CASE PRESENTATION

- A 78-year-old woman has history of increasing fatigue.
- She has no other medical problems and does not take any medications.
- On physical examination, The patient appears pale. Other examination is unremarkable.

INVESTIGATIONS

Laboratory studies:	
Hemoglobin	7.8 g/dL
Leukocyte count	2800 cells /cmm
Platelet count	100,000 cells /cmm

- Bone marrow study is hyper cellular

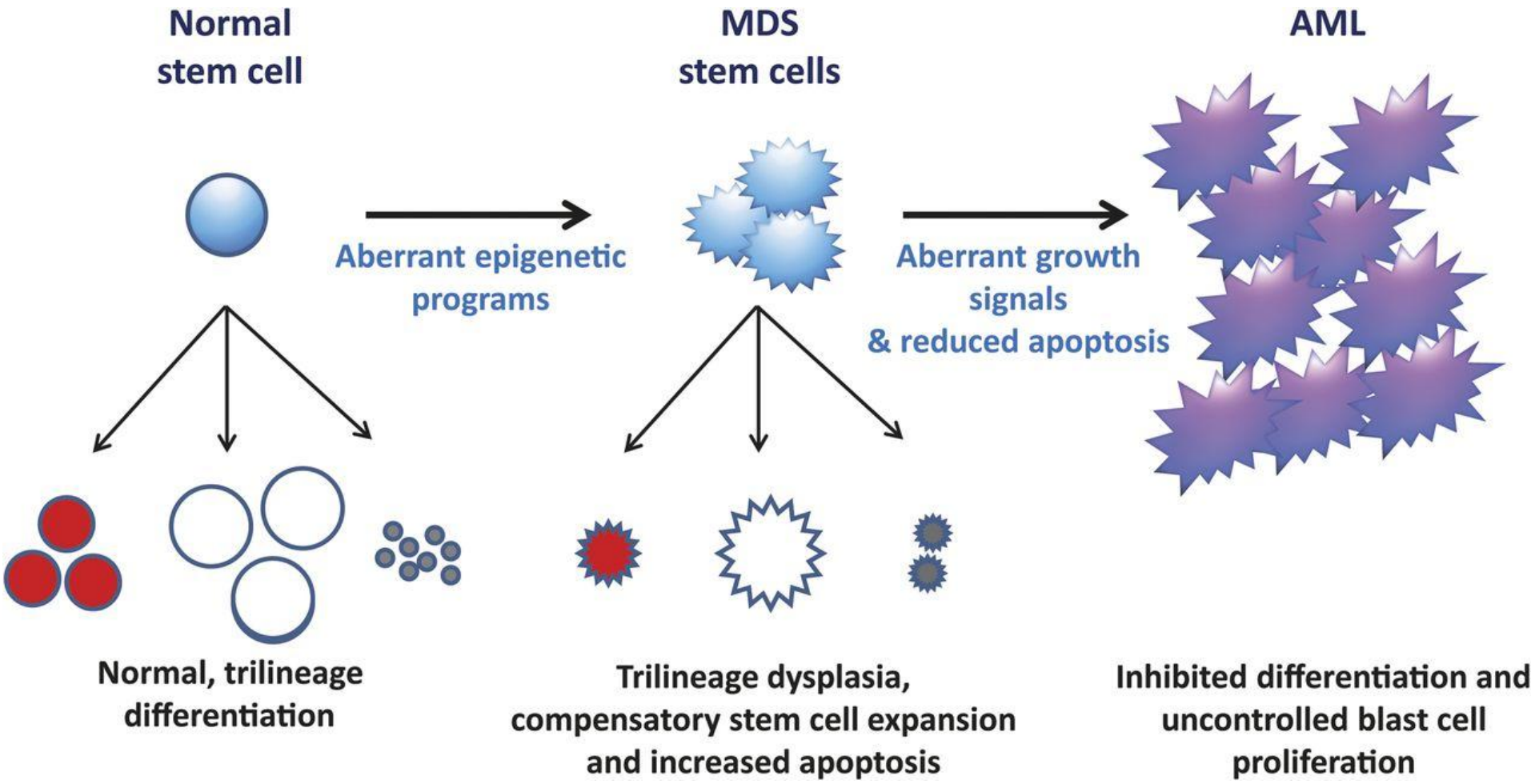
MYELODYSPLASTIC SYNDROMES

DEFINITION

- The myelodysplastic syndromes are a group of stem cell disorders characterized by:
  - ü *Cytopenias* due to impaired blood cell production,
  - ü *Dysplastic:* abnormal appearing bone marrow cells, and
  - ü *Leukaemic transformation:* 30% of patients will transform to AML during the course of their disease.

WHAT IS MYELODYSPLASIA?

In MDS, the bone marrow makes the blood cells badly (dysplasia), causing low blood counts and cells that don't work very well



AETIOLOGY

- *Idiopathic*
- *Children: Hereditary syndromes* associated with MDS.
- Secondary cause as a risk factors include:
  - ü *Benzene exposure, chemical or solvent exposure,*
  - ü *Tobacco smoke*.
  - ü *Chemotherapy drugs* (alkylating agents topoisomerase inhibitors) or
  - ü *Radiation*.

CLINICAL FEATURES

- About 20% of cases are detected incidentally.
- The hallmark clinical manifestation in MDS *is persistent or progressive bone marrow failure*:
  - Fatigue due to anemia,
  - Infections or
  - Bleeding.

SIGNS

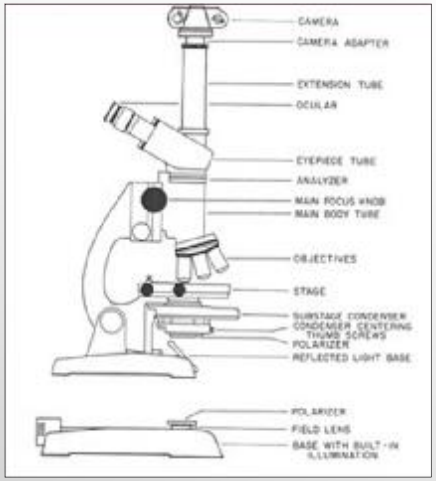
- Pallor, petechiae and/or purpura.
- Hepatomegaly, splenomegaly, and lymphadenopathy are uncommon, about 20% of patients have splenomegaly.

DIAGNOSIS

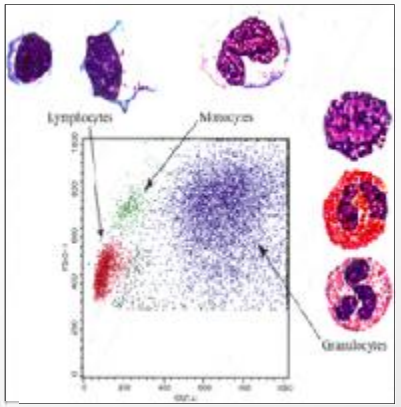
- The presence of *dysplastic changes* in the peripheral blood smear *and*
- *Dysplasia and hypercellular bone marrow*
- The presence of typical chromosomal abnormalities supports the diagnosis of MDS.

Diagnosis

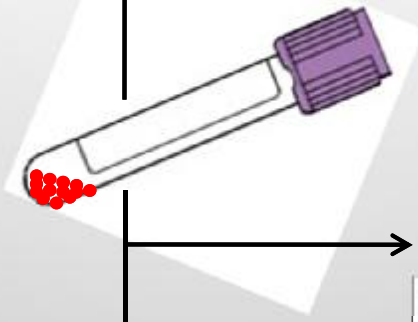
Specialist tests for myelodysplasia



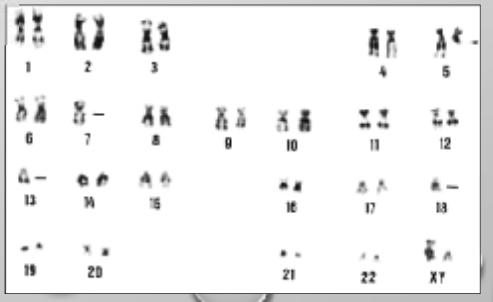
←Morphology



Flow cytometry



Cytogenetics

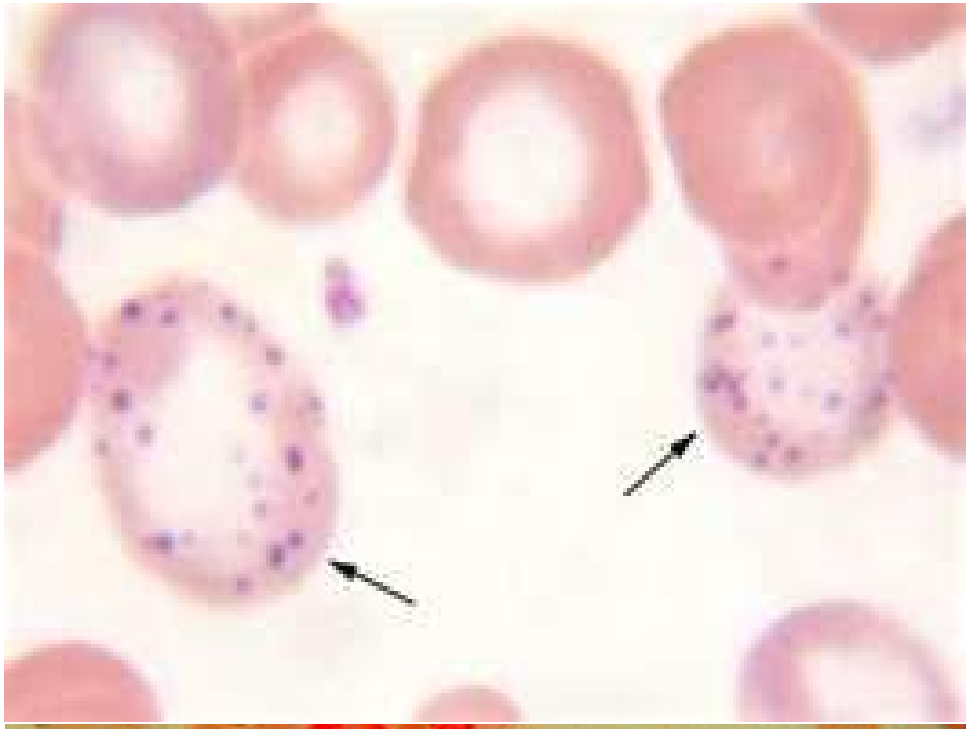


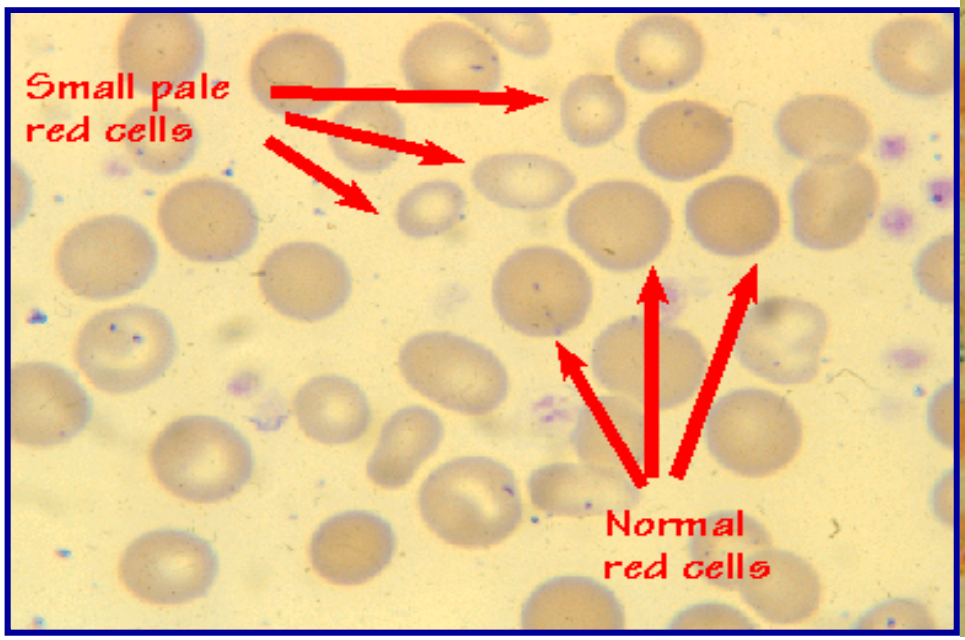
Bone marrow

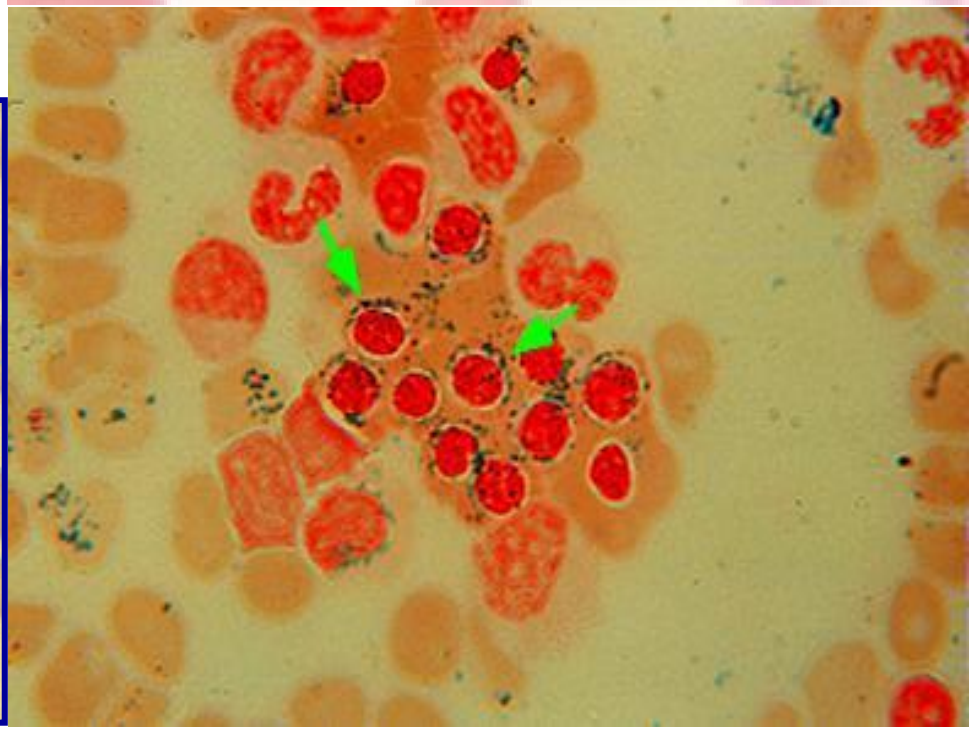
COMPLETE BLOOD COUNT

- The peripheral blood count may show a single cytopenia (anemia, thrombocytopenia, or neutropenia) in the early phase or bicytopenia or pancytopenia (3 deficient cell lines) in later stages.

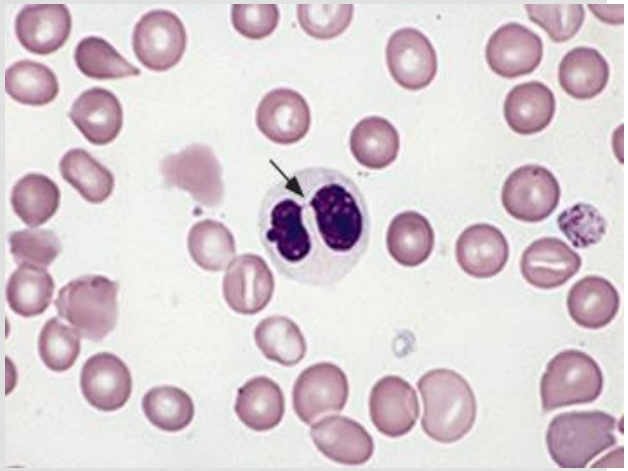
- Anemia usually macrocytic with oval-shaped RBCs.
- Dimorphic.
- Punctate basophilia
- Sideroblast

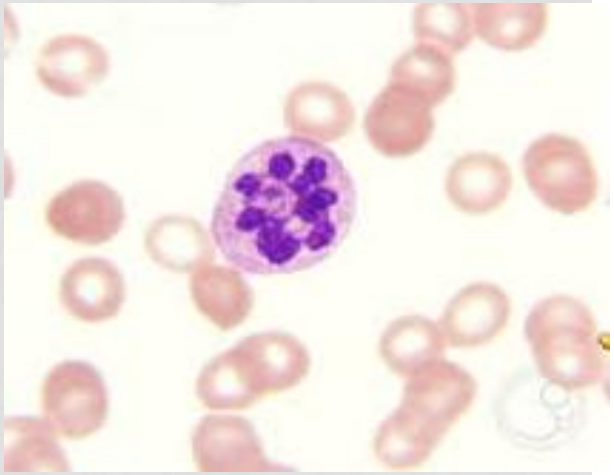




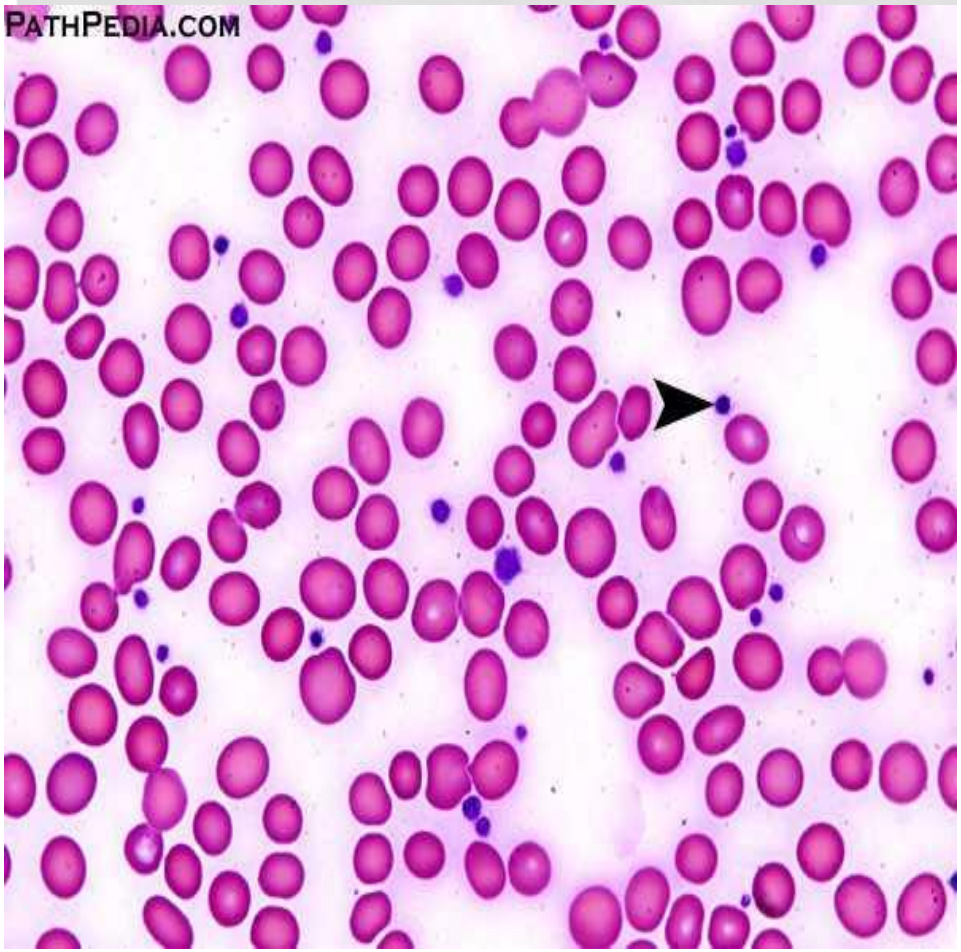


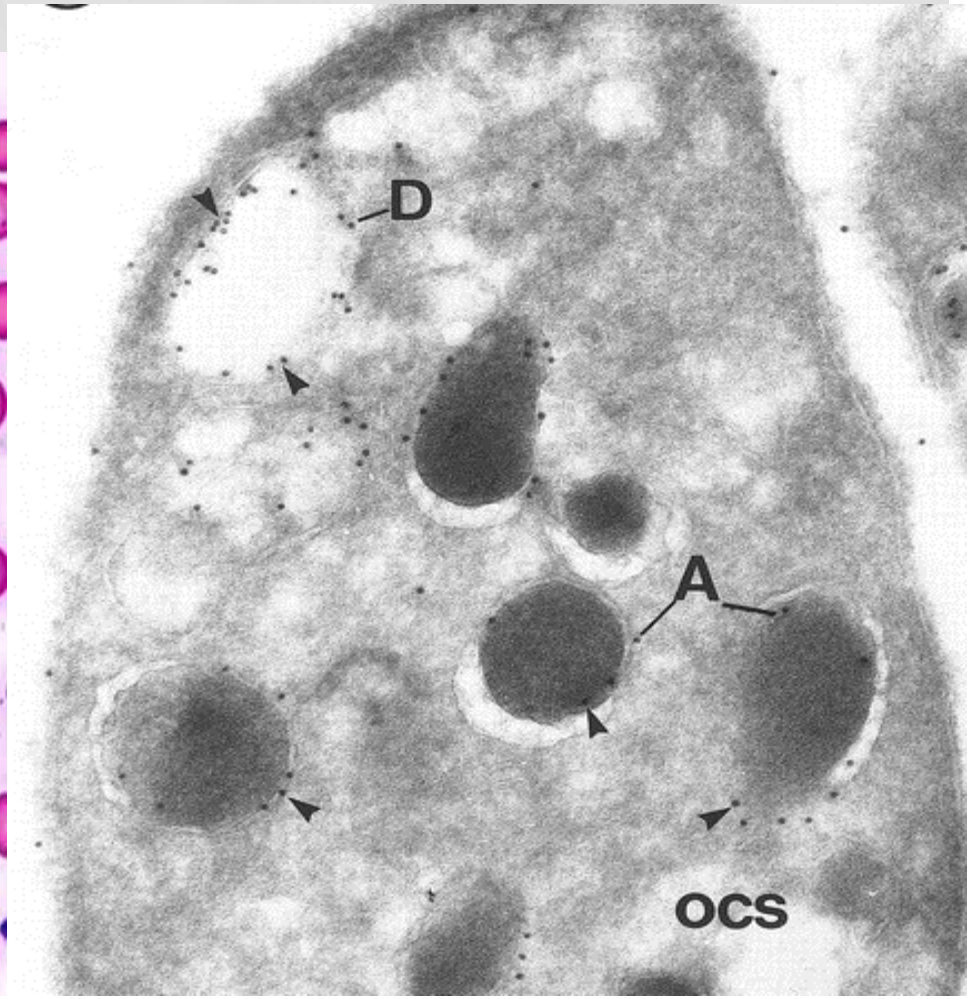
- Neutropenia with shape changes:
  - Bilobed, or unsegmented nuclei
  - Hypersegmentation on the nuclei (6-7 lobes).
  - Granulation abnormalities.
- Myeloblasts *less than 20%.*





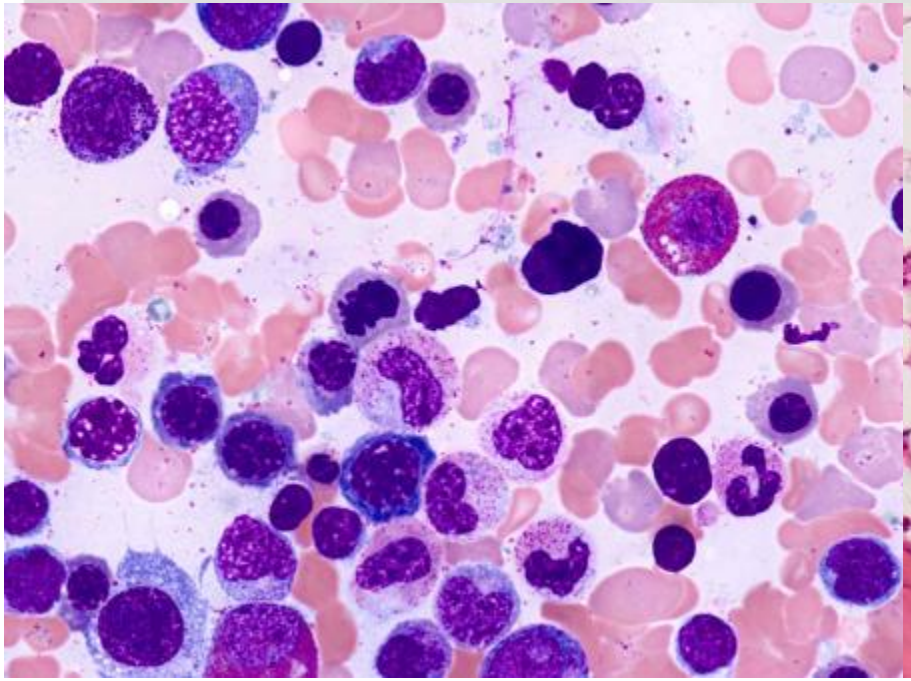
- Platelets are also large, lack granules and has abnormal functional studies.

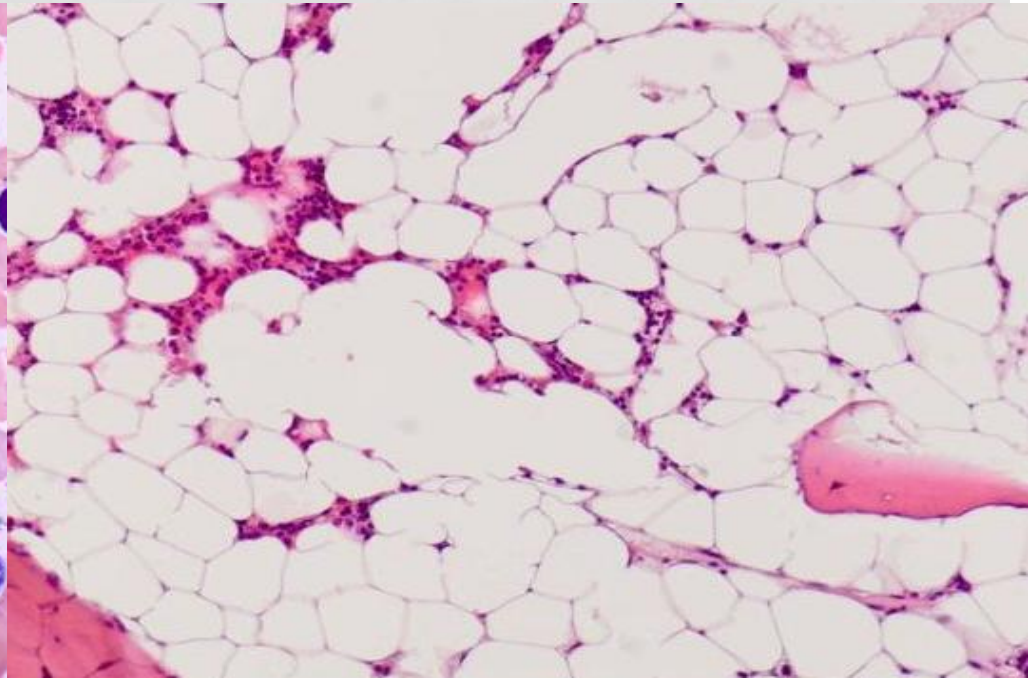




BONE MARROW

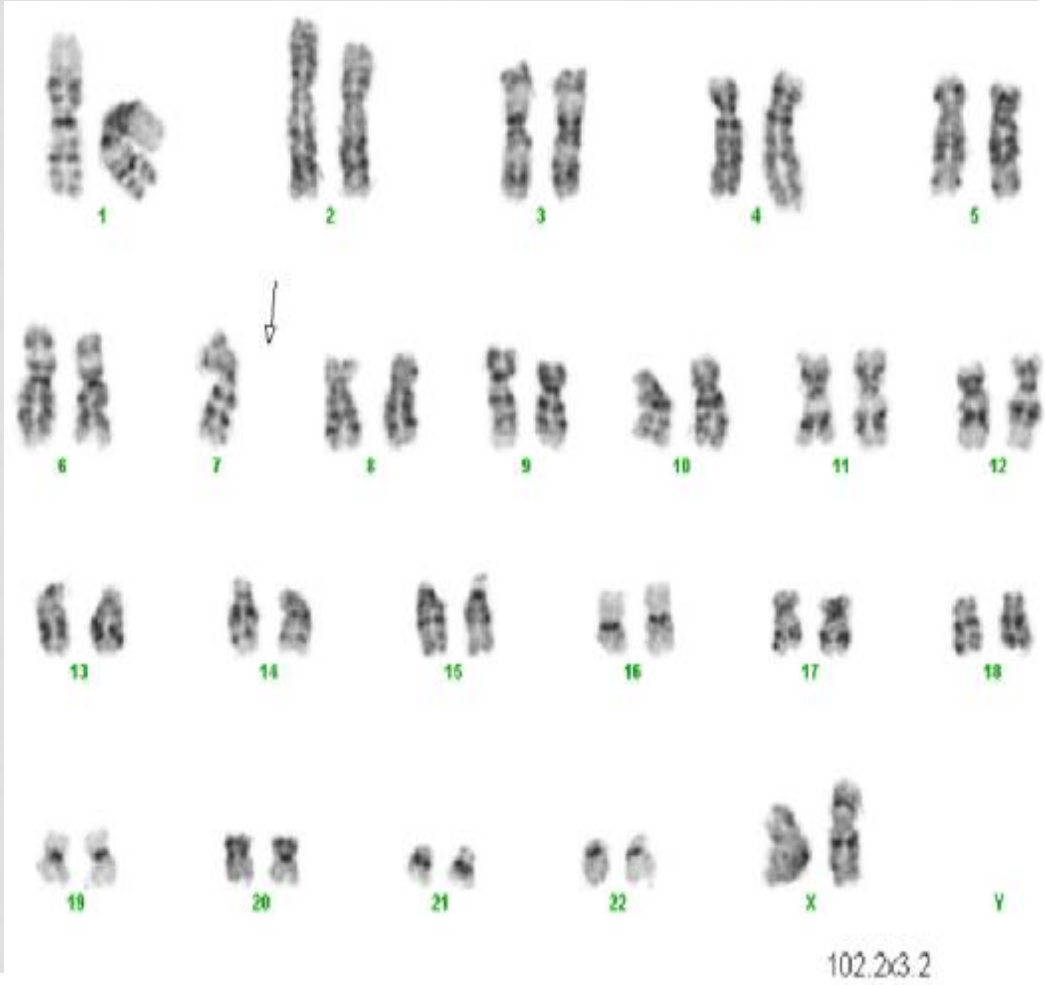
- The bone marrow is usually normal or hypercellular, but in 20% of cases it is sufficiently hypocellular to be confused with aplasia.





CYTOGENETIC STUDY

- Chromosomal abnormalities associated with MDS include isolated chromosome 5q deletion (5q−); monosomy 7; trisomy 8; ...etc.

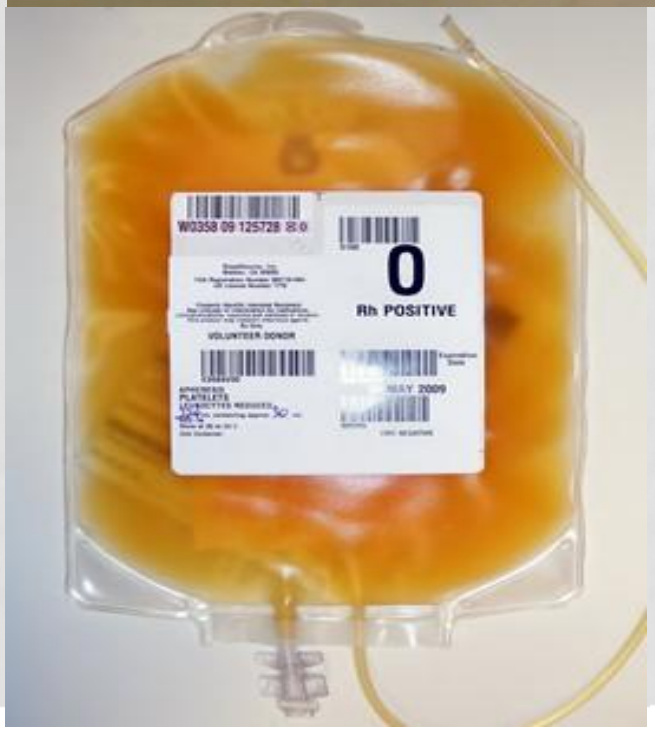


TREATMENT

- Supportive treatment:
  - ü Blood component transfusion
  - ü Hemopoietic growth factors (erythropoietin, G-CSF)
  - ü Antibiotics

SUPPORTIVE CARE

- Anemia: RBC transfusions or erythropoietin
- Thrombocytopnea:
  - ü platelet transfusion.
  - ü Aminocaproic acid may be considered for bleeding refractory to platelet transfusions or profound thrombocytopenia



- Antibiotics for bacterial infections.
- Granulocyte-colony stimulating factor (G-CSF):

  Consider use if recurrent or resistant infections in neutropenic patient.
- Iron Chelation for patient with recurrent blood transfusion.

SPECIFIC TREATMENT

- Chemotherapy (refractory to cytotoxic chemotherapy)
- Immune modulator
- Bone marrow transplant (Only treatment offers cure)

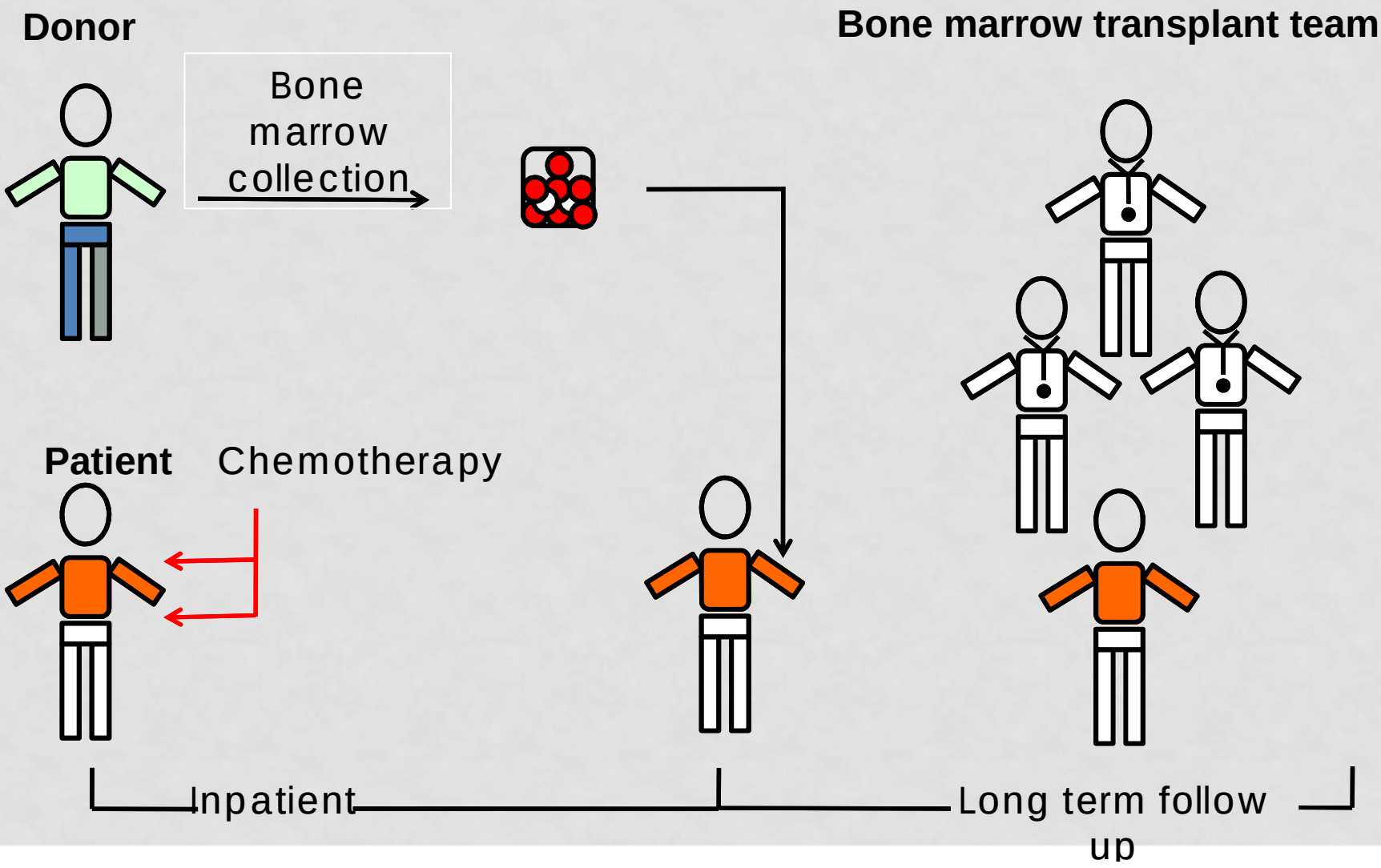
CHEMOTHERAPY

- Conventional Chemotherapy: response rates are low.
- Azacitidine:
  - Improvements in cytopenias, transfusion dependency (quality of life)
  - Time to AML progression
  - Significant improvement in median overall survival.
- Decitabine improve time to AML transformation and death.

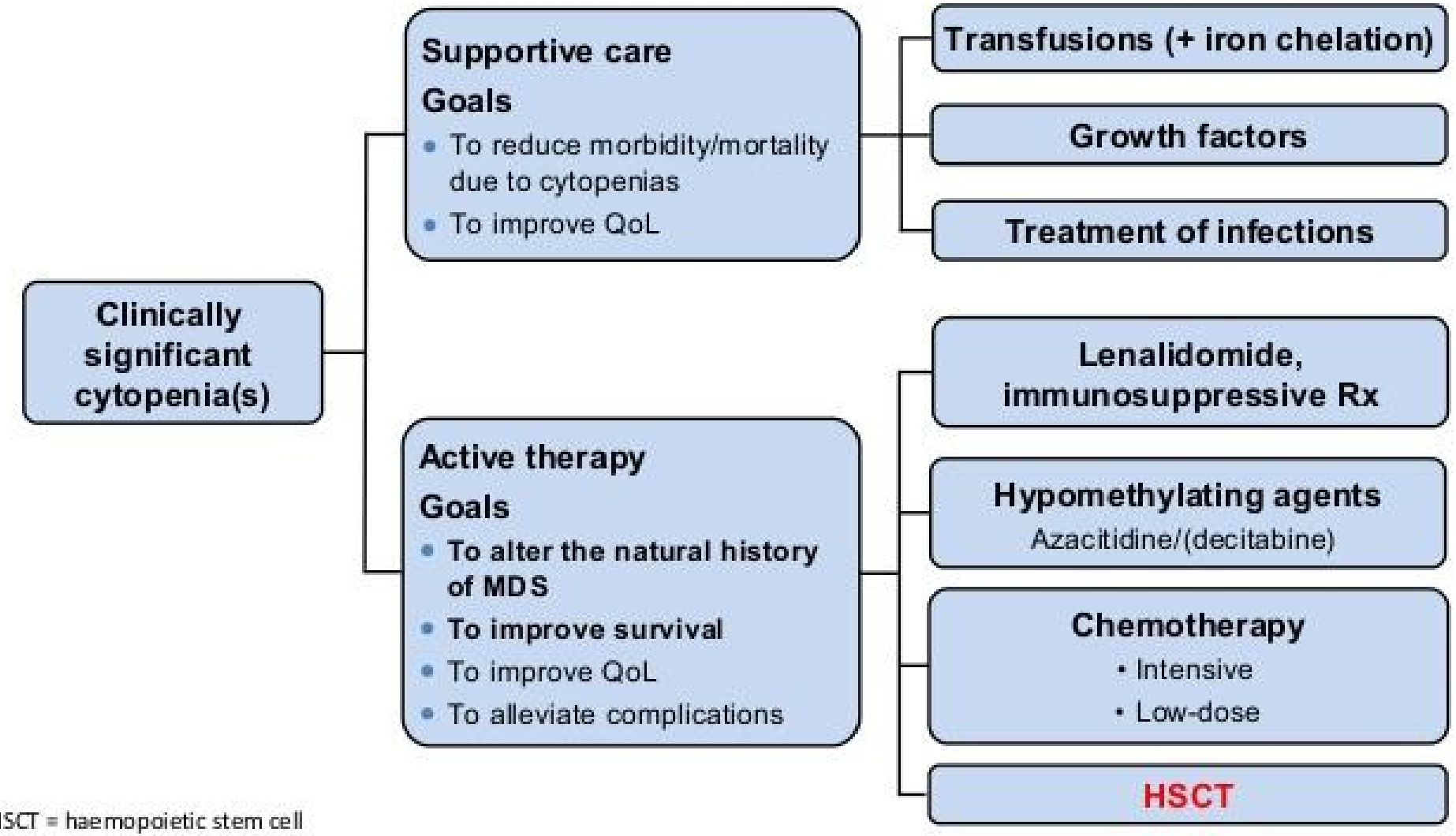
IMMUNOMODULATORS

- Lenalidomide is particularly effective in *reversing anemia in* MDS patients with del(5q) syndrome.
- Antithymocyte globulin plus cyclosporine may produce sustained independence from transfusion and improve survival.

- **Allogeneic SCT :** is the only curative option for MDS. The overall 5-year survival rate approaches 40%.



Treatment of patients with MDS: goals and options



HSCT = haemopoietic stem cell transplantation; QoL = quality of life.

CASE PRESENTATION

- Bone marrow examination shows hypercellular marrow with erythroid hyperplasia and dysplasia of the erythroid and granulocyte series. Megakaryocytes are increased with many hypolobulated cells.
- Cytogenetic studies show deletion of the long arm of chromosome 5 [del(5q-)].

NATURAL HISTORY

- The course of MDS can be subdivided in two categories:

I. 70% show progressive cytopenia.

  - 50% die of causes unrelated to MDS,
  - 50 % die due to complications of marrow failure.

II. 30% of patients evolve into AML.

SUMMARY

- Patients with MDS may present with features of anemia, thrombocytopenia, and/or neutropenia.
- The workup in includes CBC with differential, peripheral blood smear, bone marrow studies and cytogenetic study.

- Standard care typically includes supportive therapy, including transfusions, and may include bone marrow stimulation and cytotoxic chemotherapy.
- Bone marrow transplantation has a limited role but it is the only curative measure.