

An Overview of Blood and Marrow Transplantation

October 24, 2009

Stephen Couban
Department of Medicine
Dalhousie University

Objectives

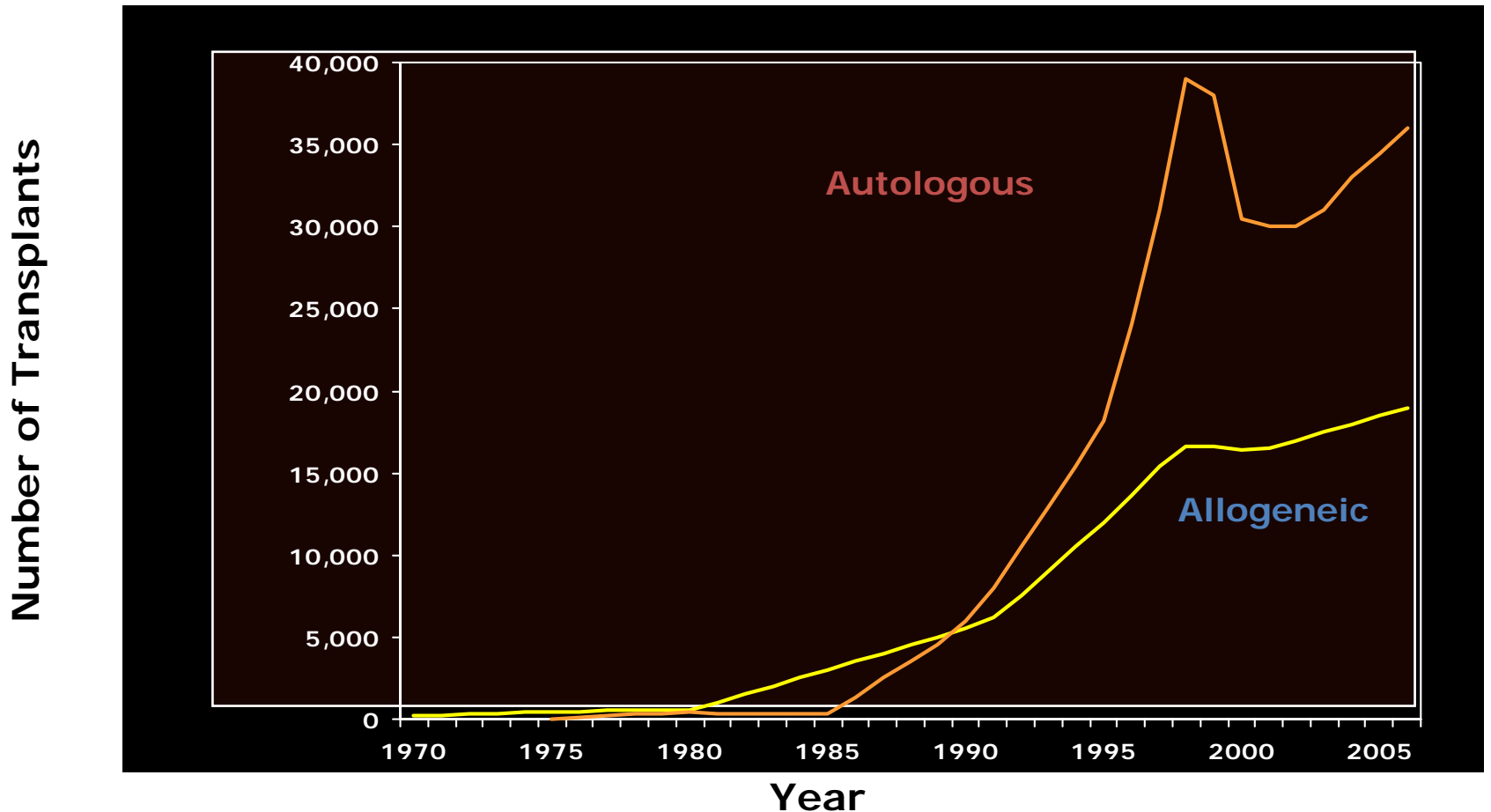
- What are the types of blood and marrow transplantation?
- Who may benefit from transplantation?
- Main diseases for which blood and marrow transplantation is undertaken
- What is graft versus host disease?

Goals of BMT

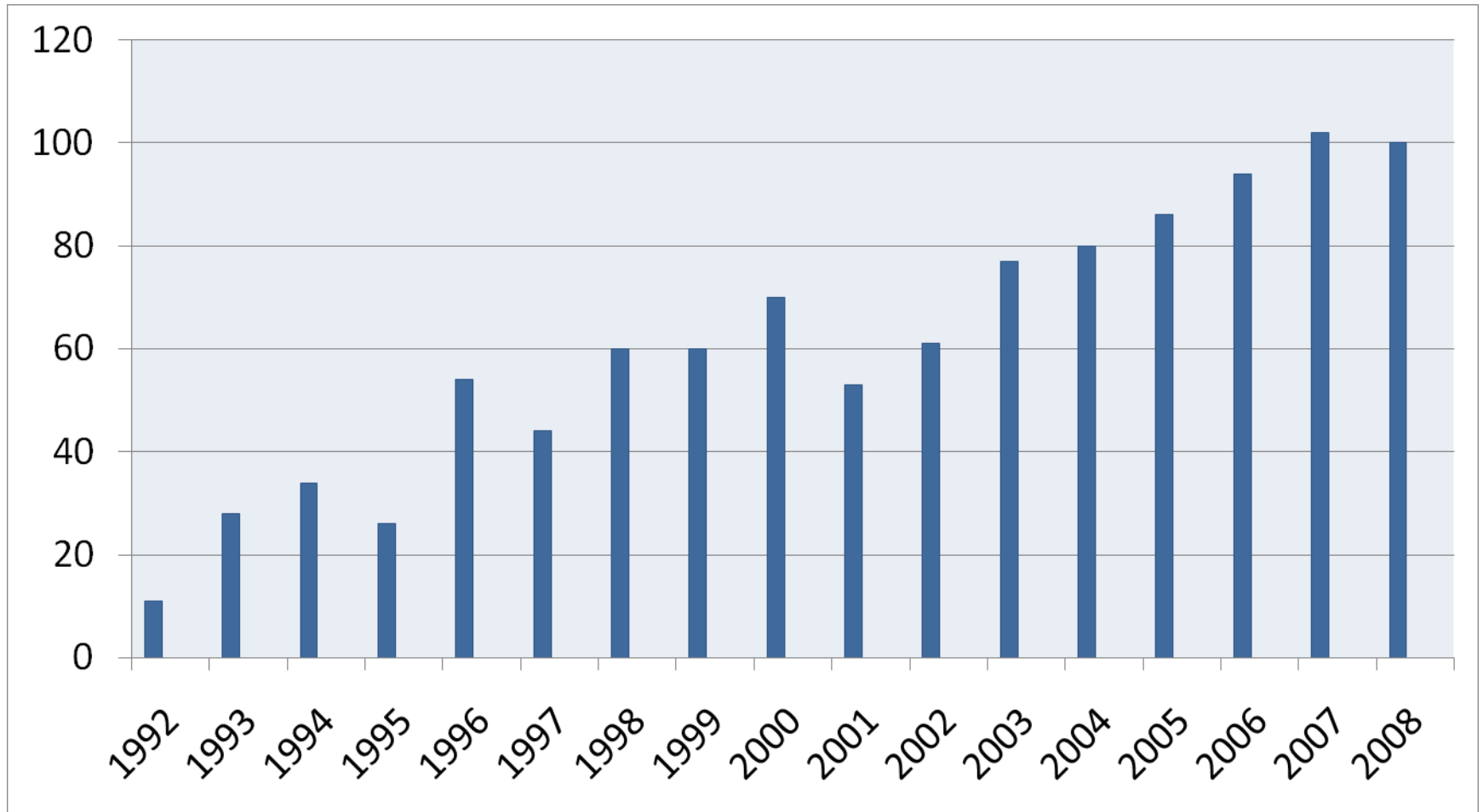
- Cancer therapy
 - Cure or prolongation of remission
- Marrow replacement
 - Aplastic anemia, thalassemia, sickle cell disease
- Developmental
 - Connective tissue diseases: scleroderma
 - Multiple sclerosis
 - Brain tumours
 - (Breast Cancer)

Annual Numbers of Blood and Marrow Transplantations, 1970-2006

- Worldwide -



Halifax Transplant Activity 1992-2008



Types of Transplant

```
graph TD; A[Types of Transplant] --> B[Autologous]; A --> C[Syngeneic]; A --> D[Allogeneic]; D --> E[Related]; D --> F[Volunteer Unrelated];
```

Autologous

Syngeneic

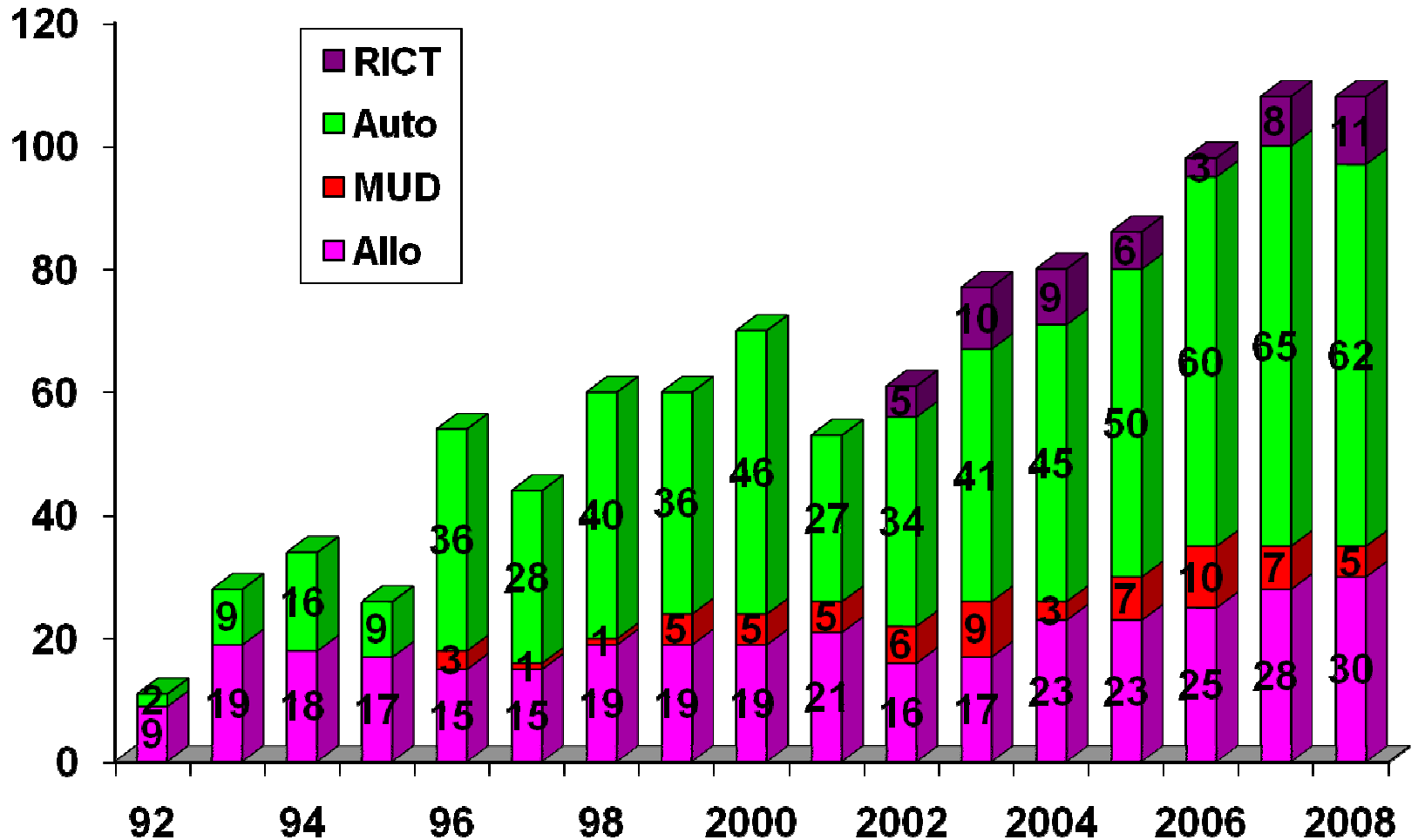
Allogeneic

Related

Volunteer
Unrelated

Halifax Transplants by Type

Auto vs Allo vs MUD vs RICT



Types of Transplant

```
graph TD; A[Types of Transplant] --> B[Autologous]; A --> C[Syngeneic]; A --> D[Allogeneic]; D --> E[Related]; D --> F[Volunteer Unrelated];
```

Autologous

Syngeneic

Allogeneic

Related

Volunteer
Unrelated

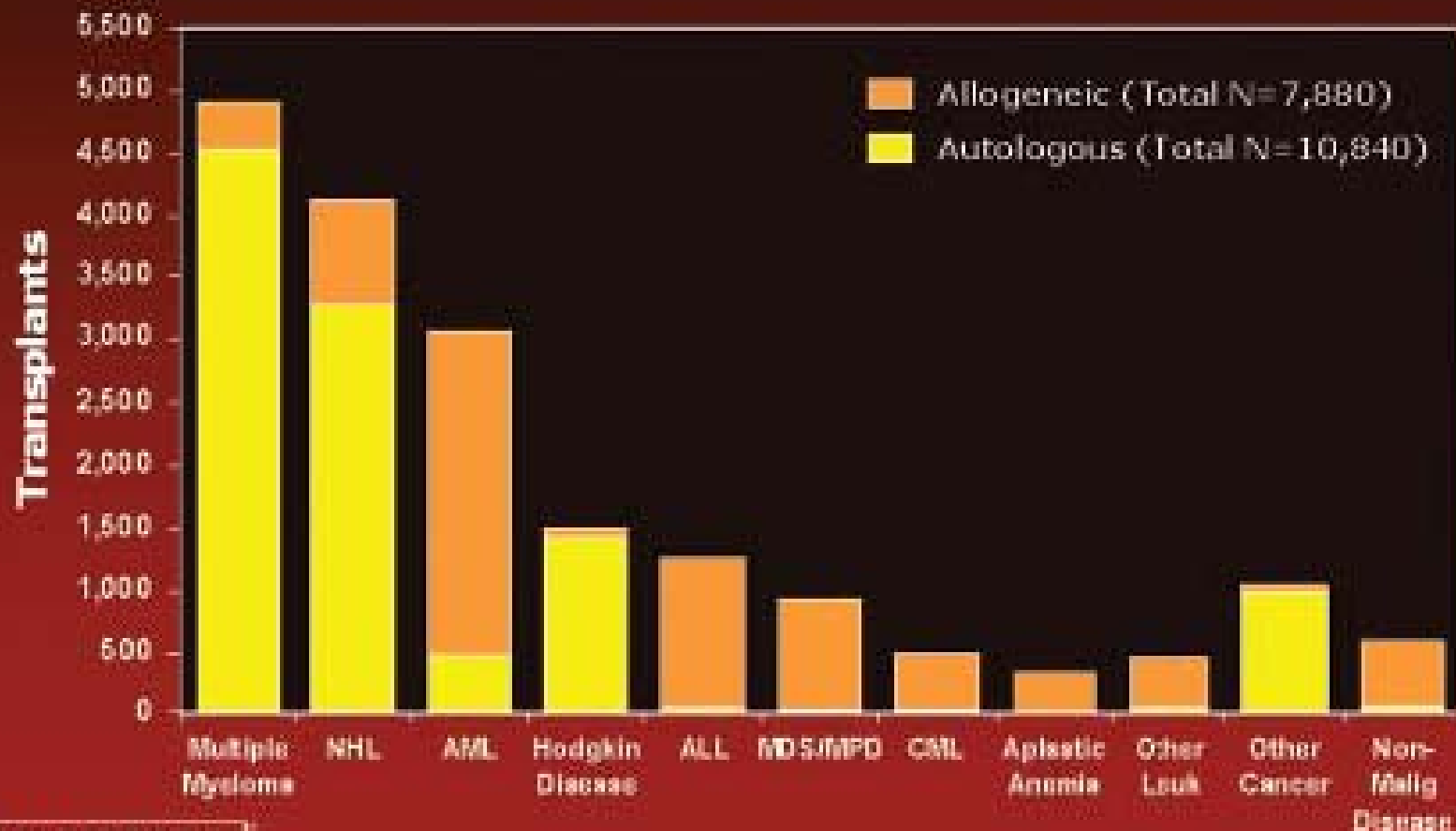
Autologous Transplant

- Age
 - ≤ 65 years old
 - ≤ 70 years old for myeloma
- Performance State
 - Organ function (heart, lungs, liver, kidneys)
- Chemosensitivity

Diseases for Autologous Transplantation

- Myeloma
 - Era of novel therapies
- Relapsed Lymphoma
 - Non-Hodgkin's lymphoma
 - Hodgkin lymphoma
- Acute Leukemia
- Solid Tumours
 - Germ cell tumour
 - (breast cancer)

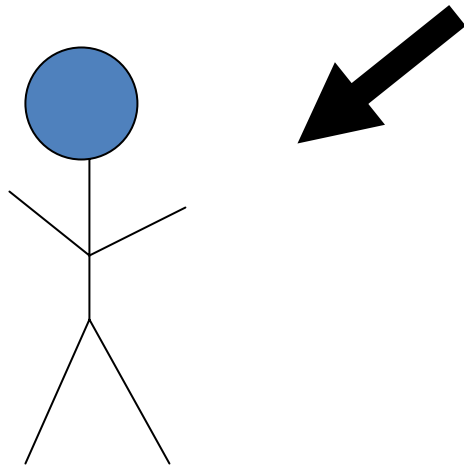
Indications for Hematopoietic Stem Cell Transplantation in North America 2005



Autologous Transplant: Stages

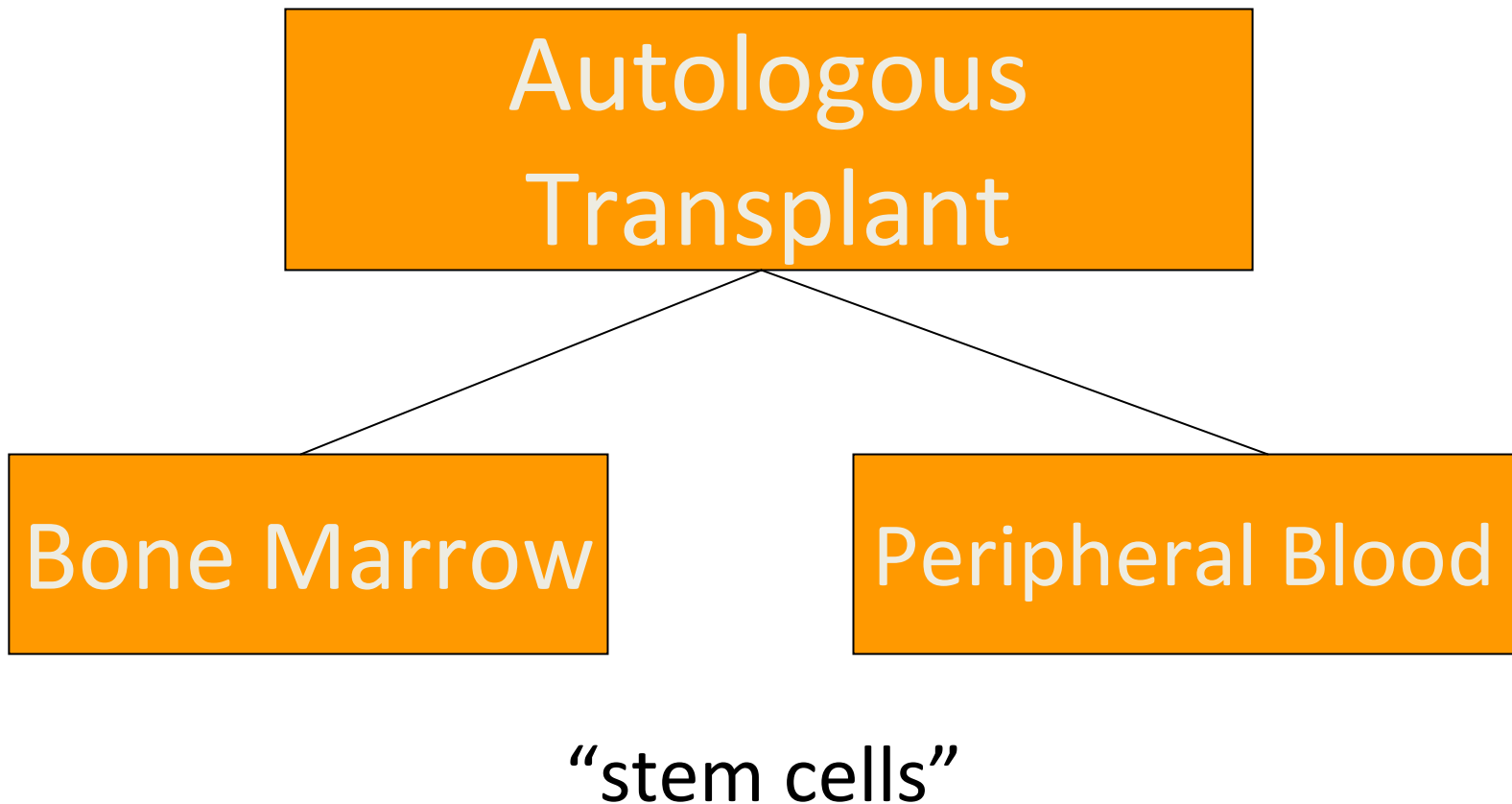
1. Pre-transplant chemotherapy
2. Harvest
3. Conditioning
4. Infusion
5. Recovery

1. Pre-Transplant Chemotherapy

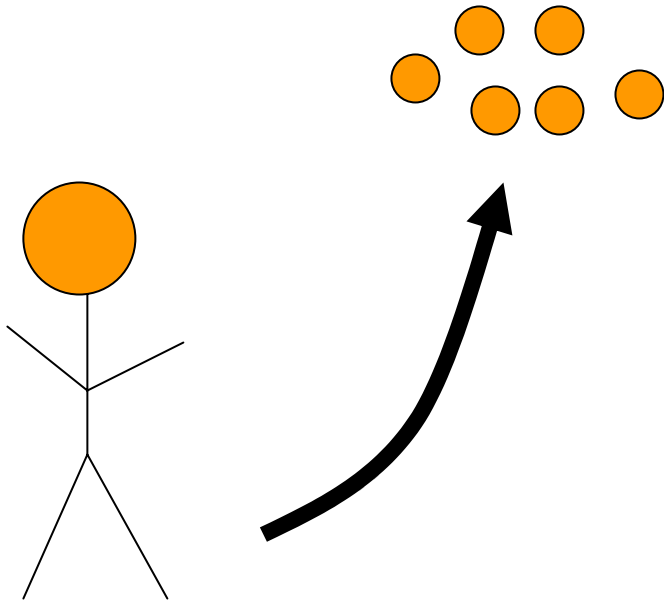


- Chemosensitivity
- In vivo purging

2. Harvest: Source of Cells

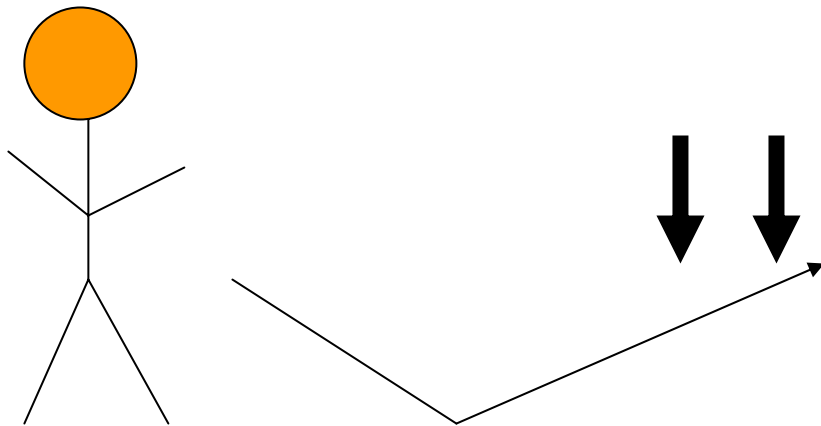


Bone Marrow Harvest



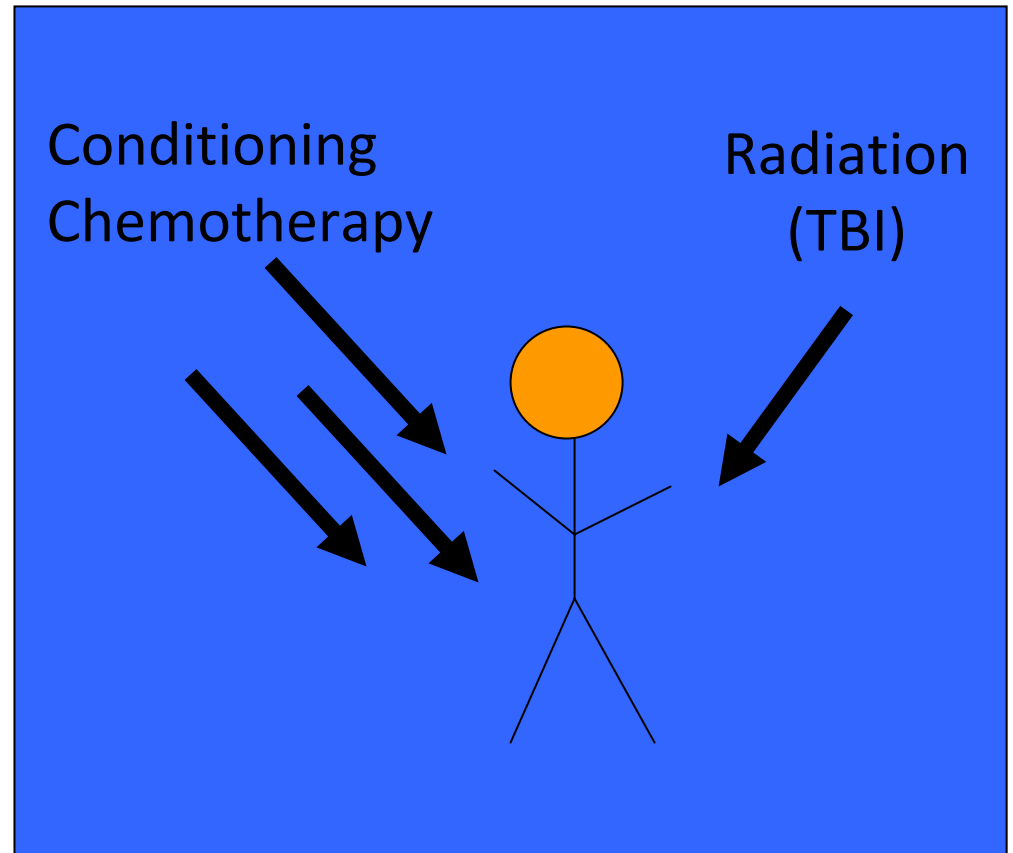
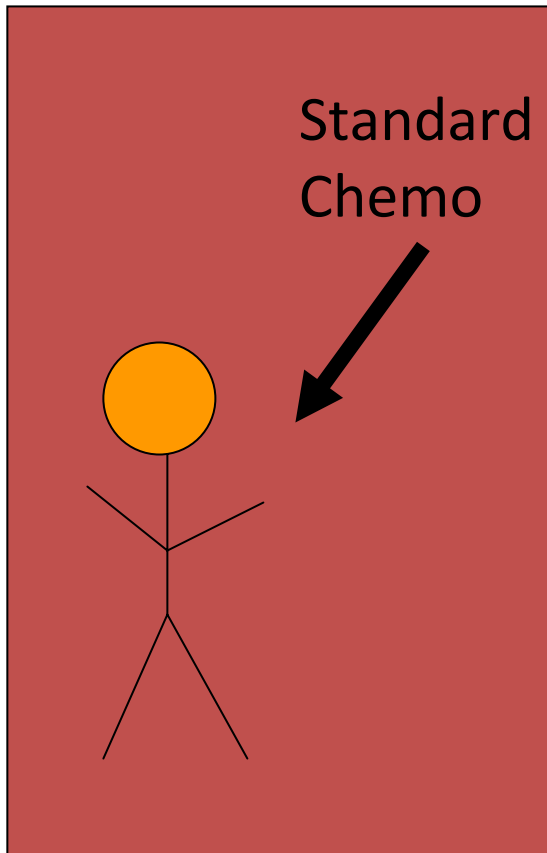
- Advantages
 - No chemotherapy
 - No growth factors
 - One day
- Disadvantages
 - General anesthetic
 - Large volume

Peripheral Blood Harvest

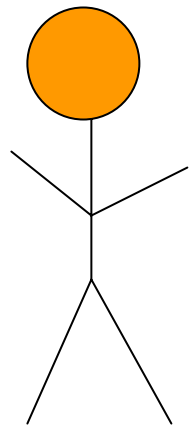


- Advantages
 - No general anesthetic
 - Small volume
 - **Engraftment**
- Disadvantages
 - Chemotherapy
 - Growth factors
 - Apheresis

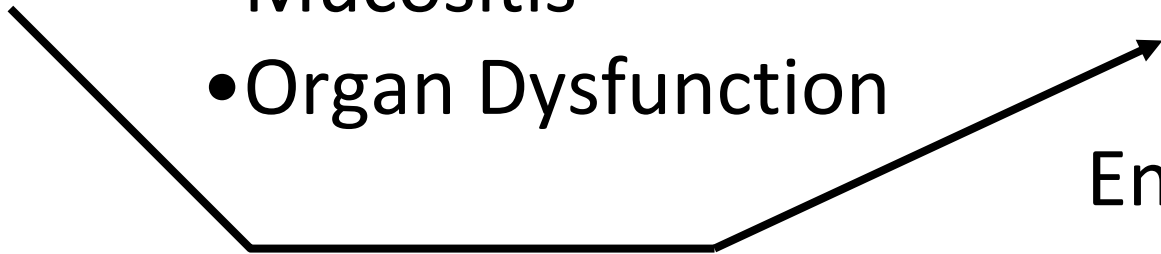
3. Conditioning



4+5. Infusion to Engraftment



- Infection
- Bleeding
- Mucositis
- Organ Dysfunction



Engraftment

Late Effects

- Organ Damage: pulmonary, cardiac, renal
- Second Cancers
- Endocrinopathies
- Cataracts
- Infertility
- Relapse

Shelley beats odds – twice



Mrs. Dymally, the patient, and her baby.

Marrow transplant patient gives birth

The Dymally family has a new member. Mrs. Dymally, 34, is a patient at the University of California Medical Center in San Francisco. She has a history of leukemia and has received a bone marrow transplant. She is now pregnant with a baby due in July.

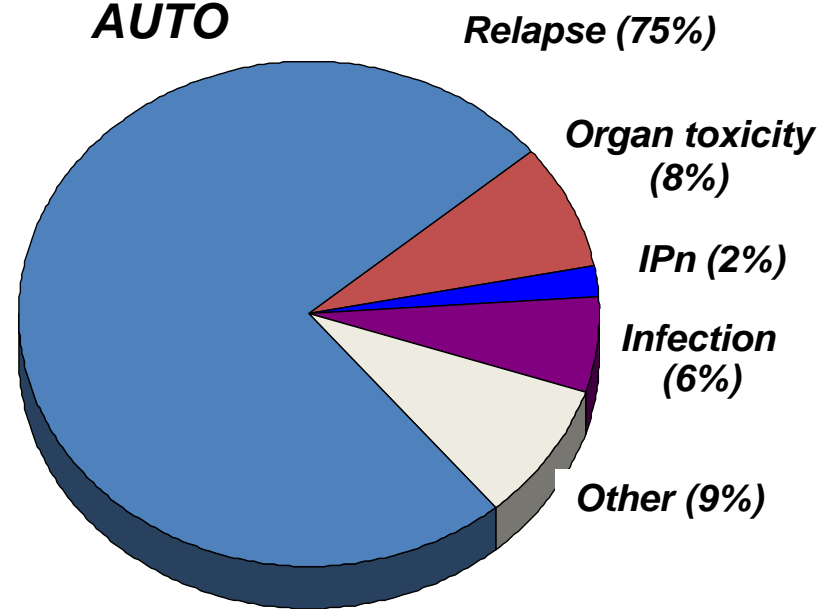
The first time Mrs. Dymally was pregnant was about two years ago. She had a healthy baby, but she had to have a cesarean section because of her leukemia. The second time she was pregnant was about a year ago. She had a healthy baby, but she had to have a cesarean section because of her leukemia. Mrs. Dymally had a very difficult pregnancy and delivery. She had to be in bed for several weeks after the birth of her baby. She is now recovering from the surgery and is doing well.

"It was something we really wanted," says Mrs. Dymally. "I was worried, but I had a positive attitude." Mrs. Dymally's doctor says, "It was something we really wanted." The baby is healthy and is doing well. Mrs. Dymally is now recovering from the surgery and is doing well.

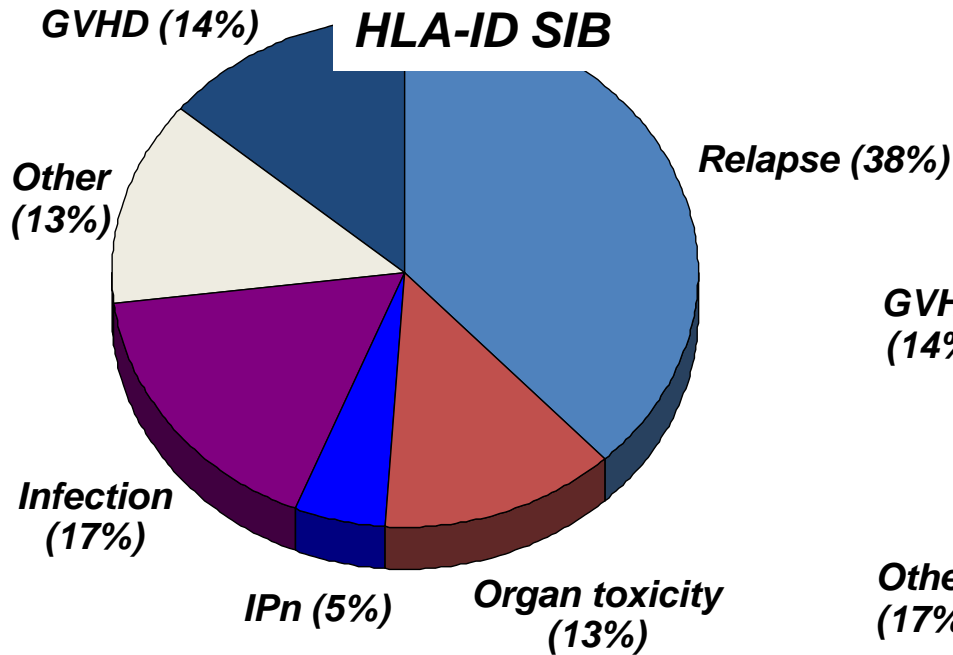
...and a healthy baby. Mrs. Dymally is now recovering from the surgery and is doing well. The baby is healthy and is doing well. Mrs. Dymally is now recovering from the surgery and is doing well. The baby is healthy and is doing well. Mrs. Dymally is now recovering from the surgery and is doing well. The baby is healthy and is doing well.

Causes of Death after Transplants

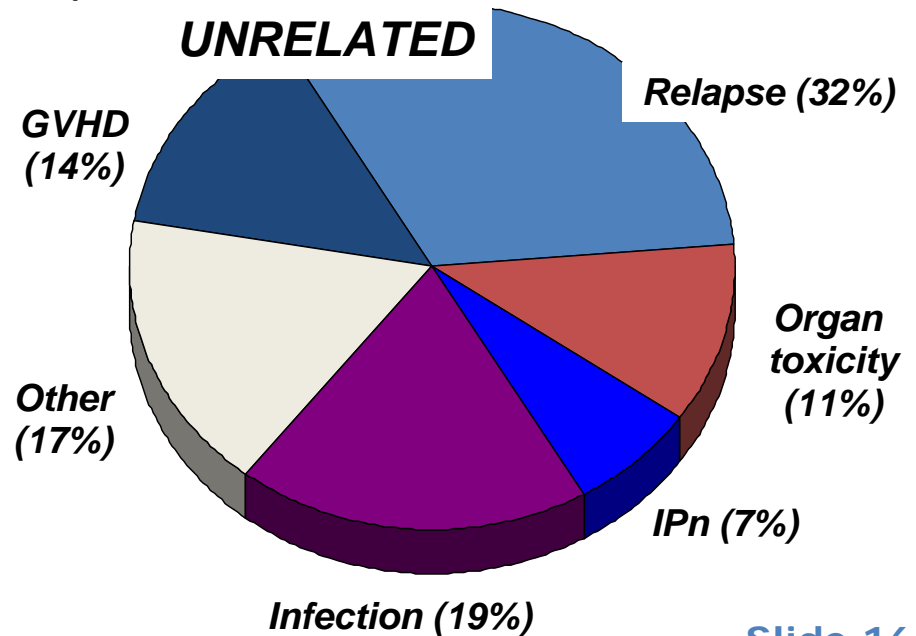
AUTO



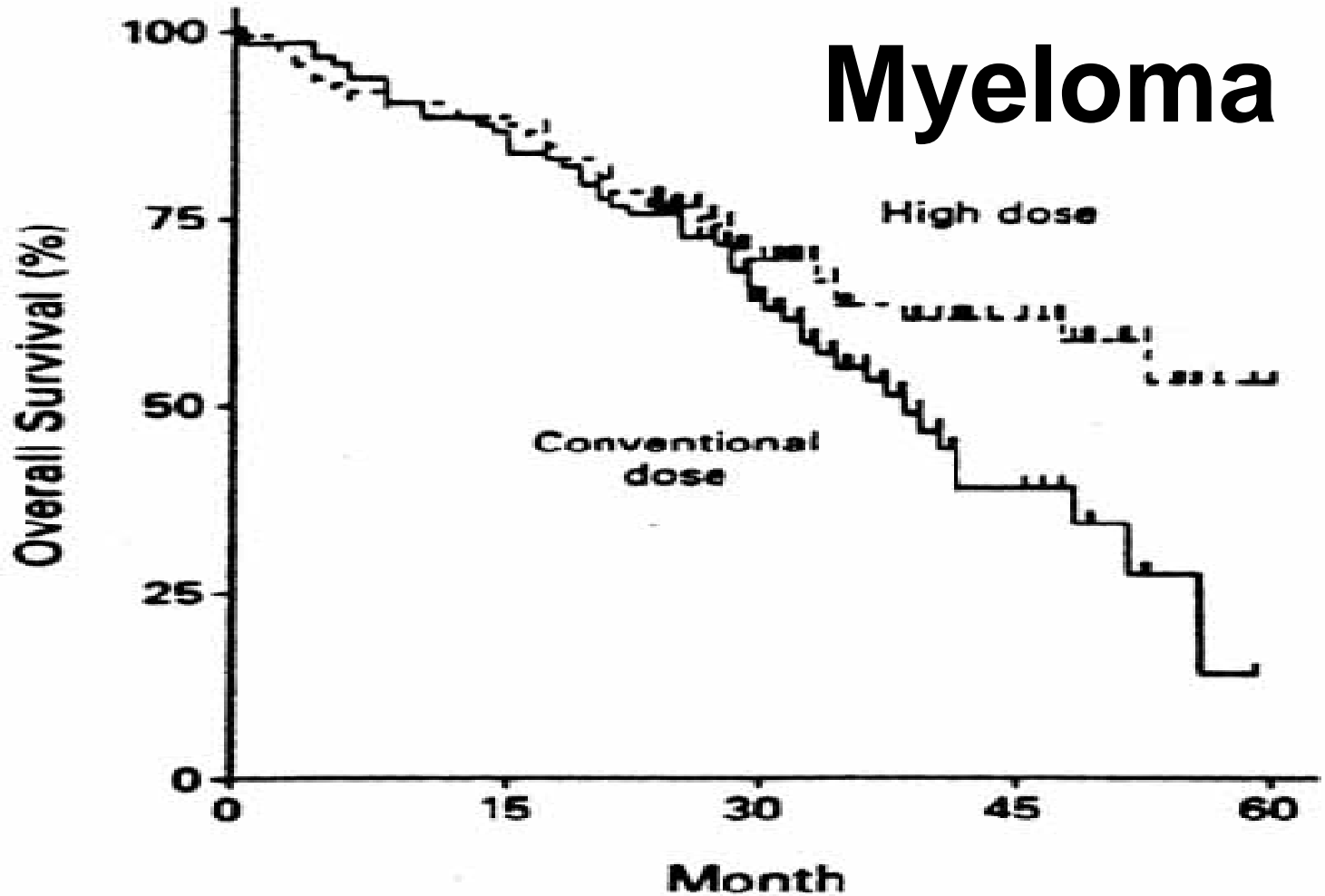
HLA-ID SIB



UNRELATED

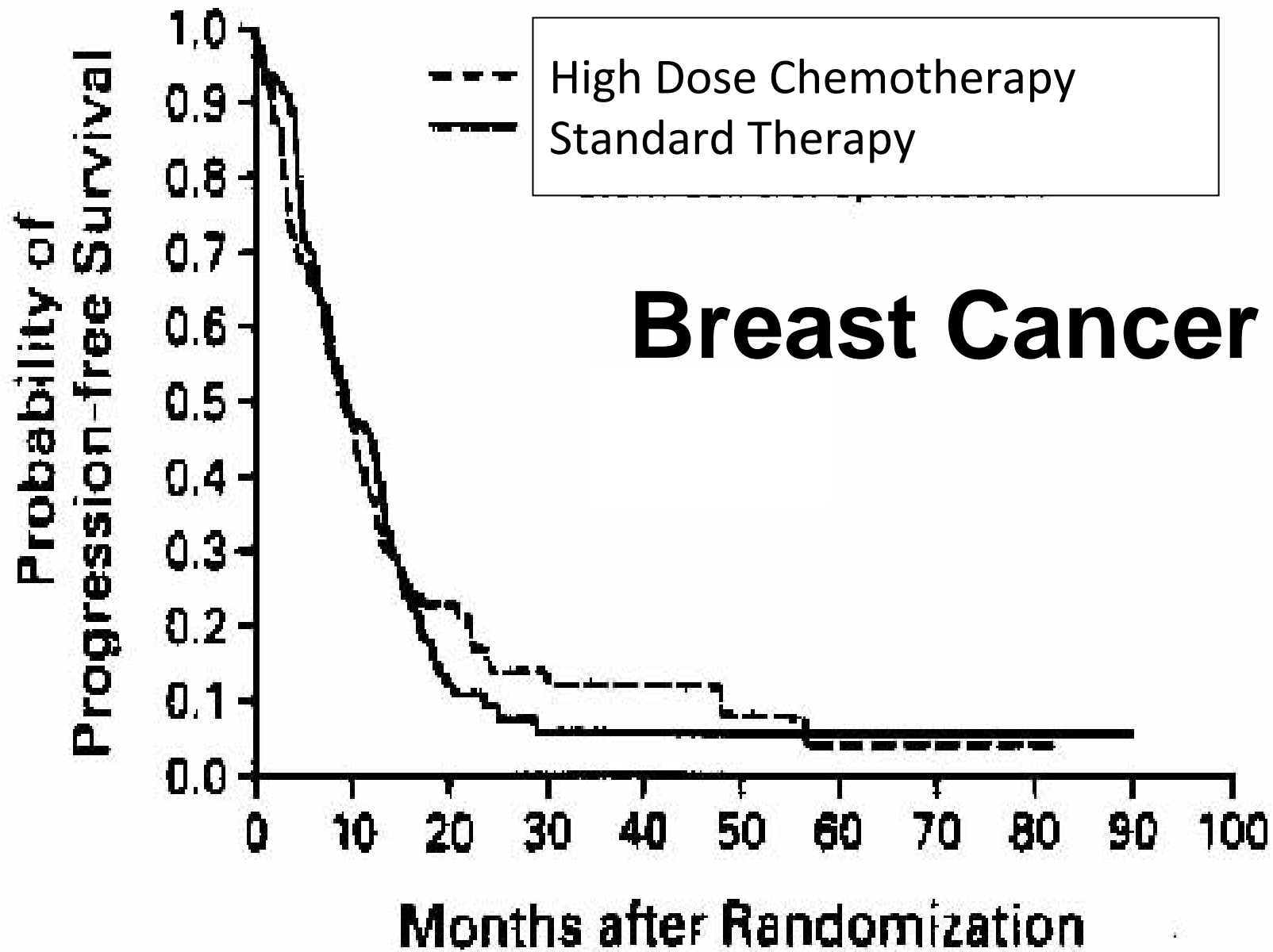


Myeloma



Conventional dose	63 (53-73)	35 (22-50)	12 (1-40)
High dose	69 (58-78)	61 (50-71)	52 (36-67)

Figure 2. Overall Survival According to Treatment Group.
 The numbers shown below the time points are probabilities of overall survival (the percentages of patients surviving) and 95 percent confidence intervals.



Allogeneic Transplantation

Types of Transplant

```
graph TD; A[Types of Transplant] --> B[Autologous]; A --> C[Syngeneic]; A --> D[Allogeneic]; D --> E[Related]; D --> F[Volunteer Unrelated];
```

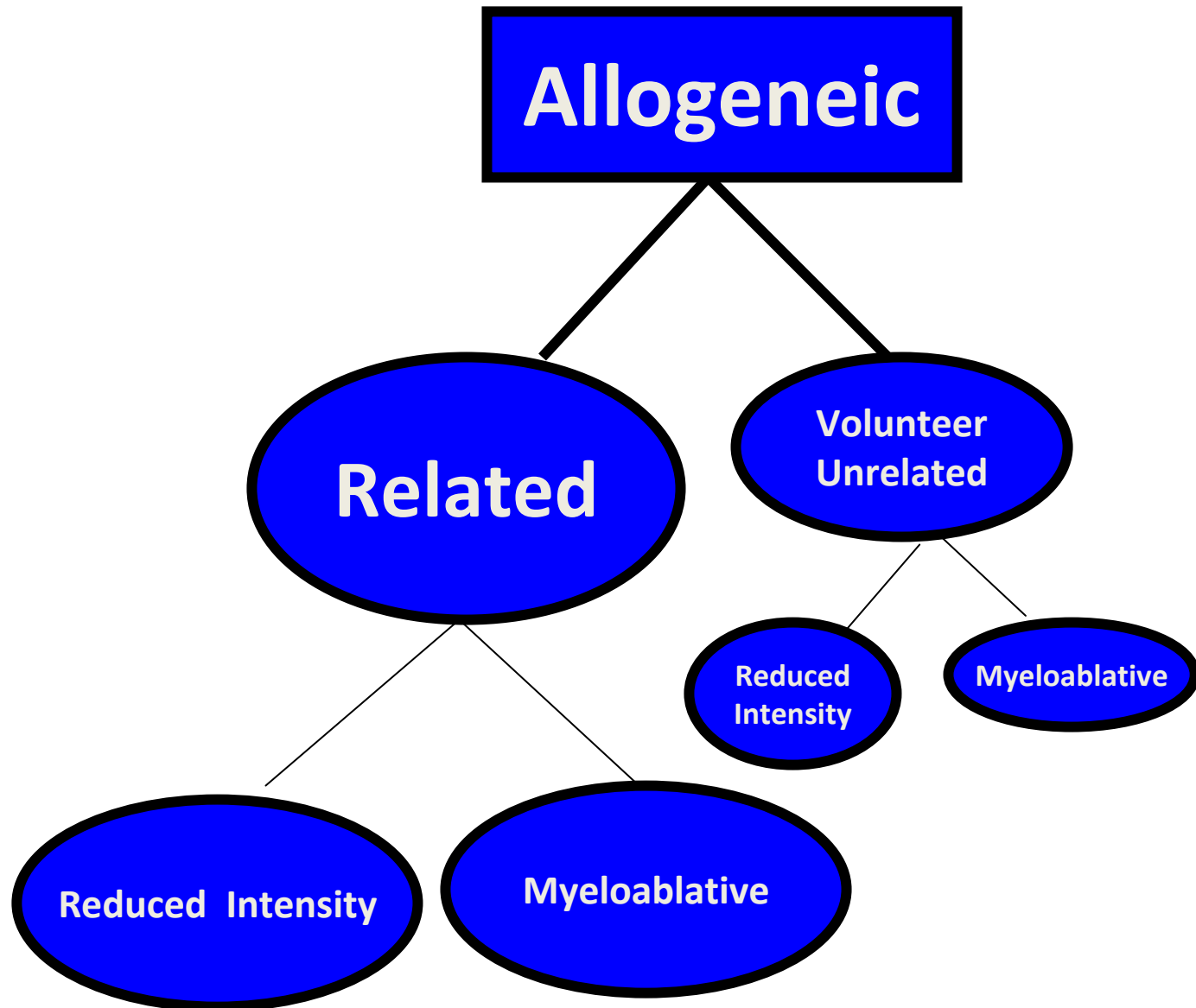
Autologous

Syngeneic

Allogeneic

Related

Volunteer
Unrelated



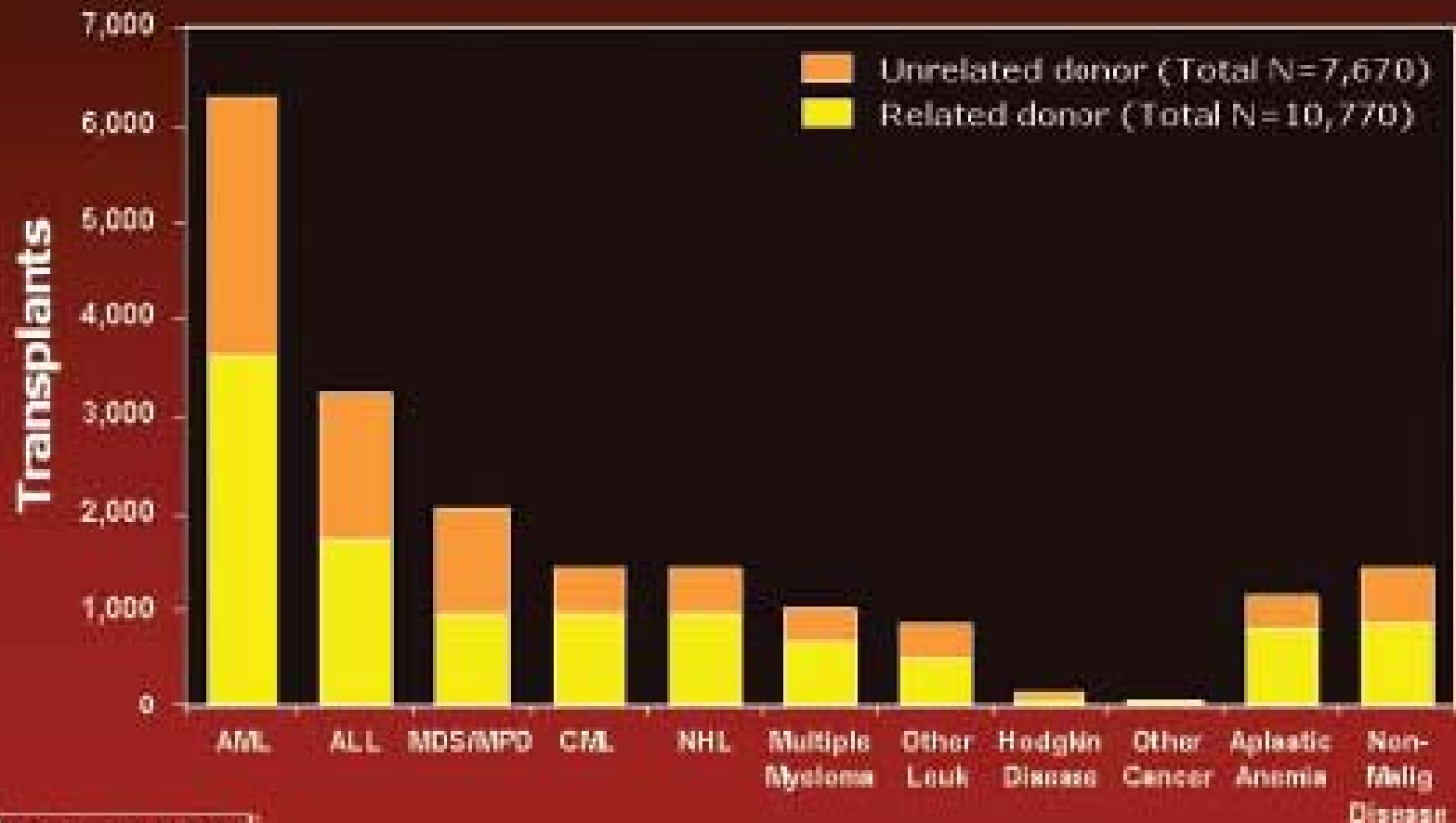
Allogeneic Transplantation

- Age
 - \leq 55 years old
 - \leq 50 years old (unrelated)
 - \leq 65 years old (reduced intensity)
- Performance State
- (Chemosensitivity)

Allogeneic Indications

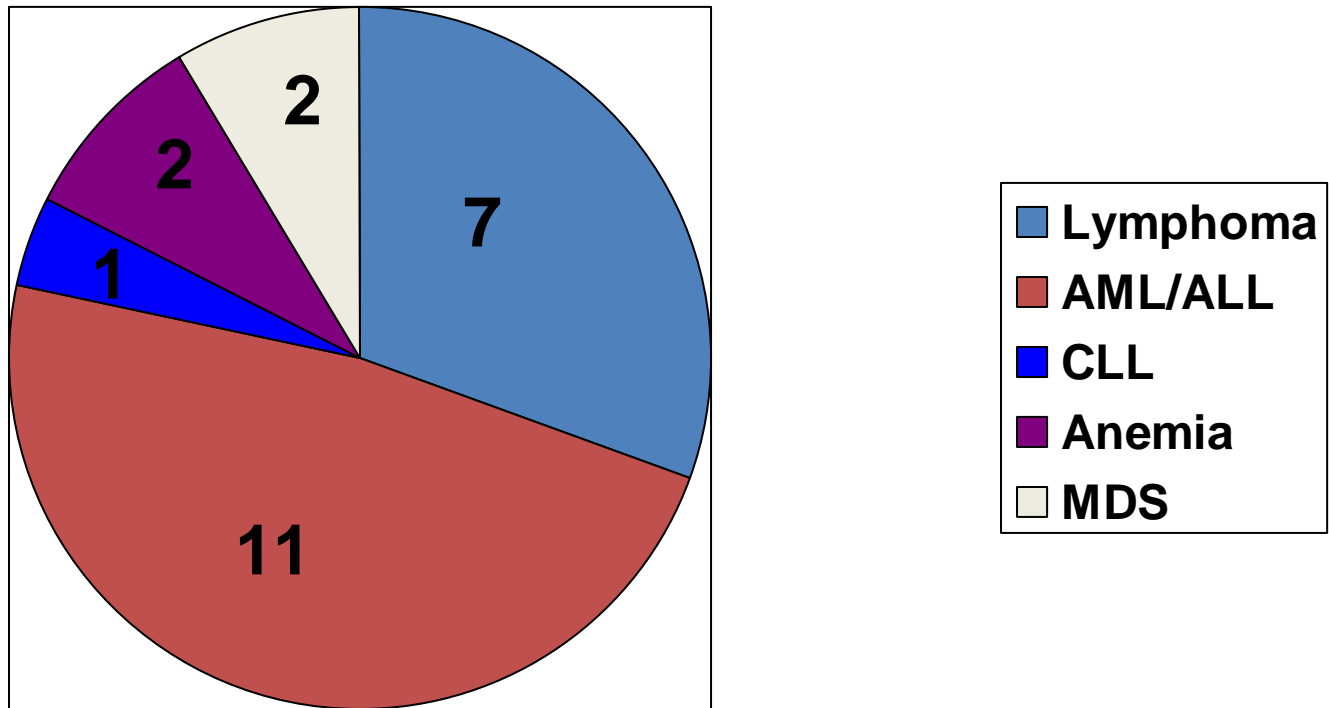
- Leukemia
 - Acute leukemia, MDS > CML, CLL
- Lymphoma
 - Indolent lymphomas
- Myeloma
 - Uncommon in 2009
- Bone marrow failure
- Diseased bone marrow

Indications for Allogeneic Hematopoietic Stem Cell Transplantation, 2005 – Worldwide



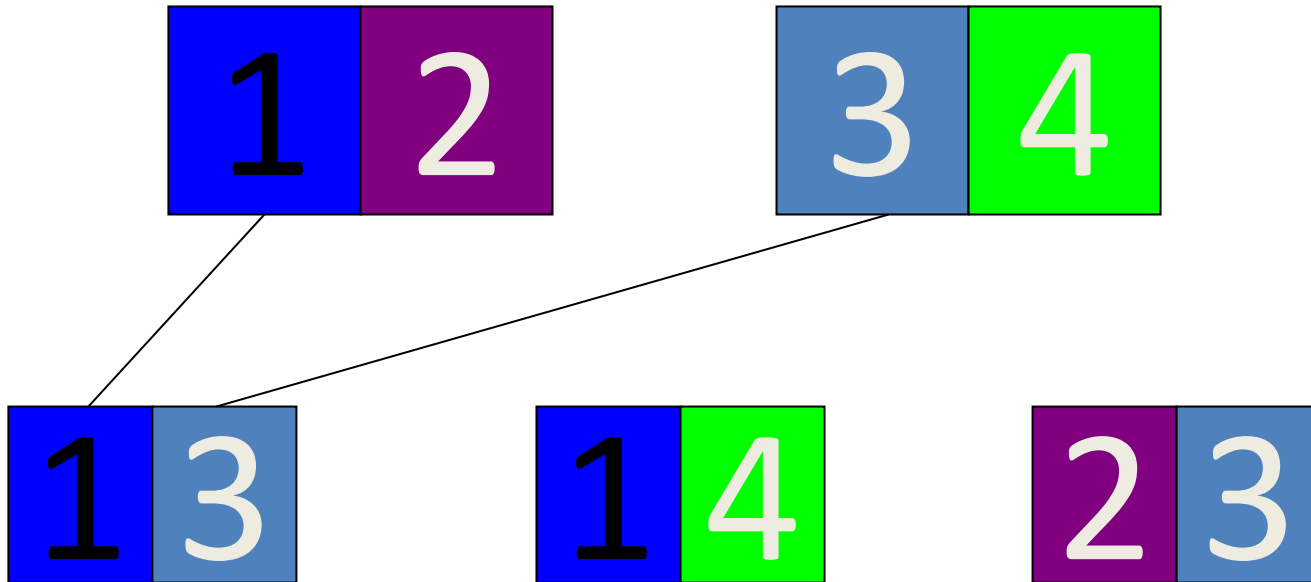
Sibling Allogeneic Transplants

Halifax: 2008

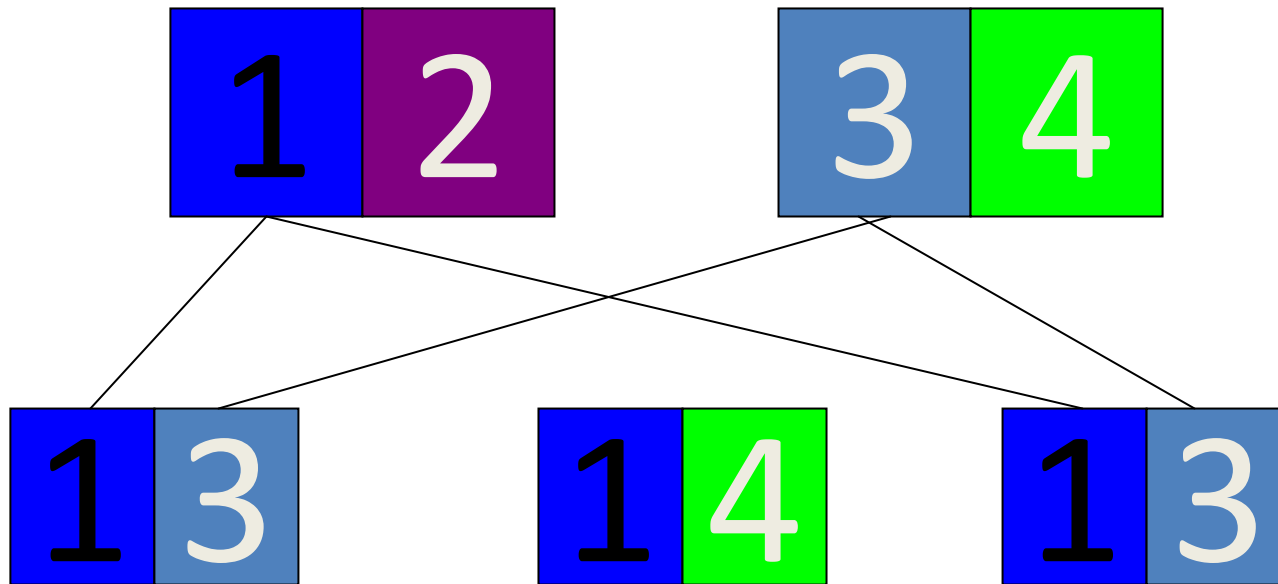


Allogeneic: The Match

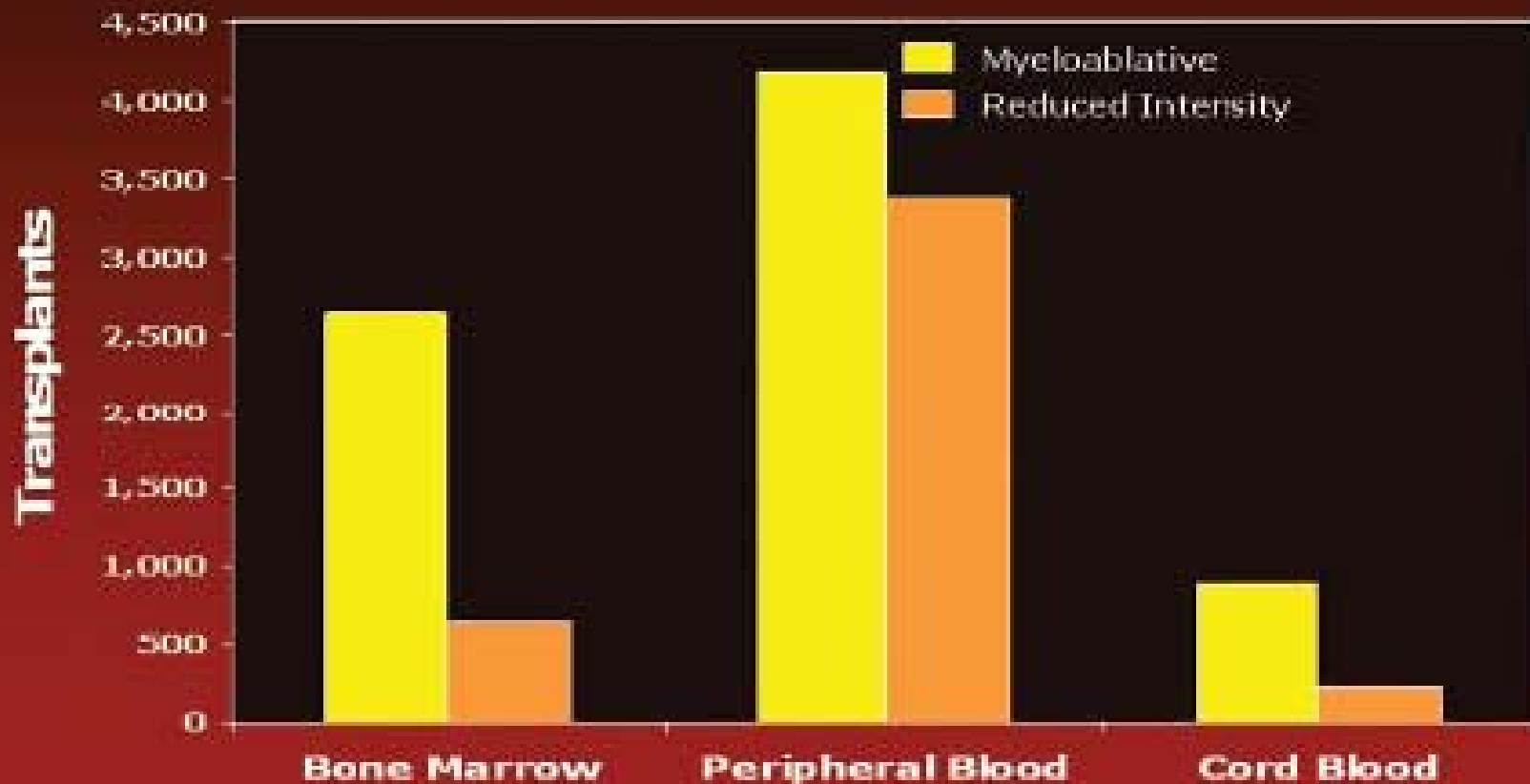
Each child inherits one set of HLA antigens from each parent

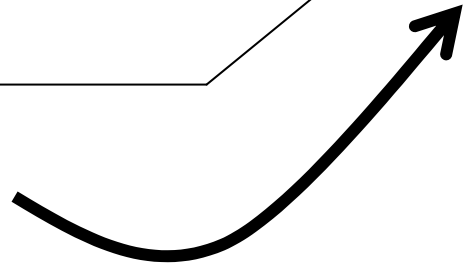


Allogeneic: The Match



Allogeneic Transplantations by Graft Source and Conditioning Regimen Intensity, Registered with the CIBMTR, 2005-2006





Graft versus Host Disease

Reverse of graft rejection

Immunologic attack of donor cells
against the recipient

Acute Graft versus Host Disease

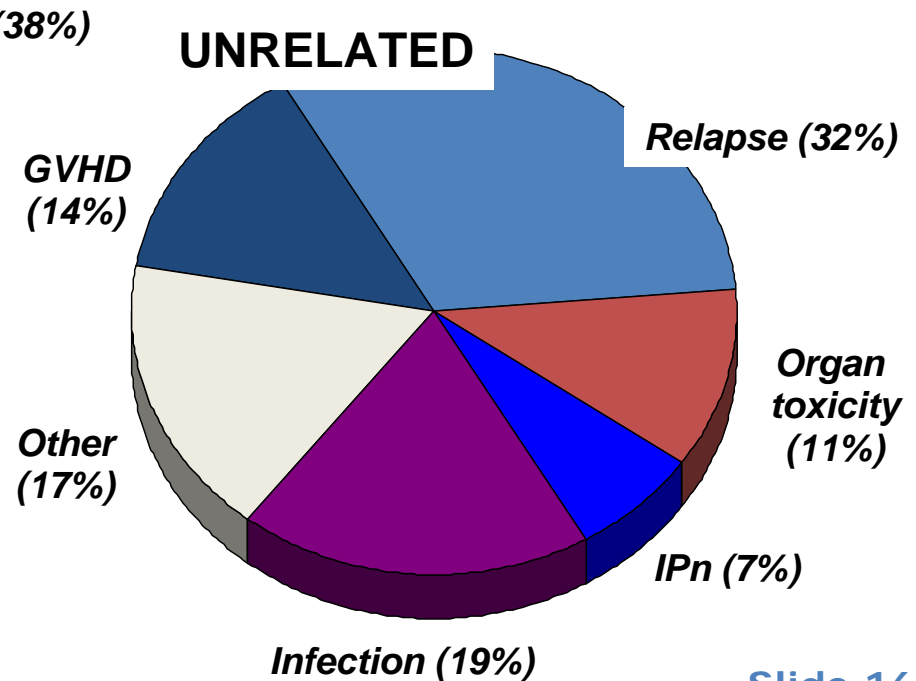
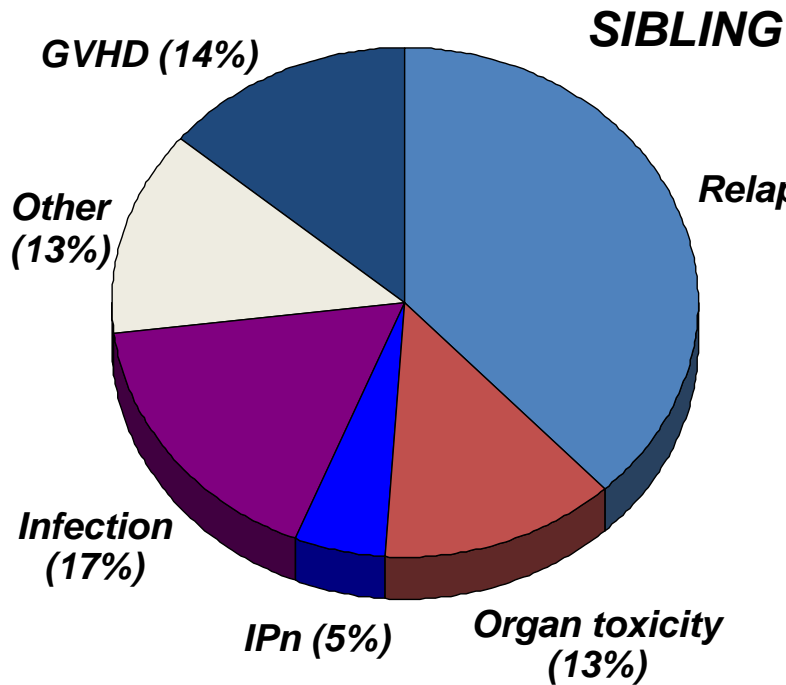
- Skin: Rash
- Liver: Inflammation
- Gut: Diarrhea
 - Characteristics

Chronic Graft versus Host Disease (cGvHD)

- Skin
 - Scleroderma
- GI tract
 - Small, dry mouth
 - Strictures
 - Chronic diarrhea
- Liver
- Eyes
 - Sicca syndrome
 - Corneal ulceration
- Nervous System
 - Peripheral neuropathy
- Lungs
 - Bronchiolitis obliterans
 - (BOOP)
- Muscles and Joints
 - Lupus-like syndrome
 - Myositis

- The Immune Effect in Allogeneic Transplant
 - A double-edged sword
 - Graft vs Host Disease
 - Graft vs Tumour Effect
 - Donor Leukocyte Infusions
 - Reduced Intensity Transplants
 - » “mini transplants”

Causes of Death after Transplants



Important Syndromes for the Internist

- Febrile Neutropenia
- CMV Infections
 - Allogeneic transplants
 - CMV pneumonia; CMV colitis; CMV hepatitis
- Pulmonary infections
 - PCP
- GvHD Syndromes
 - May mimic many connective tissue and autoimmune diseases

Important Syndromes for the Internist

- Cardiac
 - Myocardial damage related to chemotherapy, radiation
 - Acute pericarditis (GvHD)
- Pulmonary
 - Acute, subacute or chronic parenchymal lung injury from chemotherapy, radiation
 - **Bronchiolitis obliterans**
 - BOOP
 - Restriction due to scleroderma
- Renal
 - Chronic renal injury
 - Calcineurin inhibitors
- Endocrine
 - Hypothyroidism
 - Steroid-induced bone disease

Conclusions

- Autologous Transplant
 - Identifying which patients will benefit
 - cure (lymphoma)
 - disease control (myeloma)
 - Transplant schema
 - Indications
 - Risks and complications

Summary

- Identifying patients who may benefit
 - Myeloma (auto)
 - Lymphoma (auto and allo)
 - Leukemia (allo)
- Mechanics of transplantation
- Complications
 - GvHD

Conclusions

- Allogeneic Transplant
 - Identifying which patients will benefit
 - current challenge of CML
 - Transplant schema
 - Indications
 - Complications
 - Immune effect

Thank you