

Hematopoietic stem cell transplantation



HSCT - definition

Definition

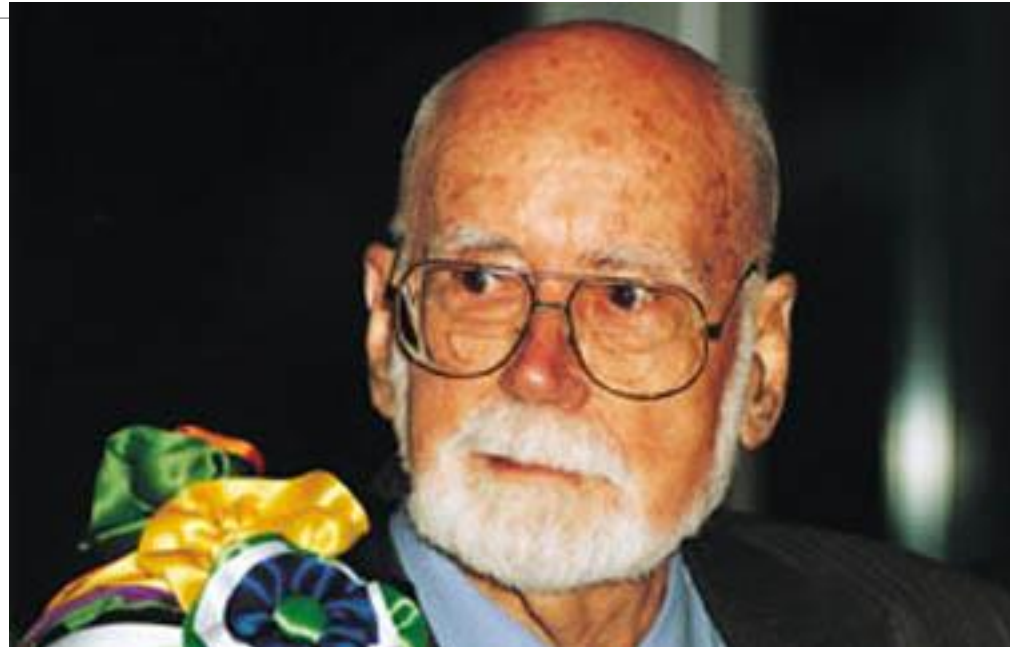
any procedure where hematopoietic stem cells of any donor and any source are given to a recipient with intention of repopulating/replacing the hematopoietic system in total or in part

History

- **Hematopoietic stem cell transplantation in the mouse**
 - the radiation protection phenomenon (mid-1950s)
- **Hematopoietic stem cell transplantation in the dog**
- **Hematopoietic stem cell transplantation in human patients**
 - 1959–1963 : first allogeneic HSCT in humans
 - beginning of the Modern Era of HSCT: the end of 60

The Nobel Prize, 1990

E. Donnall Thomas



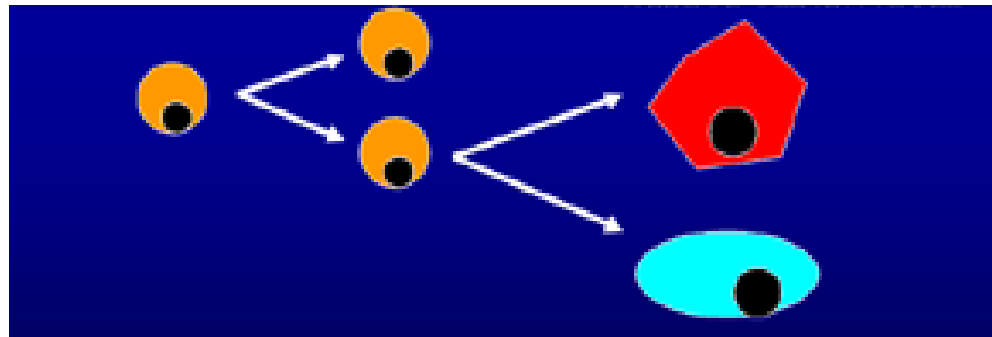
first successful HSCT in treatment of acute leukemias

Thomas ED, Lochte HL, Lu WC, Ferrebee JW. Intravenous infusion of bone marrow in patients receiving radiation and chemotherapy. N. Engl. J. Med. 1957; 257: 491.

Stem cells

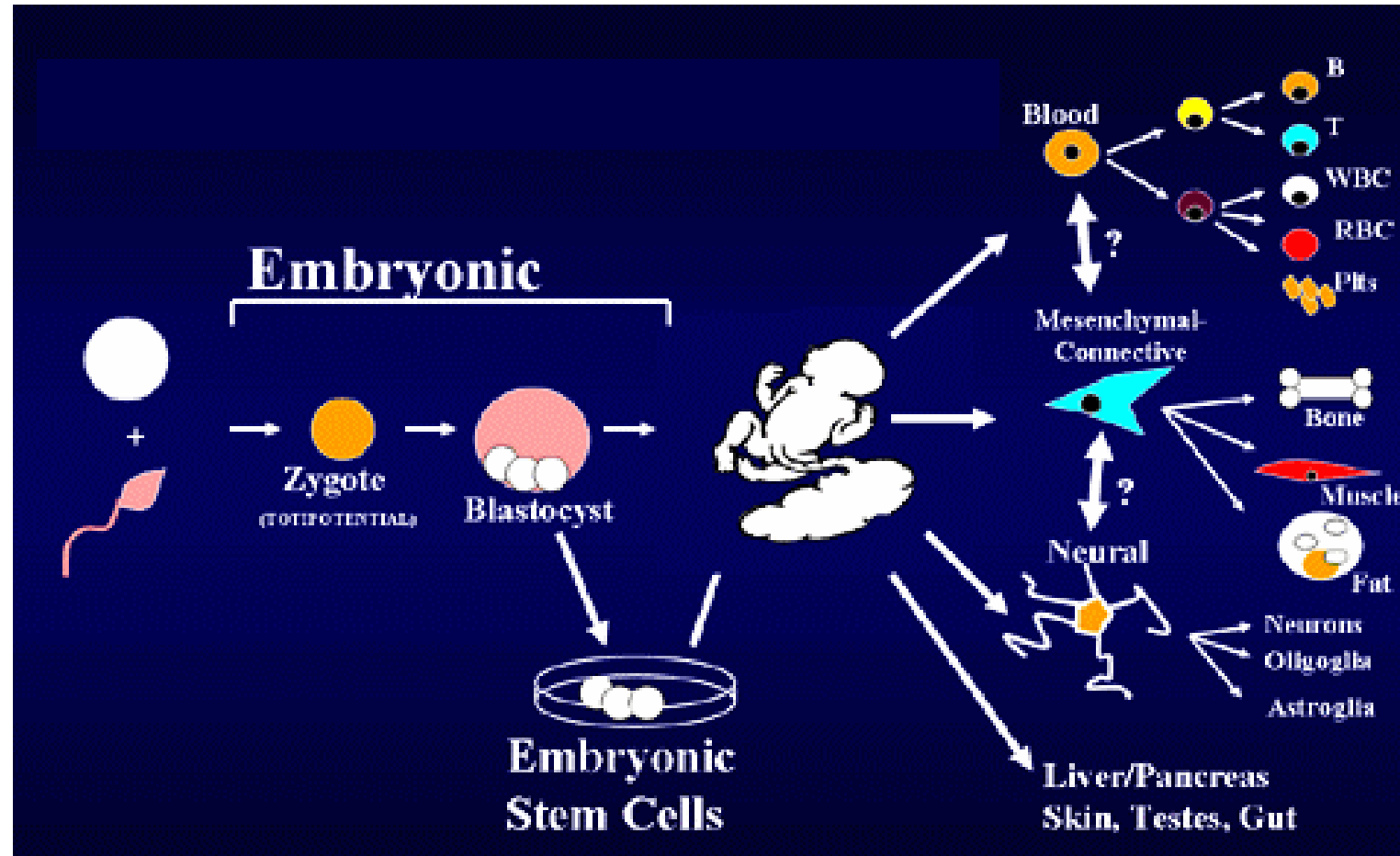
population of undifferentiated cells which are able

- **to divide for indefinite period**
- **to self renew**
- **to generate a functional progeny of highly specialised cells**



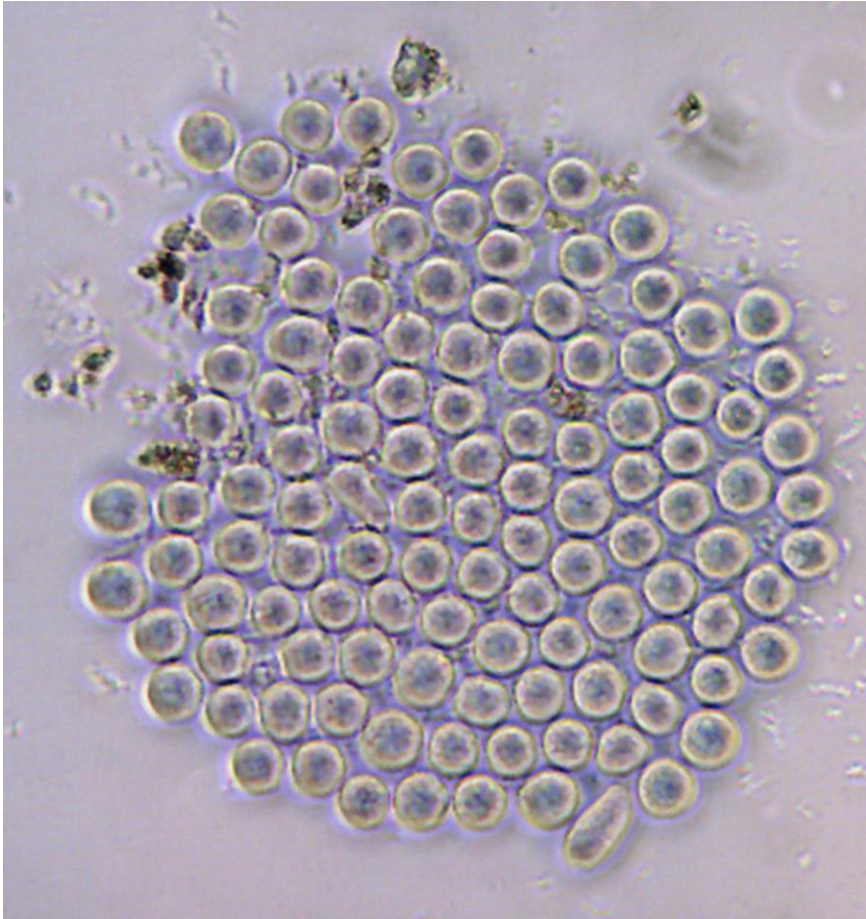
Hierarchy

- Totipotent (fertilised egg)
- Pluripotent (embryonic cell)
- Multipotent (hematopoietic)



Hematopoietic stem cells

1 / 25 000 - 100 000 of bone marrow cells



Characteristic:

- CD34
- CD133
- Lin⁻
- C-kit (CD117)
- BCRP

Blood, 15 Jan 2004

HSCT

- **Allogeneic HSCT**
 - syngeneic
 - from sibling/related donor
 - from unrelated donor
- **Autologous HSCT**

Sources of stem cells

Bone marrow

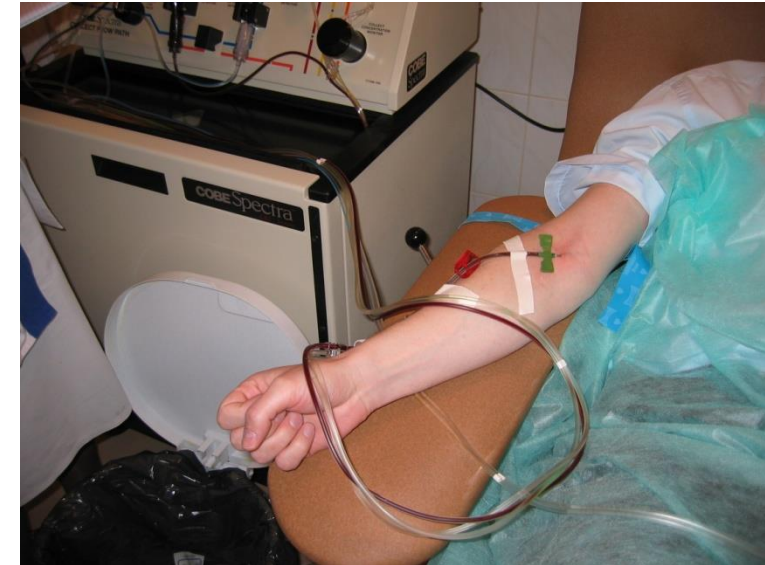
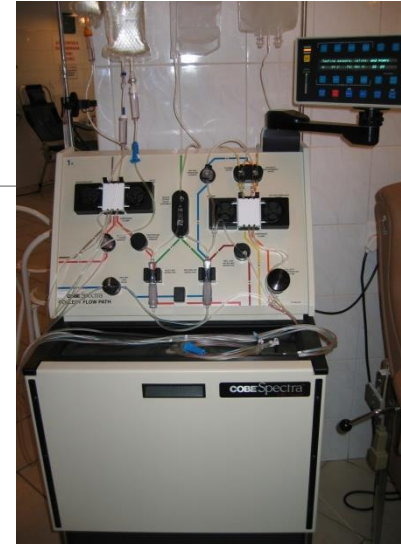
Peripheral blood

Umbilical cord blood

Donors of hematopoietic stem cells

- 1. Sibling donor, HLA identical (25%)**
- 2. Unrelated donors registry (>30 mln donors) - BMDW Registry – Bone Marrow Donor Worldwide**
- 3. Cord blood bank (>700 000 units) - Netcord, Eurocord**

Collection of hematopoietic stem cells



bone marrow

peripheral blood

Indication for HSCT

Neoplastic disorders

- Hematological malignancies
 - Lymphomas (Hodgkin and non-Hodgkin)
 - Leukemias (acute and chronic) and MDS
 - Multiple myeloma
- Solid tumors

Non-neoplastic disorders

- Aplastic anemia
- Autoimmune diseases
- Immunodeficiency
- Inborn errors of metabolism

Conditioning regimens

Principles

- „space-making” (controversial)
- immunosuppression
- disease eradication

Strategy

- Ablative therapy
 - radio/chemo
- Reduced intensity therapy
 - radio/chemo
- Non-myeloablative therapy
 - radio/chemo

Bone marrow transplantation unit



Hematopoietic stem cell infusion



Factors influencing the outcome of HSCT

Disease factors

- stage

Patient - related factors

- Age

Donor - related factors

- Histocompatibility (HLA)
- Sex
- Viral status (CMV positivity)

Peri-transplant factors

- Conditioning
- GVHD prevention
- Stem cell source and content

Post-transplant factors

- GVHD

Complication

Allogeneic

- **Early**

- infection
- aGVHD
- bleeding
- toxicity
- graft failure

- **Late**

- chGVHD
- infection
- relapse
- gonadal failure
- secondary malignancy
- toxicity

Autologous

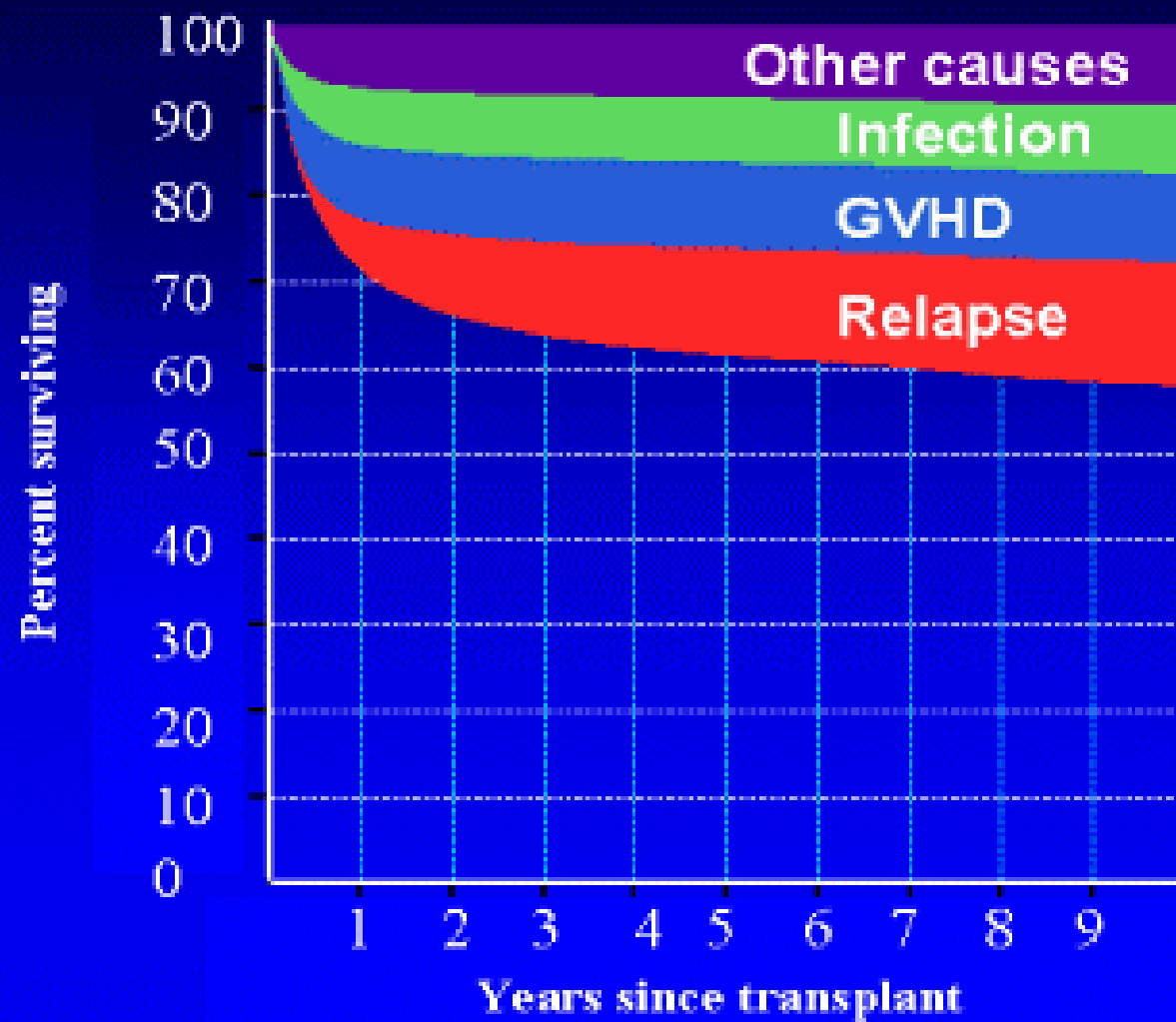
- **Early**

- infection
- bleeding
- toxicity

- **Late**

- relapse
- infection
- gonadal failure
- secondary malignancy
- toxicity

Causes of death after conventional transplant



AlloHSCT - graft versus host disease

GVHD

- Acute (1- 4°)
- Chronic (limited, extensive)

Prophylaxis

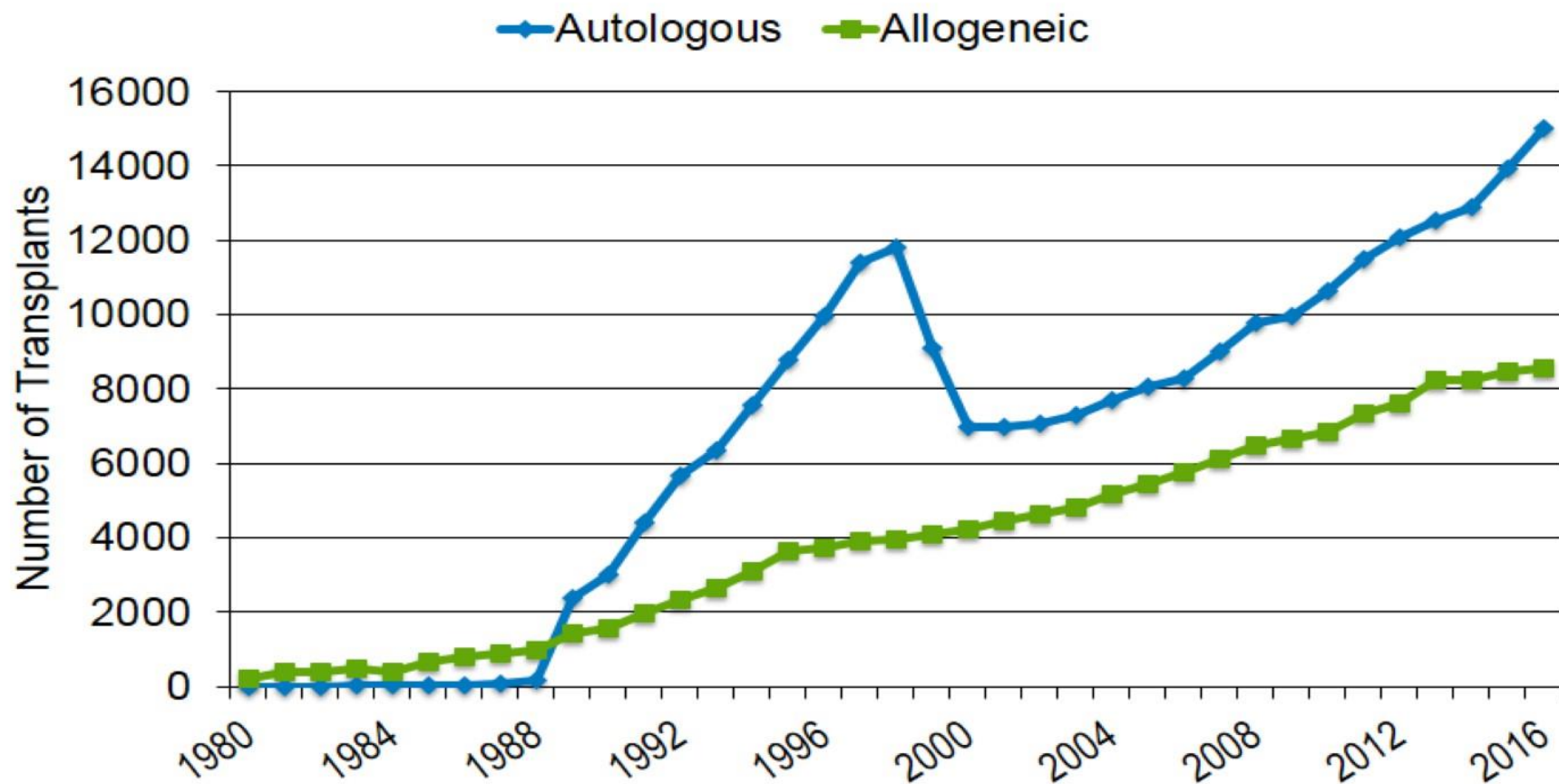
- Cyclosporine
- Metotrexate

Treatment

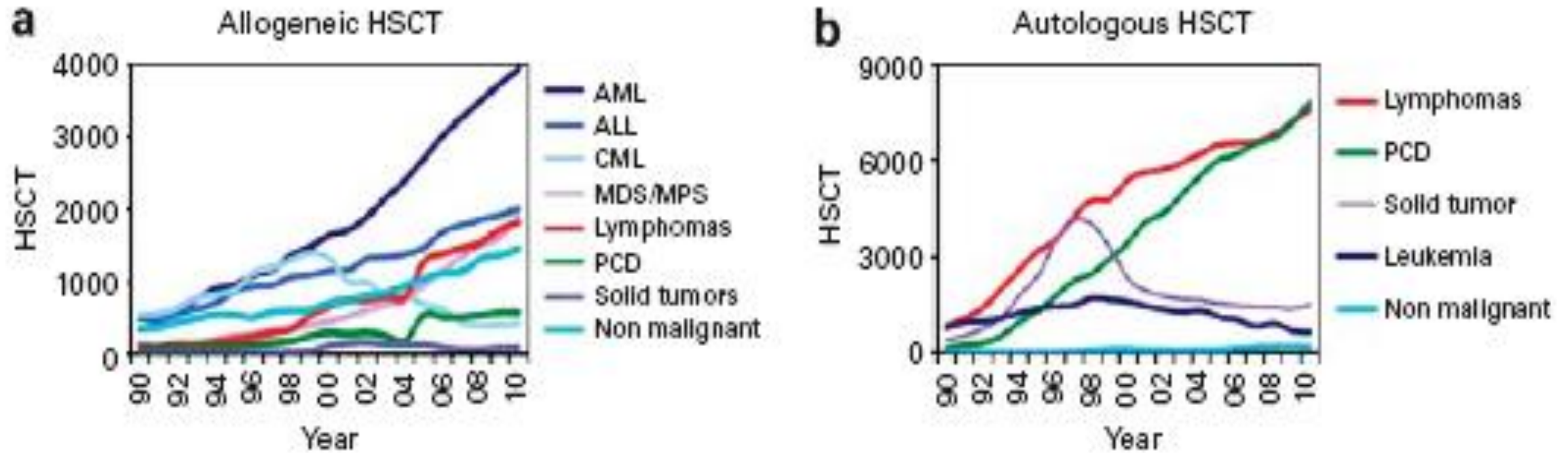
- Cyclosporine
- Steroid
- Mycophenolate mofetil
- Antithymocytic globuline
- Anti-TNF alfa, anti-Il 2



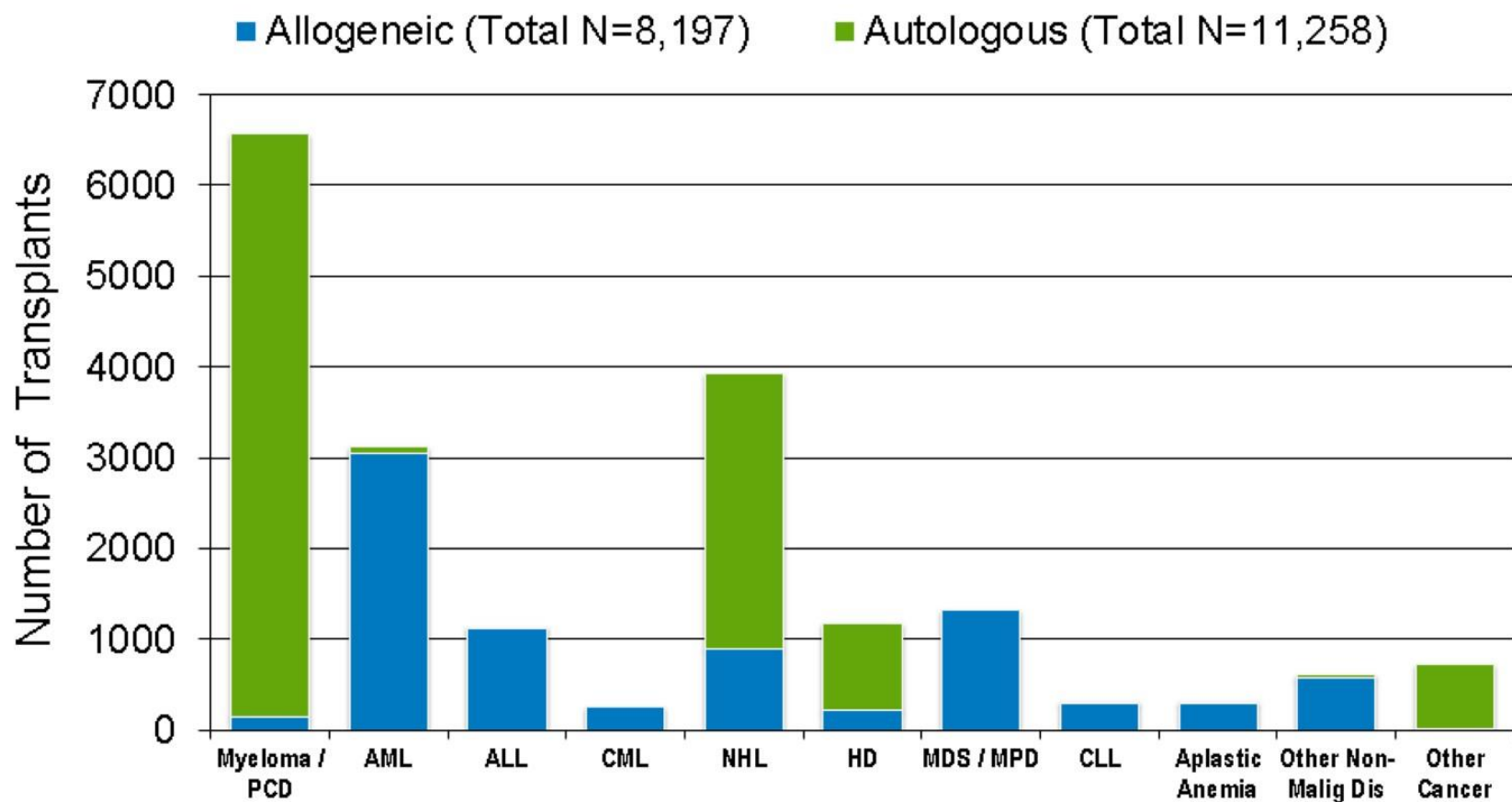
Annual Number of HCT Recipients in the US by Transplant Type



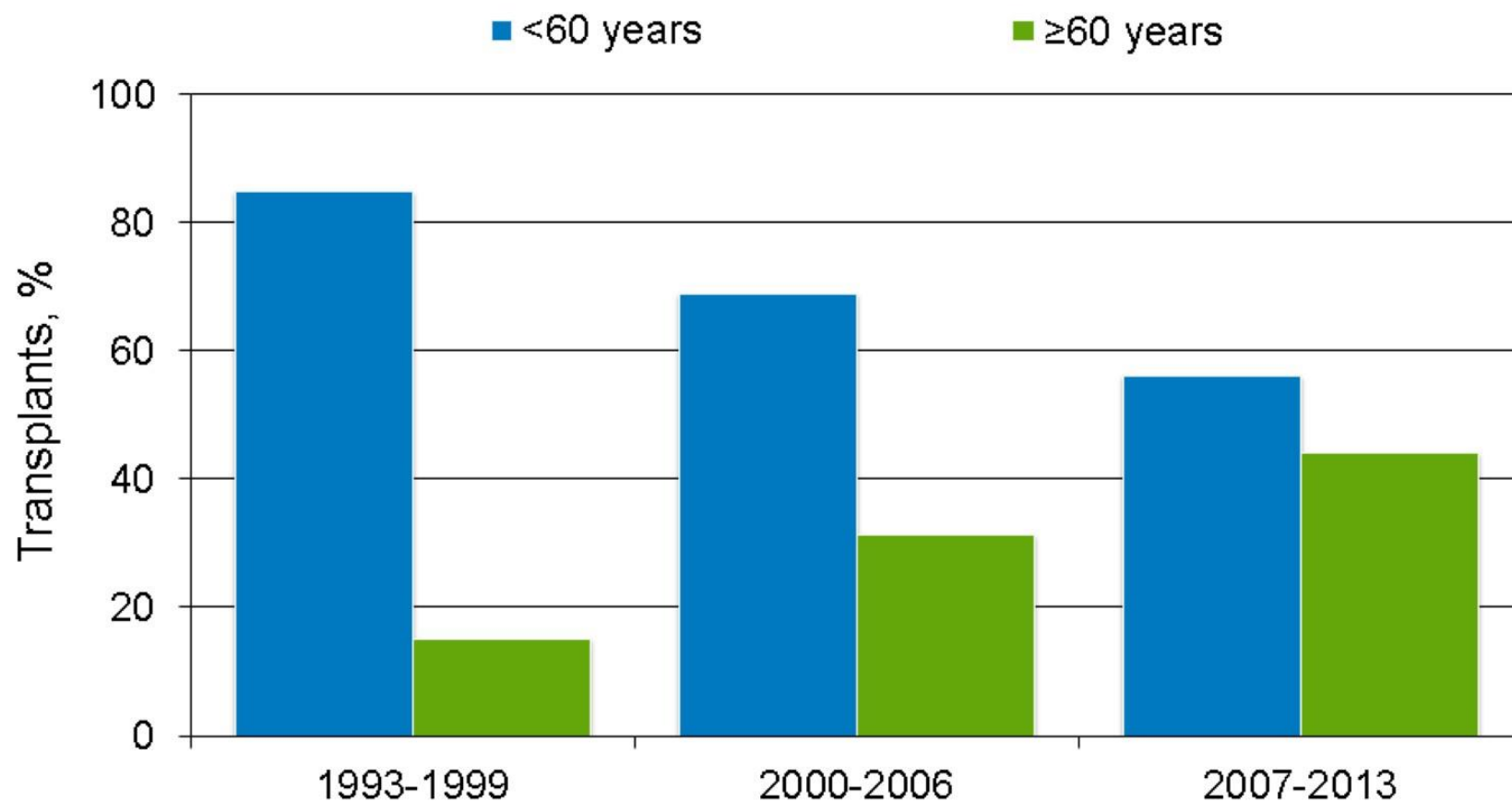
Transplant activity in Europe



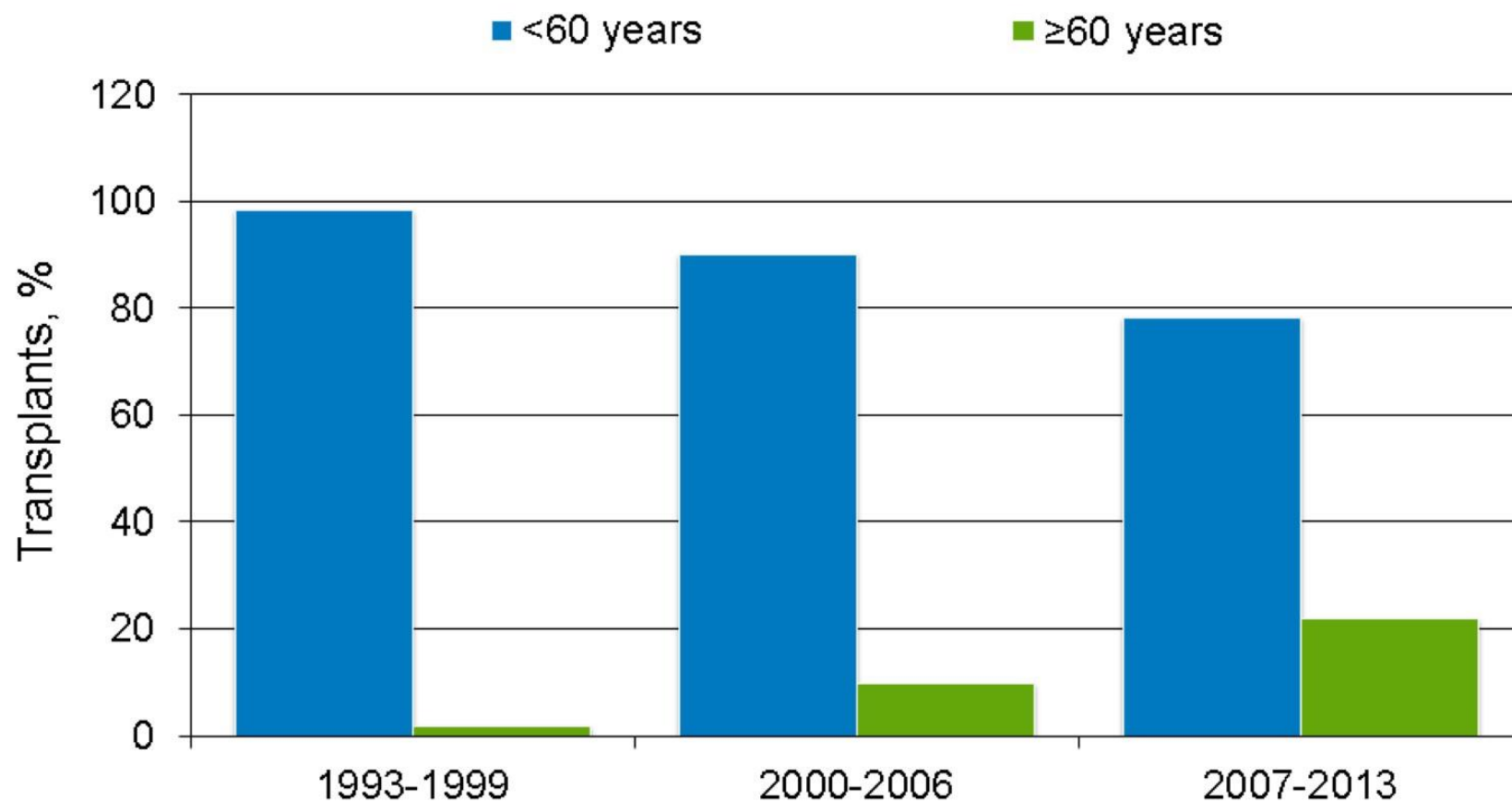
Indications for Hematopoietic Stem Cell Transplants in the US, 2013



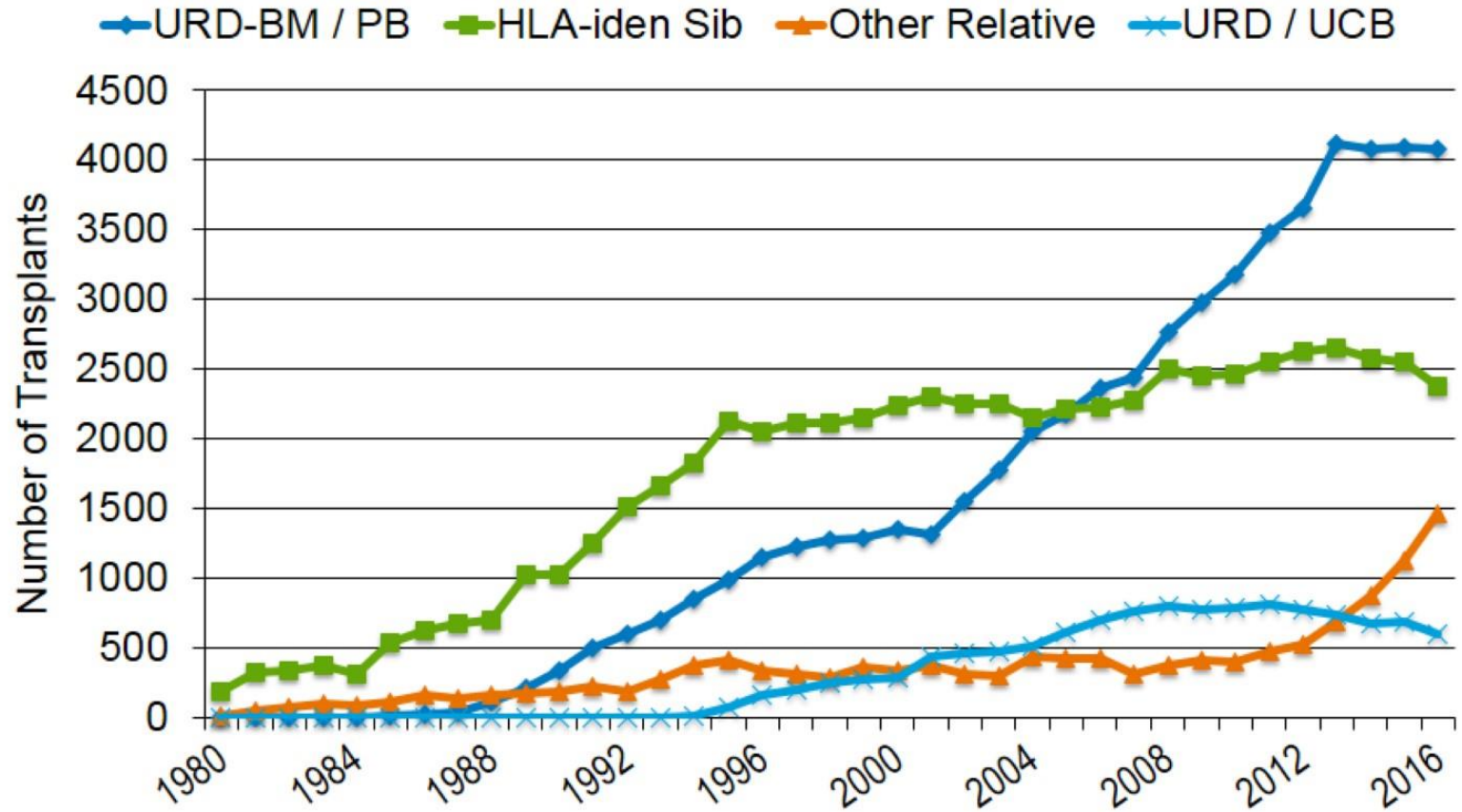
Trends in Autologous Transplants by Recipient Age*



Trends in Allogeneic Transplants by Recipient Age*



Allogeneic HCT Recipients in the US, by Donor Type



Transplant activity in Europe

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

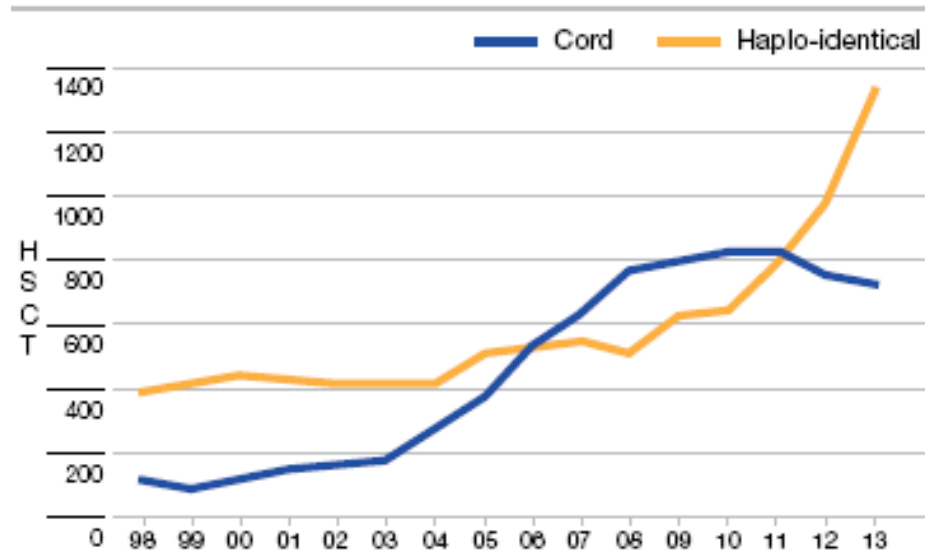
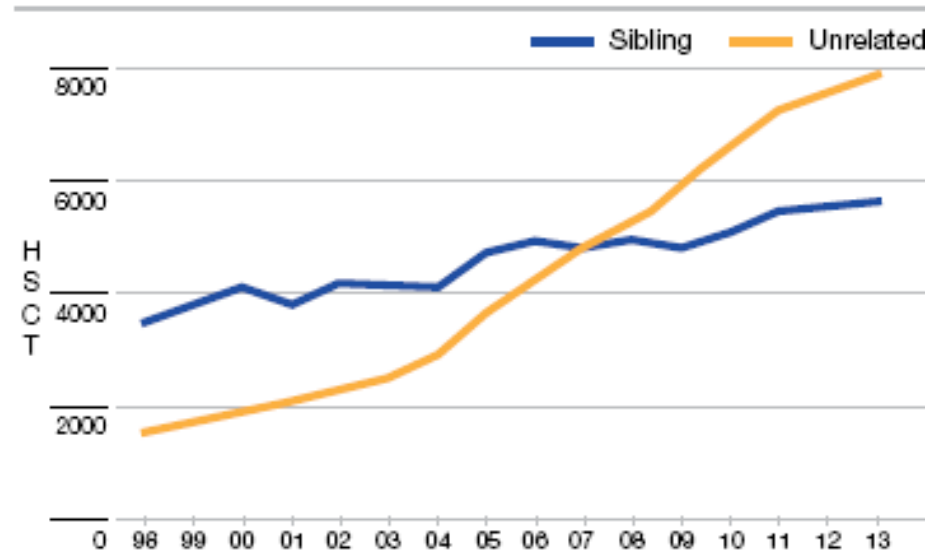


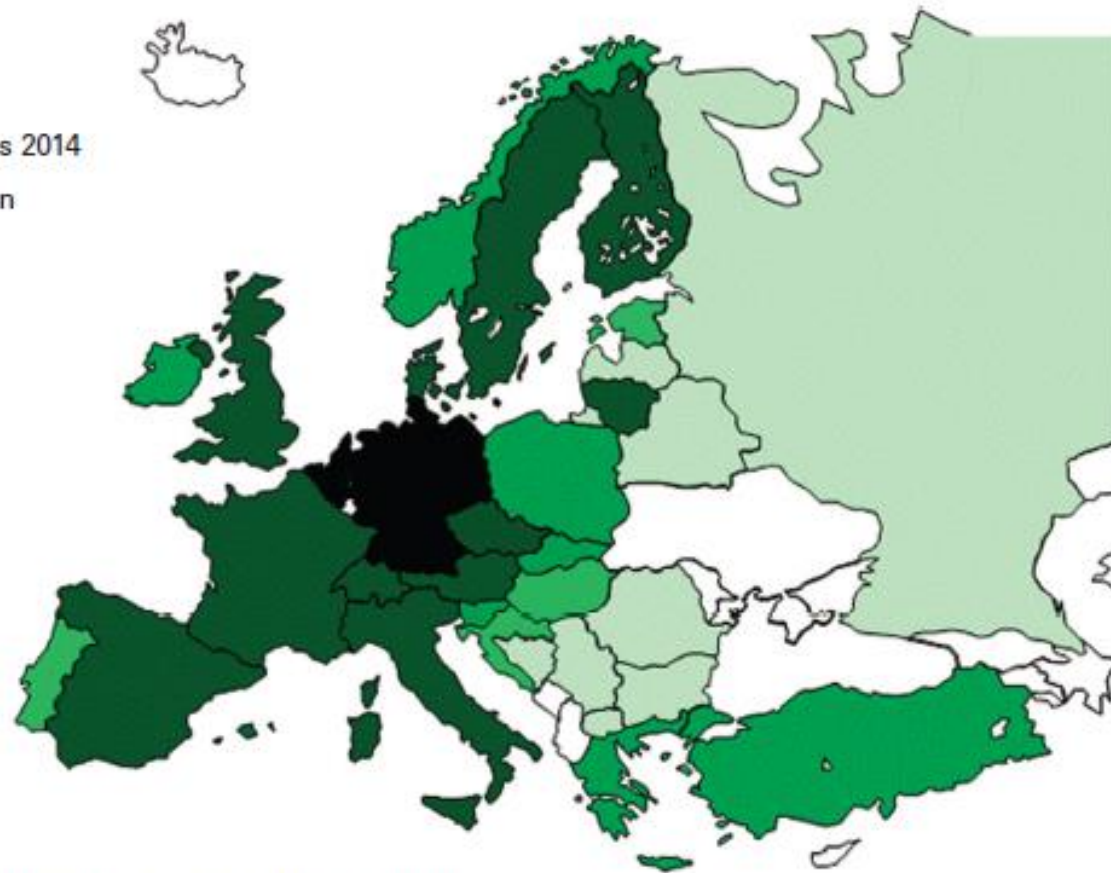
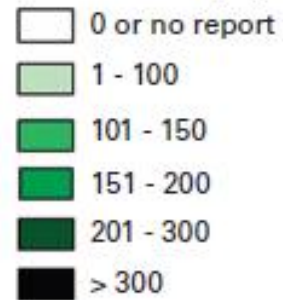
Figure 1b. Absolute numbers of sibling donor and unrelated donor HSCT in Europe 1998-2013



Transplant activity in Europe

a

N. allogeneic transplants 2014
per 10 million population



Transplant activity in Europe

b

N. autologous transplants 2014

per 10 million population

0 or no report

1 - 100

101 - 200

201 - 300

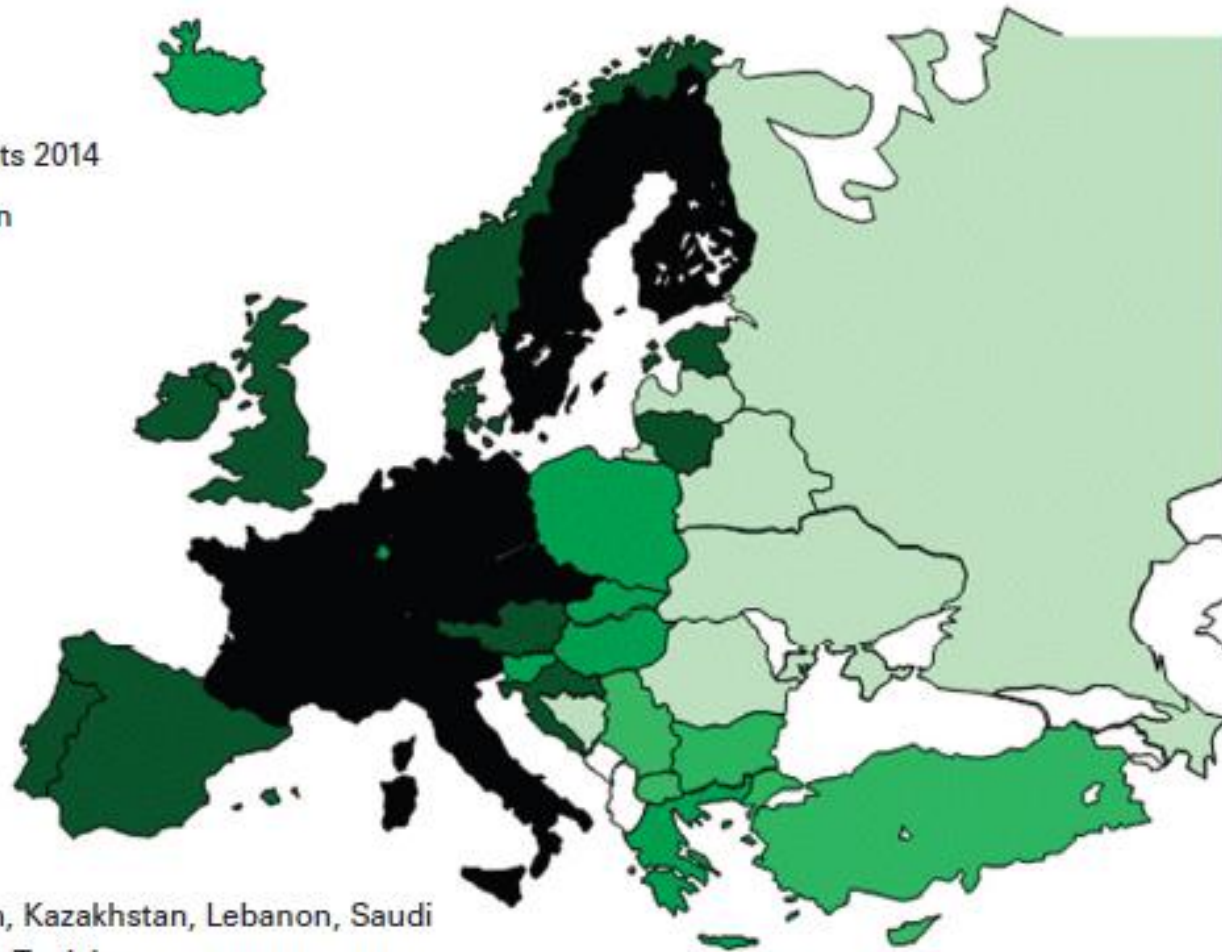
301 - 400

> 400

Nigeria

Algeria, Iran, Jordan, Kazakhstan, Lebanon, Saudi Arabia, South Africa, Tunisia

Israel



Poznan University of Medical Sciences, Department of Hematology

BMT Unit

- **first transplant - 1990**
- **>1800 transplants performed**
- **>120 procedures per year**
- **accreditation of European Group for Blood and Bone Marrow Transplantation (CIC 730; www.ebmt.org)**
- **accreditation of NMDP**

Plasticity and transdifferentiate of stem cells:
potential clinical impact in regenerative
medicine

