

An Overview of Blood and Marrow Transplantation

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Stephen Couban
Department of Medicine
Dalhousie University

Objectives

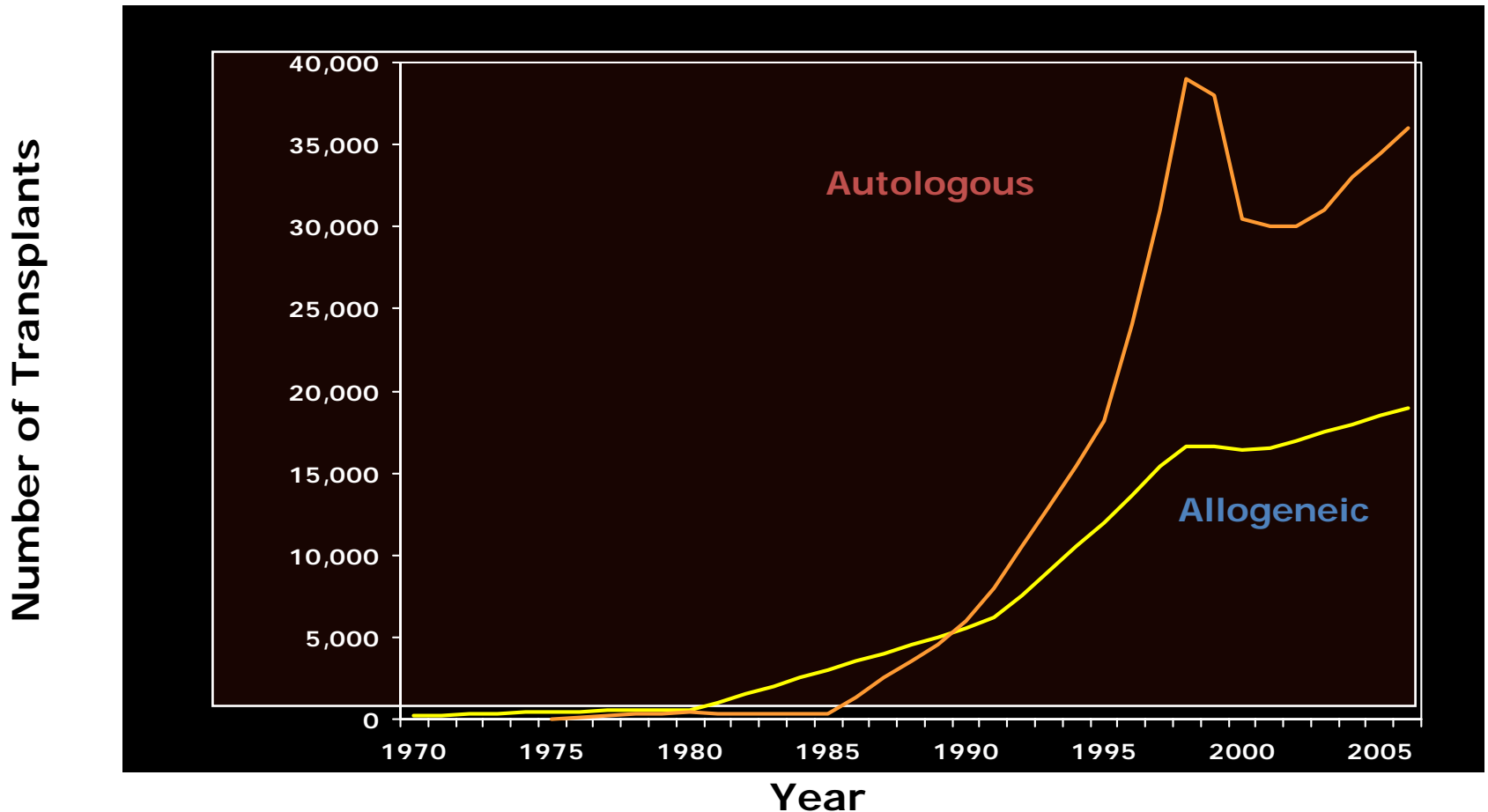
- What are the types of blood and marrow transplantation?
- Who may benefit from transplantation?
- Main diseases for which blood and marrow transplantation is undertaken
- What is graft versus host disease?

Goals of BMT

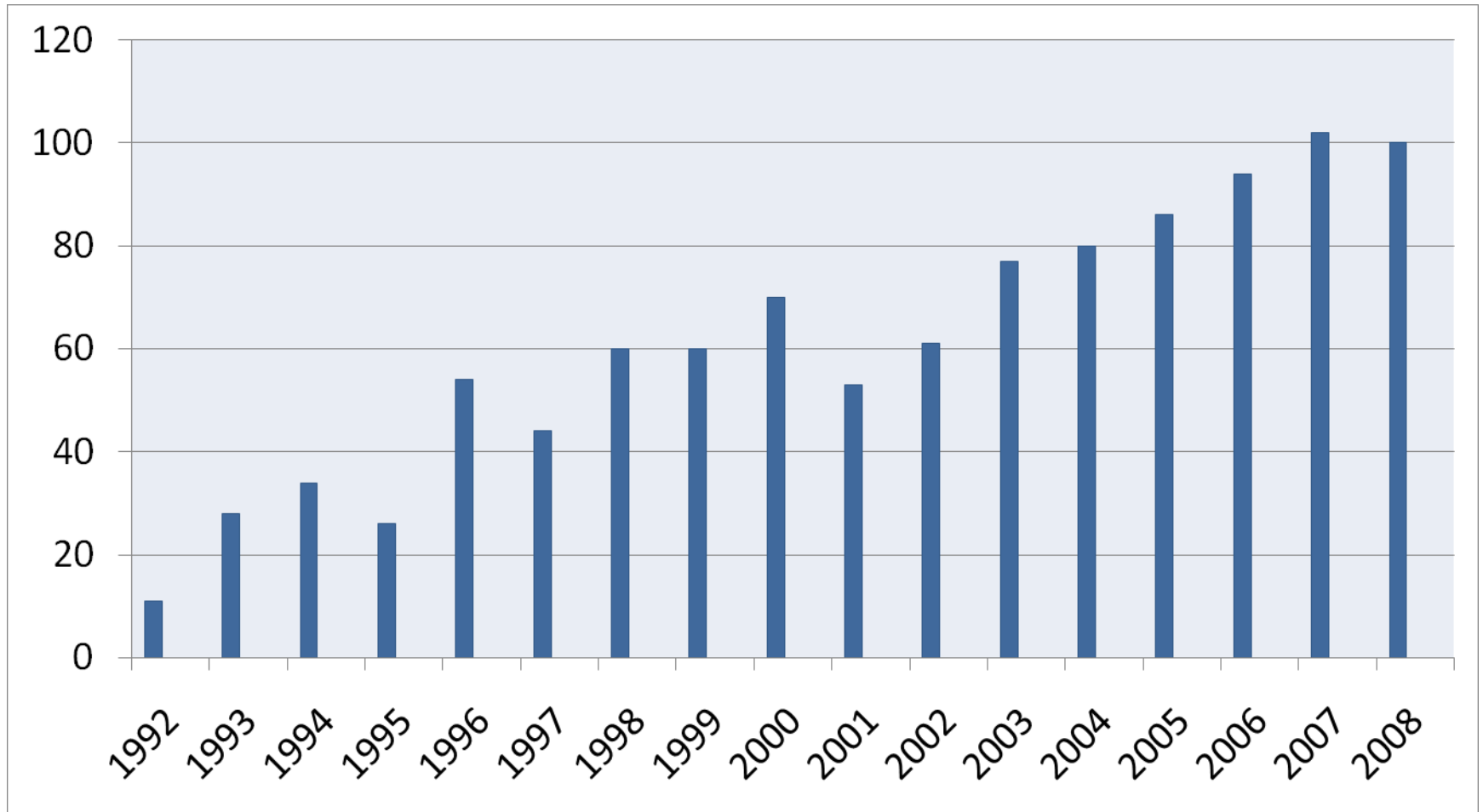
- Cancer therapy
 - Cure or prolongation of remission
- Marrow replacement
 - Aplastic anemia, thalassemia, sickle cell disease
- Developmental
 - Connective tissue diseases: scleroderma
 - Multiple sclerosis
 - Brain tumours
 - (Breast Cancer)

Annual Numbers of Blood and Marrow Transplantations, 1970-2006

- Worldwide -



Halifax Transplant Activity 1992-2008



Types of Transplant

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

Syngeneic

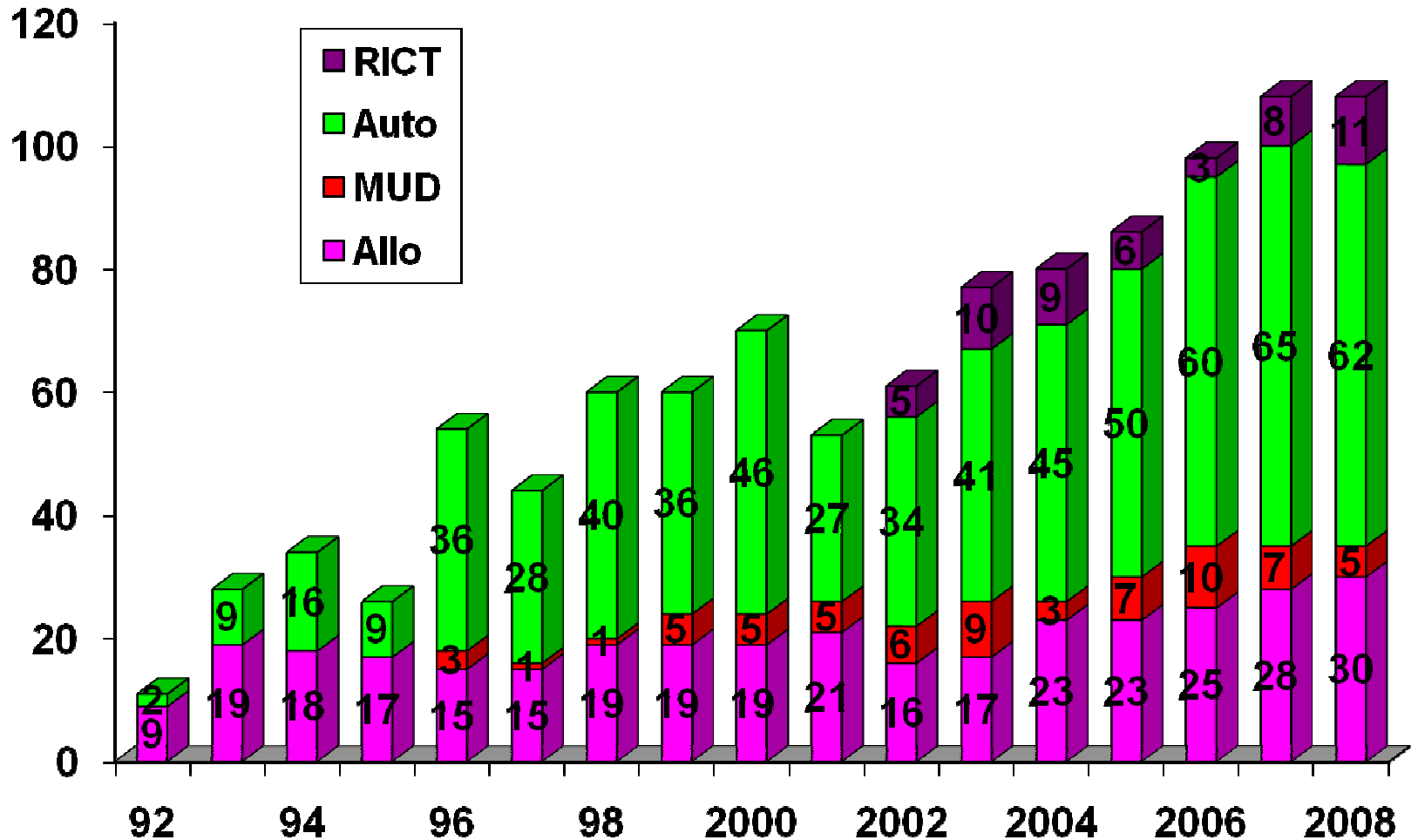
Allogeneic

Related

Volunteer
Unrelated

Halifax Transplants by Type

Auto vs Allo vs MUD vs RICT



Types of Transplant

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Autologous

Syngeneic

Allogeneic

Related

Volunteer
Unrelated

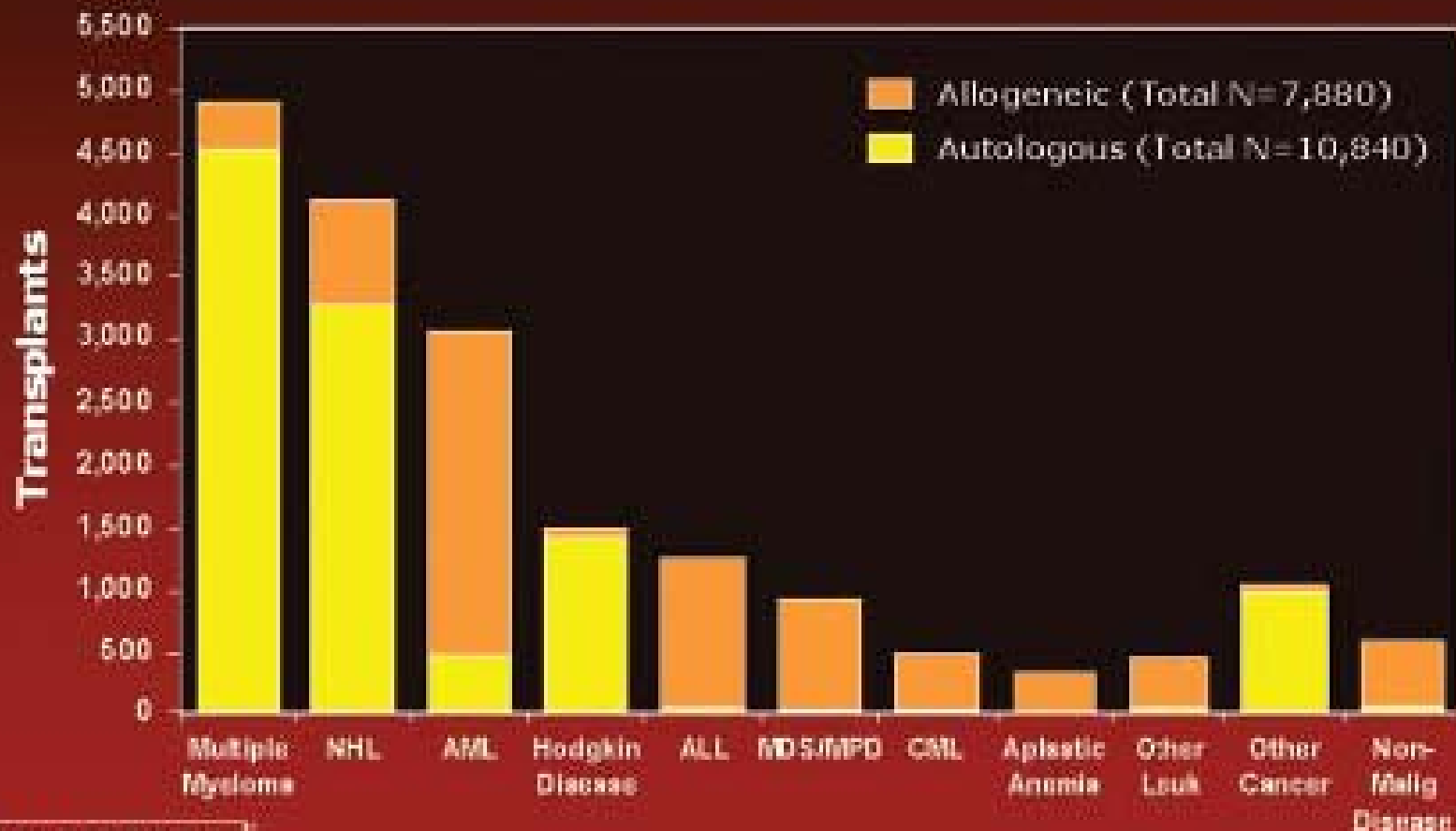
Autologous Transplant

- 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)

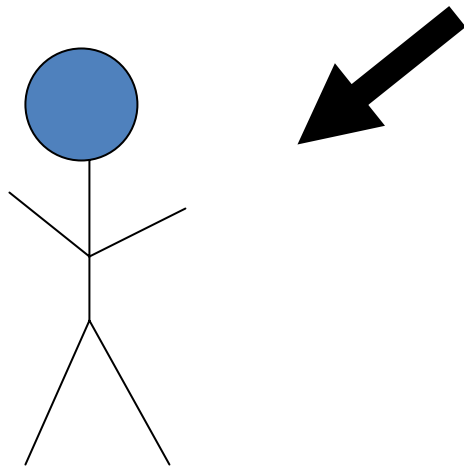
Indications for Hematopoietic Stem Cell Transplantation in North America 2005



Autologous Transplant: Stages

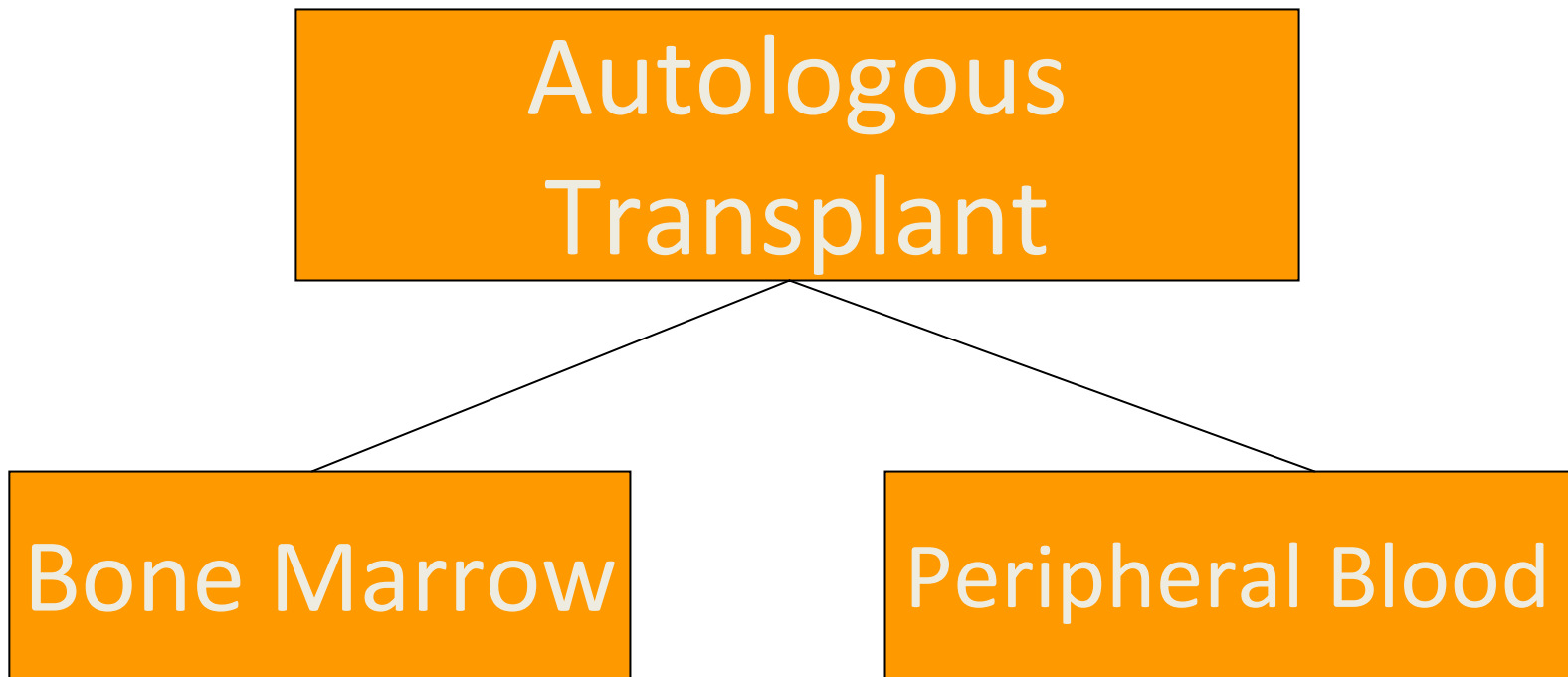
1. Pre-transplant chemotherapy
2. Harvest
3. Conditioning
4. Infusion
5. Recovery

1. Pre-Transplant Chemotherapy



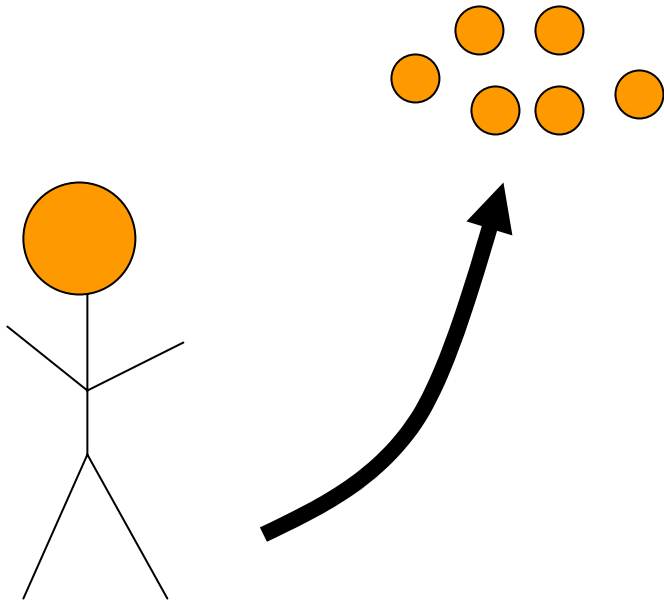
- Chemosensitivity
- In vivo purging

2. Harvest: Source of Cells



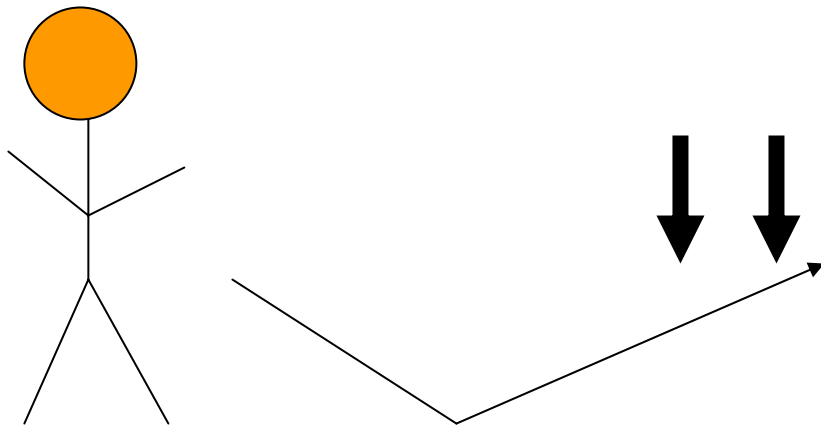
“stem cells”

Bone Marrow Harvest



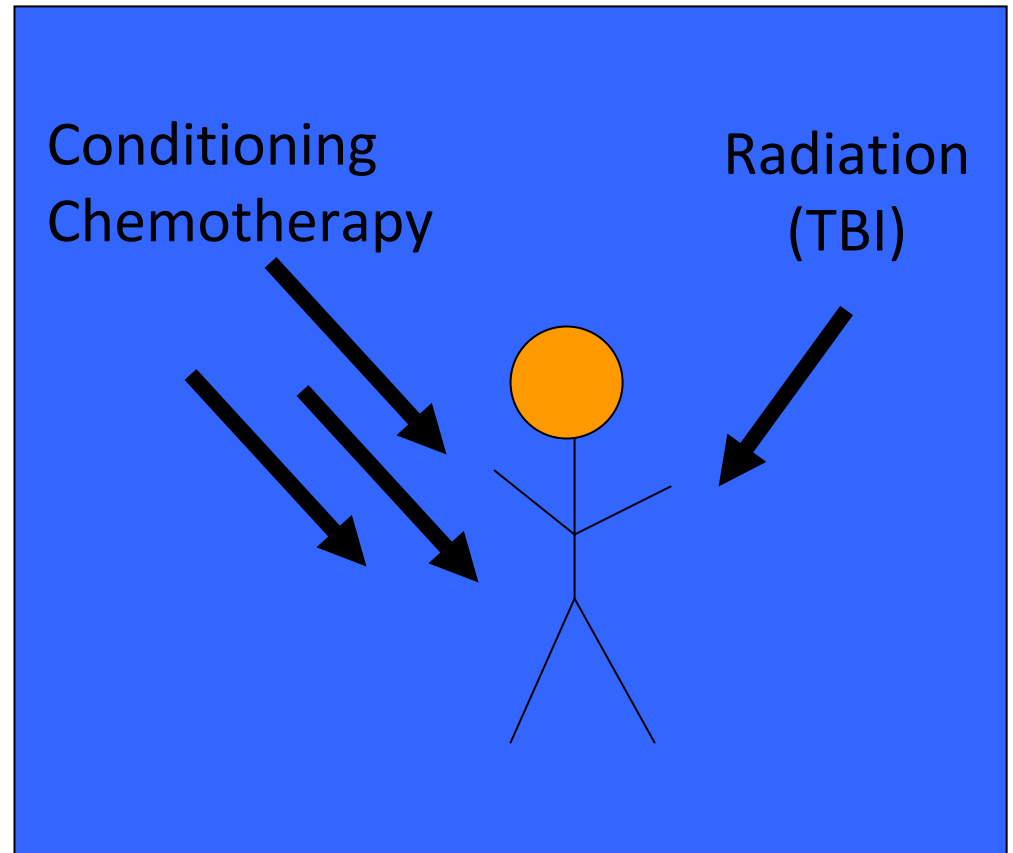
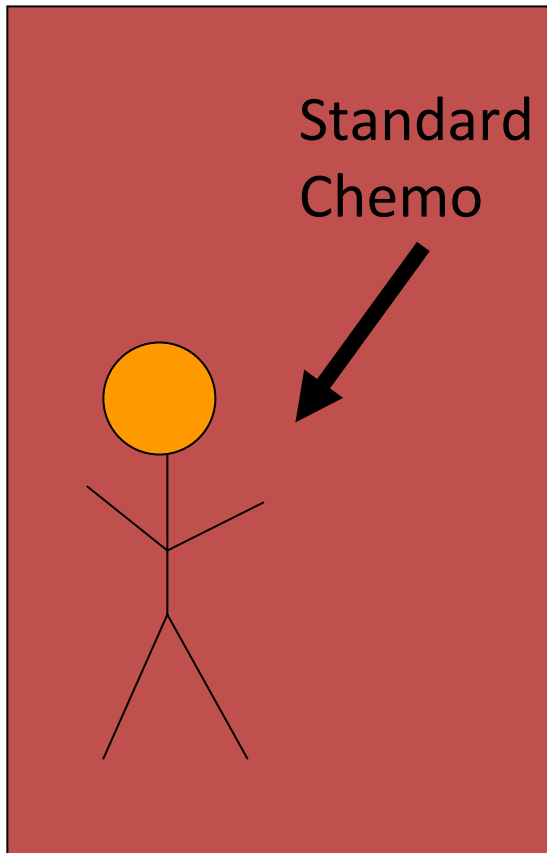
- Advantages
 - No chemotherapy
 - No growth factors
 - One day
- Disadvantages
 - General anesthetic
 - Large volume

Peripheral Blood Harvest

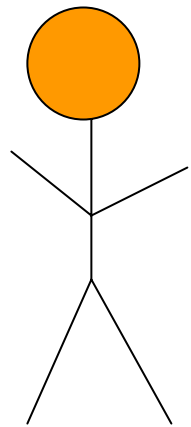


- Advantages
 - No general anesthetic
 - Small volume
 - **Engraftment**
- Disadvantages
 - Chemotherapy
 - Growth factors
 - Apheresis

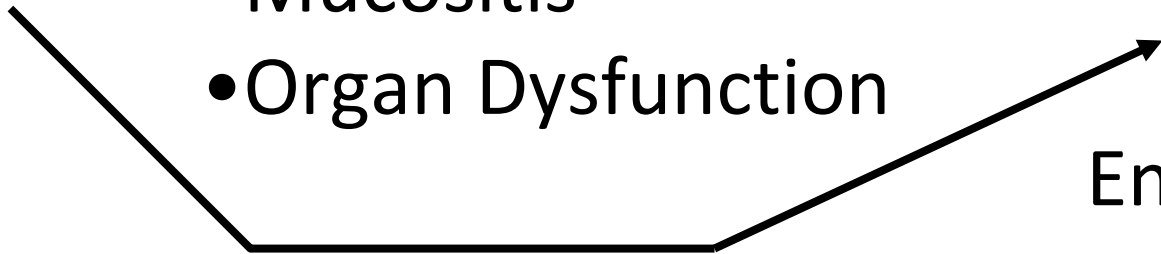
3. Conditioning



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



Marrow transplant patient gives birth

By DOBBA SCHWARTZ
The Dispatch
PHILADELPHIA — Mrs. Dymally, a 36-year-old Philadelphia housewife, has beaten the odds twice.

The first time was about four years ago, when a bone marrow transplant put her on the list to receive.

The second was Monday when she gave birth to a healthy boy — only the third success out of a number of failed attempts to have a marrow transplant patient in Philadelphia.

Mrs. Dymally had been told there was a 50-50 chance she would have a successful pregnancy.

"It's a miracle," she said. "I never thought I would be able to have a child."

She was diagnosed with acute myelogenous leukemia in 1978. After several failed attempts at chemotherapy, she was placed on the list for a bone marrow transplant.

"It was something we really wanted," she said.

She had the operation last month after taking 40 days of chemotherapy. Another 20 days was the usual 100-day course. The doctor is a specialist in leukemia, which means fighting the disease with marrow transplants is the best chance of getting better.

The hematologist and body physician, Dr. James H. Dymally, said he was sure the baby would be born healthy. He usually finds patients in the 10 to 15 week stage of pregnancy, but the baby was born two weeks earlier. There is no program for premature babies.

The baby has a growth after Mrs. Dymally stopped estrogen therapy and became pregnant.

The baby is named after Dr. Ross, father of Mrs. Dymally's father, Joseph. She was named for marrow and the first patient of the bone marrow program.

The parents will proudly name the boy.

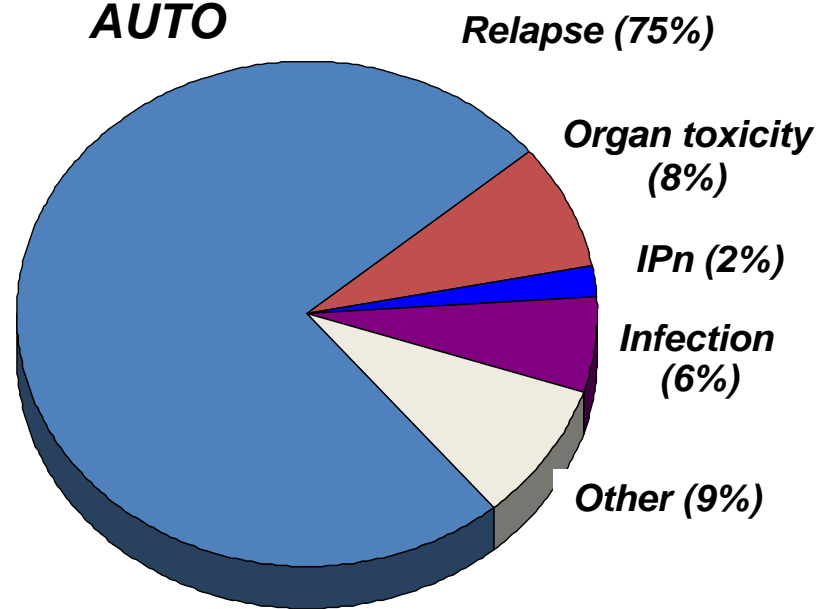
The Dispatch reporter is named

Mrs. Dymally, 36, with her newborn son, Robert, Jr., born Monday.

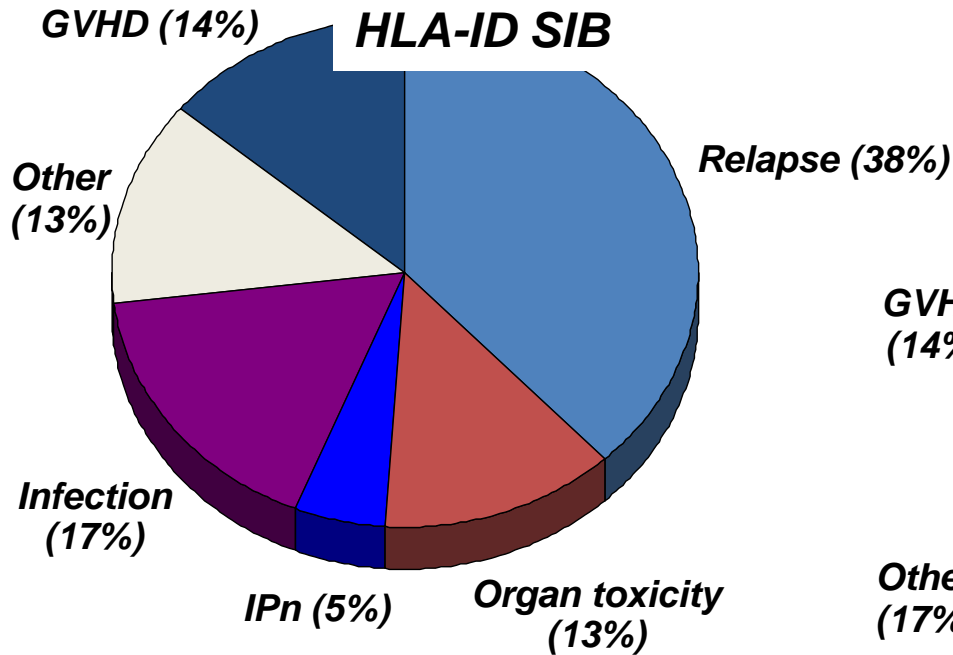
Shelley Dymally, 36, with her newborn son, Robert, Jr., born Monday.

Causes of Death after Transplants

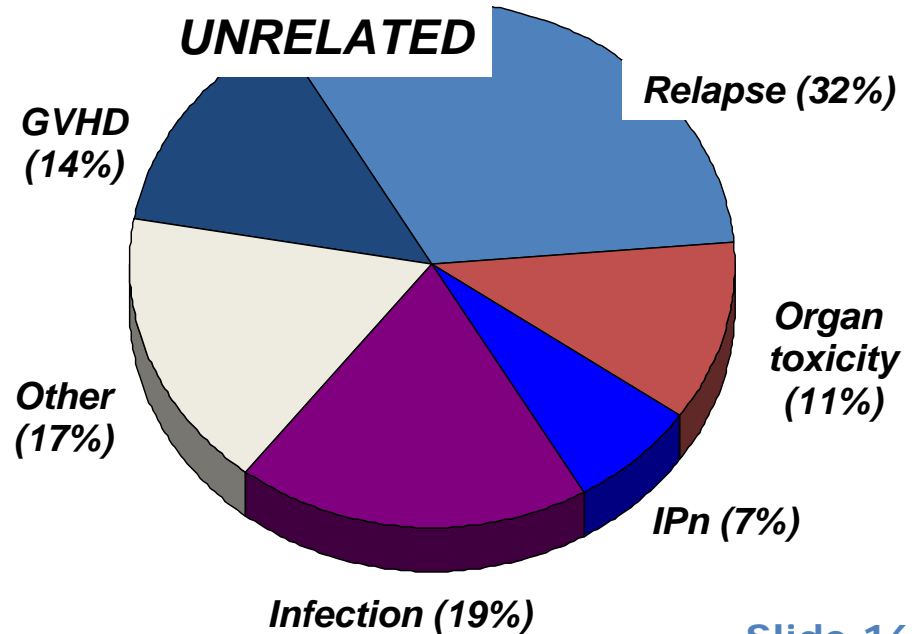
AUTO



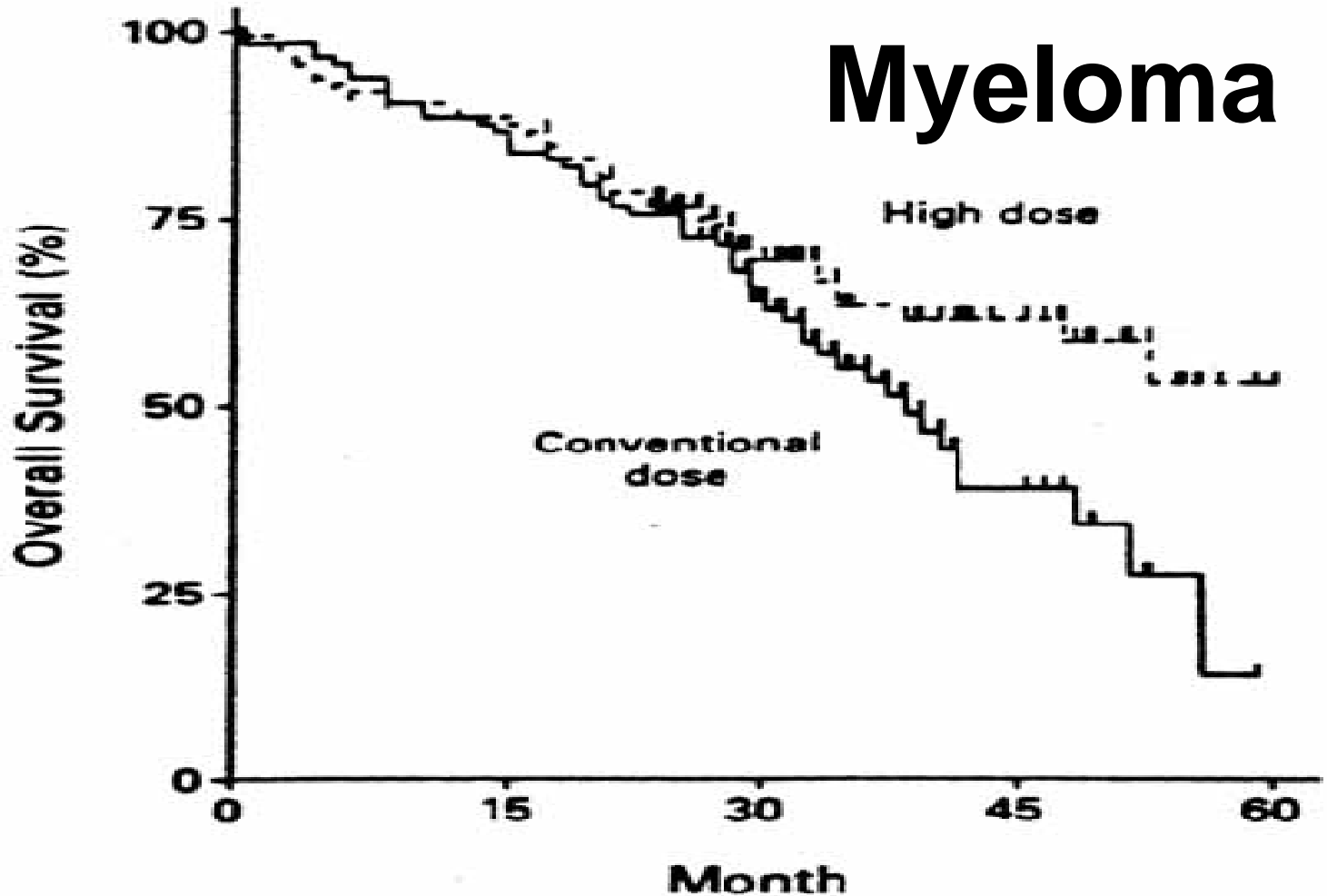
HLA-ID SIB



UNRELATED

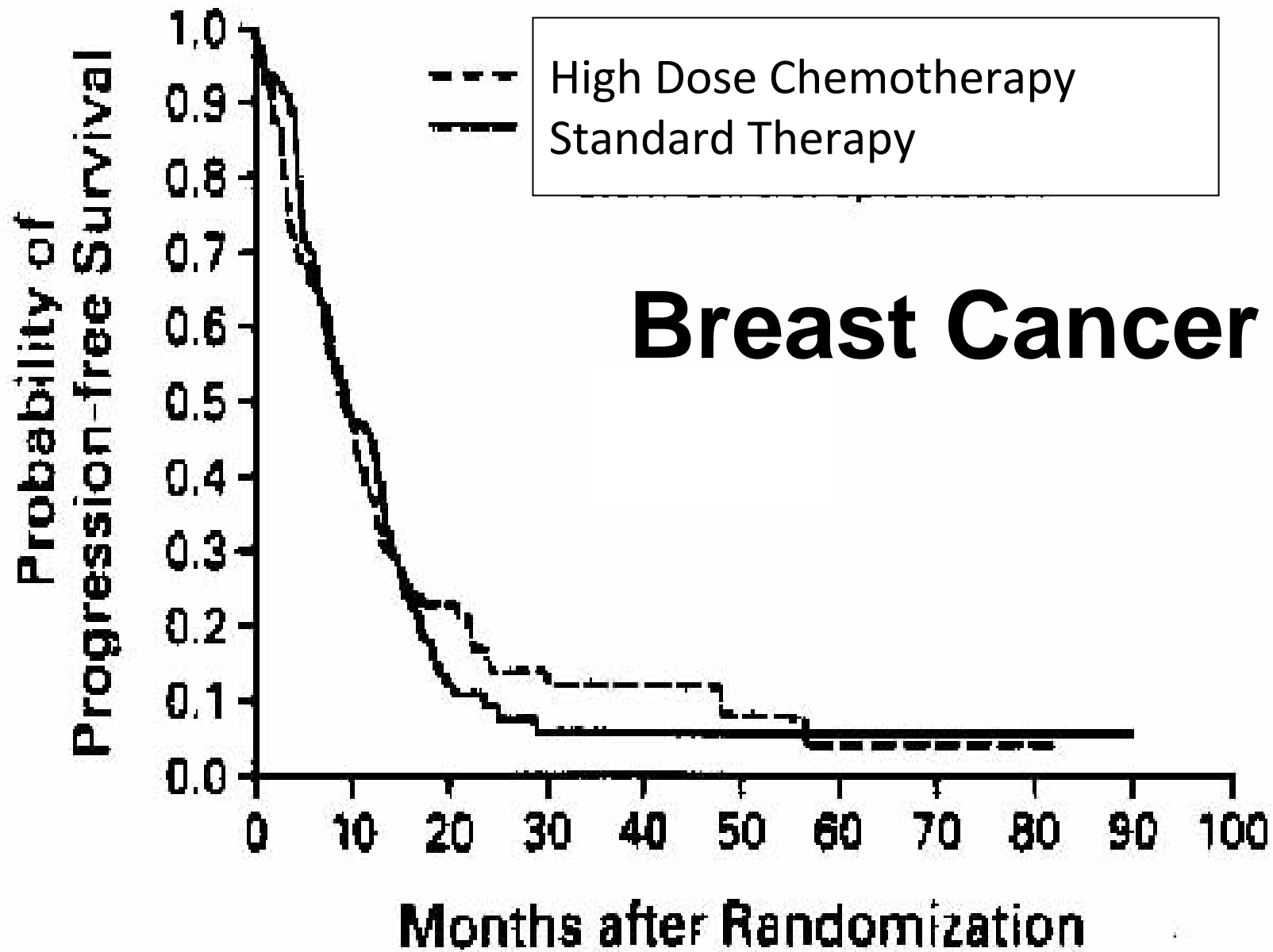


Myeloma



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

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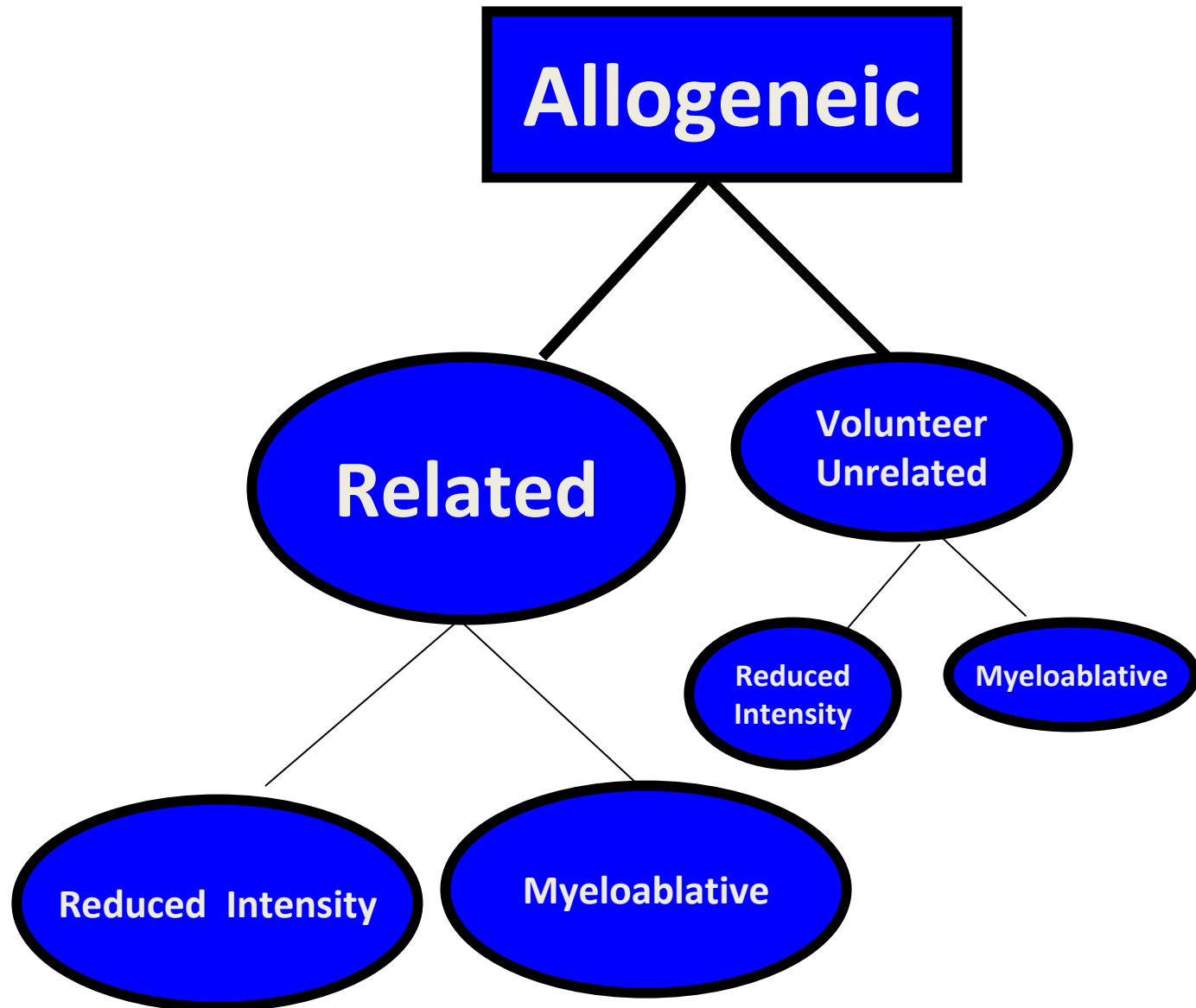
Autologous

Syngeneic

Allogeneic

Related

Volunteer
Unrelated



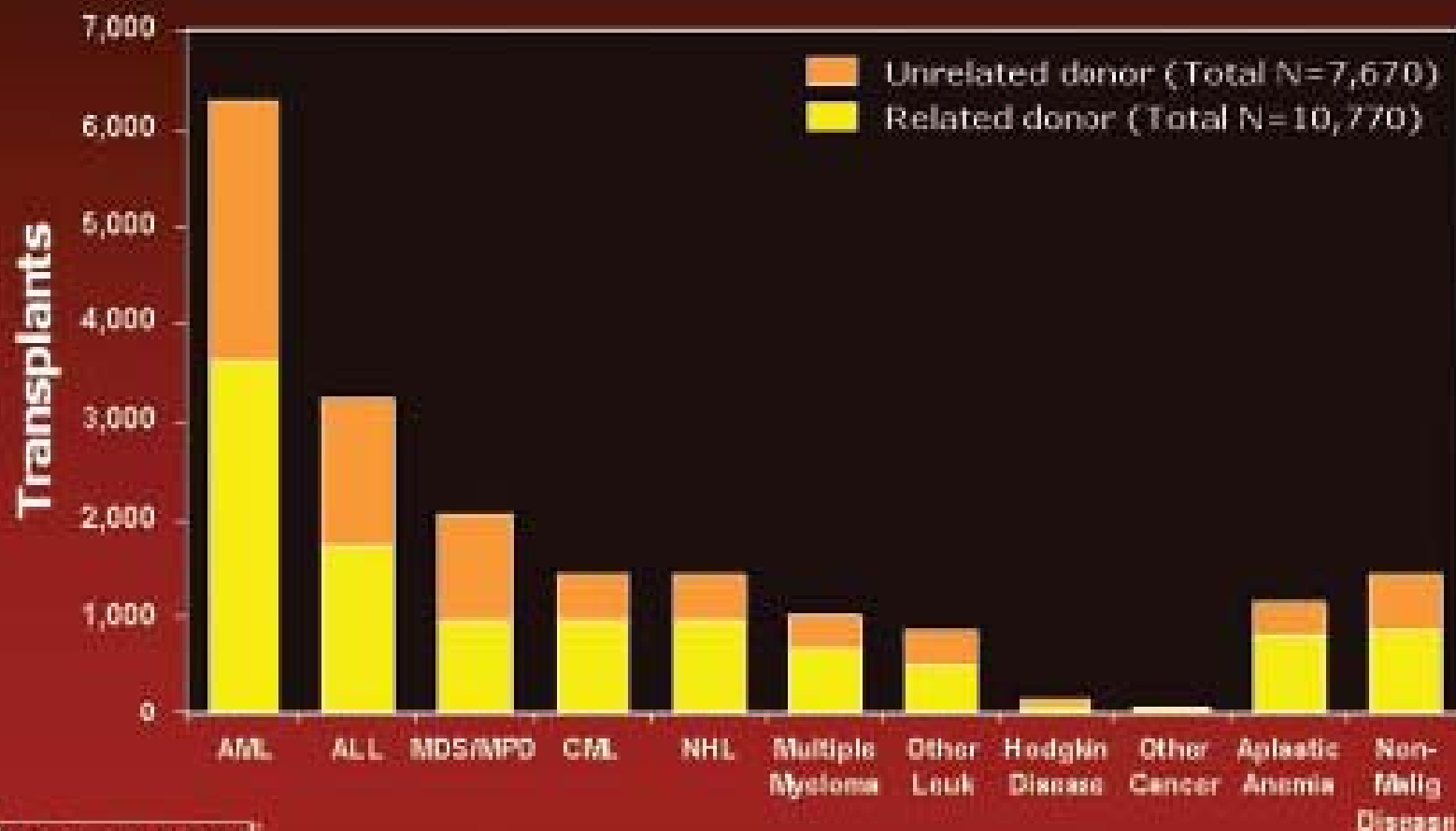
Allogeneic Transplantation

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

Allogeneic Indications

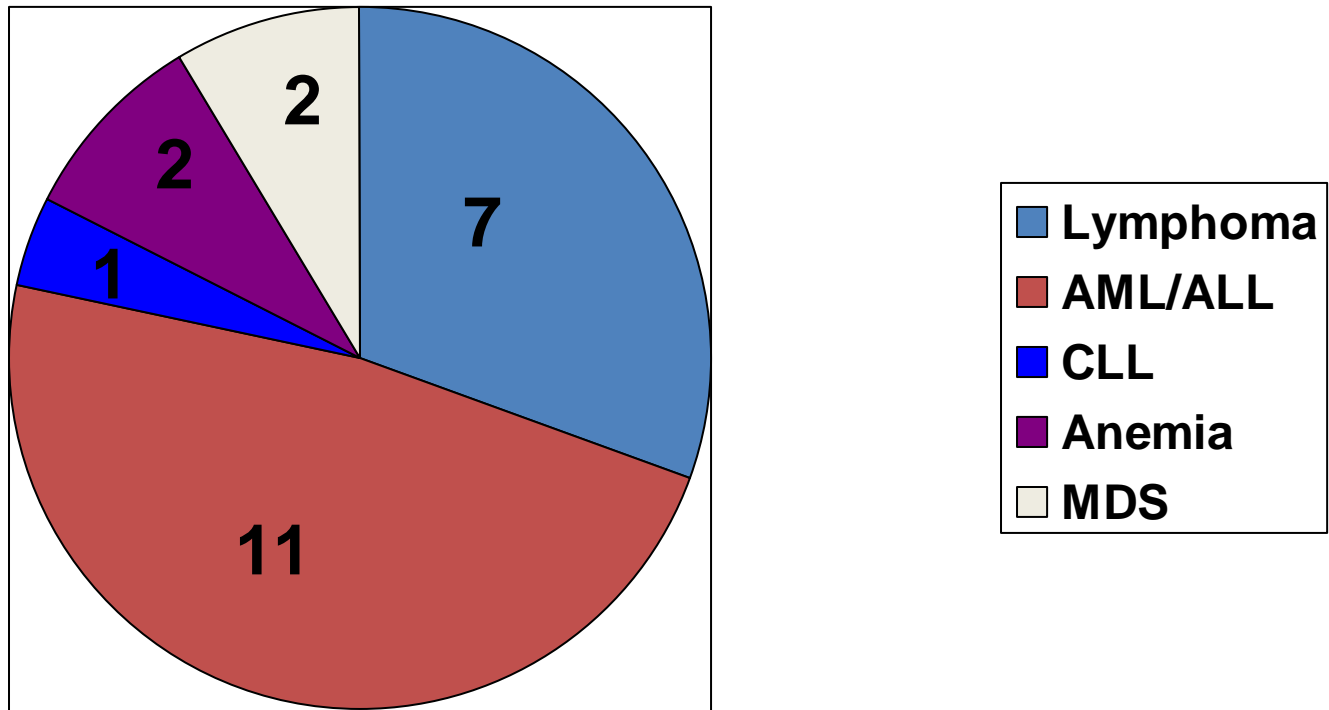
- Leukemia
 - Acute leukemia, MDS > CML, CLL
- Lymphoma
 - Indolent lymphomas
- Myeloma
 - Uncommon in 2009
- Bone marrow failure
- Diseased bone marrow

Indications for Allogeneic Hematopoietic Stem Cell Transplantation, 2005 – Worldwide



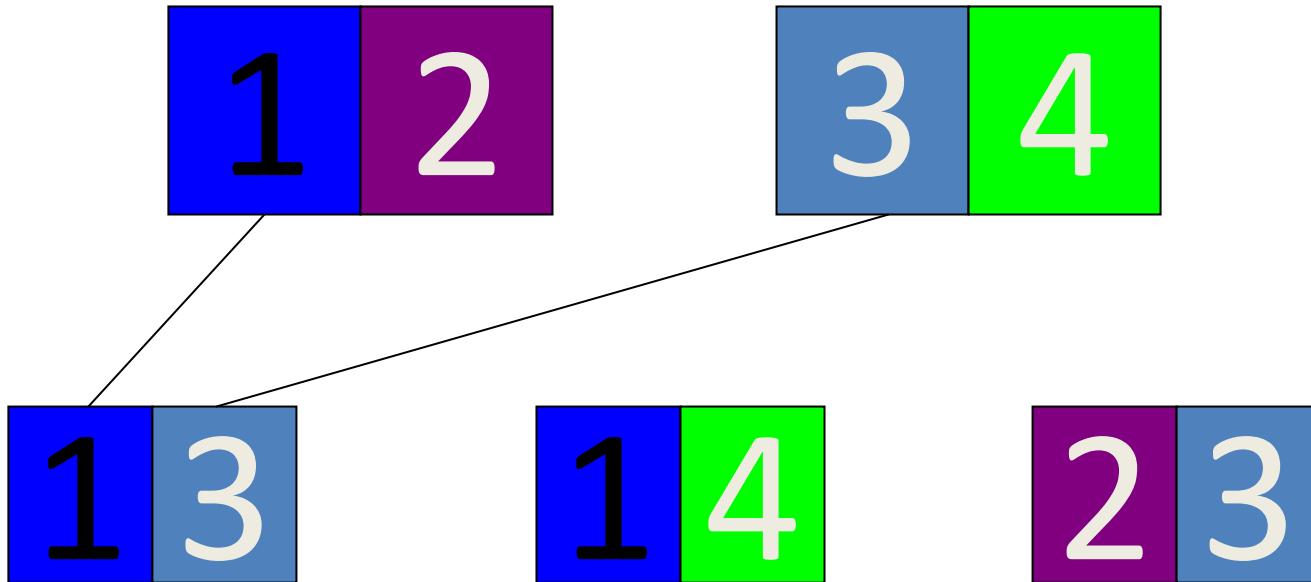
Sibling Allogeneic Transplants

Halifax: 2008

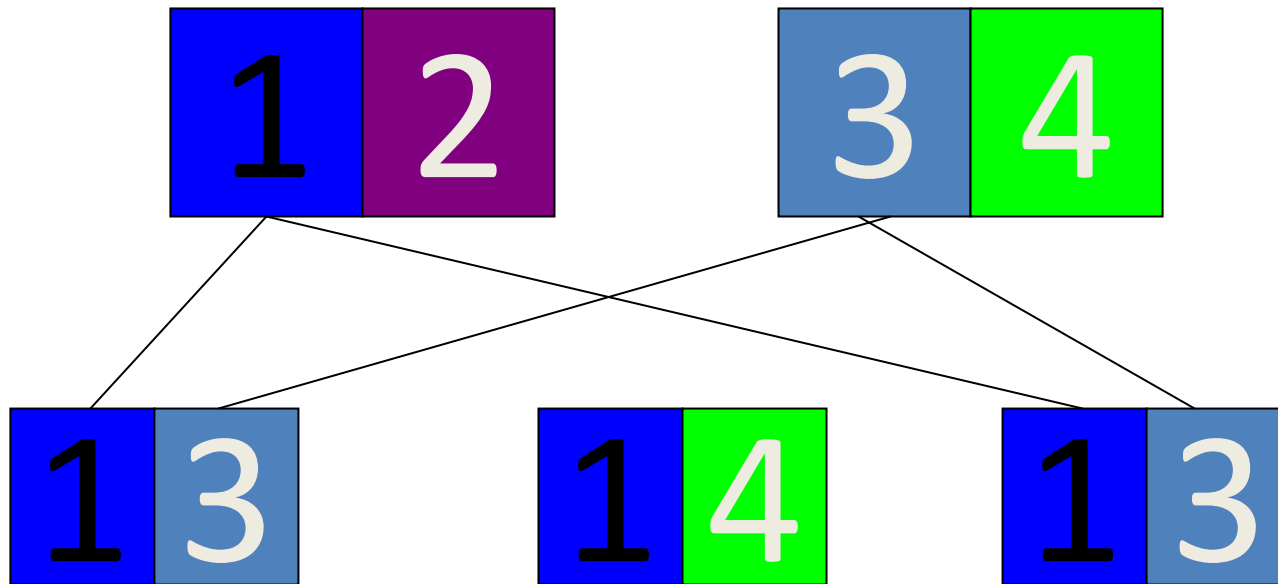


Allogeneic: The Match

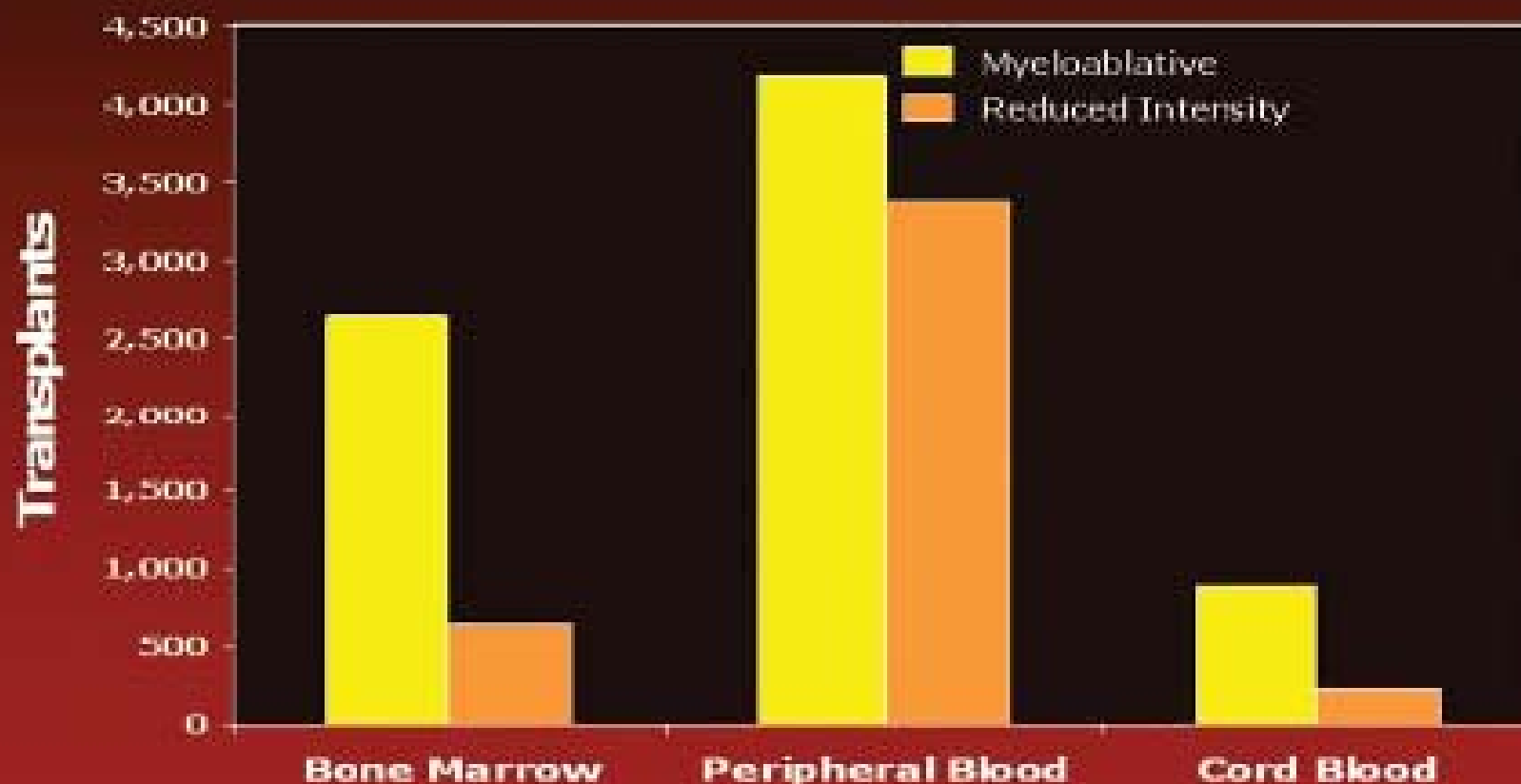
Each child inherits one set of HLA antigens from each parent

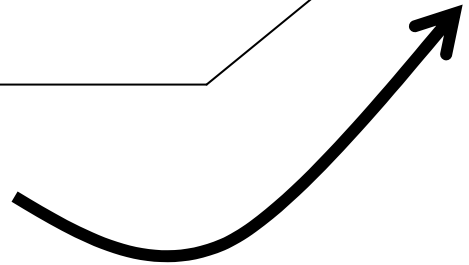
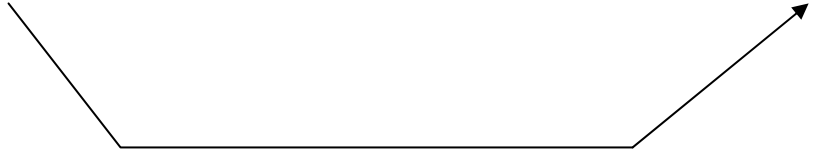


Allogeneic: The Match



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

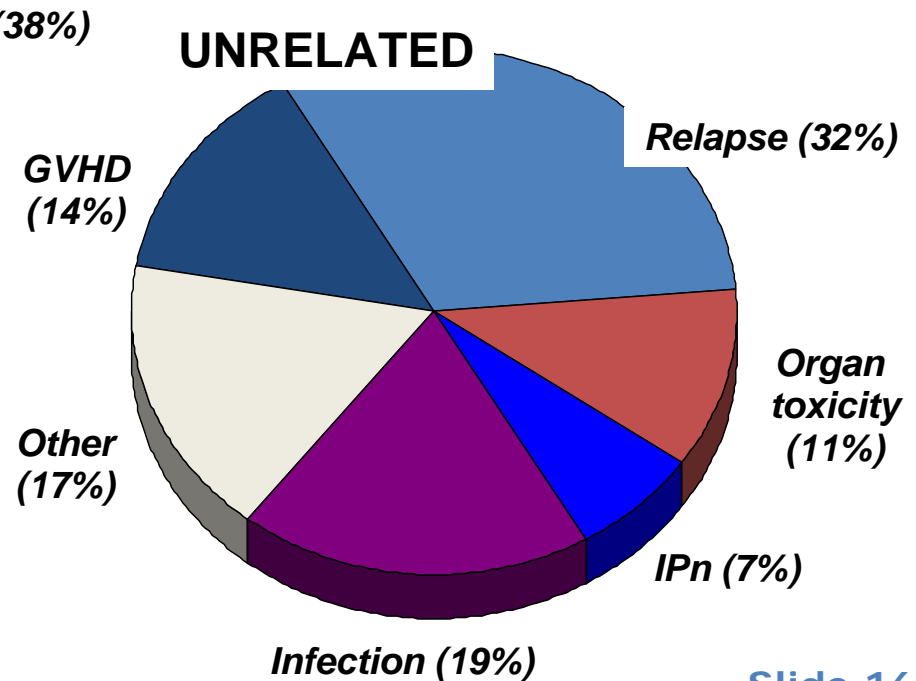
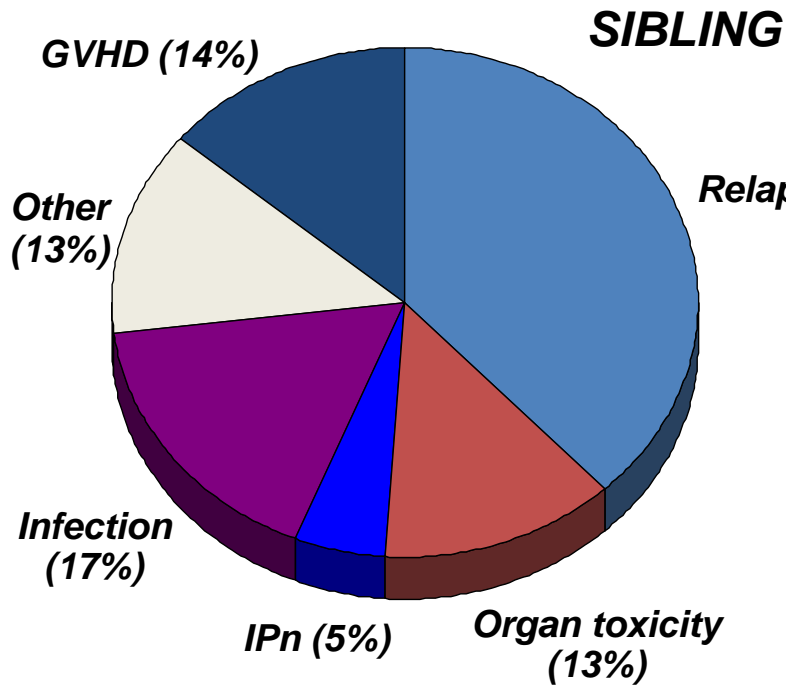
- Skin: Rash
- Liver: Inflammation
- Gut: Diarrhea
 - Characteristics

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