Hemolytic Anemia

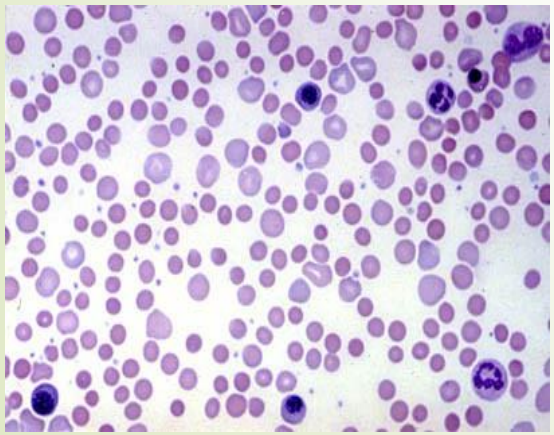
Laith Al-Showbaki, MD
Consultant Medical Oncologist,
Hematologist

Case 3

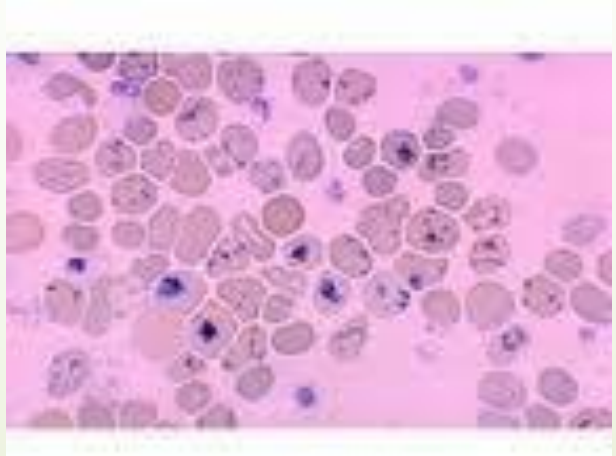
24 yr old female presented with “anemia syndrome” and jaundice. She was found to have splenomegaly.

Hb 8, wbc 12k, Plt 212k, retics© 12%, LDH 1400, bilirubin 7mg/dl,d 2.5mg/dl, DAT +3.Bld film spherocytes, polychromasia.

Bld film

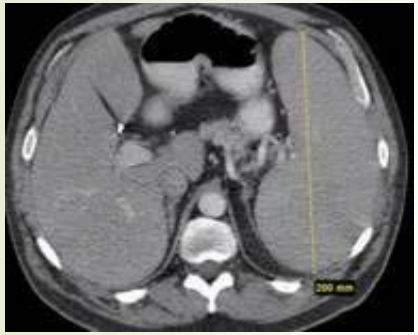


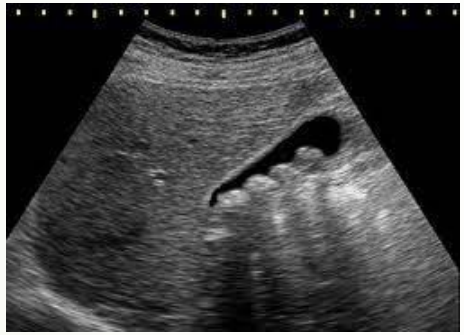
Supravital stain(retics)

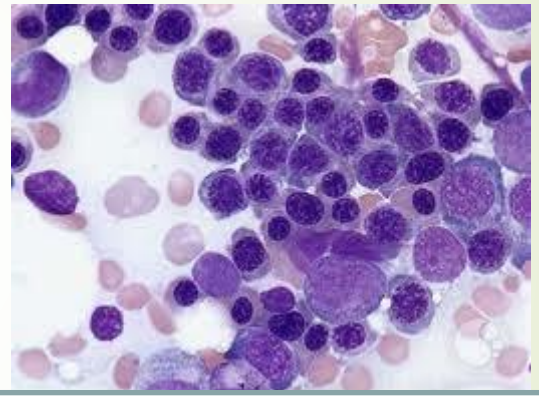


Case 3

CT Abdomen AbdominalUS BM aspirate







BM:erythroid hyperplasia with megaloblastoid changes

Diagnosis: AIHA. Treated with steroids + folic acid, complete response, but 9 months later had NHL.

Hemolysis= RBC destruction= Shortend RBC Survival with or without anemia

Hemolytic Anemias –Classification

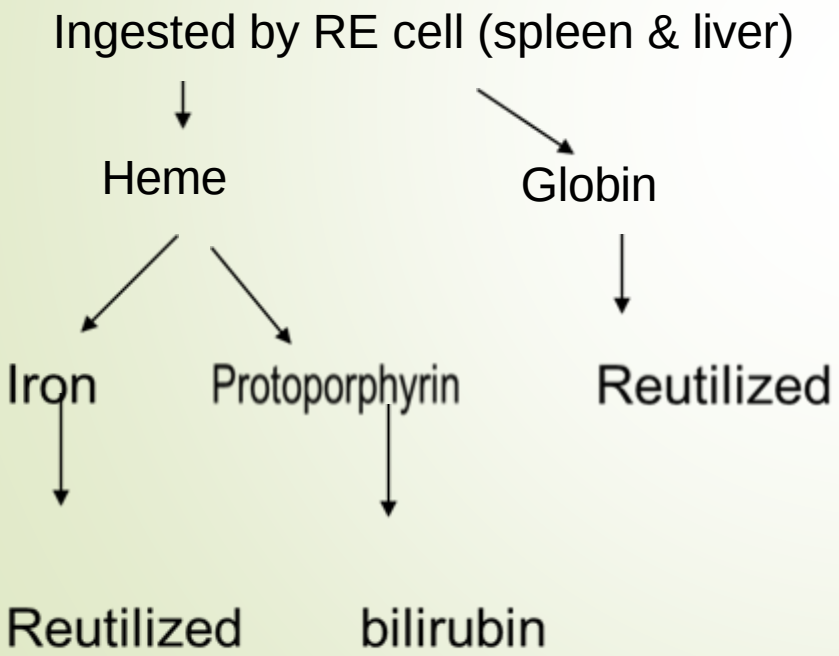
- **By sites of red cell destruction: intra *v* extravascular**

- **Acquired (immune, Non-immune).**

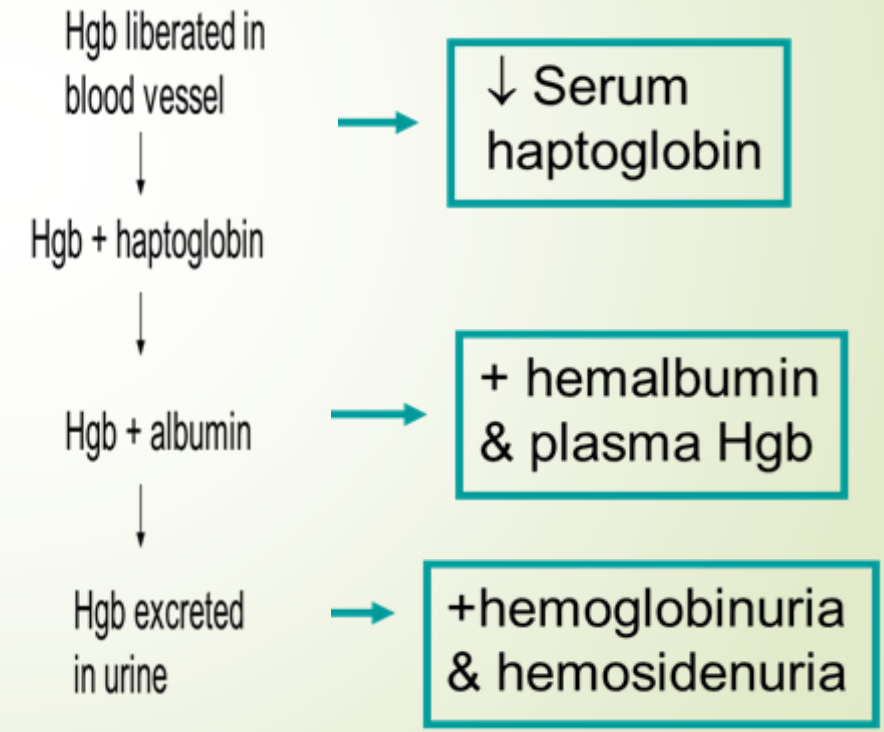
v **congenital (membrane: HS, Enzymopathies: G6PD def/PK, Hb-pathies: Thal, ss)**

- **By mechanism of red cell damage:**

Extravascular Hemolysis



Intravascular Hemolysis



Hemolysis

Evidence for increased red cell production

- **In the blood:**
  - **Elevated reticulocyte count (corrected/RPI)**
  - **Circulating NRBCs may be present**
- **In the bone marrow:**
  - **erythroid hyperplasia**
  - **reduced M/E (myeloid/ erythroid erythroid ratio)**
- **In the bone:**
  - **Deforming changes in the skull and long bones (“ frontal bossing ”)**

General Clinical Features

1 Anemia syndrome
2 Spleenomegaly
3-gallstones.
4 Dark urine (tea-colored or red)
5 Patients may have chronic ankle ulcers.
6 Aplastic crises associated with Parvovirus B19, may occur
7 Increased requirement for folate

Gallbladder stones/ biliary/ pigment stones

Parvovirus B19

- **Non-encapsulated DNA virus.**
- **Infects and lyses RBC precursors in marrow, causing 7-10d cessation of erythropoiesis.**
- **Normal individuals have no significant hematologic effect, since RBCs have normal life span.**
- **In pts with hemolytic anemias , loss of red cell production causes Aplastic Crisis**

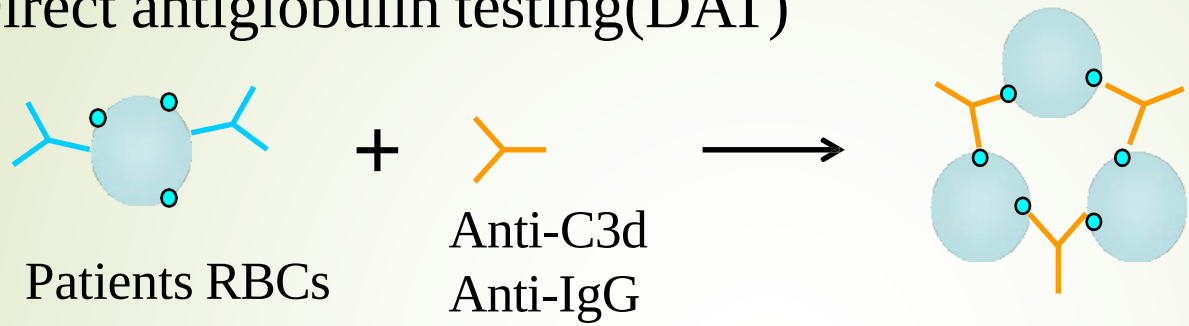
Autoimmune Hemolytic Anemia

- Warm antibodies (IgG-mediated)
  - Primary 45%
  - Secondary 40%
    - Lymphoproliferative disease
    - Connective tissue disease
    - Infectious disease
  - Drug-induced 15%

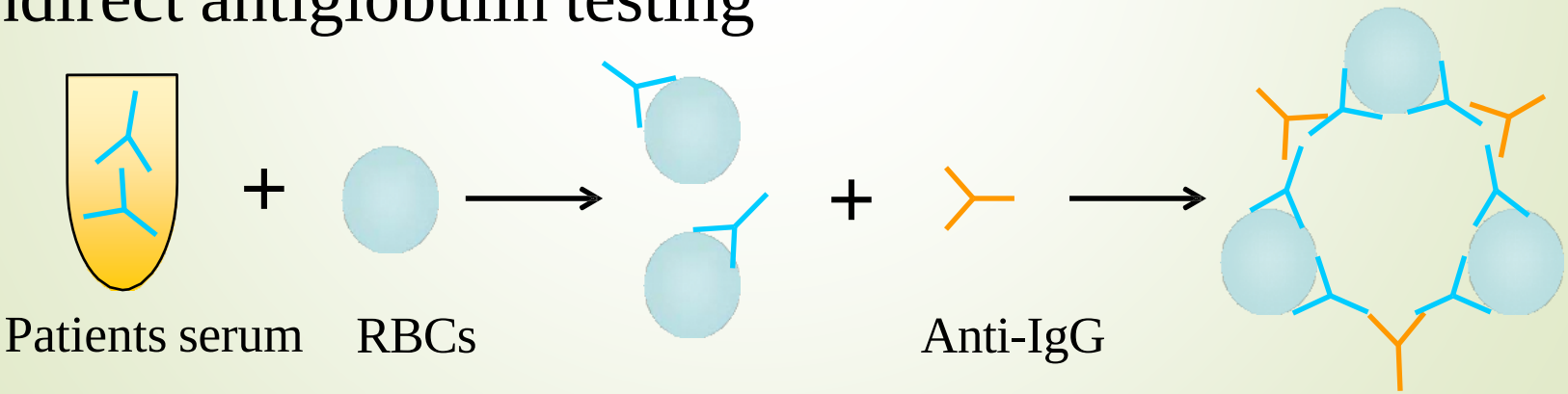
- Laboratory testing
  - Normocytic/macrocytic anemia
  - Peripheral smear - spherocytosis

Anti-Globulin (Coombs) Testing

Direct antiglobulin testing(DAT)



Indirect antiglobulin testing



Treatment of Autoimmune Hemolytic Anemia (Warm Antibody type)

- Treat underlying disease if indicated
- Prednisone (1 mg/kg/day for two weeks, then taper)
- Splenectomy ??
- Other
  - Immunosuppressive agents
  - IVIG

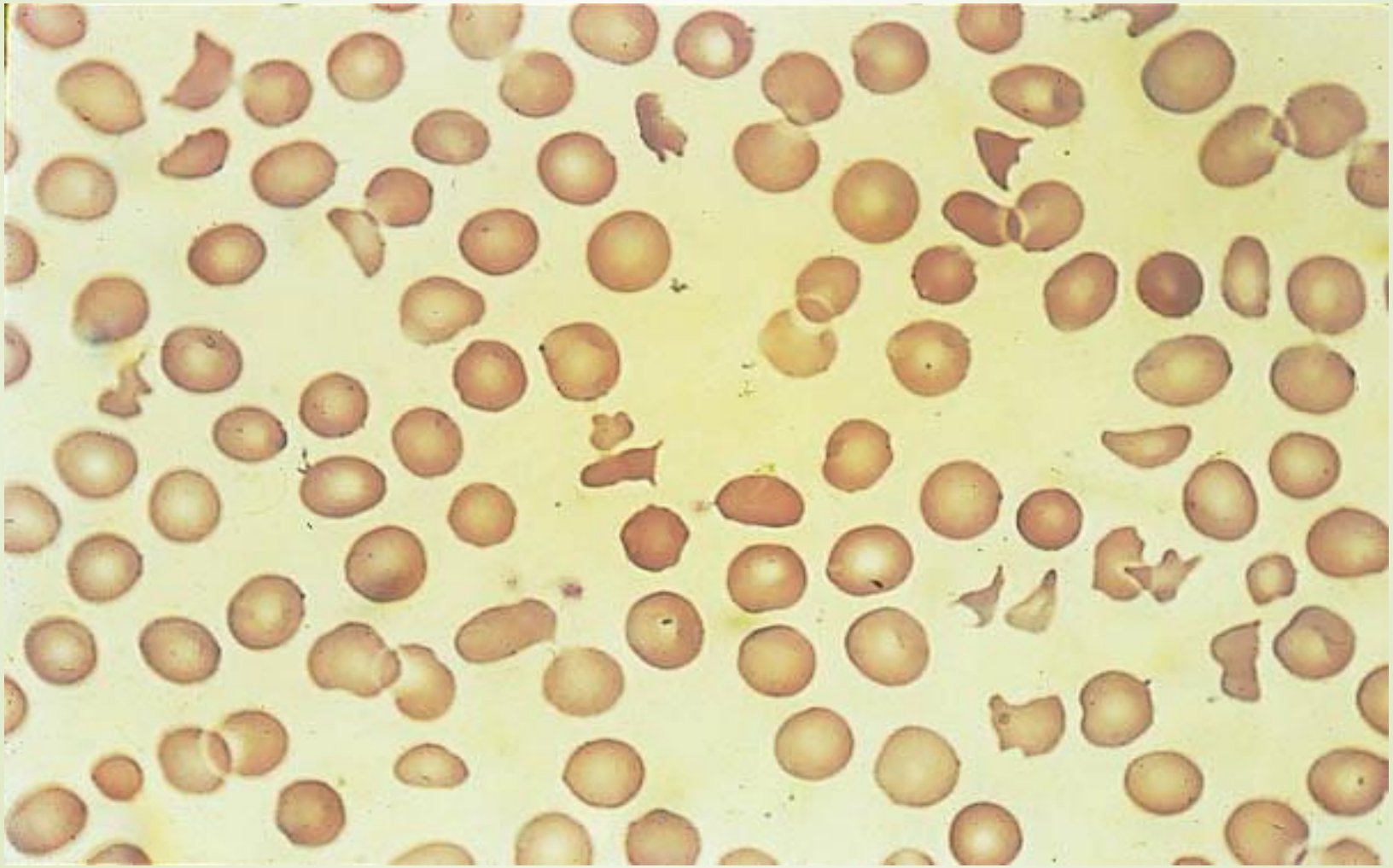
Hemolytic Anemia with Intravascular Hemolysis

- Mechanical damage (Microangiopathic hemolytic anemia)
- Chemical damage (Burns)
- Infection (Malaria or Babesiosis)
- Transfusion reaction (ABO incompatibility)

Differential Diagnosis of Microangiopathic Hemolytic Anemia

- Thrombotic thrombocytopenic purpura (TTP)
- Hemolytic uremic syndrome (HUS)
- Disseminated intravascular coagulation (DIC)
- Vasculitis
- Malignant hypertension
- Metastatic neoplasm with vascular invasion
- Preeclampsia/HELLP syndrome of pregnancy

Schistocytes: Microangiopathic Hemolytic Anemia



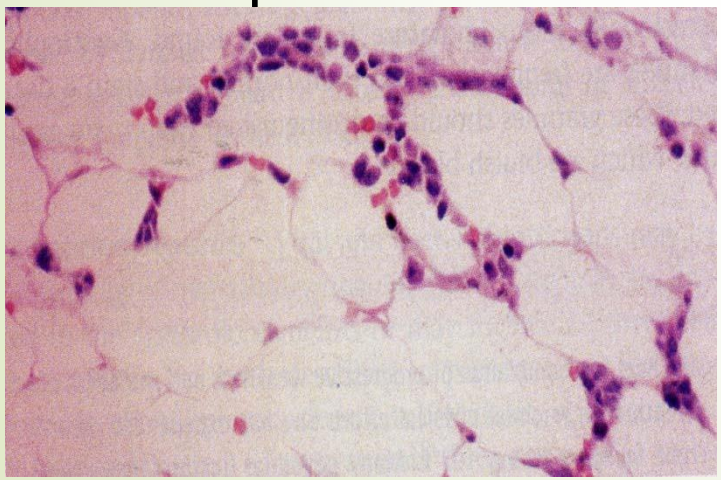
Case 3 B

19 yr old male presented with “anemia syndrome”, fever and easy bruising. No splenomegaly

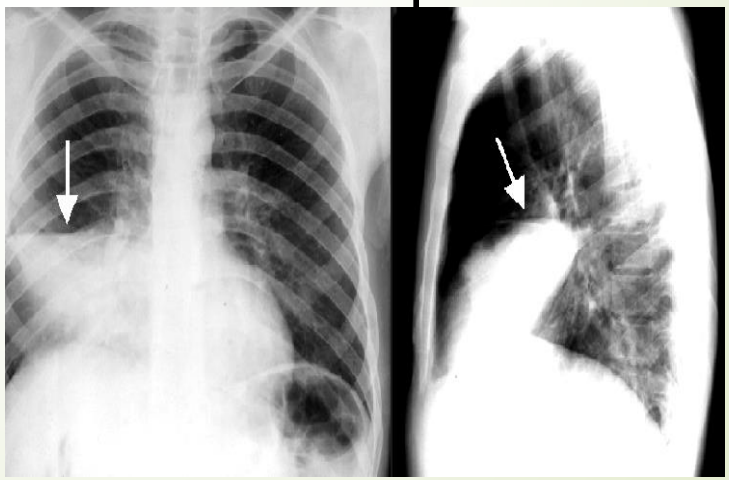
Hb 6 g/dl,WBC 1500 : N10%, L 80%, others 10%.

Retics© 0,001%.MCV 105fl,Plt 20k.

BM/ Trephine



CXR/lobar pneumonia



APLASTIC ANEMIA

- Aplastic anemia is a severe, life threatening syndrome in which production of erythrocytes, WBCs, and platelets has failed.
- Aplastic anemia may occur in all age groups and both genders.
- The disease is characterized by peripheral pancytopenia and accompanied by a hypocellular bone marrow.

APLASTIC ANEMIA

- The primary defect is a reduction in or depletion of hematopoietic precursor stem cells with decreased production of all cell lines
  - This may be due to quantitative or qualitative damage to the pluripotential stem cell.
  - In rare instances it is the result of abnormal hormonal stimulation of stem cell proliferation
  - or the result of a defective bone marrow microenvironment
  - or from cellular or humoral immunosuppression of hematopoiesis.

Causes of Bone Marrow Failure

Acquired

-Idiopathic

-PNH

Secondary

-Drugs

-- radiation

-Viruses

Inherited

-Fanconi anemia

-Diamond-Blackfan Anemia

-Other rare conditions

Clinical manifestations of AA

- »Anemia syndrome
- »Neutropenia syndrome
- »Thrombocytopenia syndrome
- »Combination of the above

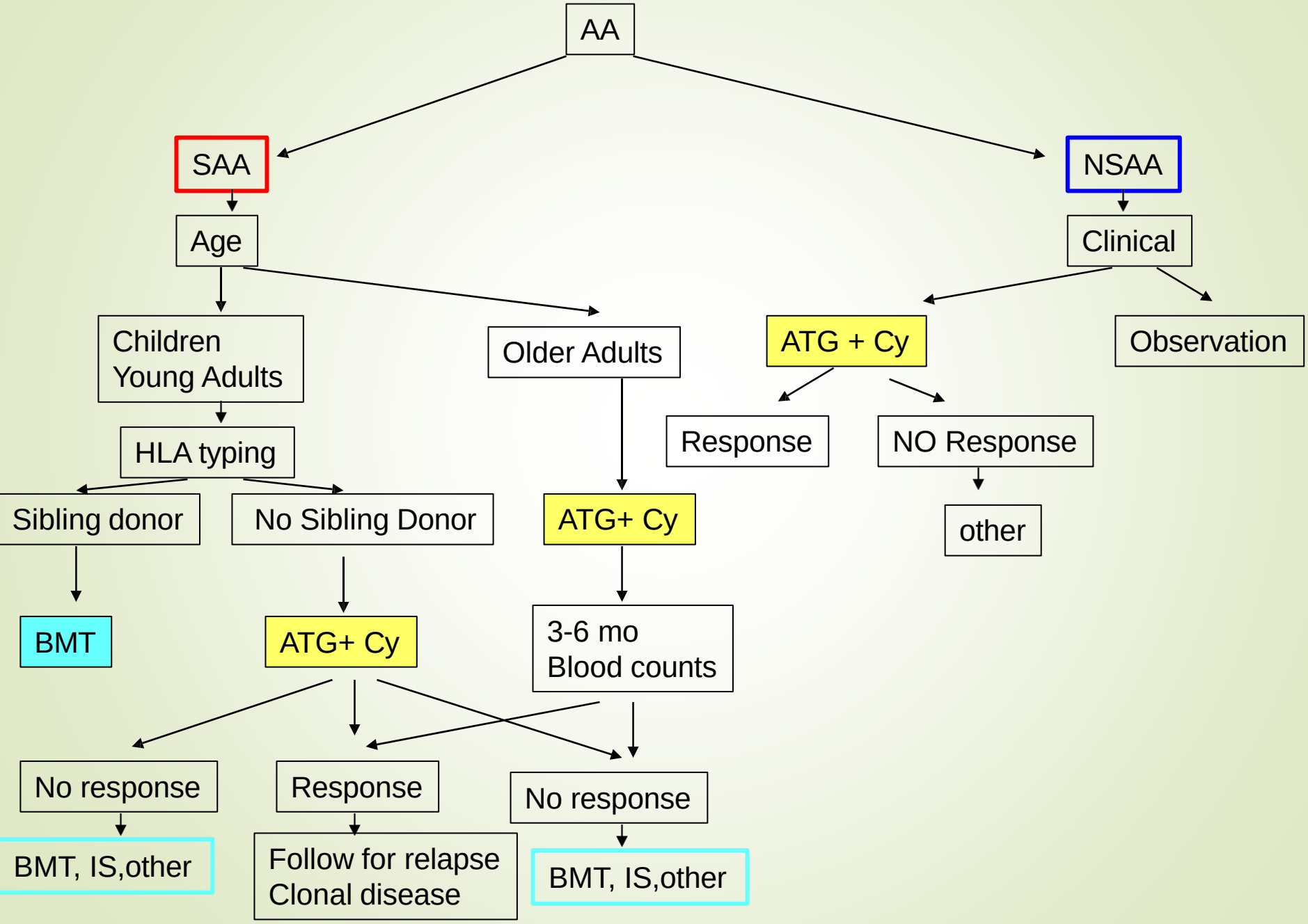
Presenting Symptoms of Aplastic Anemia

Symptoms	Number of Patients
Bleeding	41
Anemia	27
Bleeding and anemia	14
Bleeding and infection	6
Infection	5
Routine examination	8
Total	101

Classification of aplastic anemia

Classification	Criteria
Severe	BM cellularity < 25% (or < 50% if < 30% of BM is hematopoietic cells) AND ≥ 2 of the following: • Peripheral blood neutrophil count < 0.5×10^9/L • Peripheral blood platelet count < 20×10^9/L • Peripheral blood reticulocyte count < 20×10^9/L
Very severe	As above, but peripheral blood neutrophil count must be < 0.2×10^9/L
Nonsevere	Hypocellular BM with peripheral blood values not meeting criteria for severe aplastic anemia

Treatment Algorithm for AA

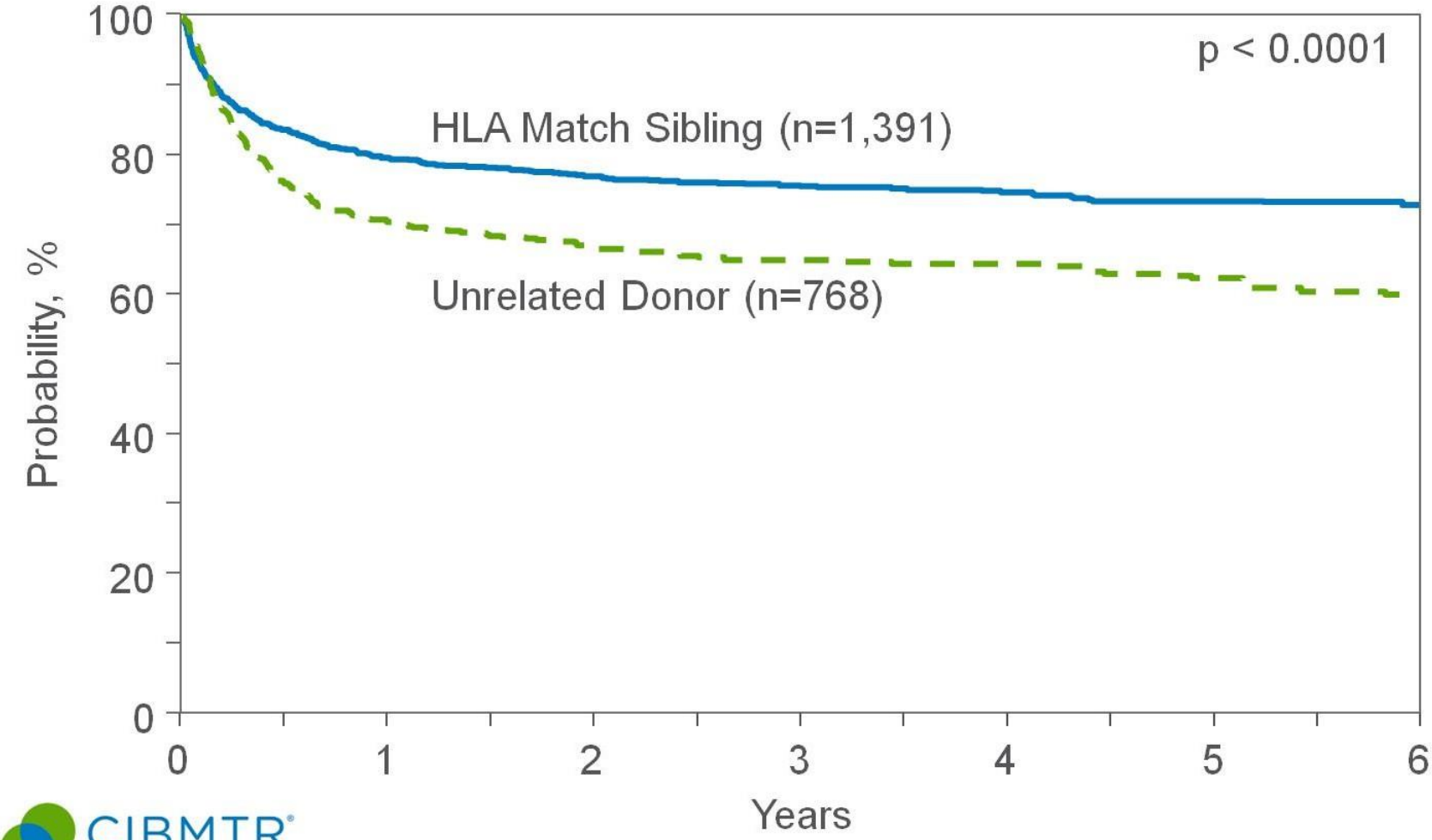


Treatment of AA

- Remove causative agent, if known
- Supportive care
  - RBC transfusions
  - Treat infections
  - Treat Bleeding
- **Bone marrow transplant**
- Immune suppression
  - CSA
  - ATG

Combination of the above

Survival after Allogeneic Transplants for Severe Aplastic Anemia, ≥ 20 Years, 2002-2012



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By Donor Type

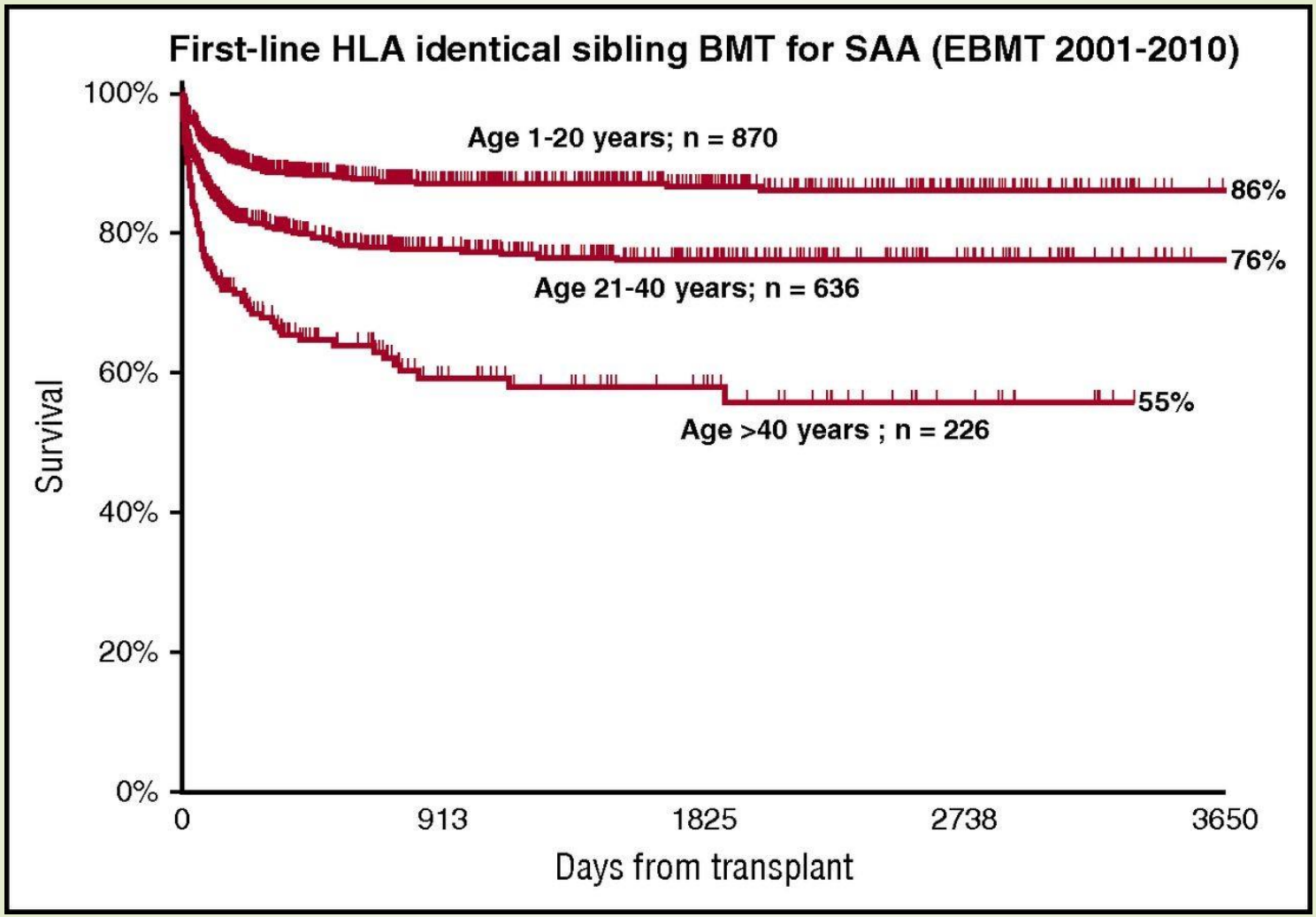
Immunosuppression for AA

Table 1. Intensive immunosuppression (ATG plus cyclosporine) for severe aplastic anemia

Study	N	Median Age (years)	Response	Relapse	Clonal Evolution	Survival
German[108]	84	32	65%	19%	8%	58% at 11 yrs
EGMBT[71]	100	16	77%	12%	11%	87% at 5 yrs
NIH[70]	122	35	61%	35%	11%	55% at 7 yrs
Japan*[72]	119	9	68%	22%	6%	88% at 3 yrs
NIH*[81]	104	30	62%	37%	9%	80% at 4 yrs

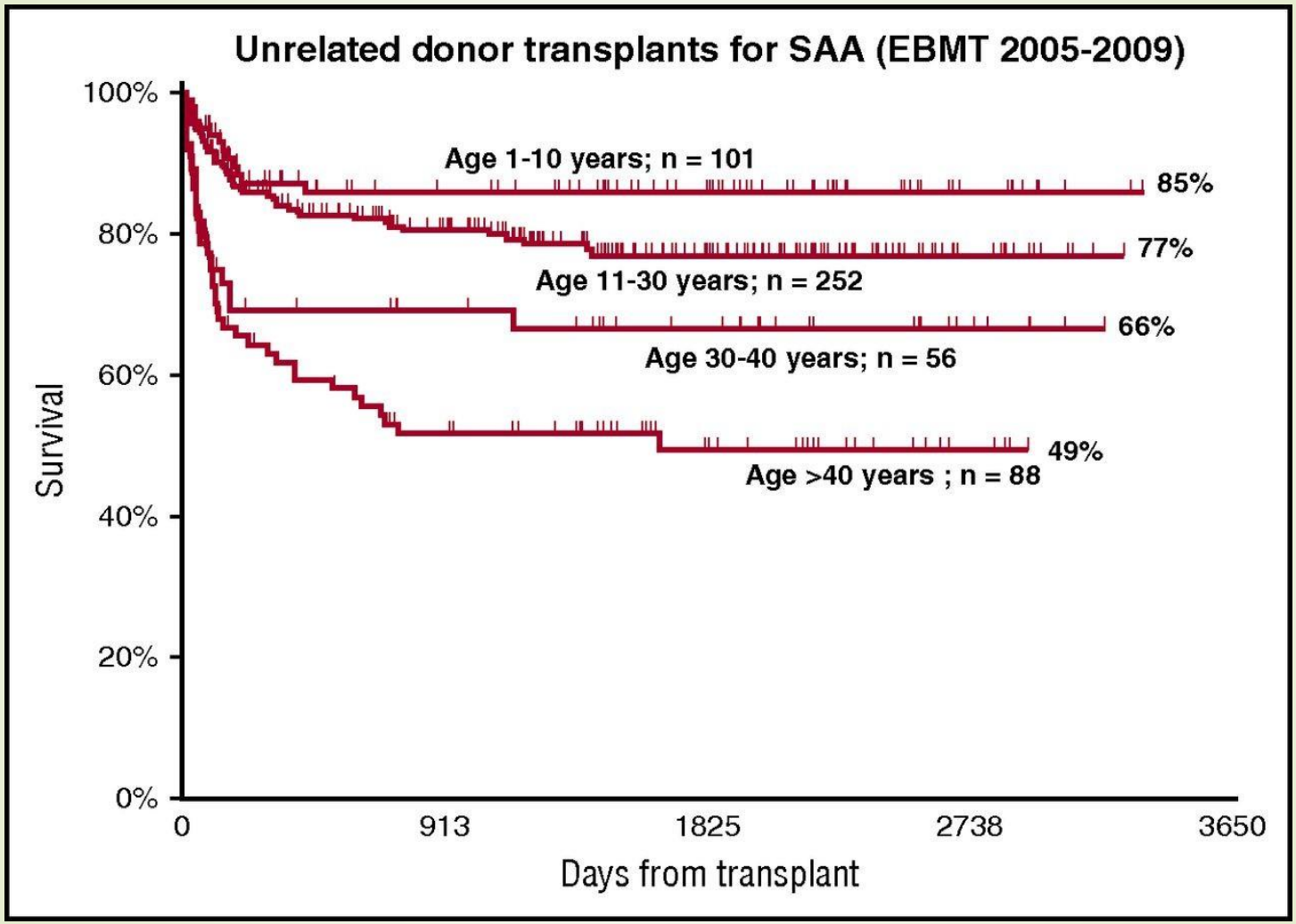
Young NS et al BLOOD 2006

A strong age effect in patients with aplastic anemia, after transplantation from an HLA identical sibling.



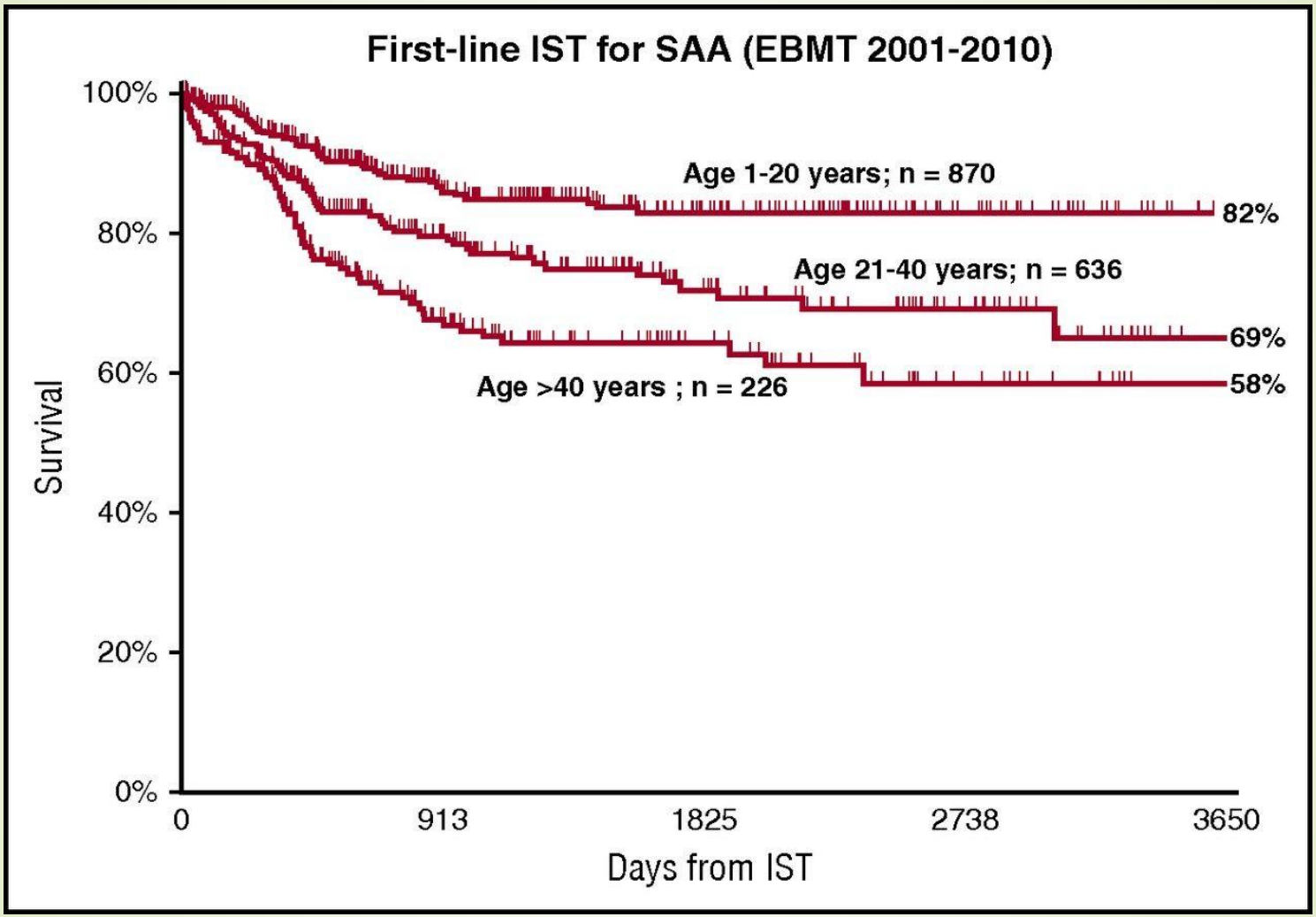
Andrea Bacigalupo Blood 2017;129:1428-1436

The age effect in UD transplants: best outcome is seen for very young patients, for whom first-line UD BMT may be considered.



Andrea Bacigalupo Blood 2017;129:1428-1436

The age effect in patients receiving first-line IST. Data from the EBMT registry.



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RELATED DISORDERS

1- Disorders in which there is peripheral pancytopenia, but the bone marrow is normocellular, hypercellular, or infiltrated with abnormal cellular elements (Myelopthesic anemia)

– replacement of bone marrow by fibrotic, granulomatous, or neoplastic cells

2 Pure red Cell aplasia

3 Myelodysplastic syndrome (MDS)