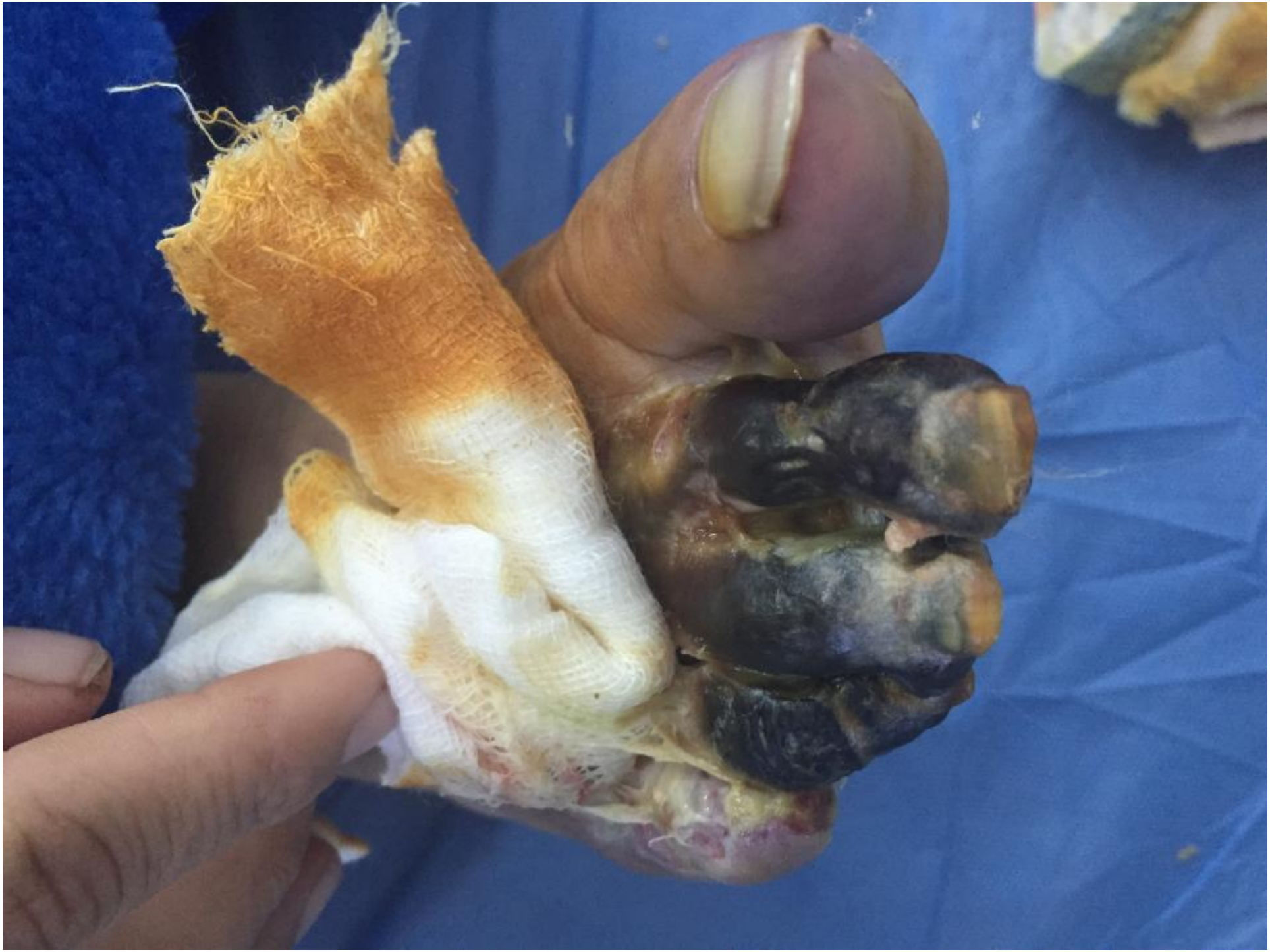
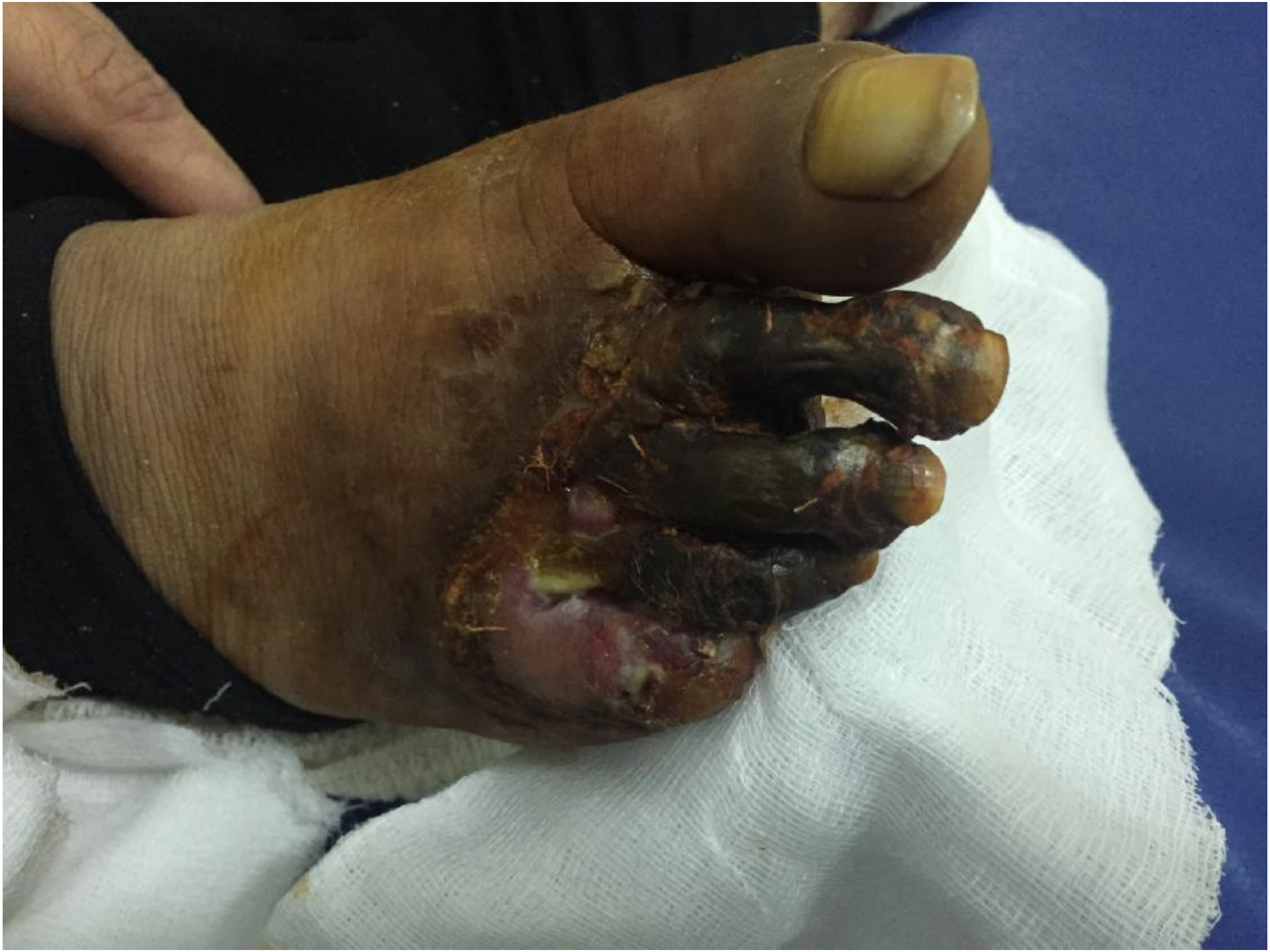
Myeloproliferative disorder

Essential thrombocythemia

Primary myelofibrosis



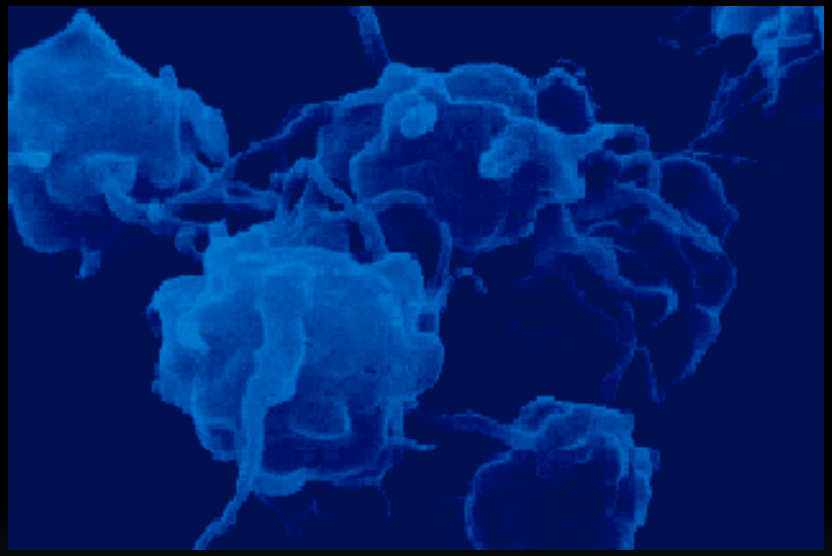


- 45 years old female presented with gangrenous both feet
- She has negative chronic illness
- on examination she look pale, positive distal pulse

- CBC and differential

- Platelets count= 1.7 million

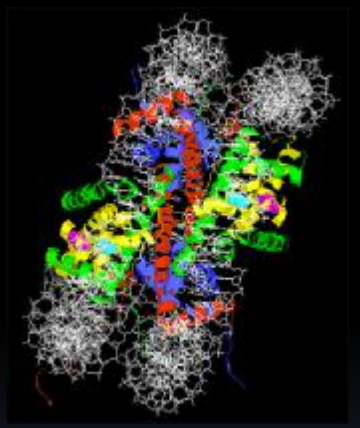
DEFINITION OF THROMBOCYTOSIS



PLATELET COUNT > 450,000/ML

MAJOR CAUSES OF THROMBOCYTOSIS

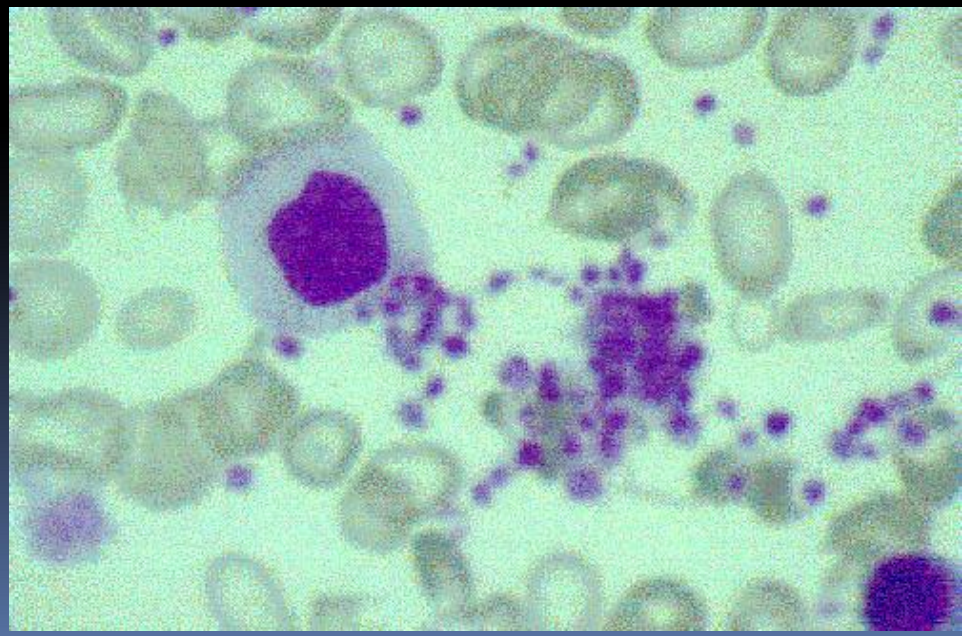
- CLONAL THROMBOCYTOSIS
  - ü CML
  - ü ESSENTIAL THROMBOCYTHEMIA
  - ü POLYCYTHEMIA VERA
  - ü MYELOFIBROSIS
- REACTIVE THROMBOCYTOSIS
- FAMILIAL THROMBOCYTOSIS



Differential diagnosis of thromboctosis

3. Reactive thrombocytosis:

- Infection & Chronic inflammation
- Tissue damage
- Malignancy
- Renal disorders
- Hemolytic anemia
- Post splenectomy
- Blood loss



Essential thrombocythemia

- Essential thrombocytosis (ET) is a MPD of unknown etiology involving manifested clinically by overproduction of platelets without a definable cause.

Epidemiology

- ET is the most frequent among the MPDs.
- The median age at diagnosis is 60 years.
- Females are more affected than males.

Clinical Features

- ET may be totally asymptomatic at presentation.
- *Hypervescosity symptoms*, atypical chest pain, erythromelalgia.

§ Thrombosis and hemorrhage:

Ø Thrombotic events: include stroke, TIA, retinal artery or venous occlusions, IHD, etc.

Ø Bleeding manifestations: In some patients with ET and platelet count >1 million/ microL, acquired von Willebrand disease may be present.

- In most individuals the condition is chronic, with the platelet count gradually increasing.
- A very small percentage may transform to PV, PMF, or AML.

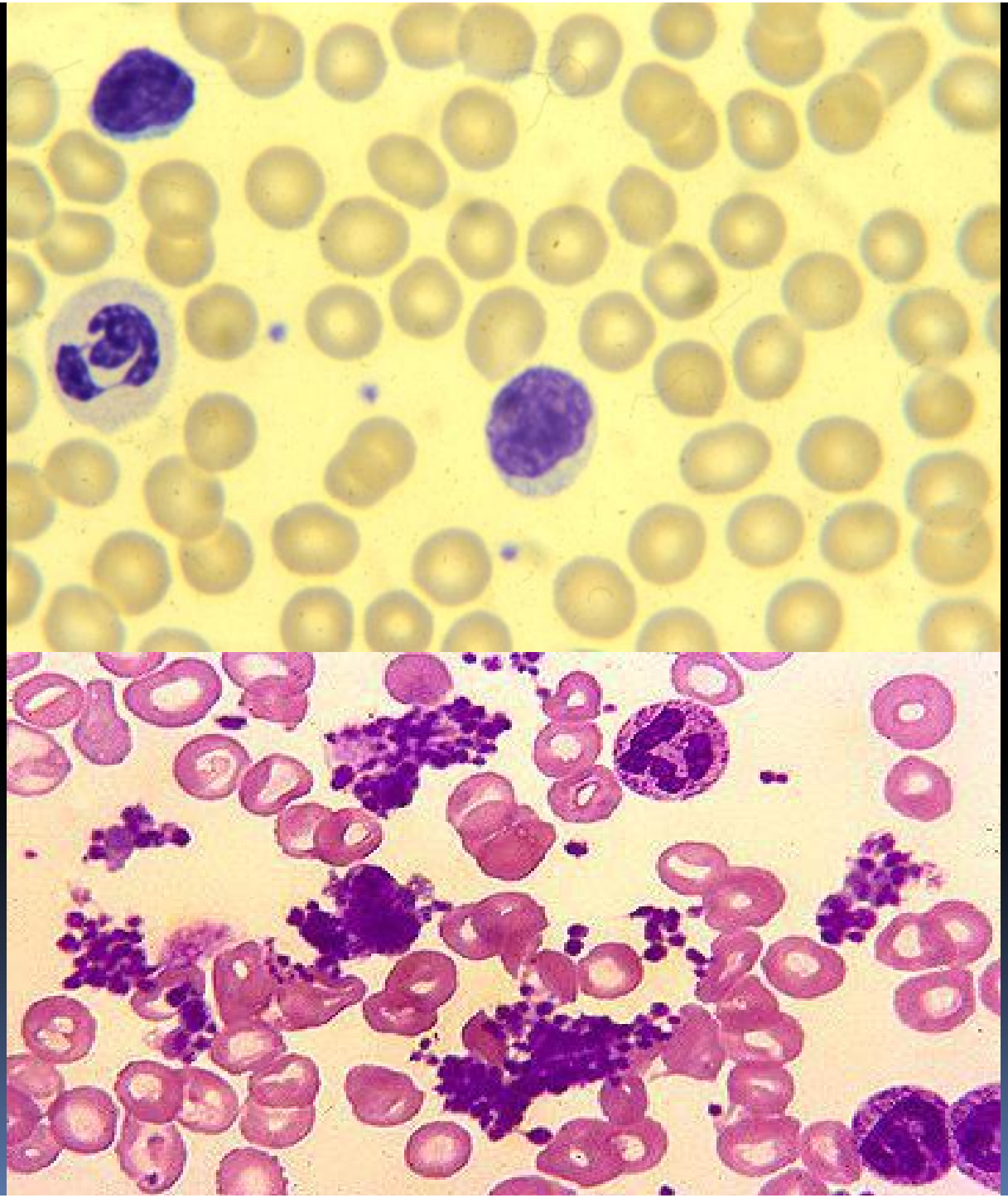
Physical examination

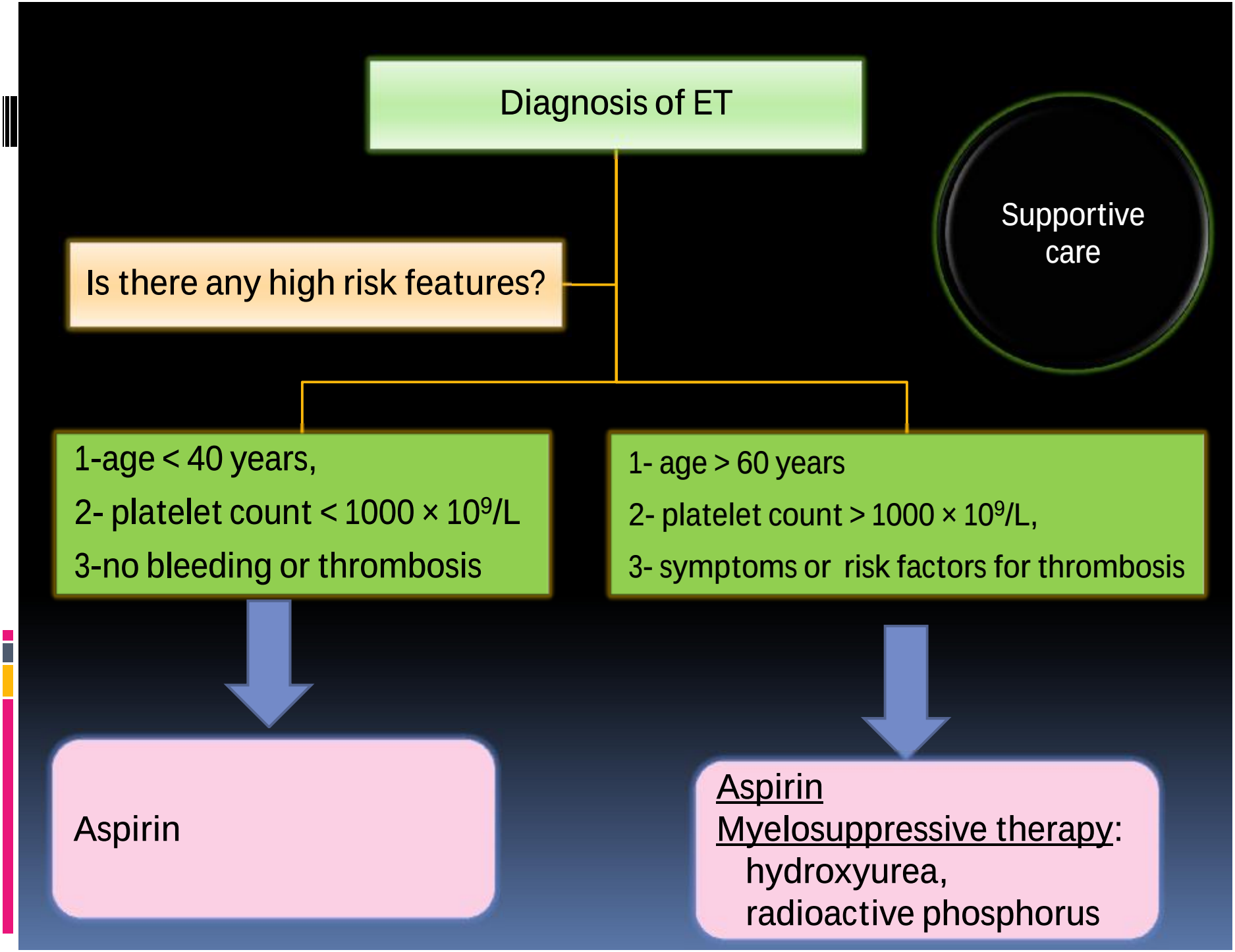
- In most patients with ET, physical examination findings are unremarkable.
- Approximately 40-50% of patients present with splenomegaly; 20% present with hepatomegaly.

Investigation

- Complete blood cell (CBC) count show thrombocytosis. Leukocytosis, and erythrocytosis may be found.
- Marrow biopsy usually reveals megakaryocyte hyperplasia and hypertrophy, as well as an overall increase in marrow cellularity.

- The identification of the *JAK2* mutation now provides a very useful positive diagnostic criterion for approximately 50% of ET patients.





Supportive care

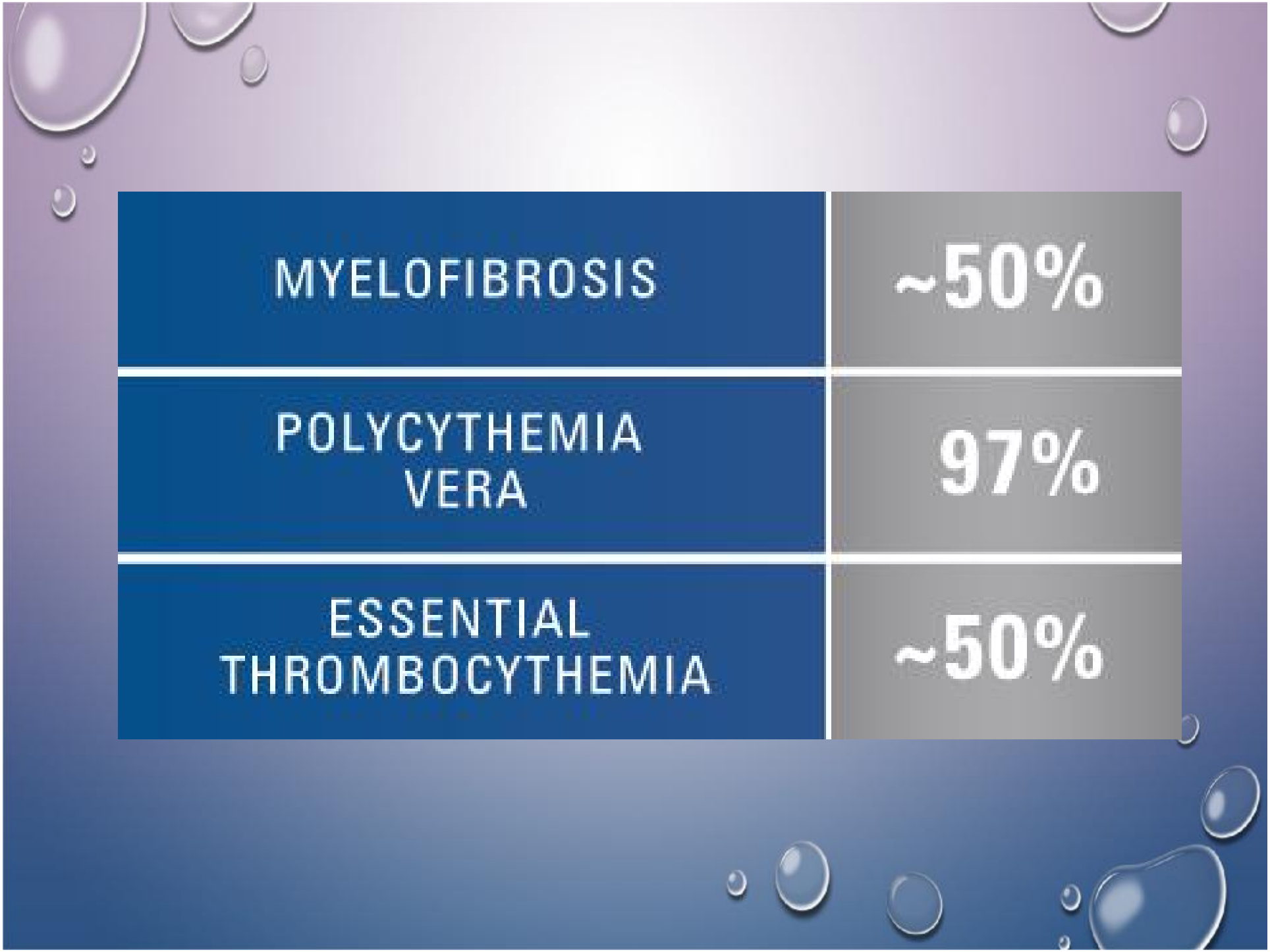
- Recommend lifestyle modifications (eg, weight loss, smoking cessation).
- ET-associated acute thrombosis should be managed with both systemic anticoagulation and concomitant cytoreductive therapy.

Primary Myelofibrosis

- PMF is a clonal disorder of unknown etiology characterized by *marrow fibrosis*, *extramedullary haemopoiesis*, *splenomegaly*, and *leucoerythroblastic blood picture*.
- Idiopathic myelofibrosis needs to be distinguished from causes of secondary myelofibrosis.

Etiology

- The etiology of PMF is unknown.
- Chromosome abnormalities are common.
- *JAK2* is present in approximately 50% of PMF.



Epidemiology

- PMF is the least common chronic MPD.
- The median age is sixth decade or later.
- Men equal to female.
- Survival in PMF is shorter than in patients with PV or ET.

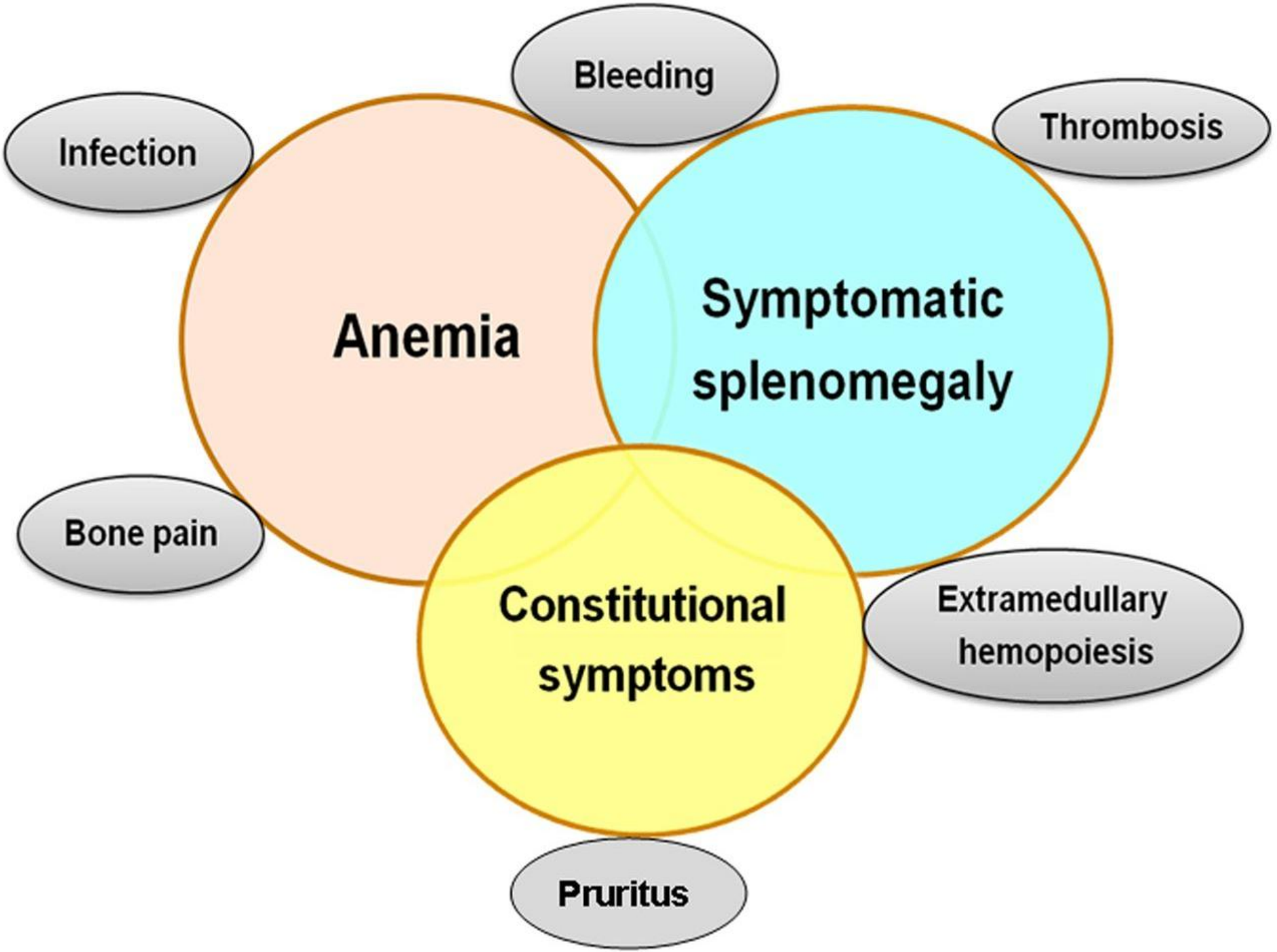
pathogenesis

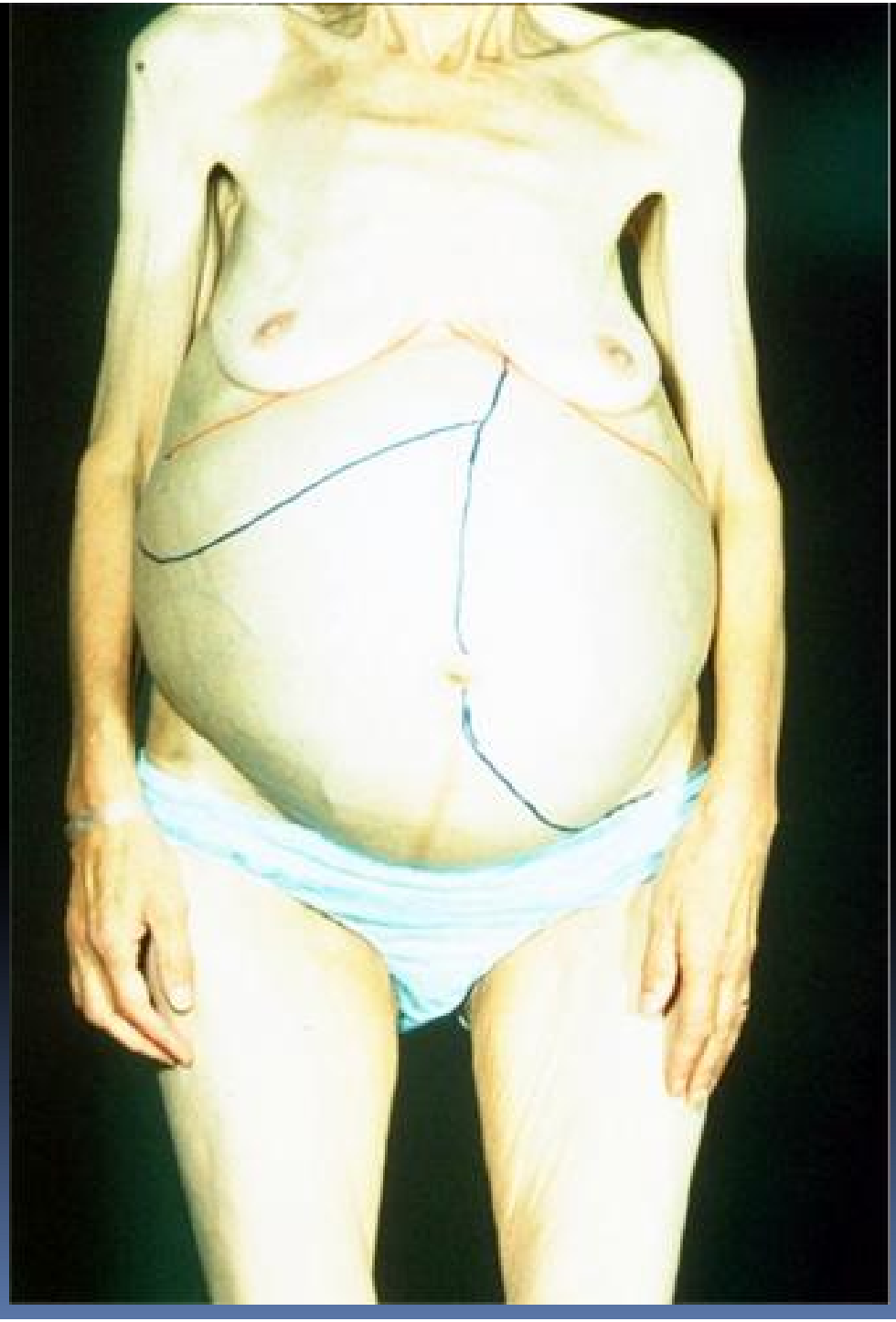
- Production of cytokines such as fibroblast growth factor by the abnormal hematopoietic cell clone leads to:
  - Replacement of the hematopoietic tissue of the bone marrow by collagen fibrosis,
  - Impairing the patient's ability to generate new blood cells and
  - Resulting in a progressive pancytopnia.

- As a result, *extramedullary hematopoeisis* (blood cell formation occurring in sites other than the bone marrow), particularly in the liver and spleen. This causes an *enlargement of these organs*.
- Enlargement of the spleen commonly results in hypersplenism, which also contributes to causing pancytopenia.

Clinical Features

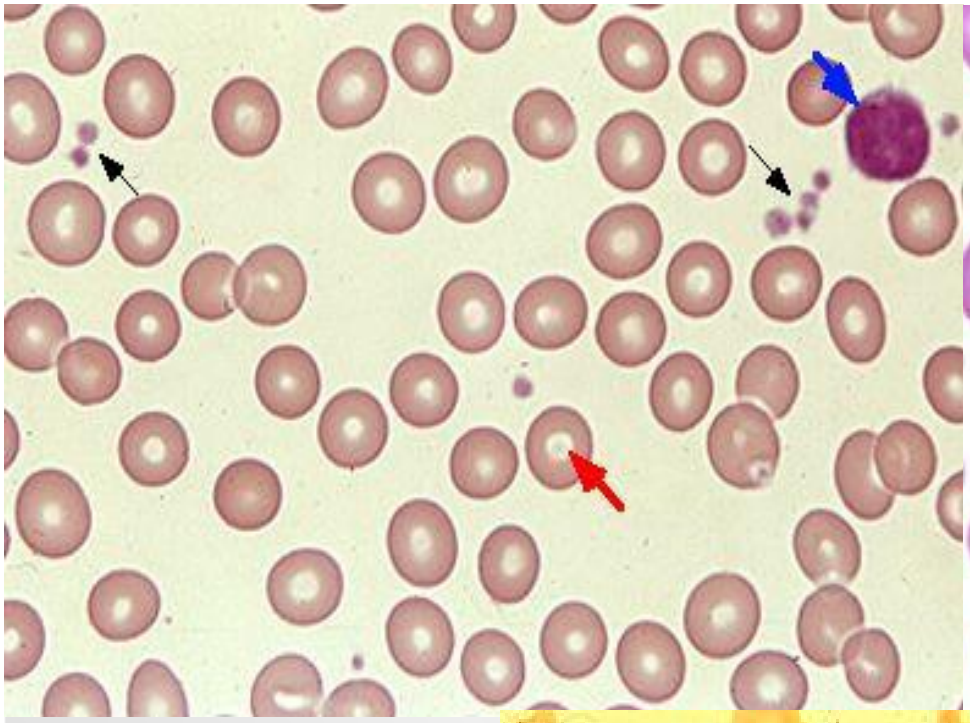
- Asymptomatic (the diagnosis being accidentally).
- The most common presenting complaint is that of severe fatigue, weight loss, low grade fever.
- Enlargement of the liver and spleen (early satiety, LUQ pain).

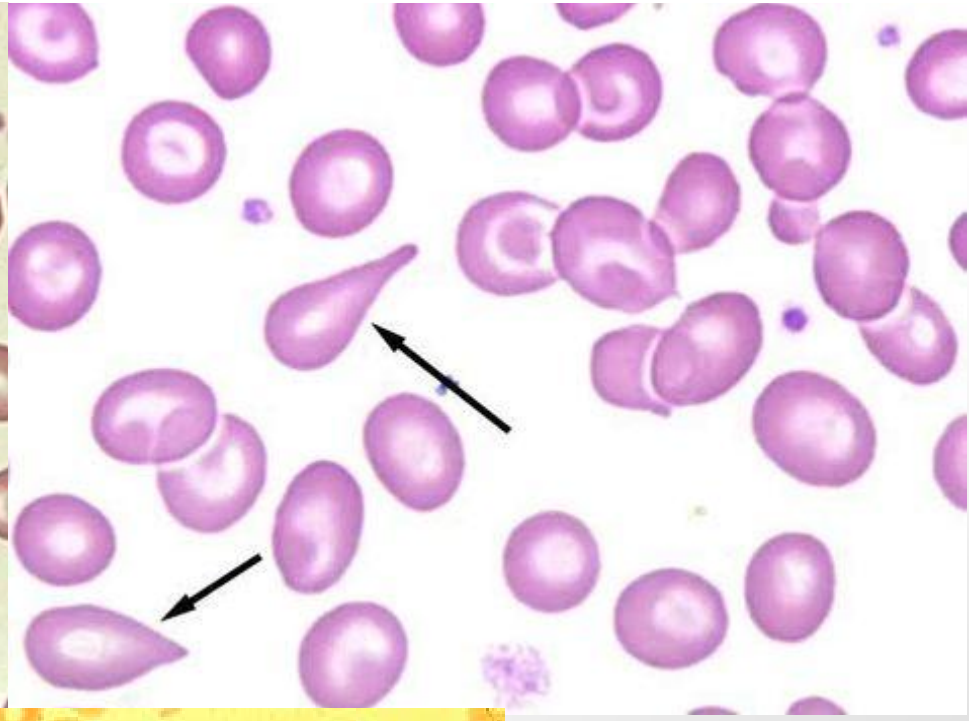


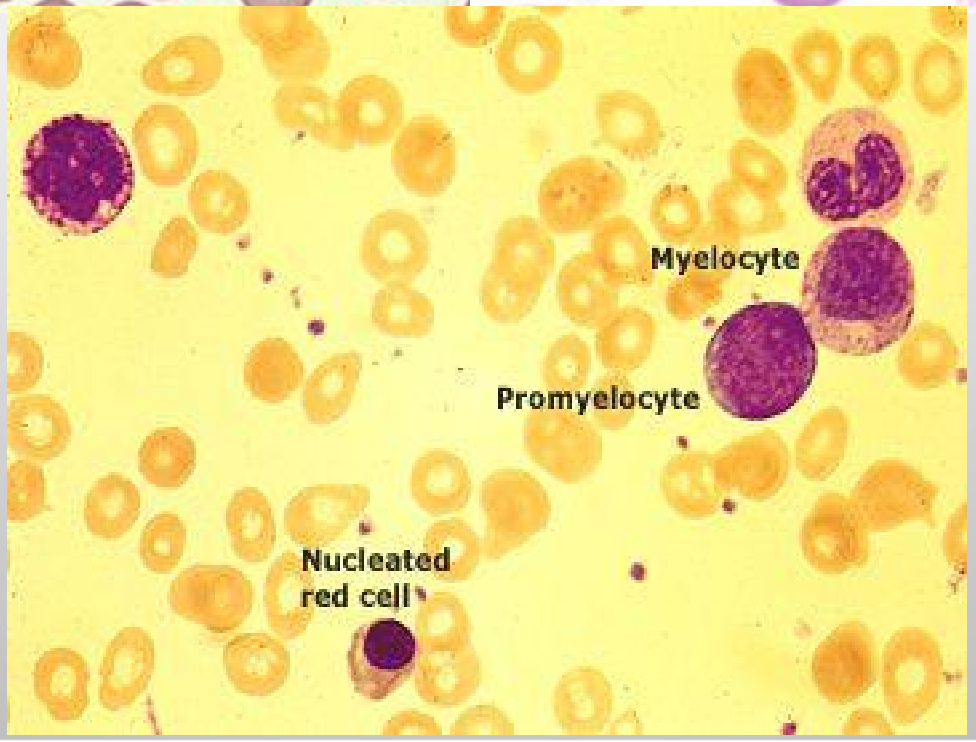


Diagnosis

- A blood smear will show *leucoerythroblastic blood picture* (immature red and white cells in the peripheral blood).
- Anemia is the rule, while the leukocyte and platelet counts are either normal or increased, but either can be depressed.





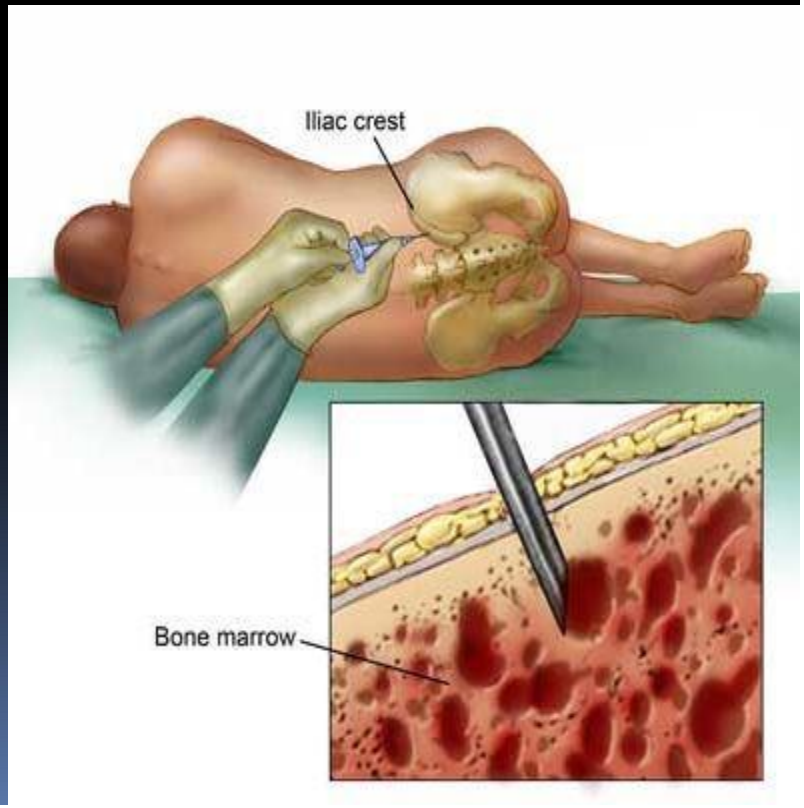


Bone marrow study

- Bone marrow biopsy is essential to make a diagnosis of PMF. The biopsy shows *increased reticulin and fibrous* tissue and progressively replaces hemopoiesis.

- The bone marrow aspirate usually yielding a "dry" tap

- The presence of a *JAK-2* mutation supports the diagnosis



Complications

1. Blood cell transfusion–dependent
2. About 10% transform to acute leukemia.
3. Extramedullary hematopoiesis can cause ascites; portal, pulmonary, or intracranial hypertension; intestinal or ureteral obstruction; pericardial tamponade; spinal cord compression; or skin nodules.
4. Splenic infarction.

5. Increase the incidence of arterial and venous thrombosis.
6. They developing infectious complications.
7. Osteosclerosis and periostitis may result in significant pain and discomfort.
8. Gout or urate stones.

Treatment

- No specific therapy exists for PMF. The only curative treatment for PMF is allogeneic BMT.
- In the remaining cases therapy remains supportive and aimed at alleviating symptoms.

- *Anemia* responds to treatment with androgens, corticosteroids and human recombinant erythropoietin.
- *Cytoreductive therapy* can be useful in the management of hepatosplenomegaly, constitutional symptoms and thrombocytosis.
- *Allopurinol* can control significant hyperuricemia.
- *Bisphosphonates* can help with bone pain.

- Splenectomy may be required for a grossly enlarged spleen or symptomatic pancytopenia.
- Splenic irradiation is an alternative to splenectomy in some cases and can significantly reduce splenic size.

- Ruxolitinib is indicated for treatment of patients with intermediate or high-risk myelofibrosis, including primary MF, post–polycythemia vera MF and post–essential thrombocythemia MF.