

# New Advances in Pediatric Aplastic Anemia

Evan Shereck, MD

Clinical Assistant Professor  
Department of Pediatrics  
British Columbia Children's Hospital  
University of British Columbia



# Outline

- What is Aplastic Anemia?
- Treatment
- Advances

# Children are **NOT** Little Adults

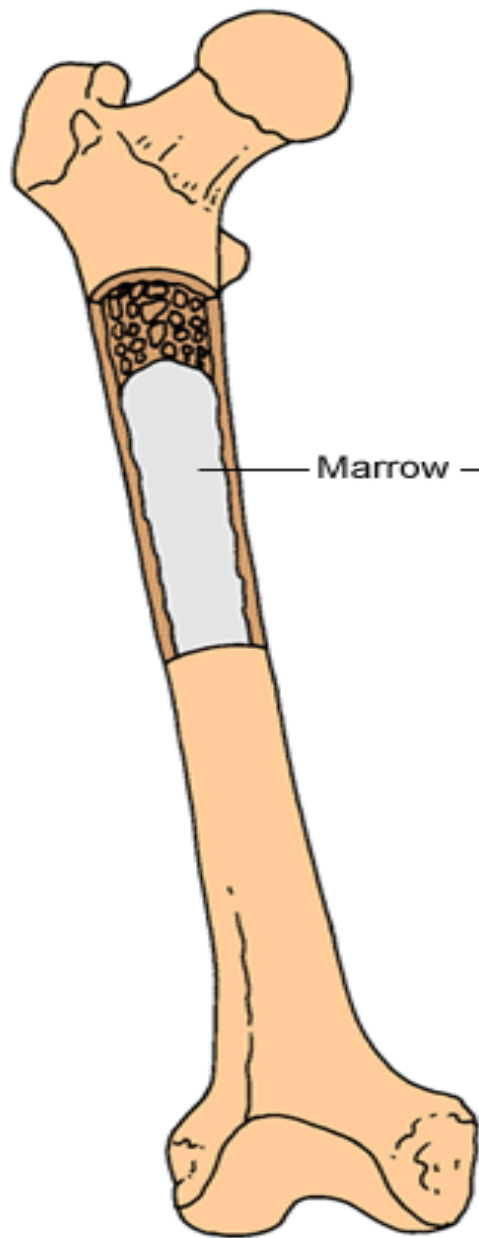


# Aplastic Anemia

- First described in 1888, Paul Ehrlich
  - Autopsy of pregnant woman
  - Fatal illness with bleeding, fever, anemia
- Aplastic Anemia coined in 1904

# Aplastic Anemia

- Empty bone marrow
  - Low white blood cells
  - Low red blood cells
  - Low platelets

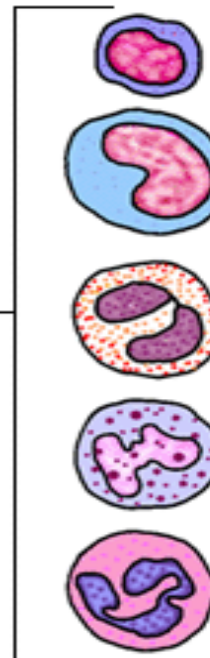


Red Blood Cells



Marrow

White Blood Cells



Lymphocyte

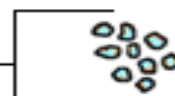
Monocyte

Eosinophil

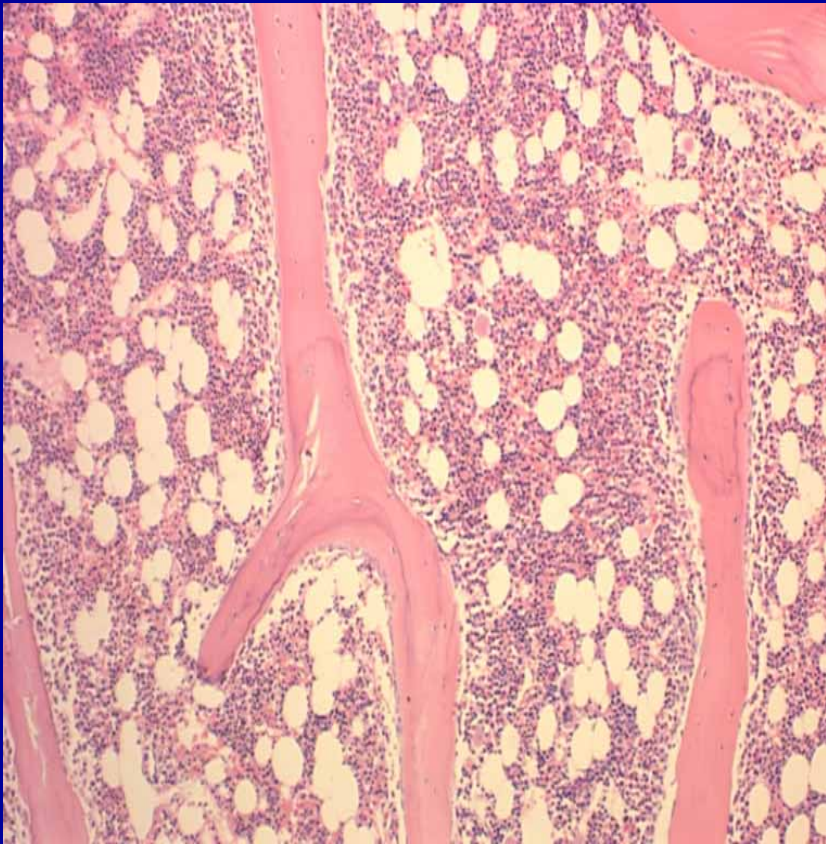
Basophil

Neutrophil

Platelets



# Bone Marrow Biopsies



**White Blood  
Cells Protect!**

**...from infection**





# Low White Blood Cells



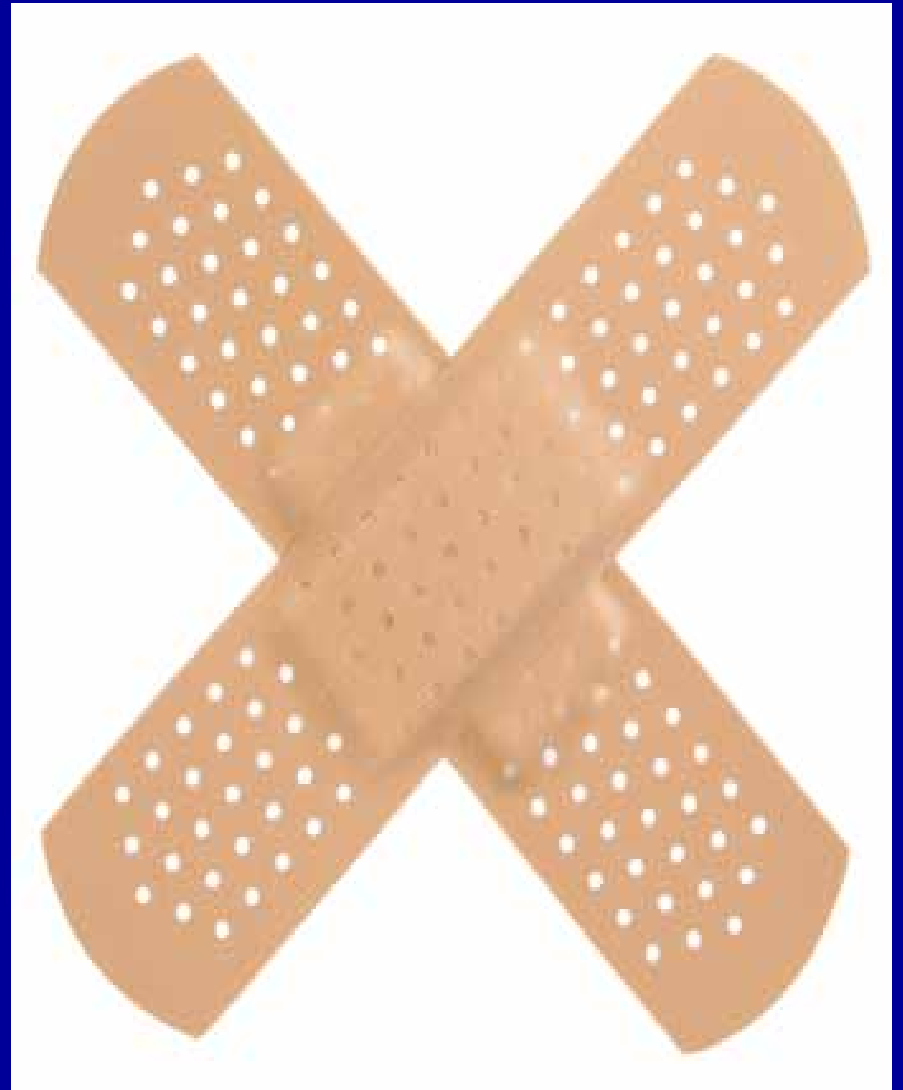


Red Blood Cells  
carry oxygen, which  
gives you energy

# Low Red Blood Cells



Platelets prevent  
bleeding



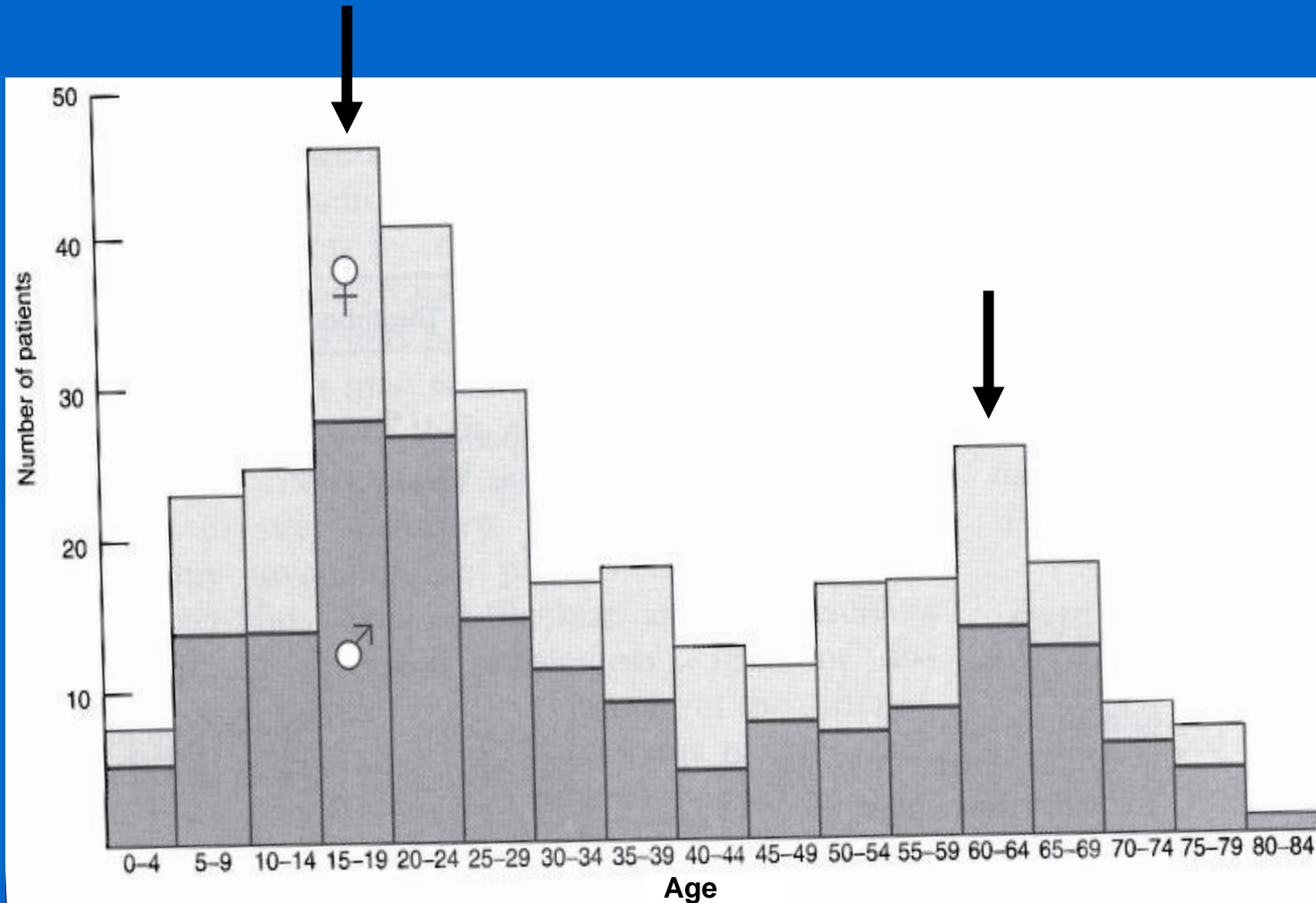
# Low Platelets



# Severe Aplastic Anemia

- Two of the following:
  - Neutrophils  $< 500/L$  (1500-5000)
  - Platelet count  $< 20 \times 10^9/L$  (180-440)
  - Abs. Reticulocyte count  $< 40 \times 10^9/L$  (20-80)
- Bone Marrow biopsy  $< 25\%$  cellularity

# Age Distribution







# How do you get aplastic anemia?

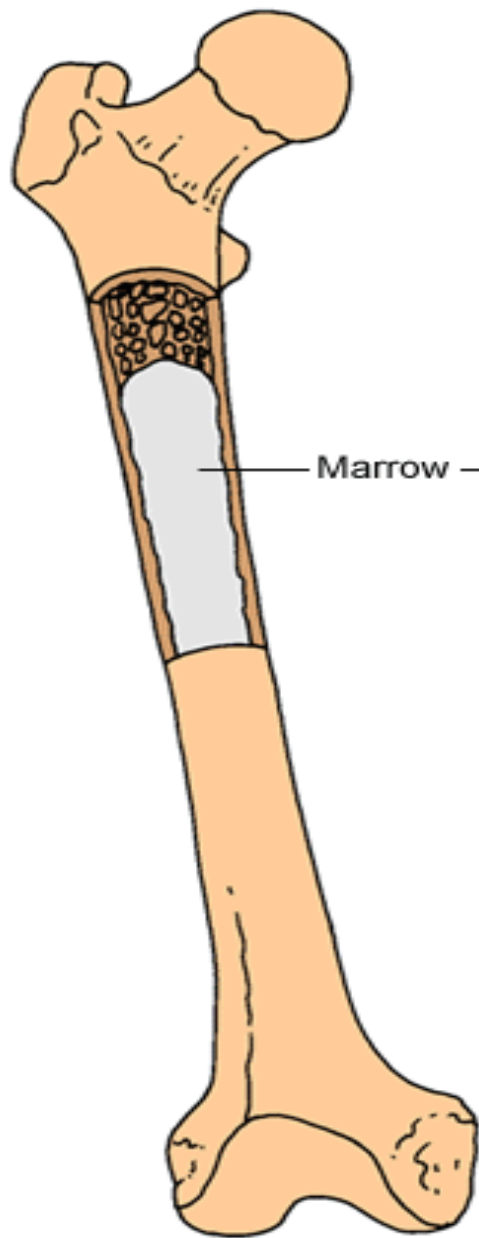
- Inherited
- Acquired

# Acquired

- Pregnancy
- Infections
- Benzene
- Ionizing radiation
- Drugs
- Idiopathic

# Pathophysiology

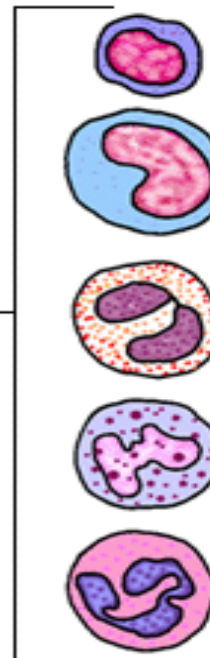
- Lymphocytes attack own stem cells in bone marrow
- With less stem cells, less red blood cells, white blood cells, and platelets are produced



Red Blood Cells



White Blood Cells



Lymphocyte

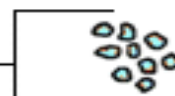
Monocyte

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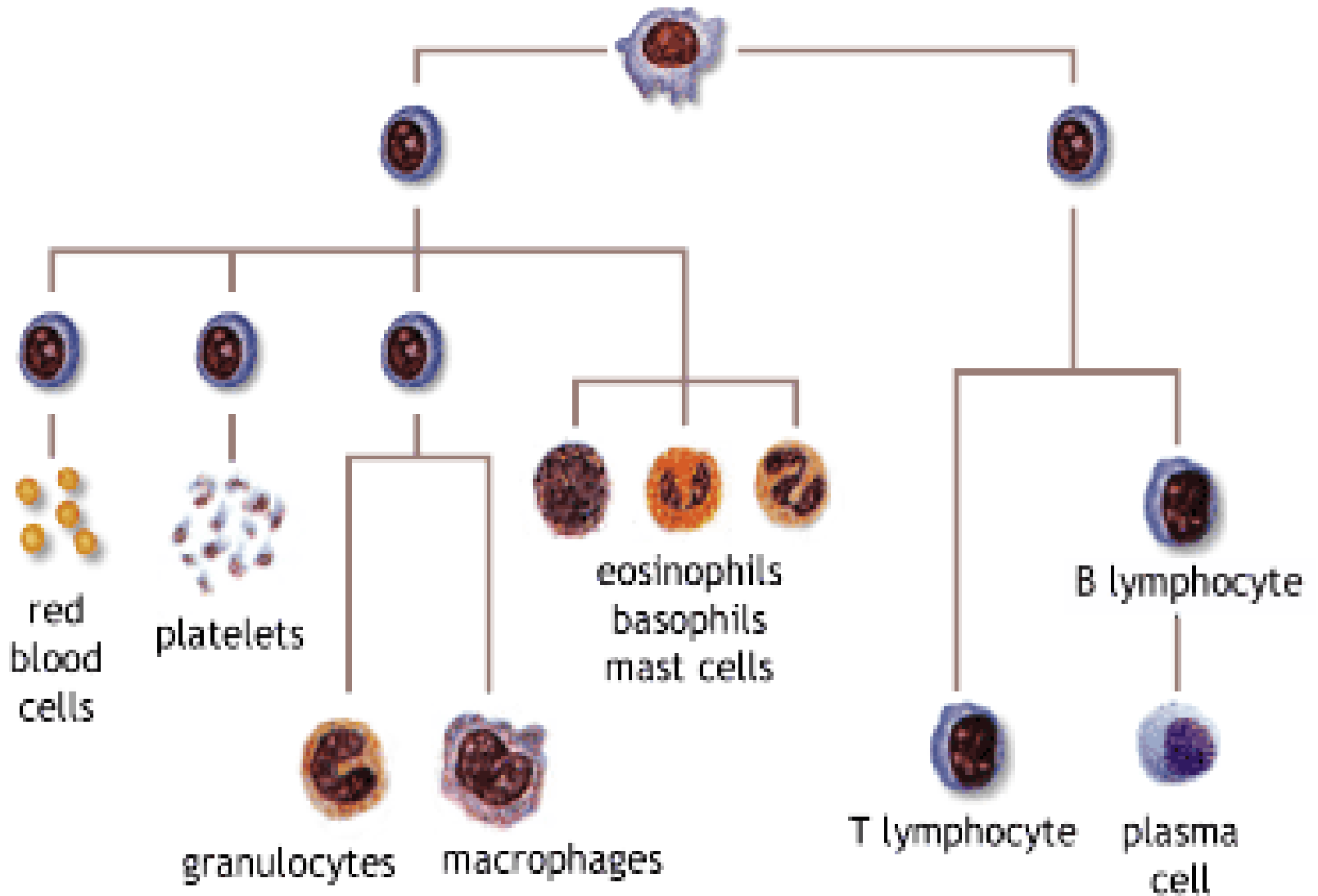
Basophil

Neutrophil

Platelets

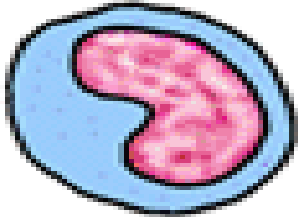


# Stem Cell

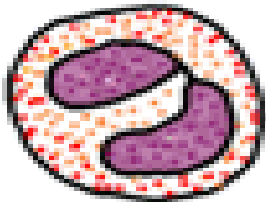




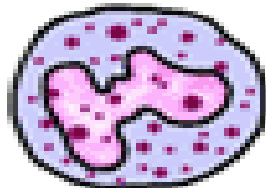
Lymphocyte



Monocyte



Eosinophil



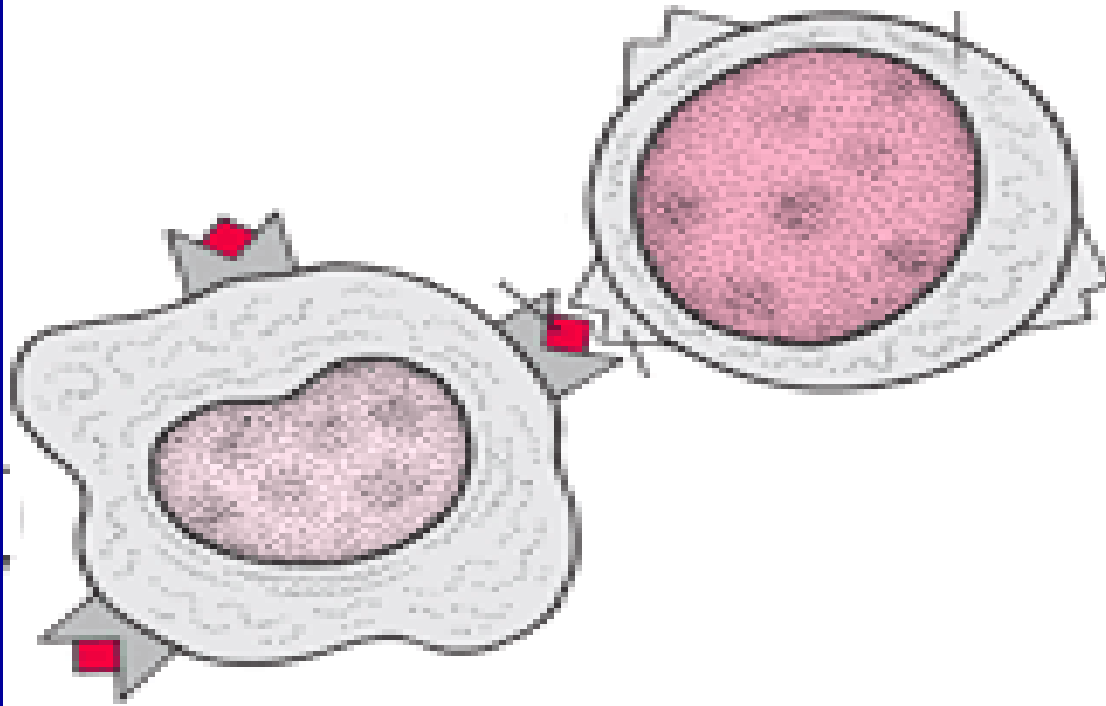
Basophil



Neutrophil

Each type of white blood cell has a unique function to help protect your body

**T-lymphocyte**



**Infected Cell**

**Stem Cell**

T lymphocyte





# Supportive Care

- Blood transfusions
- Platelet transfusions
- Soft toothbrushes
- Stool softeners
- Avoidance of aspirin/ibuprofen, etc
- Avoidance of trauma
- Investigation of fever

# Treatment

- Immunosuppressive therapy (IST)
- Hematopoietic stem cell transplantation (HSCT)

# Immunosuppressive Therapy

- If no matched related donor
- Response rate 55-77%
- ~70% disease free @ 10 years

Scheinberg et al *J Peds* 2008

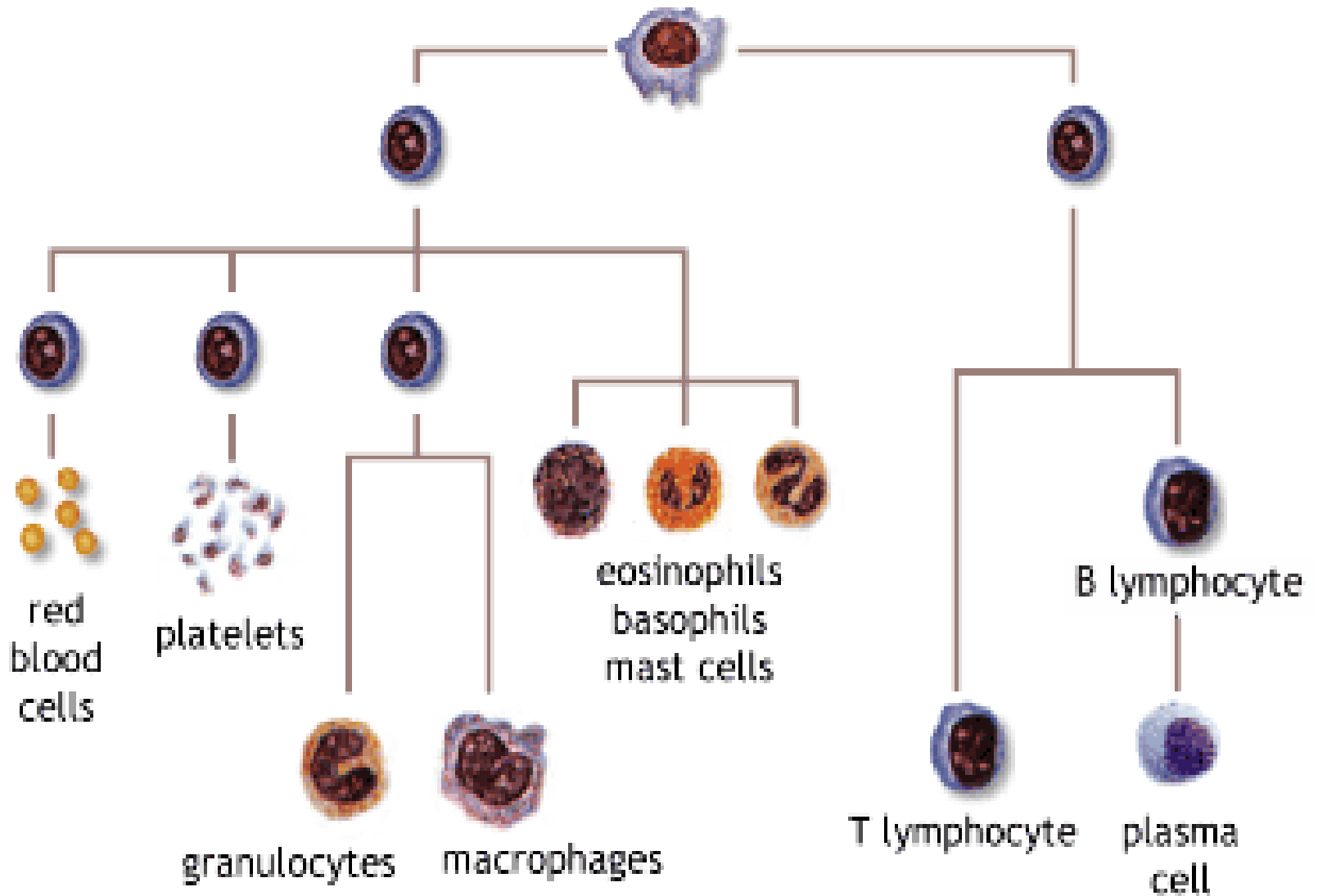
# Immunosuppressive Therapy

- Antithymocyte Globulin (ATG)
- Cyclosporine

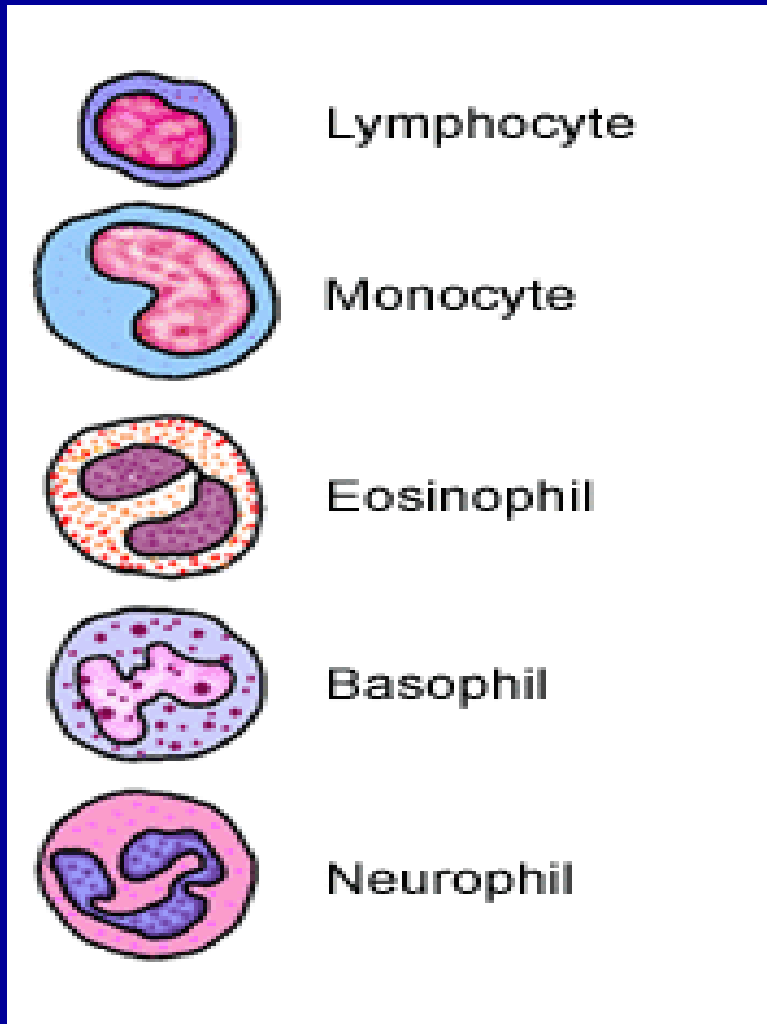
# ATG



# Stem Cell



# Cyclosporine



Inhibits T-lymphocytes

# IST Risks

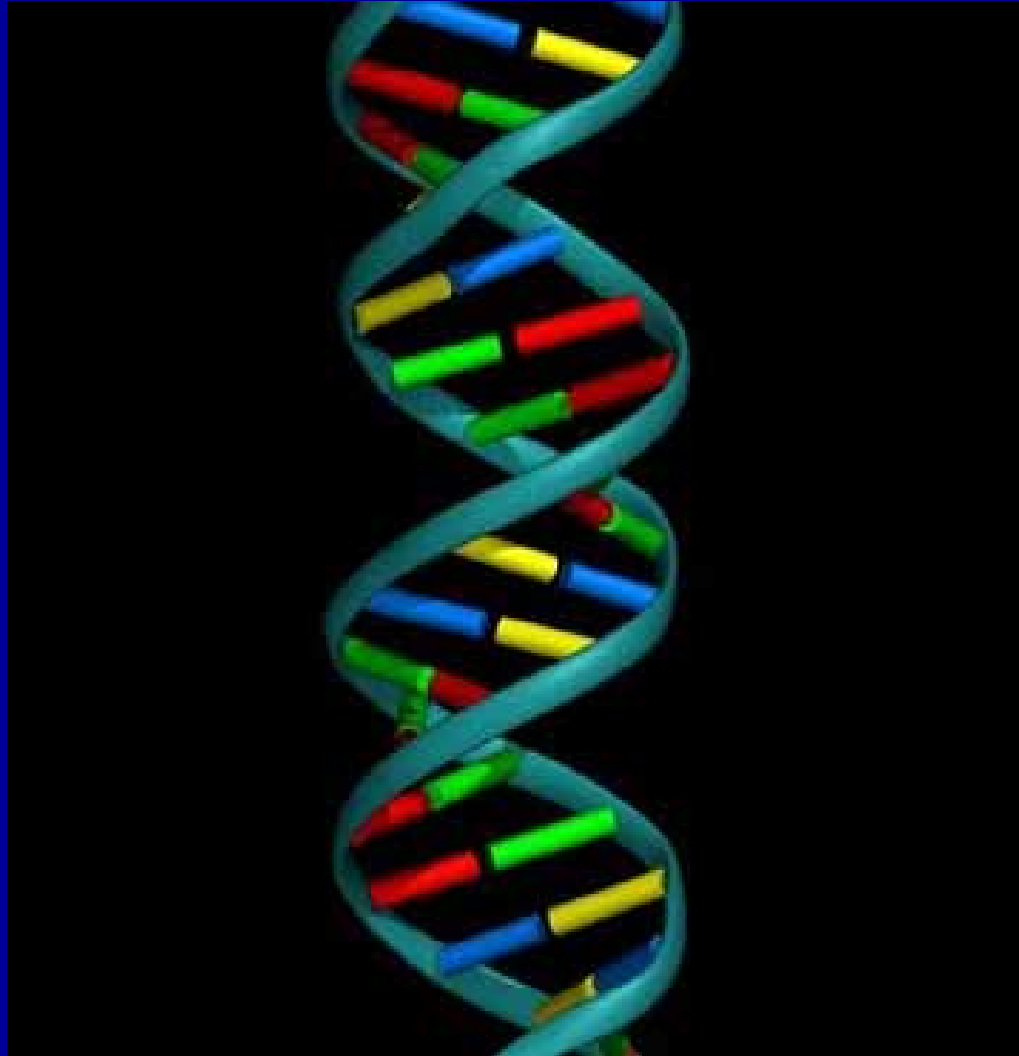
- Myelodysplasia
- Relapse

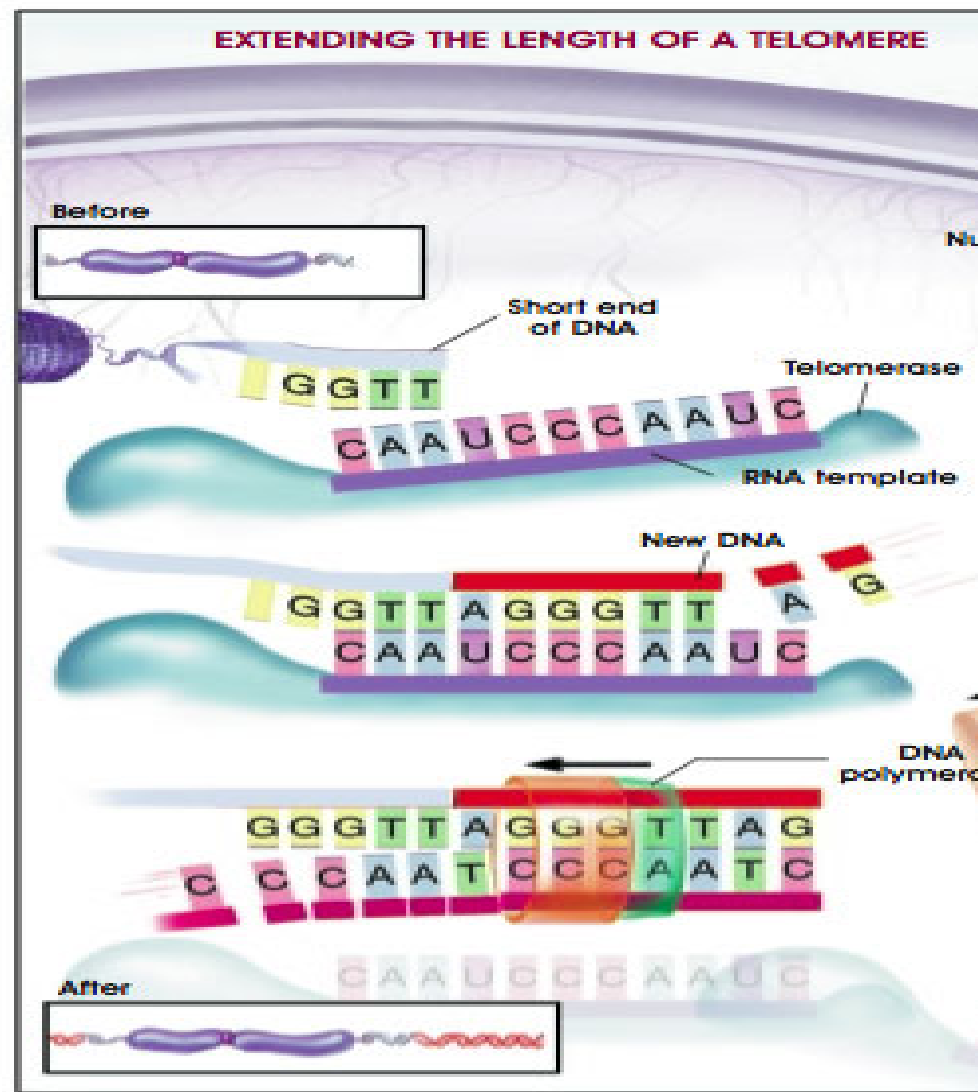
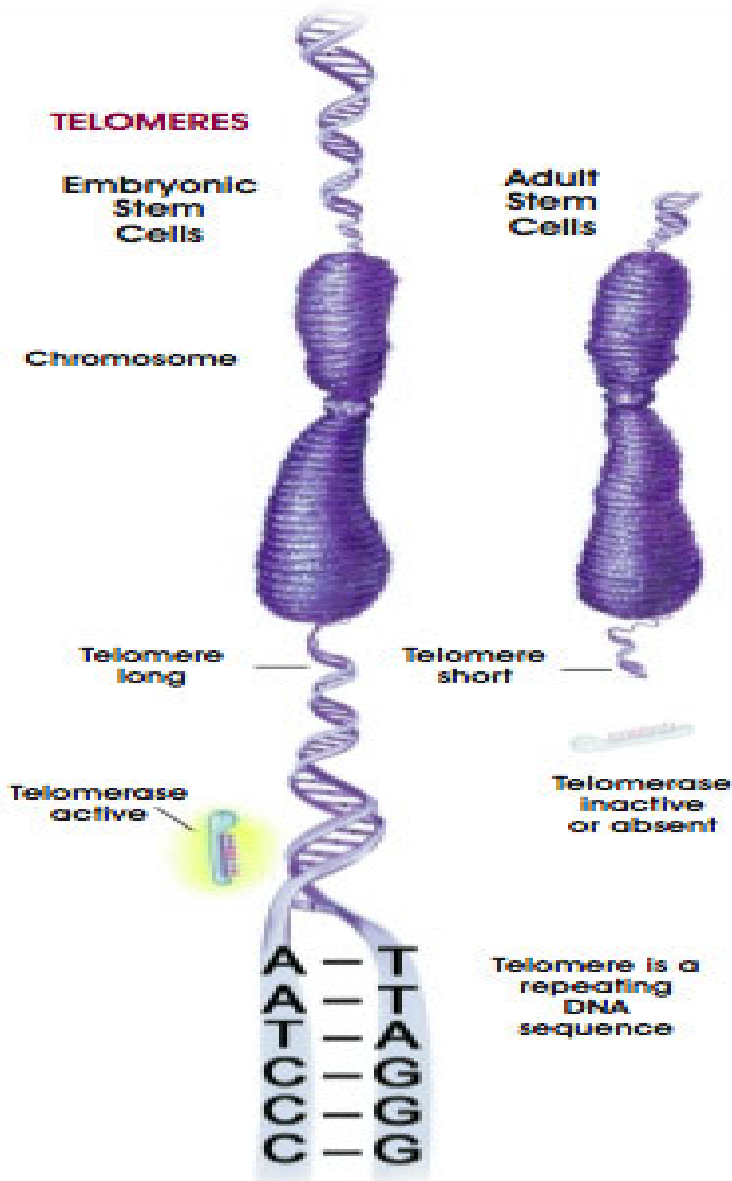


# Is there a way to Predict Response to IST?

- Telomeres

# DNA is Organized into a Double Helix





# Bone Marrow Transplantation

- 70-97% failure free survival

Kojima et al *Br J Haem* 2000

- Less risk for MDS or leukemia

# BMT limitations

- Only 53-65 % chance of finding match for African, Hispanic, Asian patients

Maier M et al Human Immunol 2006

- Graft versus host disease
  - 20-25% risk

# BMT Late Effects

- Infertility
- Reduced height
- Abnormal thyroid function
- Secondary malignancies

# Recent Improvements in treatment

- Improved graft versus host medications
- Alternative donor sources
  - Matched unrelated adult donors
  - Cord Blood

# Alternate Donors

- Increased graft rejection
- Increased graft versus host disease
- CB may contain too few cells



# Alternate Donor Advances

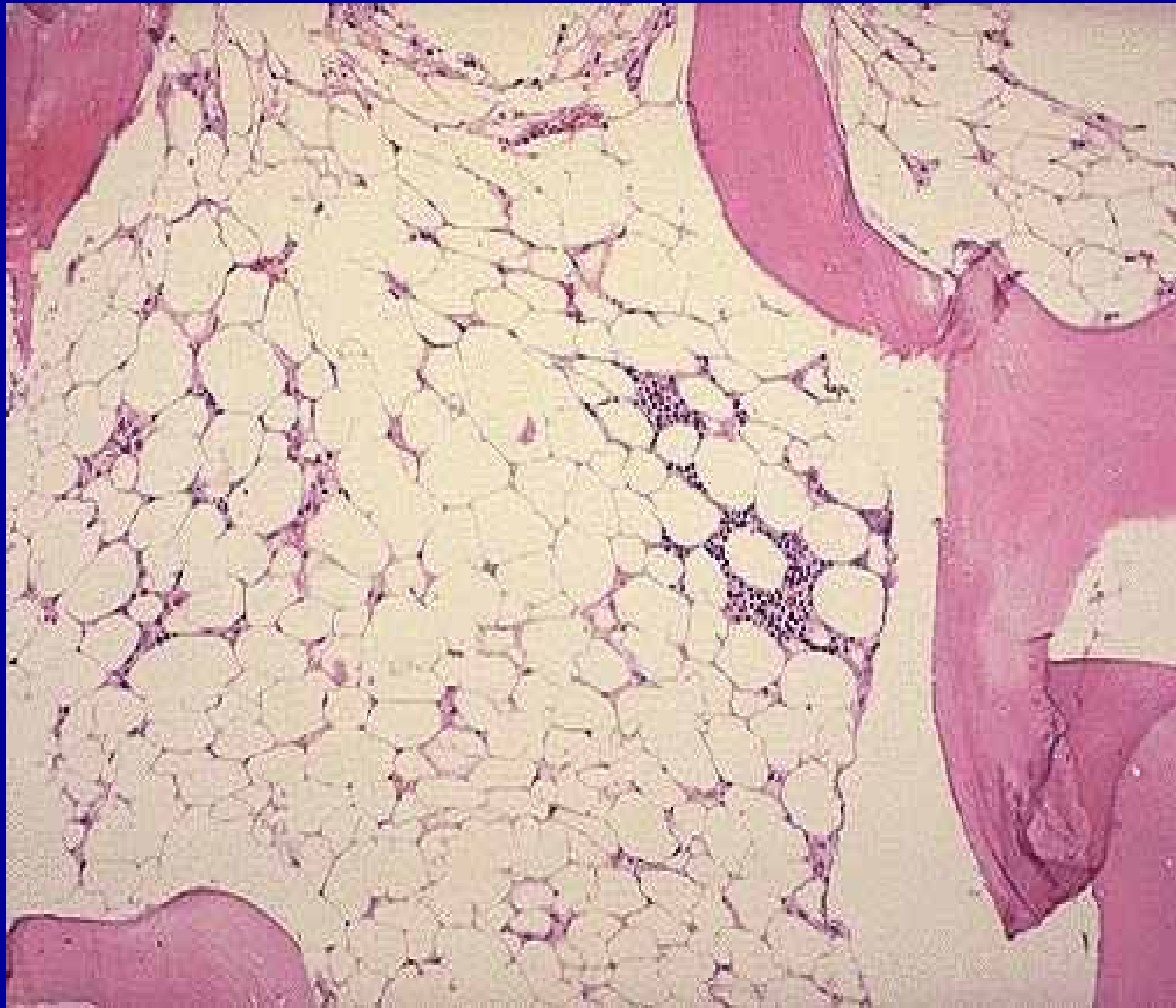
- Conditioning
- Better GVHD meds
- Improvements in HLA typing
- Double cords?

# “Typical” Case

- MD, a 7 year old boy
- Presented in Oct. 2007 with:
  - Easy bruising, fatigue

# MD's CBC

- WBC-  $2.5 \times 10^9/L$
- HGB- 6 g/L
- Platelet-  $6 \times 10^9/L$
- Neutrophils-  $0.3 \times 10^9/L$
  
- Bone Marrow Showed...



# MD Cont'd

- MD had no matched sibling
- Started IST
- 6 months later- 2<sup>nd</sup> IST
- 3 months later, still no response

# MD Cont'd

- MD telomeres- short
- Underwent 10/10 MUD
- Now, 4 months later...

MD Is doing well with normal counts!



# Conclusion

- Aplastic anemia is when the bone marrow fails to make cells
- Treatment may be with IST or BMT
- Advances are constantly being made



Any Questions?

