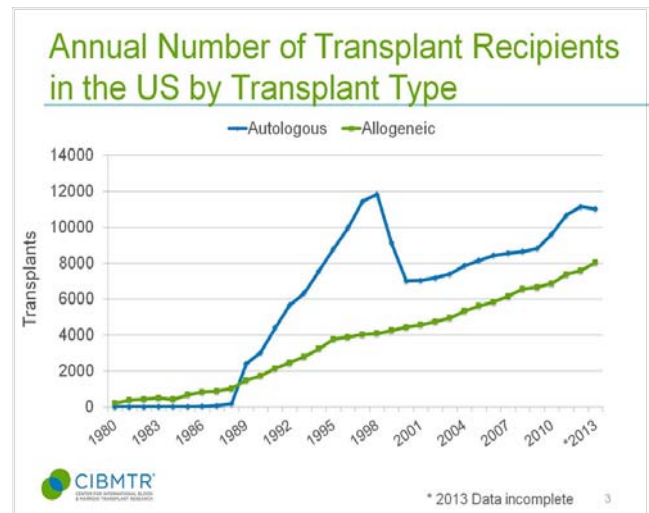
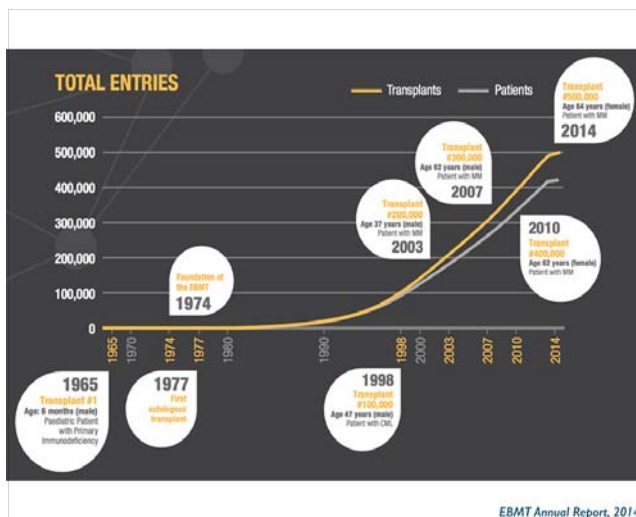
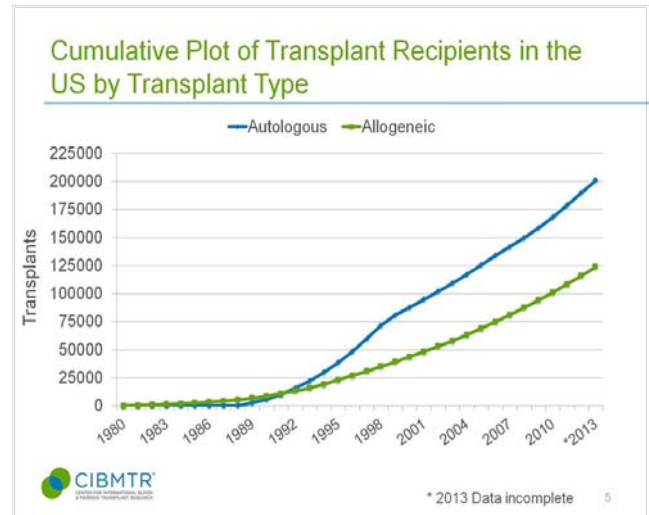
## Indication

- Hematologic malignancies
- Non-malignant hematologic diseases
- Chemo-sensitive solid cancer
- Immune disease
- Inborn error of metabolism

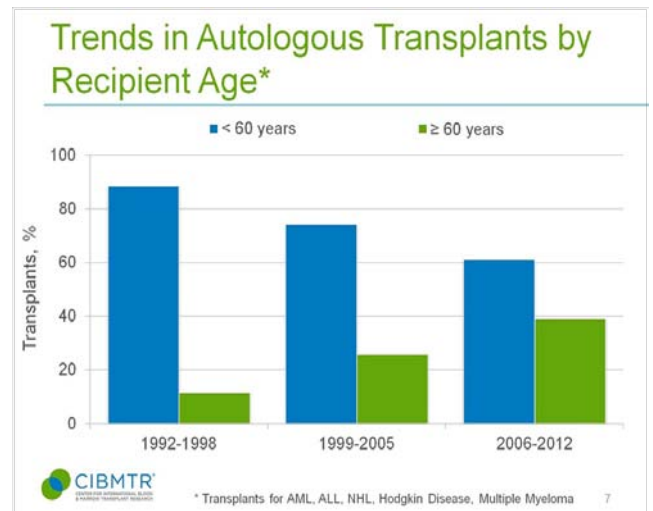
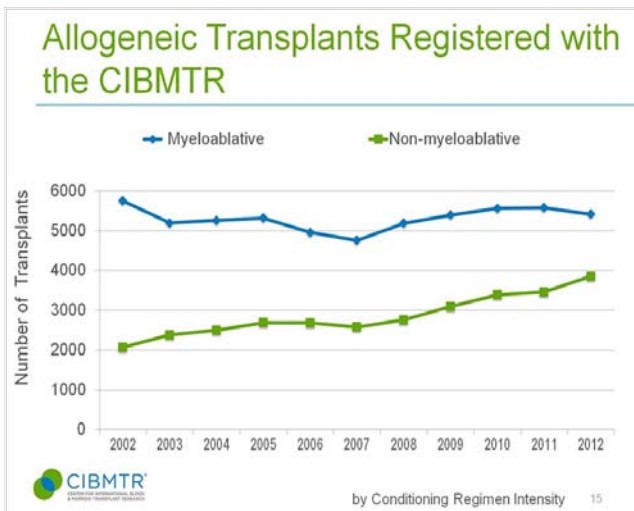
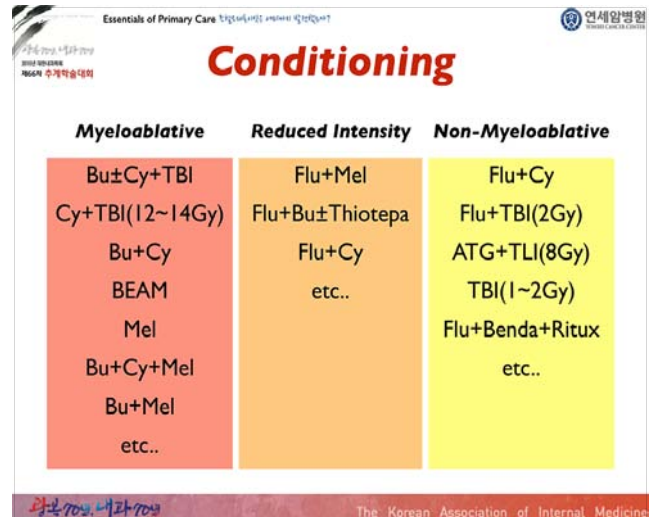
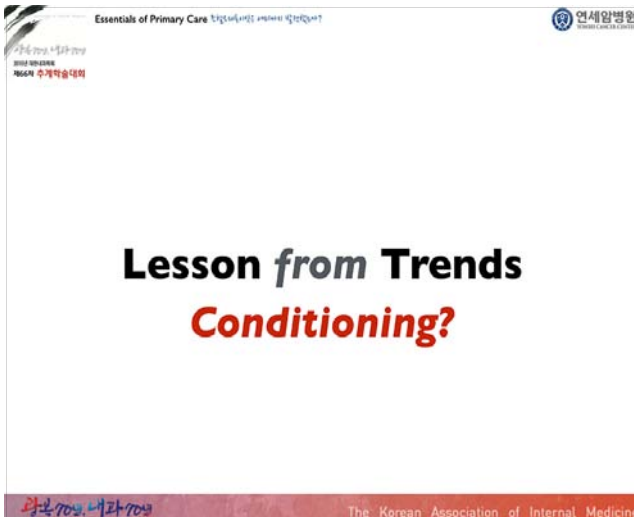
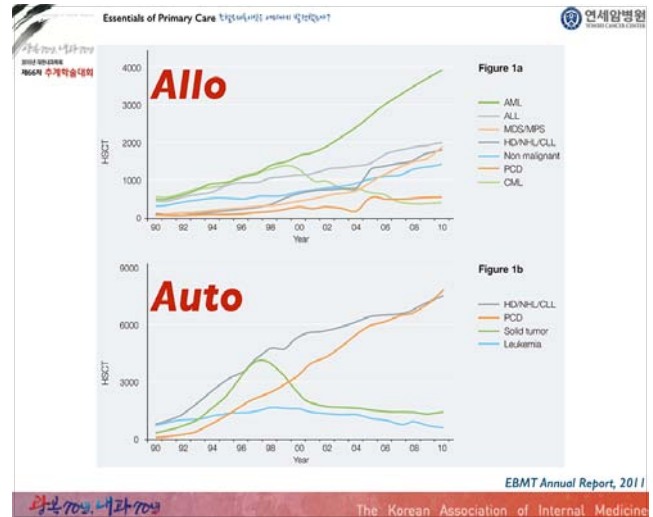
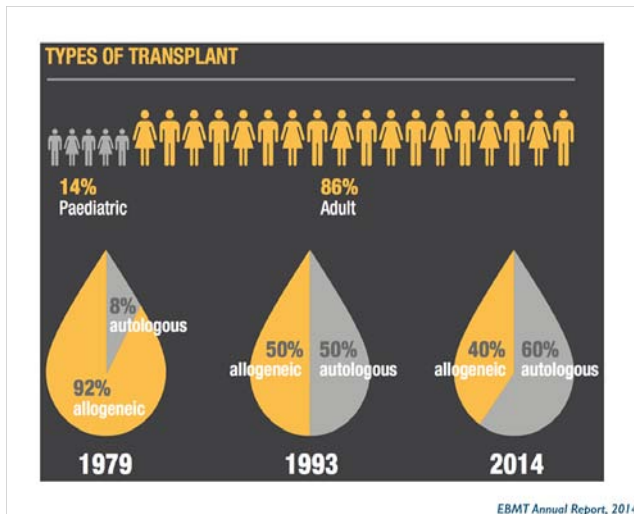
Rambam Mainmonides Med J 2014; 5:e0028

라온 70년, 내과 70년

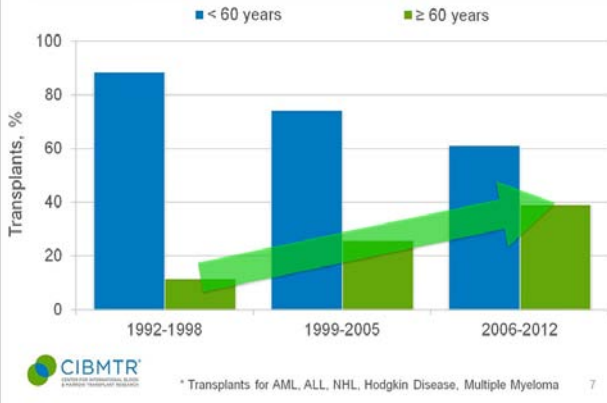
The Korean Association of Internal Medicine



— 정준원. 조혈모세포이식은 어디까지 발전했는가? —



## Trends in Autologous Transplants by Recipient Age\*



## Allogeneic Transplants for Age > 20 years, Registered with the CIBMTR

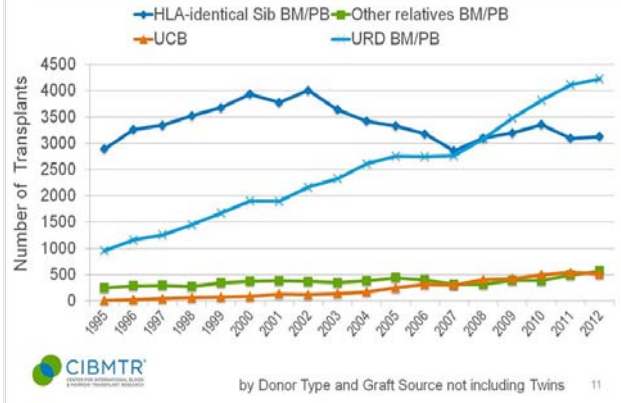


Figure 1a. Absolute numbers of haplo-identical and cord blood HSCT in Europe 1998-2013

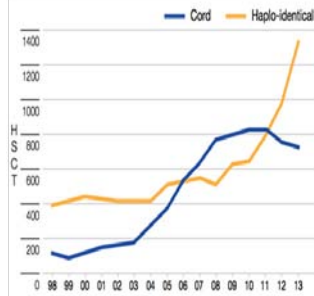
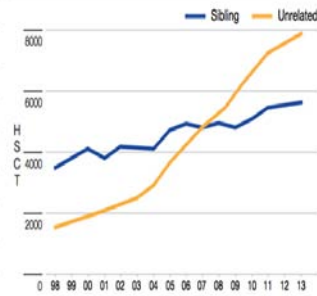
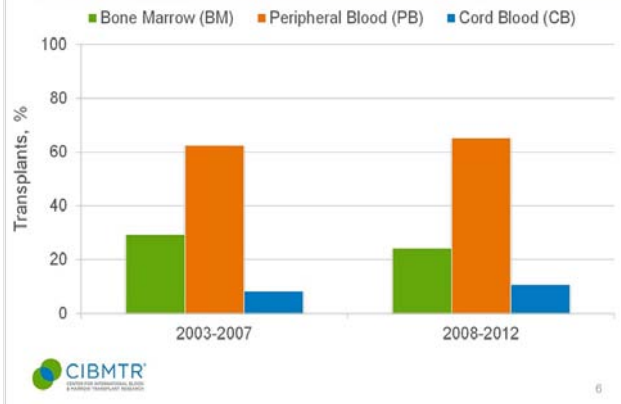


Figure 1b. Absolute numbers of sibling donor and unrelated donor HSCT in Europe 1998-2013

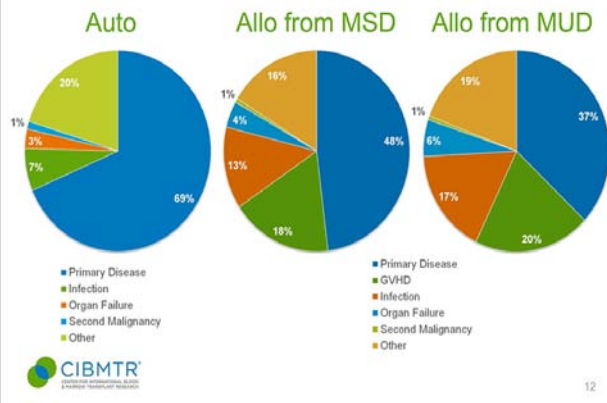


EBMT Annual Report, 2014

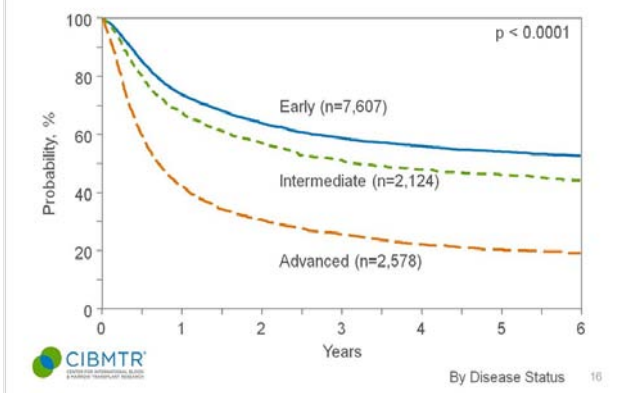
## Stem Cell Sources for Allogeneic Transplants by Year



## Causes of Death in 2011-2012

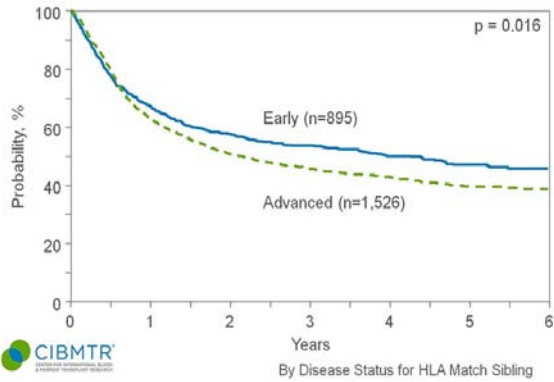


## Survival after HLA Match Sibling Donor Transplants for AML, 2002-2012

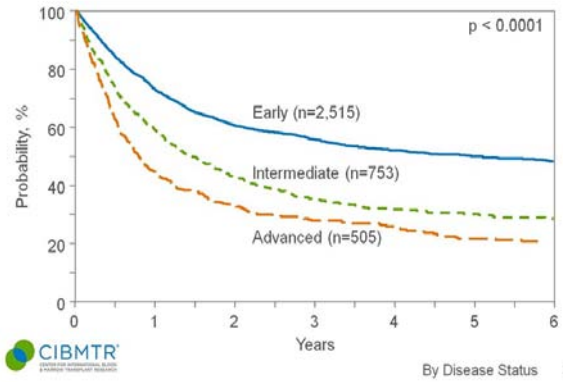


— 정준원. 조혈모세포이식은 어디까지 발전했는가? —

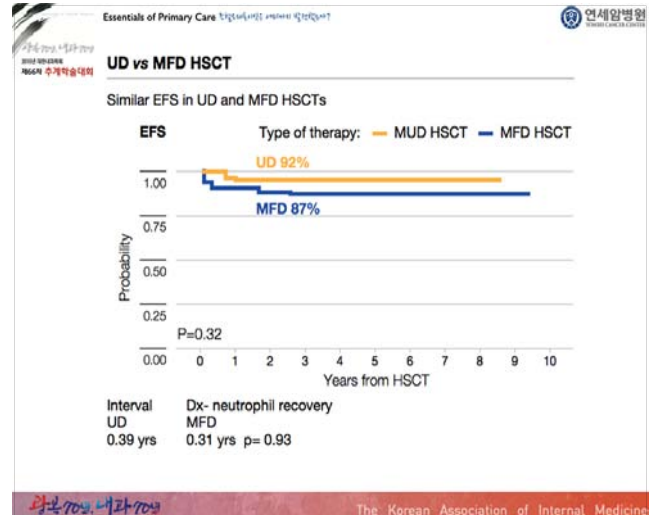
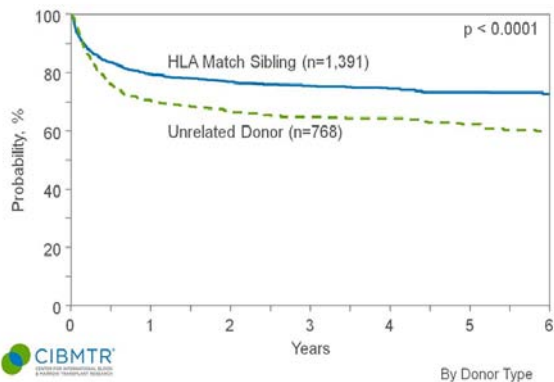
### Survival after Allogeneic Transplants for MDS, 2002-2012



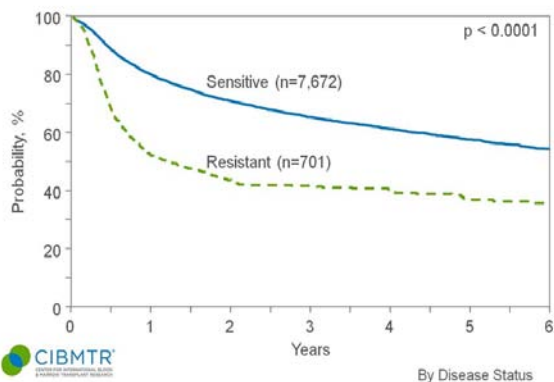
### Survival after HLA Match Sibling Donor Transplants for ALL, Age $\geq 20$ Years, 2002-2012



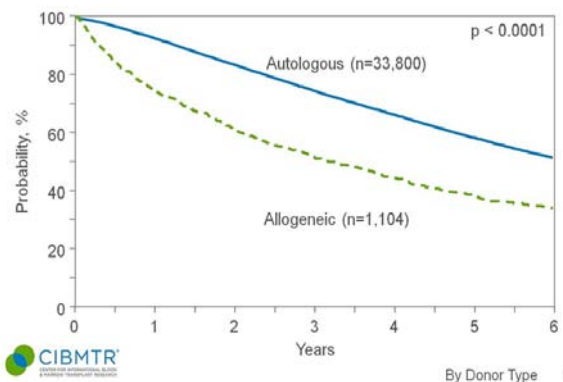
### Survival after Allogeneic Transplants for Severe Aplastic Anemia, $\geq 20$ Years, 2002-2012



### Survival after Autologous Transplants for DLBCL, 2002-2012



### Survival after Transplants for Multiple Myeloma, 2002-2012



Essentials of Primary Care 진료실에서의 핵심적인 질문들

2015 연세암병원  
연세대학교  
연세암병원  
연세대학교  
연세암병원  
연세대학교

## 2. Lesson from Trends

**HSCT is still being expanded!**  
; Quantity, Indication, Source, Donor, Patients, etc  
**HSCT is still exceeding obstacles!**  
**However, HSCT is still not the best!**

라온 70년, 내과 70년

The Korean Association of Internal Medicine

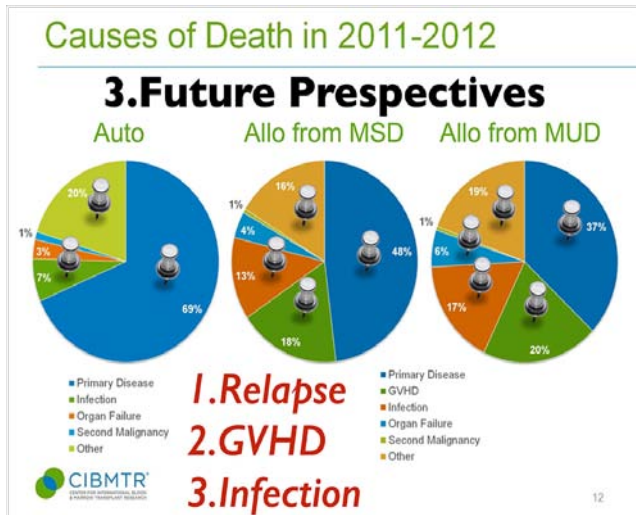
Essentials of Primary Care 진료실에서의 핵심적인 질문들

2015 연세암병원  
연세대학교  
연세암병원  
연세대학교  
연세암병원  
연세대학교

## 3. Future Perspectives

라온 70년, 내과 70년

The Korean Association of Internal Medicine



Essentials of Primary Care 진료실에서의 핵심적인 질문들

2015 연세암병원  
연세대학교  
연세암병원  
연세대학교  
연세암병원  
연세대학교

## HSCT

To reduce relapse, GVHD, & infection,...

Pre-HSCT Preparation	Conditioning	Transplant	Post-HSCT Management
+Novel drugs +Novel cell therapy	+Novel drugs	-Alloreactive T cells +Treg cells - $\alpha\beta$ CD19+ T cells + $\gamma\delta$ TCR+T cells +NK cells +MSC	+Anti-tumor vaccine +MSC +DSC - $\alpha\beta$ CD19+ T cells + $\gamma\delta$ TCR+T cells +NK cells +TAA-specific T cells +Anti-viral CTLs

라온 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진료실에서의 핵심적인 질문들

2015 연세암병원  
연세대학교  
연세암병원  
연세대학교  
연세암병원  
연세대학교

## ClinicalTrials.gov

Graft manipulations  
Pre- or Post-HSCT cell therapy or chemotherapy  
Biomarkers  
Supportive care

Indication widening  
Combined solid organ & HSC transplantations

라온 70년, 내과 70년

The Korean Association of Internal Medicine

Essentials of Primary Care 진료실에서의 핵심적인 질문들

2015 연세암병원  
연세대학교  
연세암병원  
연세대학교  
연세암병원  
연세대학교

## "Epilogue"

**HSCT is evolving**  
to break through any obstacles  
for better outcomes  
of more patients with various diseases

라온 70년, 내과 70년

The Korean Association of Internal Medicine