Anemia (3).ms 18.11.2020

Hemolytic Anemia

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- hemolytic anemia: premature, early distruction of RBCs, so the bone marrow is not able to compensate with the Erythrocytes loss
- could be conginital or acquired

Case 3

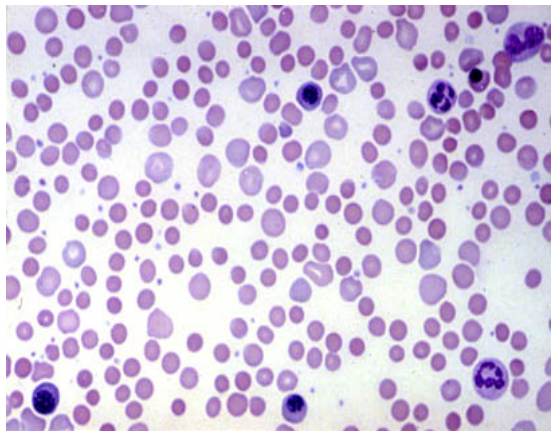
24 yr old female presented with “anemia syndrome” and jaundice. She was found to have splenomegaly.

over production

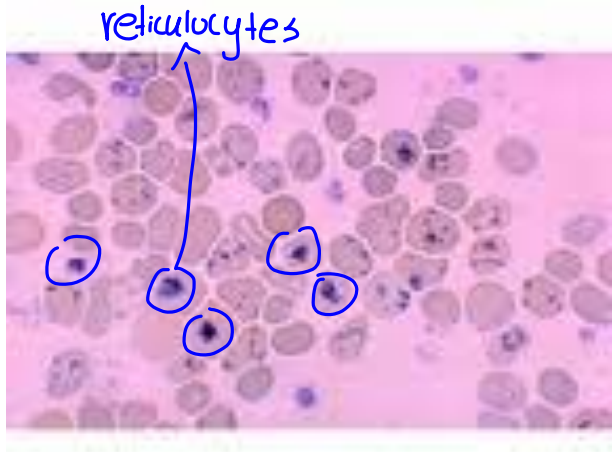
Hb 8, wbc 12k, Plt 212k, retics© 12%, LDH 1400, bilirubin 7mg/dl,d 2.5mg/dl, DAT +3.Bld film spherocytes, polychromasia.

it is used to detect autoimmune hemolysis

Bld film

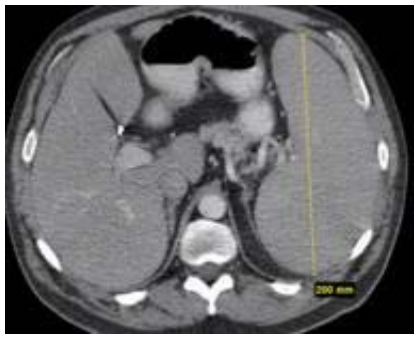


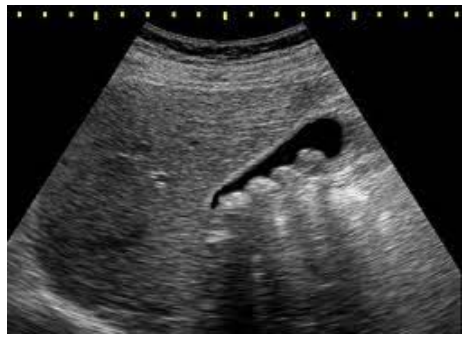
Supravital stain(retics)

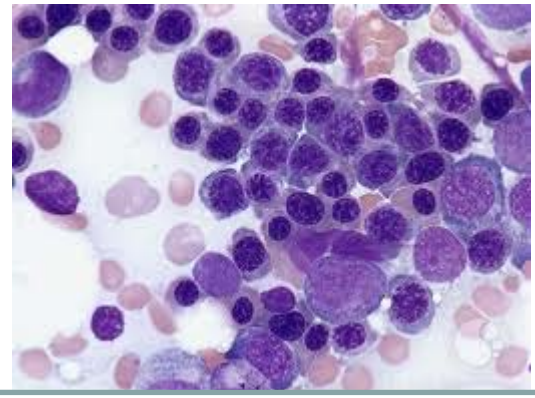


Case 3

CT Abdomen AbdominalUS BM aspirate







BM:erythroid hyperplasia with megaloblastoid changes

autoimmune hemolysis anemia

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

Treatment by steroids

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

classification types

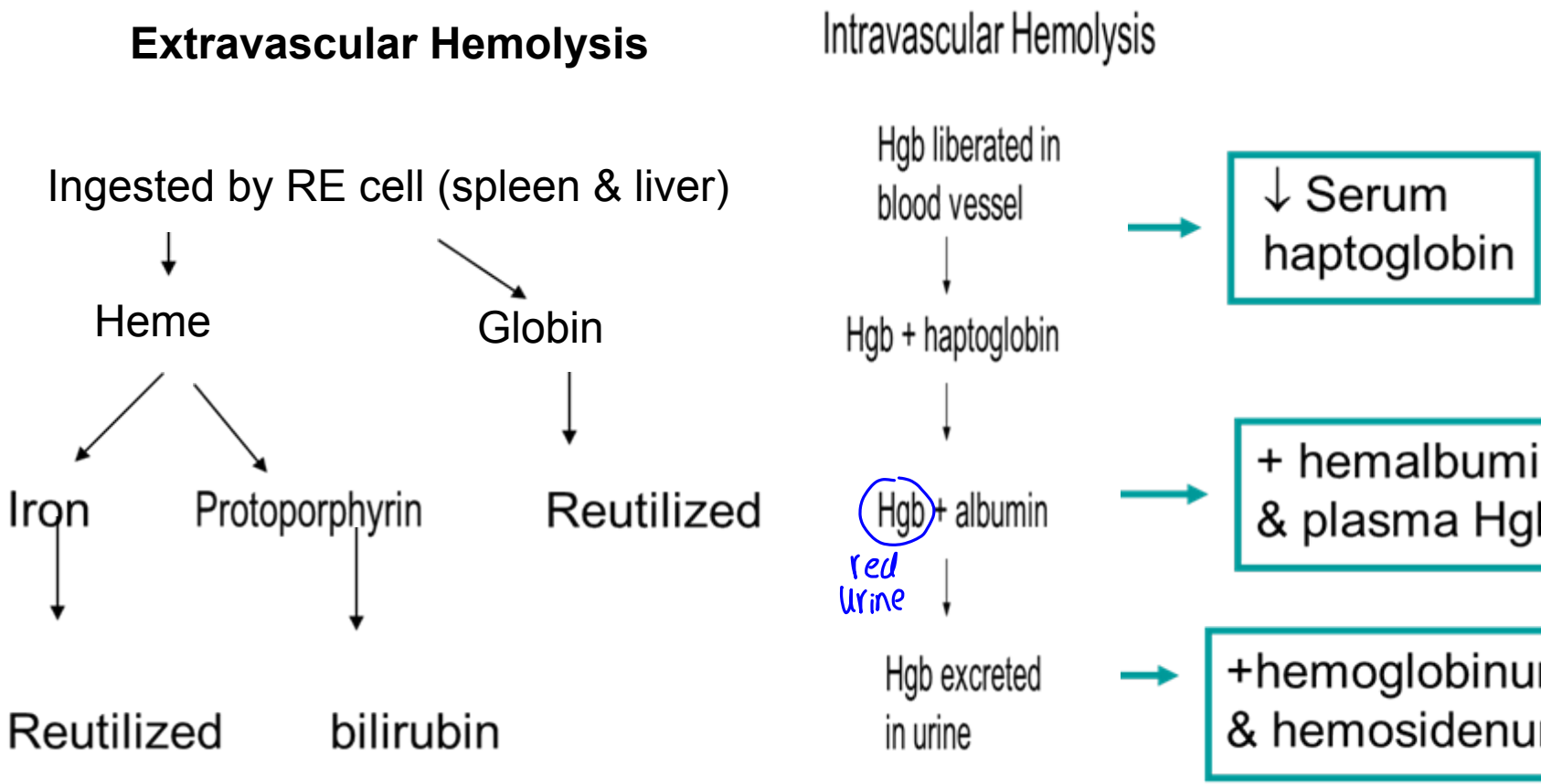
Hemolytic Anemias –Classification

(1) • **By sites** of red cell destruction: intra *v* extravascular

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

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

• By mechanism of red cell damage:


Extravascular Hemolysis
Ingested by RE cell (spleen & liver)
Heme
Globin
Iron
Protoporphyrin
Reutilized
Reutilized
bilirubin
Intravascular Hemolysis
Hgb liberated in blood vessel
Hgb + haptoglobin
Hgb + albumin
red urine
Hgb excreted in urine
↓ Serum haptoglobin
+ hemalbumi
& plasma Hgl
+hemoglobinu
& hemosidenu

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 expansion long bones (“ frontal bossing ”)

General Clinical Features

1- **Anemia syndrome**
2- **Spleenomegaly**
3-**gallstones.** extravascular type
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 to viral or bacterial infections 40%
    - Lymphoproliferative disease
    - Connective tissue disease
    - Infectious disease
  - Drug-induced 15%

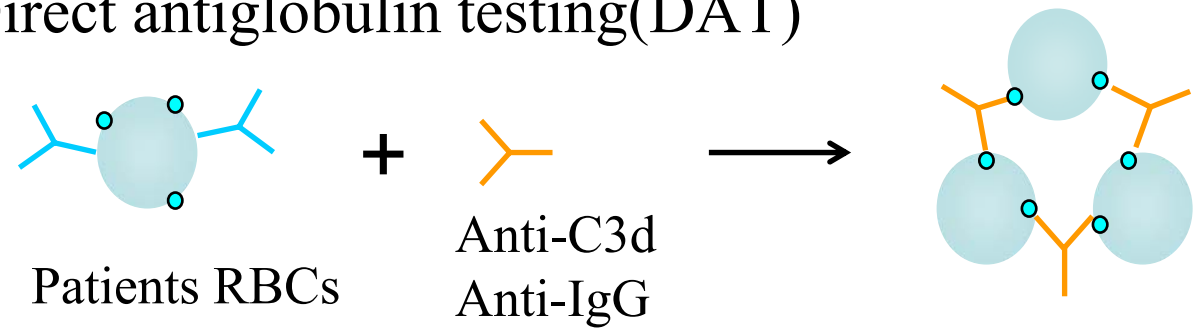
- mycoplasma pneumonia
- covid infection

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

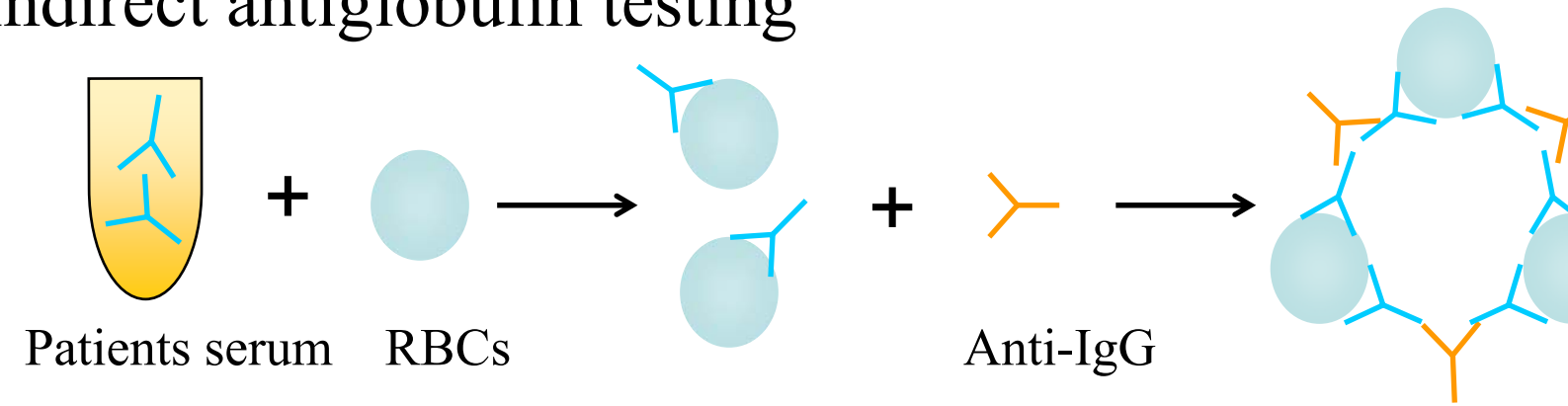
you applied agent have RBCs antibodies if the patient RBCs are coated with antibodeis —>interaction->agglutination
⊕ test

Anti-Globulin (Coombs) Testing

Direct antiglobulin testing(DAT)



Indirect antiglobulin testing



Treatment of Autoimmune Hemolytic Anemia (Warm Antibody type)

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

Corticosteroids are the first line therapy

Hemolytic Anemia with Intravascular Hemolysis

1

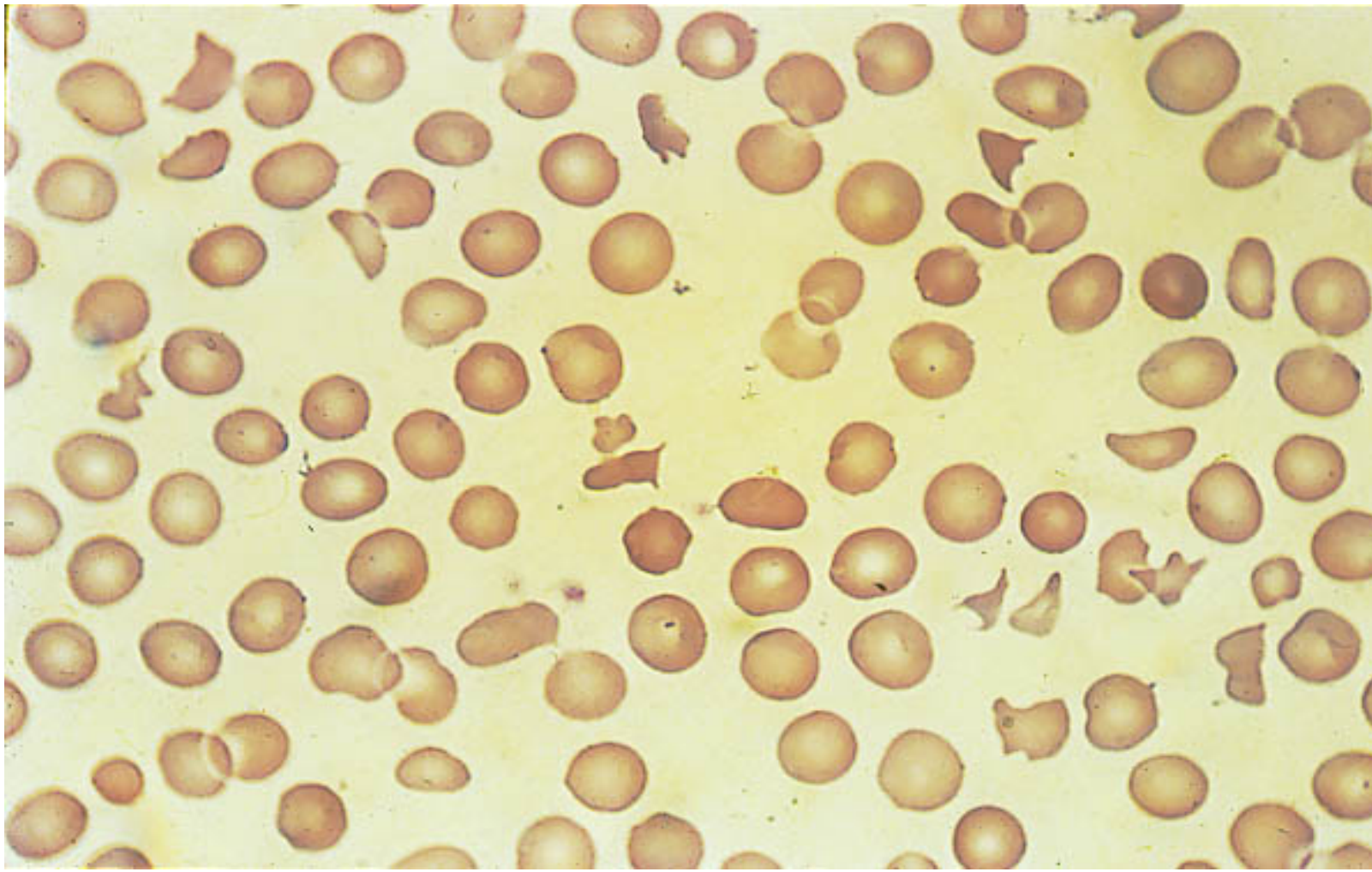
- Mechanical damage (Microangiopathic hemolytic anemia)
  prostathic heart values
- Chemical damage (Burns) inhalition injurys or sever burns
- Infection (Malaria or Babesiosis)
- Transfusion reaction (ABO incompatibility)

Differential Diagnosis of Microangiopathic Hemolytic Anemia

- Thrombotic thrombocytopenic purpura (TTP) is a disease churichtrized by presence of many shistocytes
- Hemolytic uremic syndrome (HUS)
- Disseminated intravascular coagulation (DIC)
- Vasculitis
- Malignant hypertension
- Metastatic neoplasm with vascular invasion
- Preeclampsia/HELLP syndrome of pregnancy

Schistocytes: Microangiopathic Hemolytic Anem

fragmented cells



Aplastic anemia because of BM failure

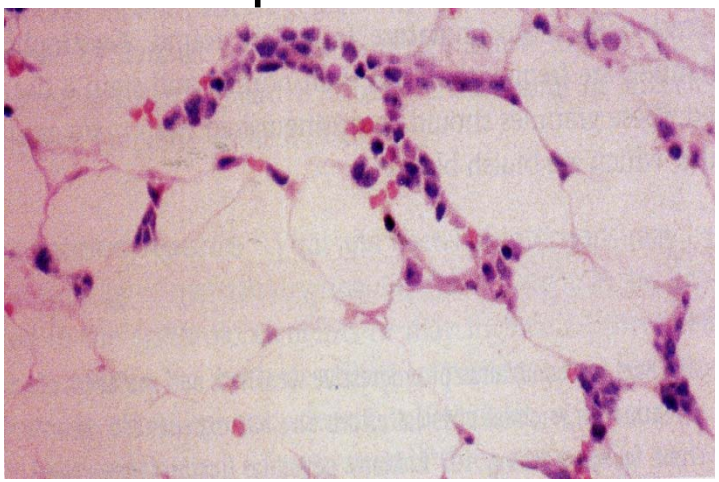
Case 3 B

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

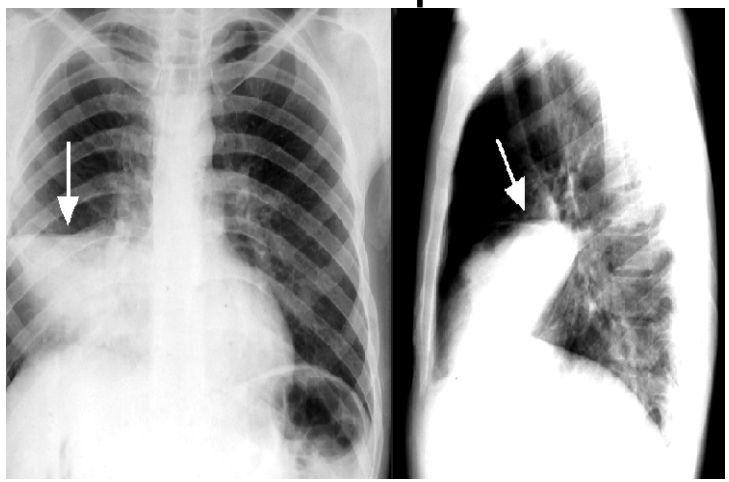
Hb 6 g/dl,WBC 1500 : N10%, L 80%, others 10%.

Retics© 0,001%.MCV 105fl,Plt 20k.

BM/ Trephine



CXR/lobar pneumonia



APLASTIC ANEMIA

Could be acquired or idiopathetic

- 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

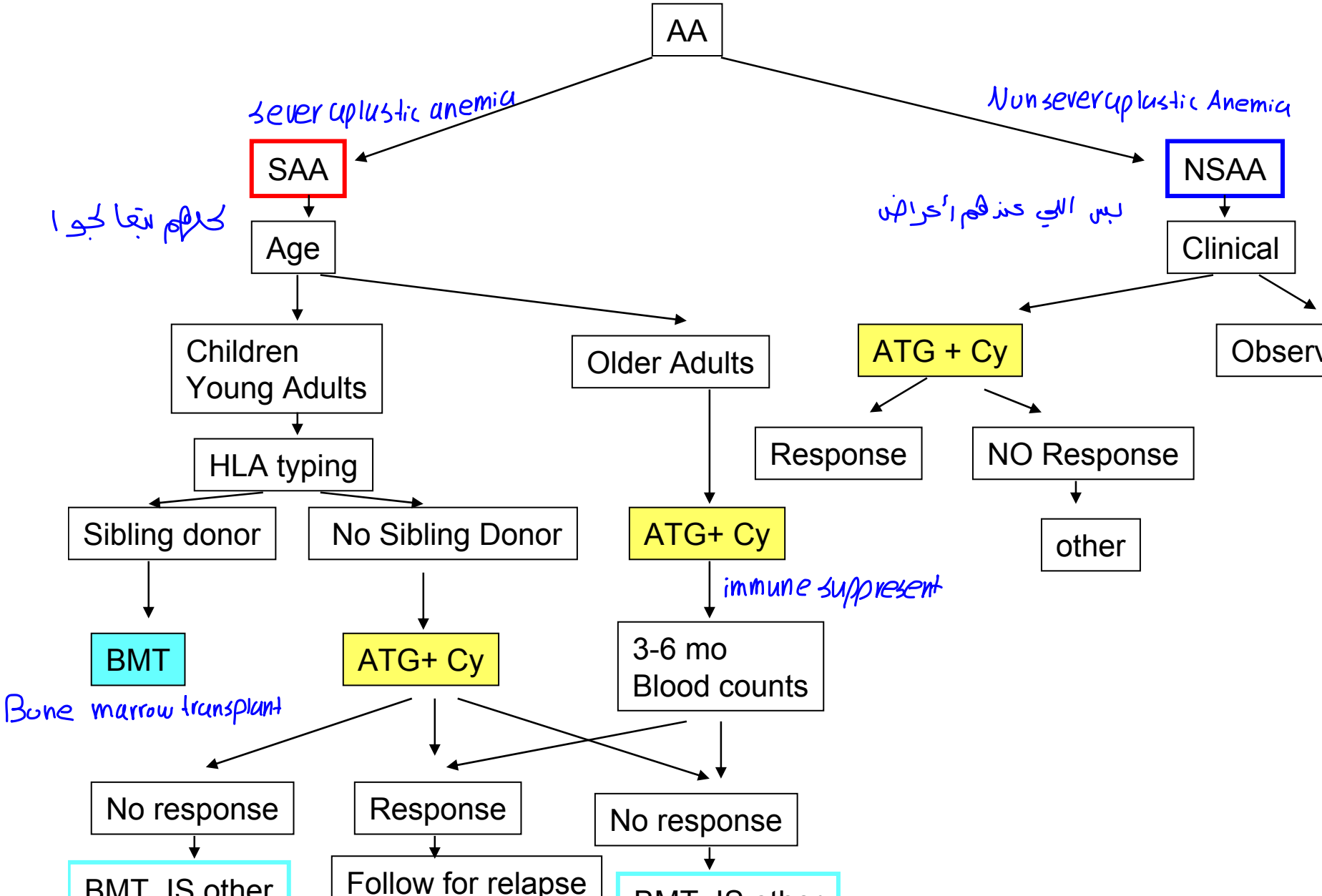
Symptoms	Number of Patients
Bleeding	41
Anemia	27
Bleeding and anemia	14
Bleeding and infection	6
Infection	5
Routine examination	8
Total	101

less plts count higher age and more risk of bleeding

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 prophylaxis
- Treat Bleeding

» **Bone marrow transplant**

» Immune suppression

- _ CSA
- _ ATG

Combination of the above

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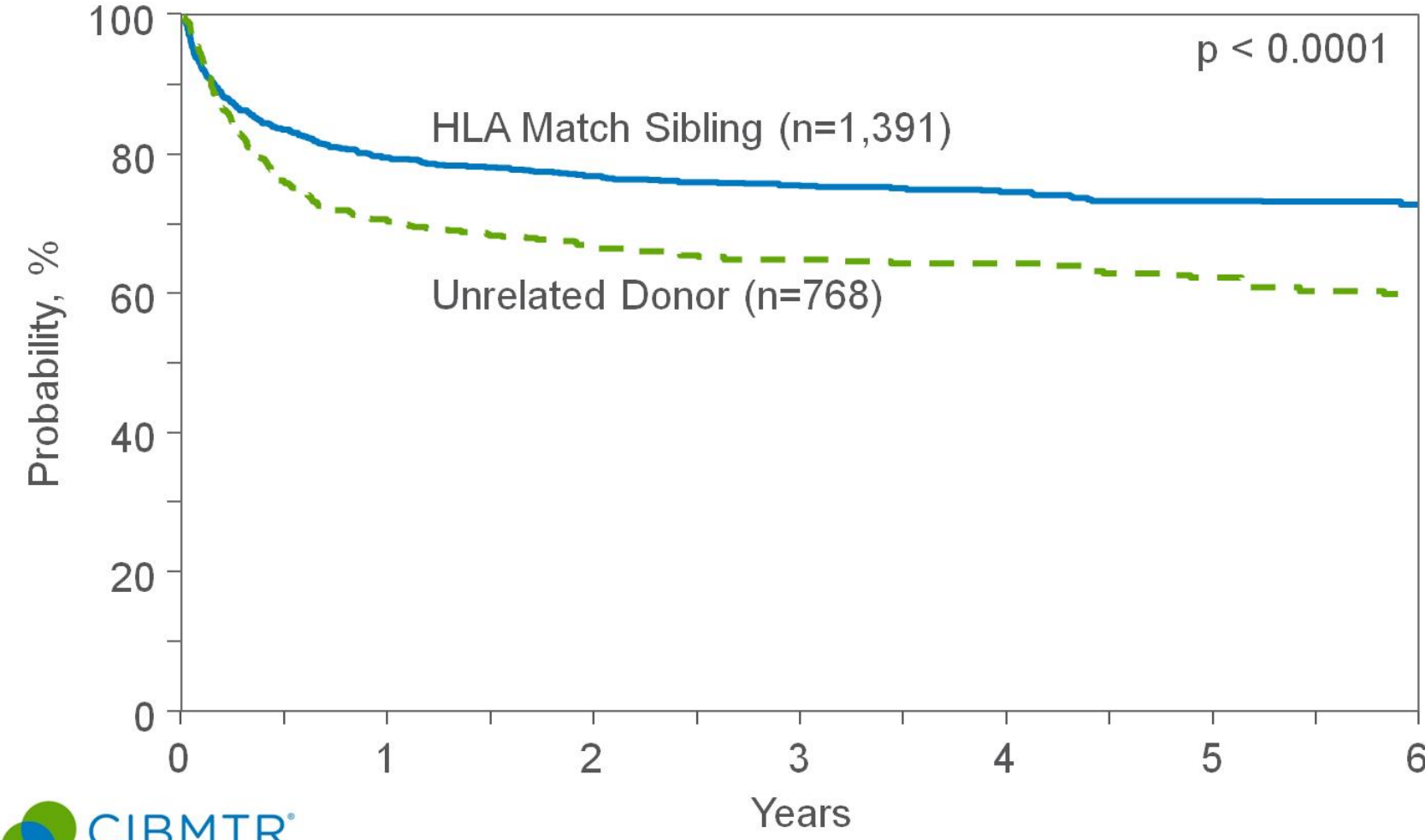
Survival after Allogeneic Transplants for Sever Aplastic Anemia, ≥ 20 Years, 2002-2012



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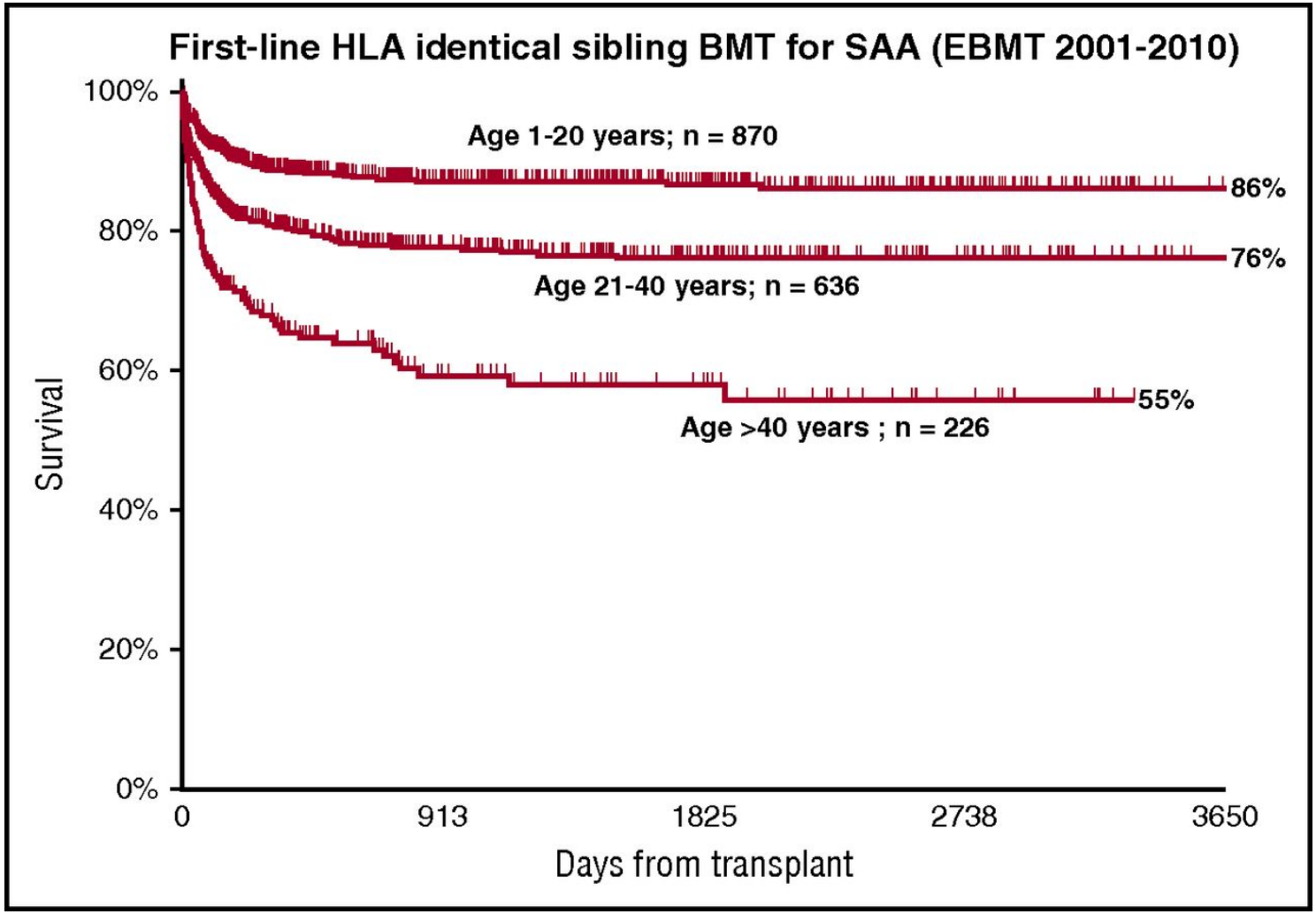
Immunosuppression for AA

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

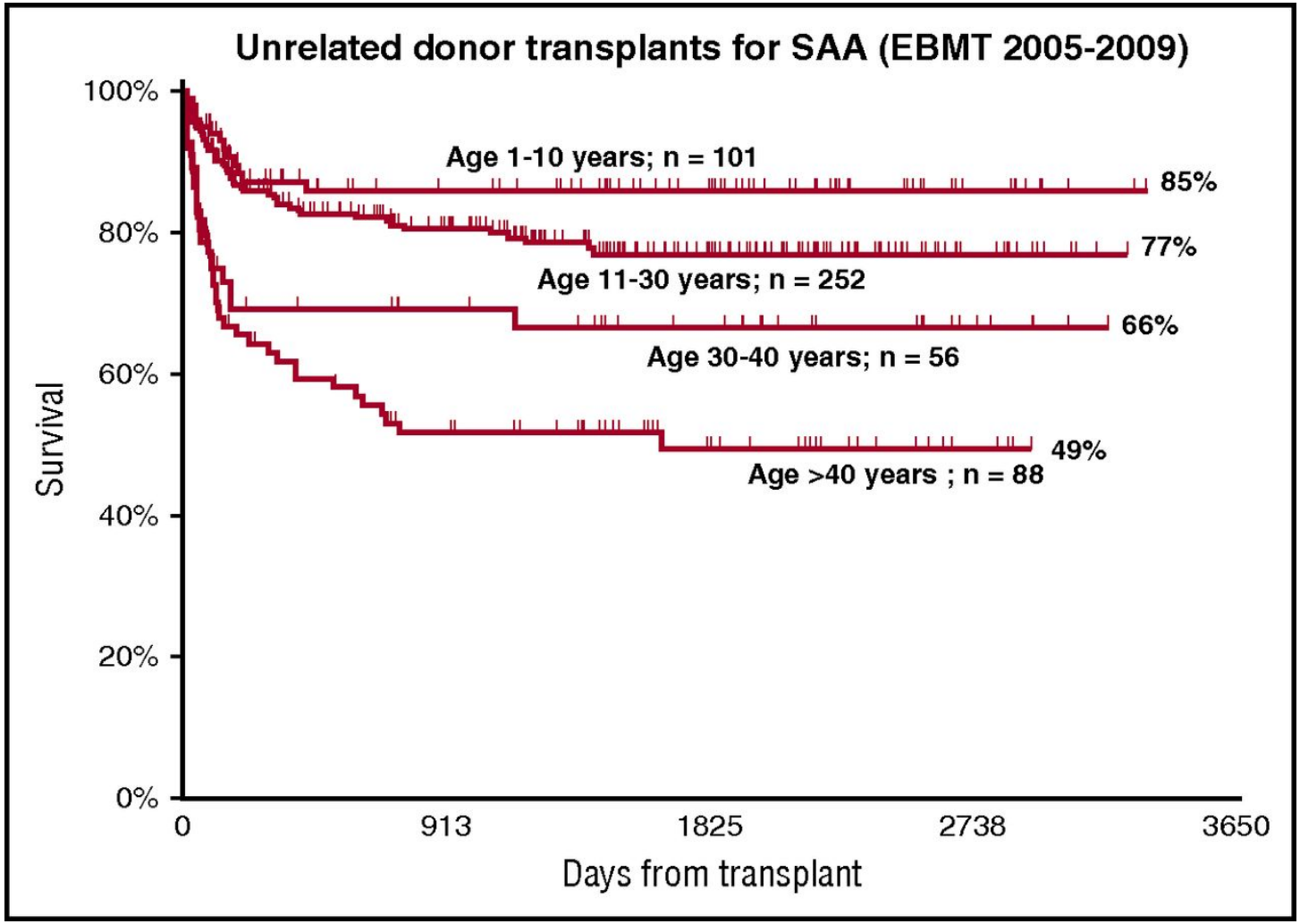
Young NS, et al BLOOD 2006

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



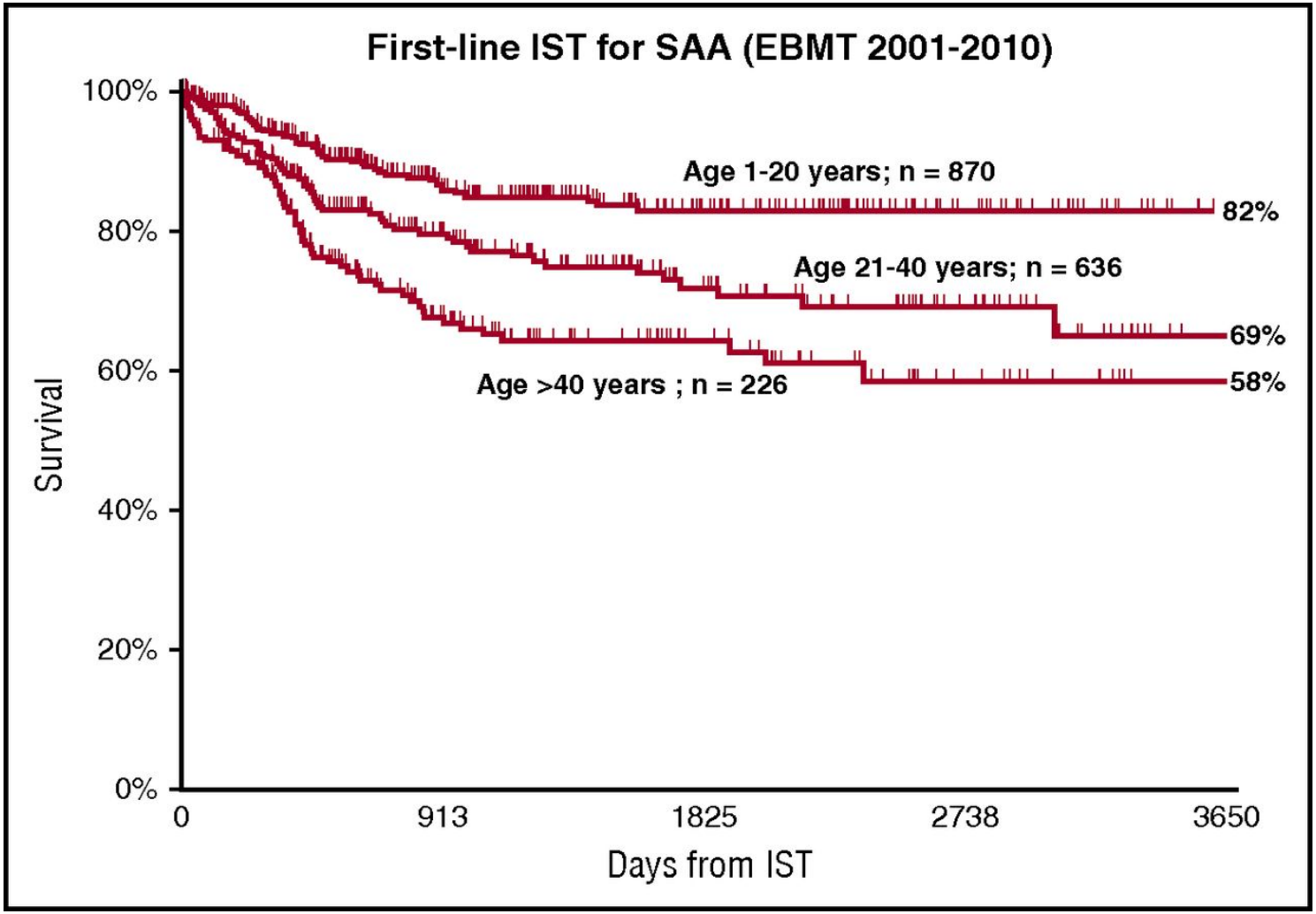
Andrea Bacigalupo Blood 2017;129:1428-1436

The age effect in UD transplants: best outcome is seen for very young patients, for whom first 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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- peripheral cytopenia but normal bone marrow

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)