

Anemia (3).ms 13.02.2020

Hemolytic Anemia

Abdallah Abbadi

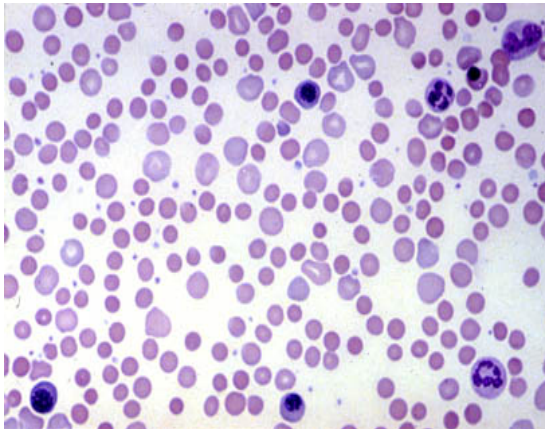
Feras Fararjeh

Case 3

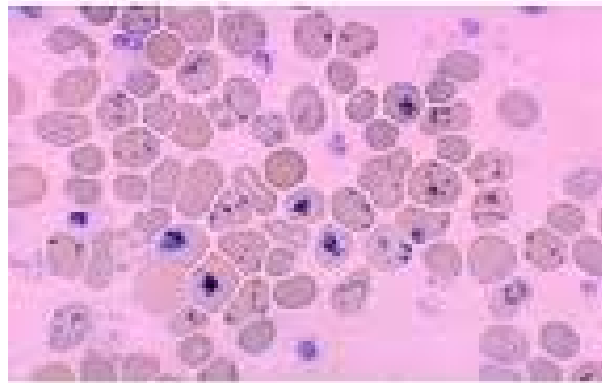
24 yr old female presented with “anemia syndrome” and jaundice. She was found to have splenomegaly.

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

Bld film

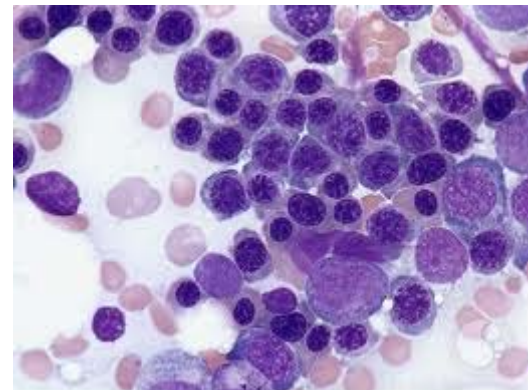


Supravital stain(retics)



Case 3

CT Abdomen AbdominalUS BM aspirate



BM:erythroid hyperplasia with
megaloblastoid changes

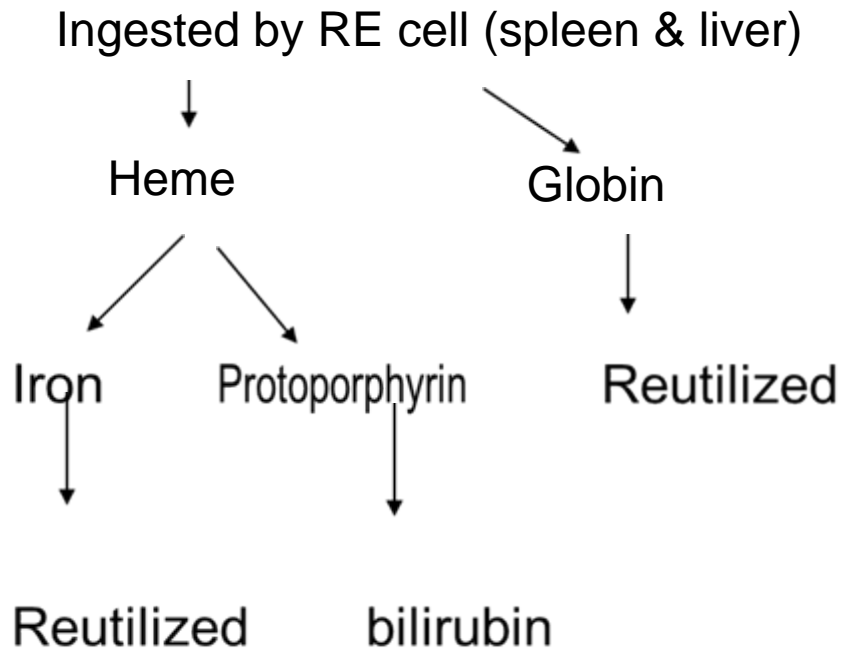
Diagnosis: AIHA. Treated with steroids + folic acid, complete response, but 9 months later had NHL.

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

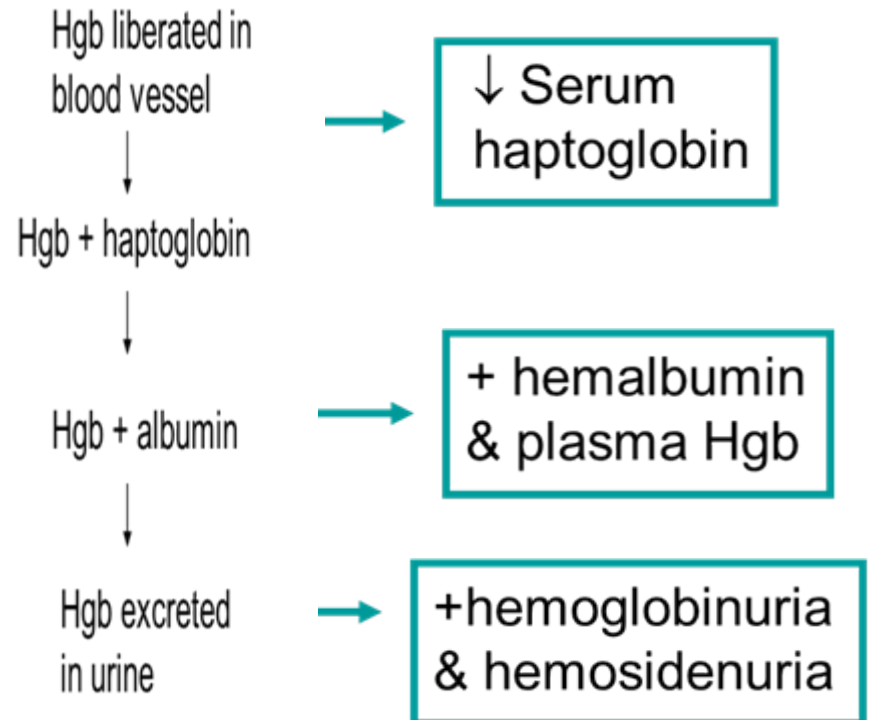
Hemolytic Anemias –Classification

- **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- **Splenomegaly**
- 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

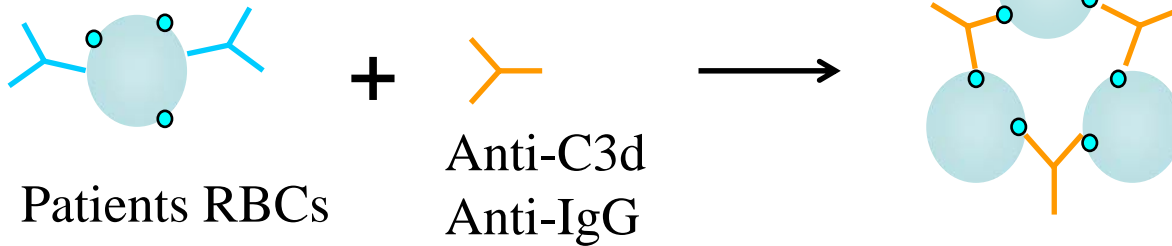
- **Non-encapsulated DNA virus.**
- **Infects and lyses RBC precursors in marrow, causing 7-10d cessation of erythropoiesis.**
- **Normal individuals have no significant hematologic effect, since RBCs have normal life span.**
- **In pts with hemolytic anemias , loss of red cell production causes Aplastic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

Autoimmune Hemolytic Anemia

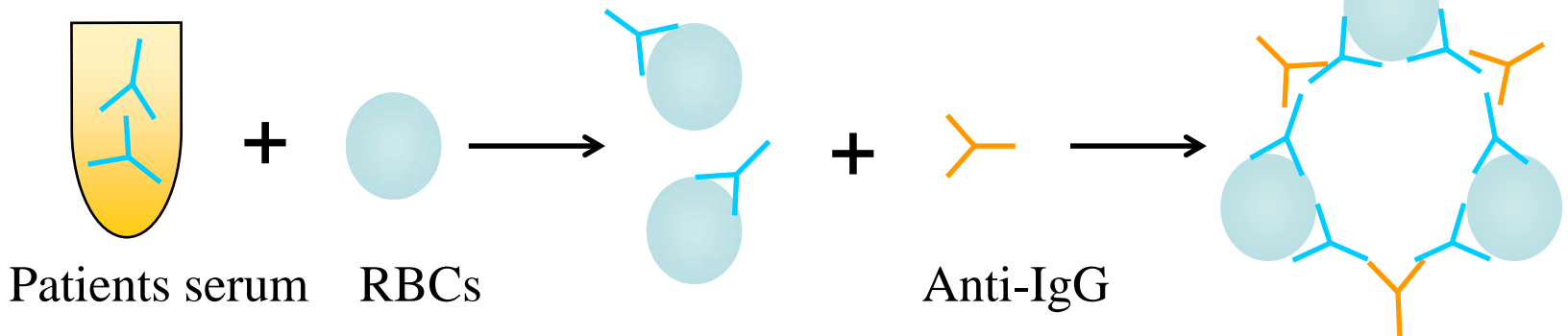
- Warm antibodies (IgG-mediated)
 - Primary 45%
 - Secondary 40%
 - Lymphoproliferative disease
 - Connective tissue disease
 - Infectious disease
 - Drug-induced 15%
- Laboratory testing
 - Normocytic/macrocytic anemia
 - Peripheral smear - spherocytosis

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

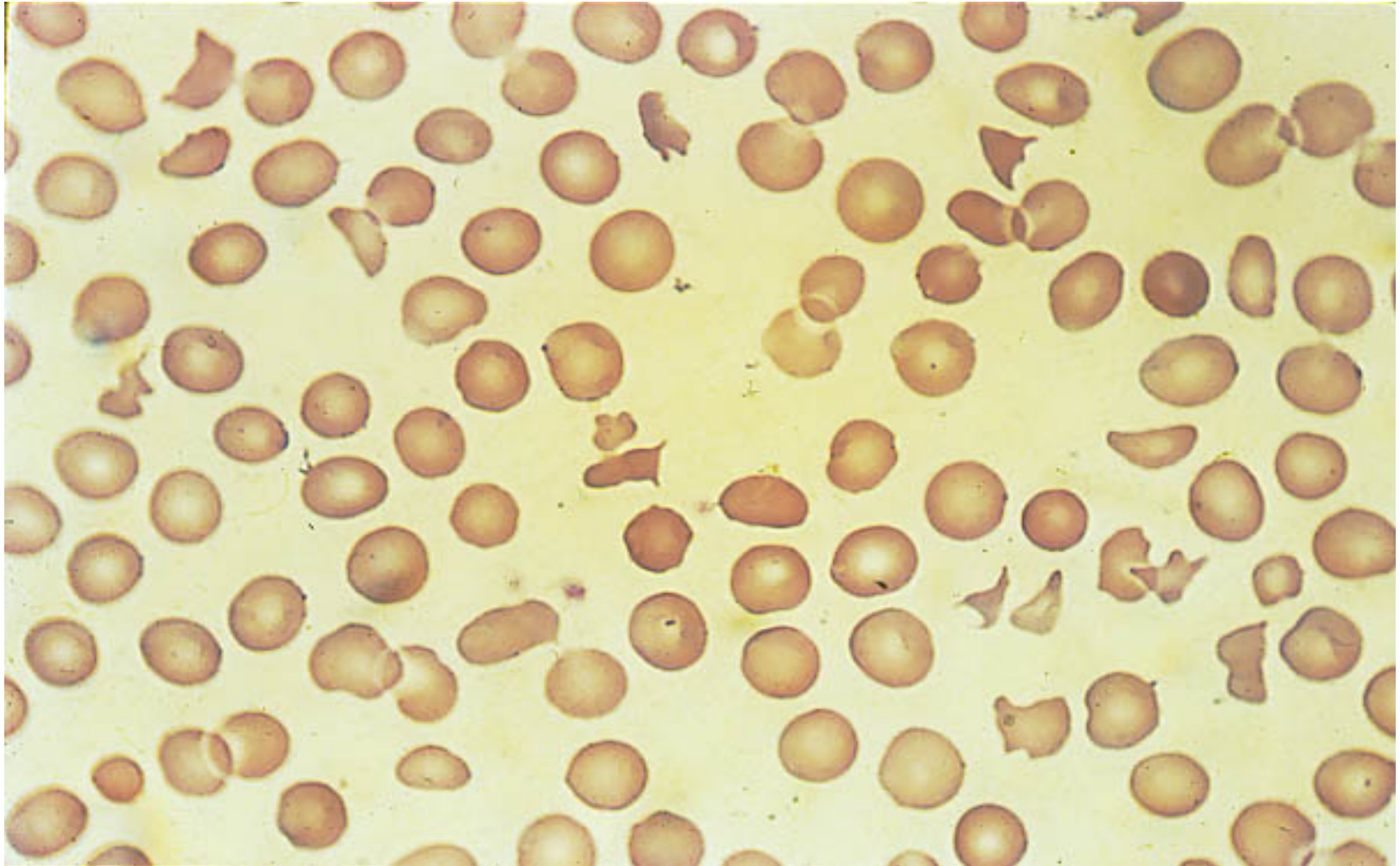
Hemolytic Anemia with Intravascular Hemolysis

- 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



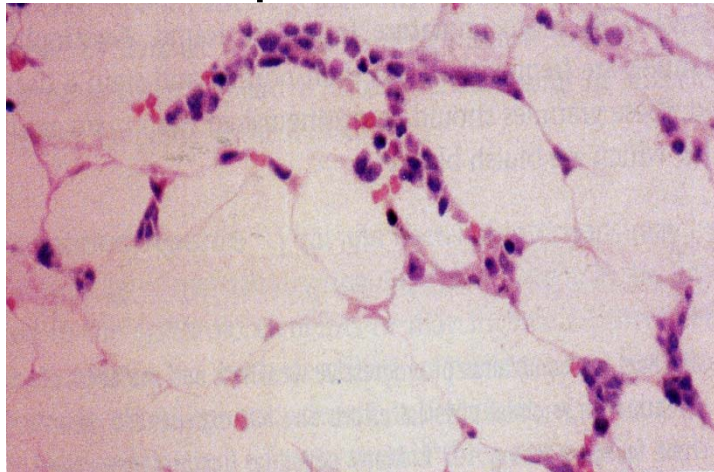
Case 3 B

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

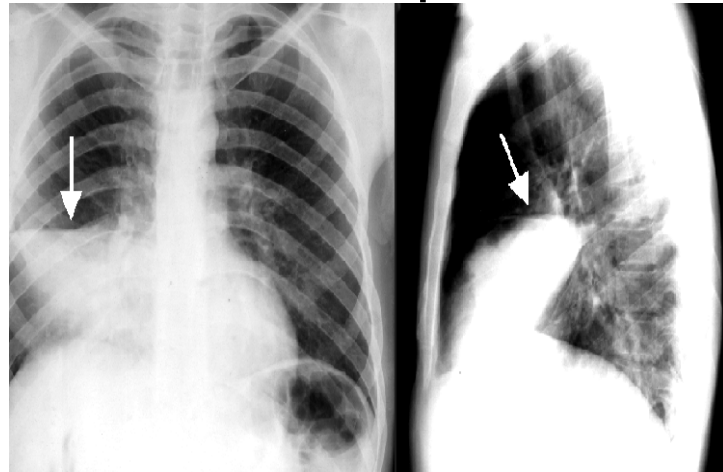
Hb 6 g/dl, WBC 1500 : N10%, L 80%, others 10%.

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

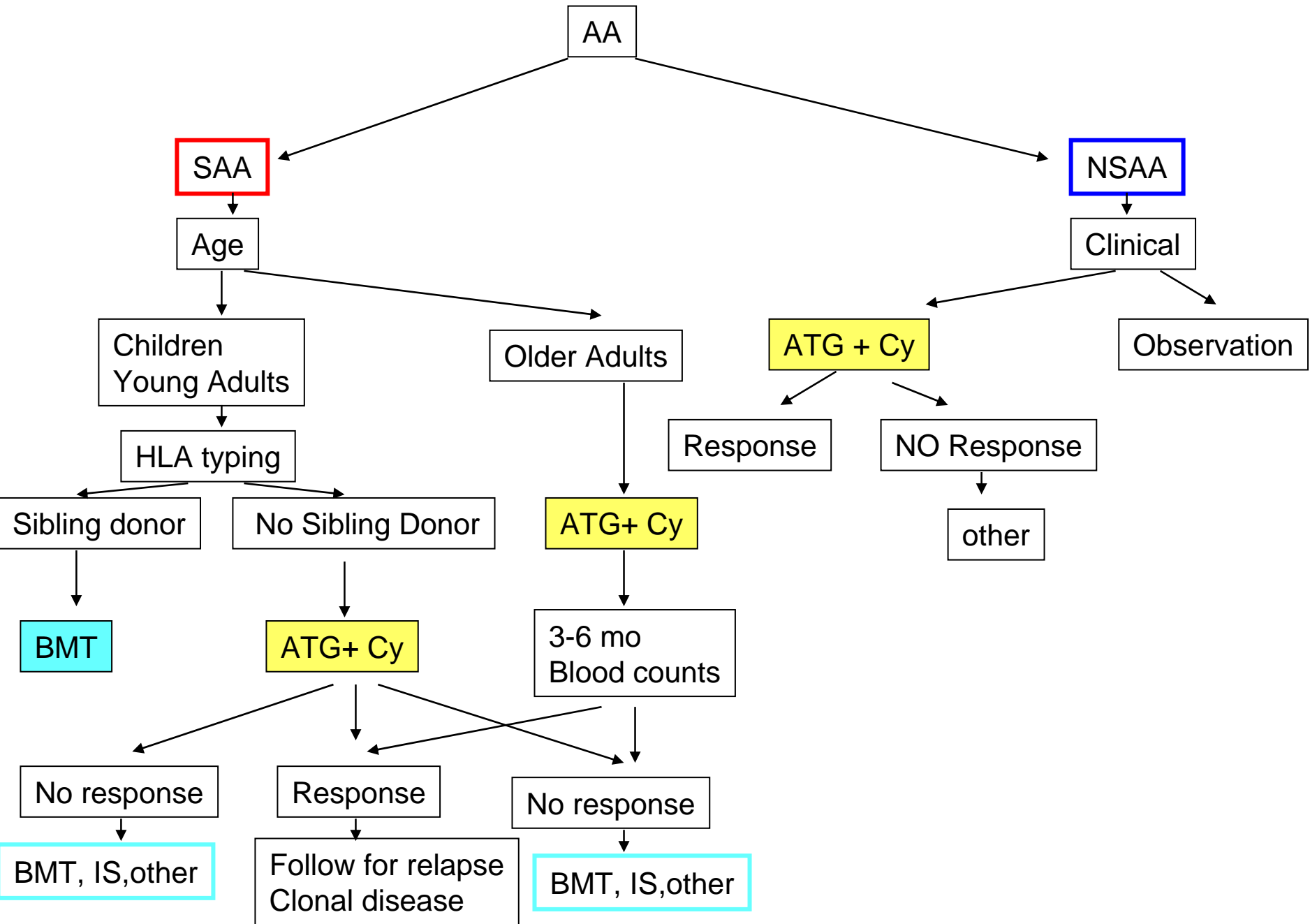
Presenting Symptoms of Aplastic Anemia

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: <ul style="list-style-type: none">• Peripheral blood neutrophil count < $0.5 \times 10^9/L$• Peripheral blood platelet count < $20 \times 10^9/L$• Peripheral blood reticulocyte count < $20 \times 10^9/L$
Very severe	As above, but peripheral blood neutrophil count must be < $0.2 \times 10^9/L$
Nonsevere	Hypocellular BM with peripheral blood values not meeting criteria for severe aplastic anemia

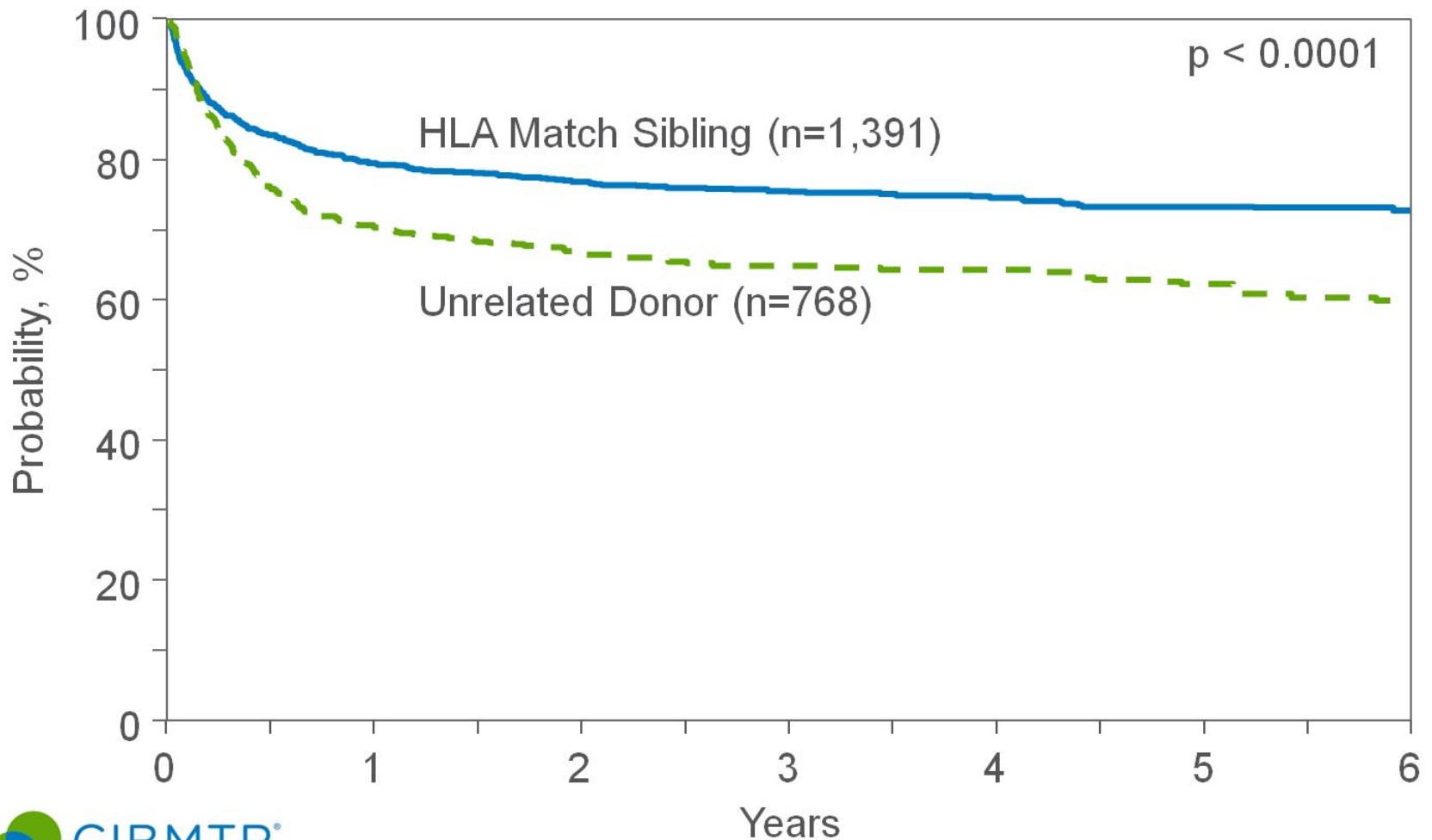
Treatment Algorithm for AA



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

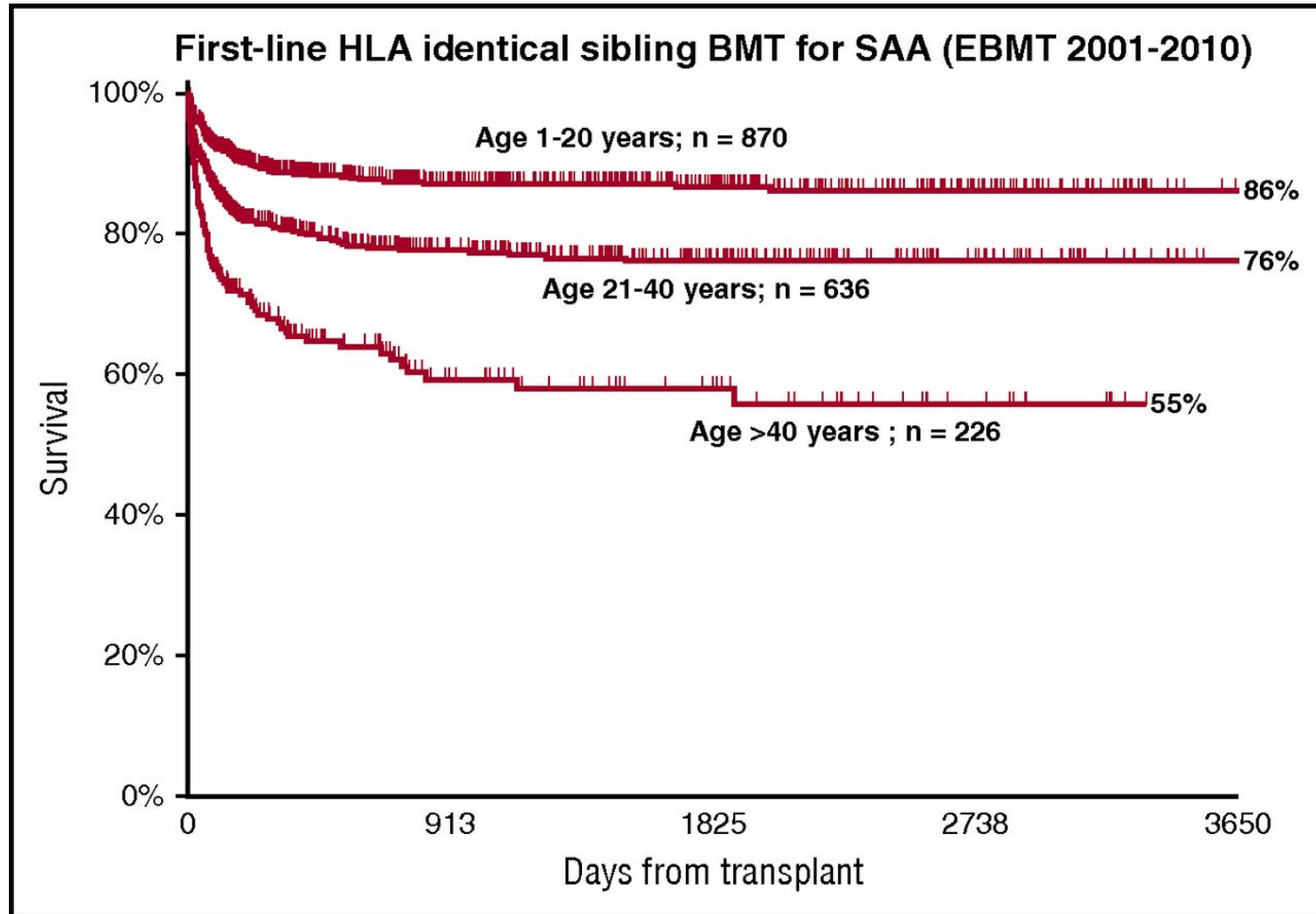


Immunosuppression for AA

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

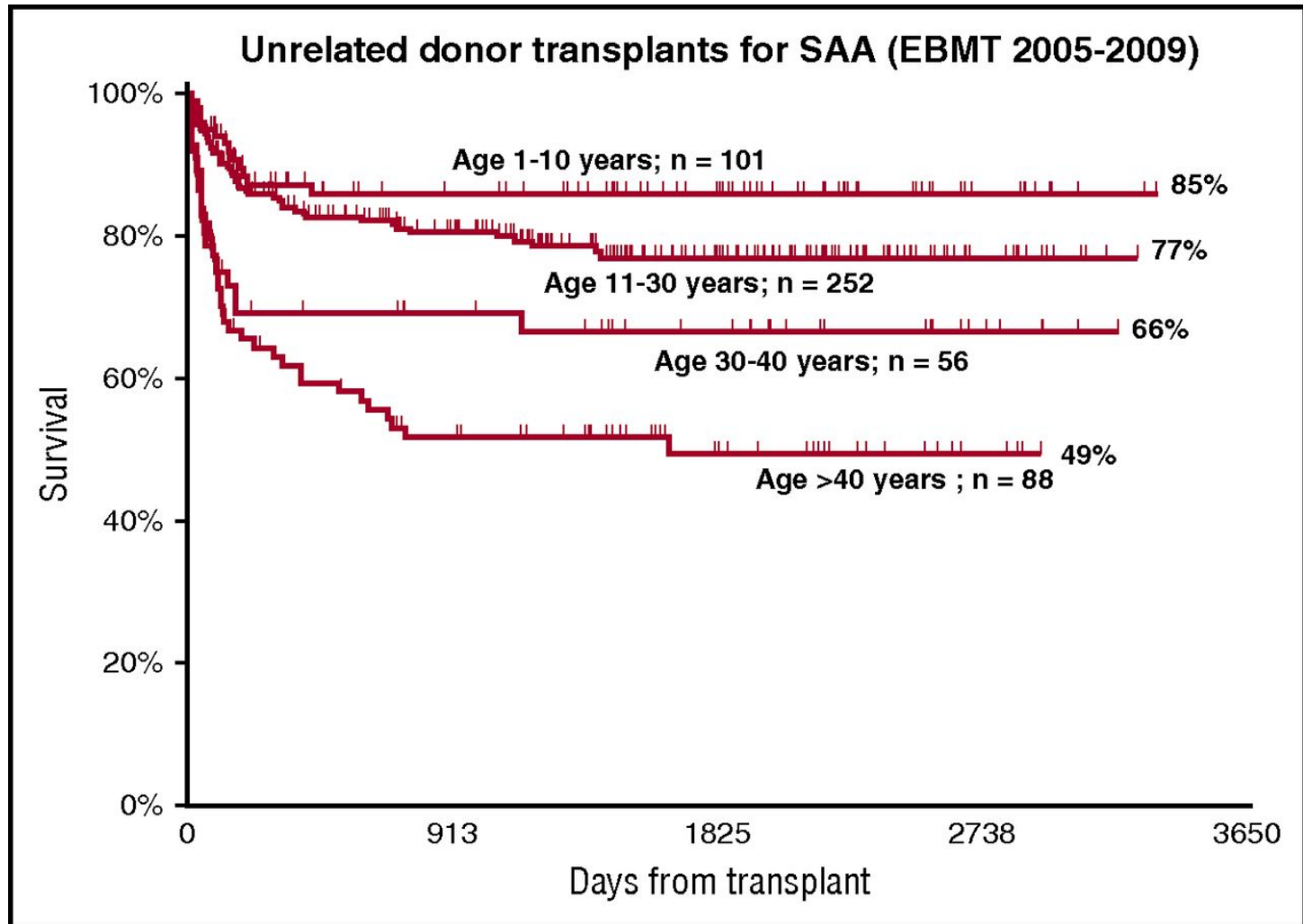
Study	N	Median Age (years)	Response	Relapse	Clonal Evolution	Survival
German ¹⁰⁸	84	32	65%	19%	8%	58% at 11 yrs
EGMBT ⁷¹	100	16	77%	12%	11%	87% at 5 yrs
NIH ⁷⁰	122	35	61%	35%	11%	55% at 7 yrs
Japan* ⁷²	119	9	68%	22%	6%	88% at 3 yrs
NIH* ⁸¹	104	30	62%	37%	9%	80% at 4 yrs

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



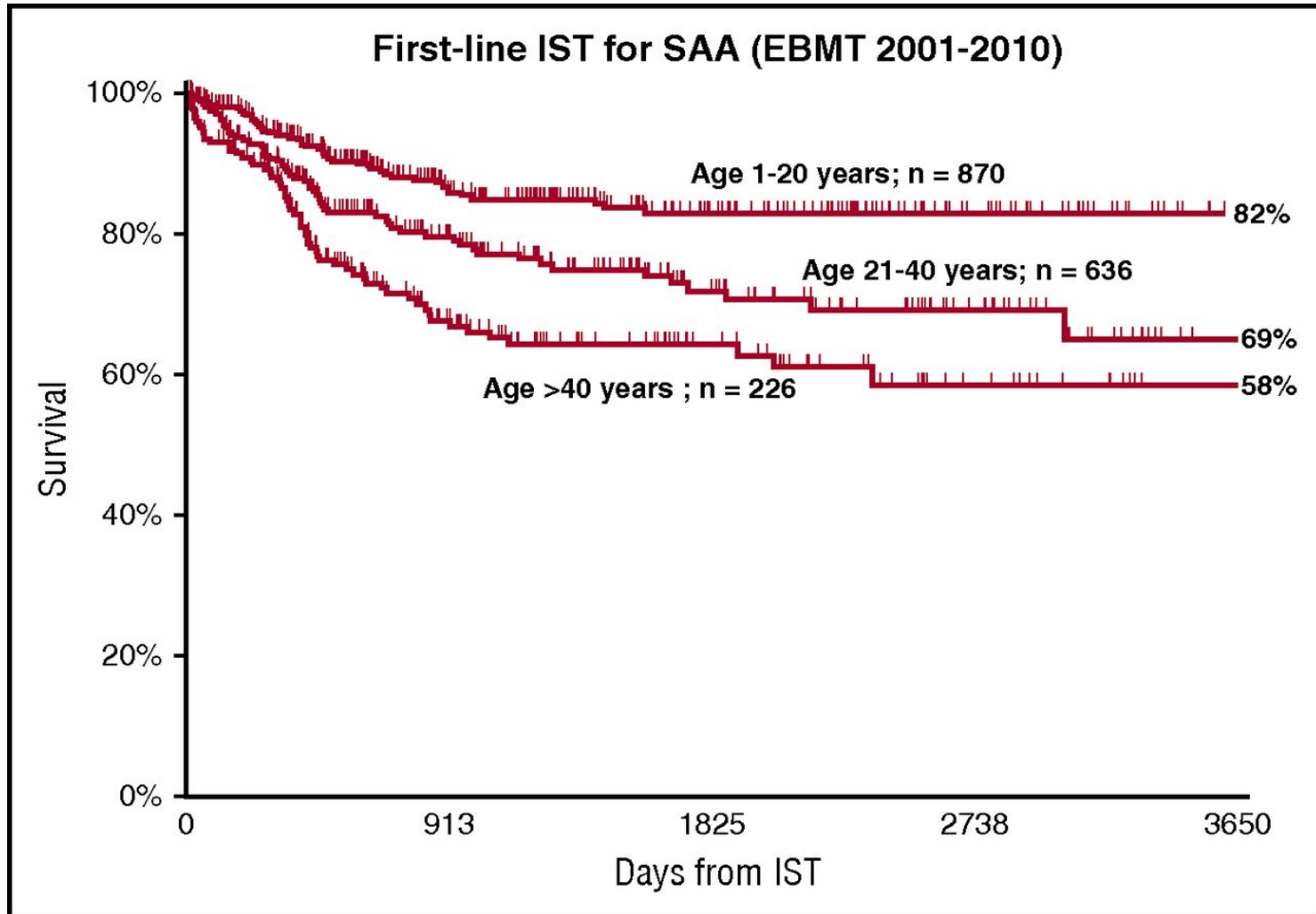
Andrea Bacigalupo Blood 2017;129:1428-1436

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.



Andrea Bacigalupo Blood 2017;129:1428-1436



RELATED DISORDERS

- 1- Disorders in which there is peripheral pancytopenia, but the bone marrow is normocellular, hypercellular, or infiltrated with abnormal cellular elements (Myelophthestic anemia)
 - replacement of bone marrow by fibrotic, granulomatous, or neoplastic cells
- 2- Pure red Cell aplasia
- 3- Myelodysplastic syndrome (MDS)