APLASTIC ANEMIA

The basic problem is failure of the pluripotent stem cells, producing hypoplasia of the bone marrow with a pancytopenia in the blood(pancytopenia with bone marrow hypocellularity). The diagnosis depend on exclusion of other causes of secondary aplastic anemia . and rare congenital causes such as Fanconi's anemia..

The main causes of aplastic anemia are:

- **Idiopathic** (in above 65% of cases).
- **Chemicals** (benzene and related compounds).
- **Drugs** (chloramphenicol, gold salts, D-peniciline, Cytotoxic drugs ,Immunosuppressives-as azathioprine
- **Radiation**.
- **Viruses** (hepatitis C, parvovirus B19, Epstein-Barr virus, cytomegalovirus).
- **Congenital (Fanconi anemia).**
- **Other** (connective tissue disease(SLE),pregnancy, Paroxysmal nocturnal hemoglobinuria(PNH.)

Fanconi's Anemia:

Fanconi's anemia is inherited as an autosomal recessive trait. When the patient suffering from aplastic anemia have also bone malformations, skin abnormalities and some other type of malformation, is likely suffering from Fanconi anemia

Physical Abnormalities in Fanconi's Anemia

Skin hyperpigmentation , Short stature, Upper Hypogonadism and genital abnormalities (males), Other skeletal. Anomalies of eyes, eyelids. Renal abnormalities

Clinical features and investigations of A.A.

Patients present with symptoms of bone marrow failure, usually anemia or bleeding, and less commonly infections.

Findings of hepatosplenomegaly and lymphadenopathy should suggest an alternative diagnosis such as leukemia and lymphoma rather than aplastic anemia.

Aplastic anemia is diagnosed with blood and bone marrow studies. An full blood count demonstrates pancytopenia, low reticulocytes and often macrocytosis. Teardrop cells, poikilocytes, and leukoerythroblastic changes suggest an alternative diagnosis .

Bone marrow aspiration and trephine reveal hypocellularity less than 30% with fatty replacement.

The severity of aplastic anemia is graded according to the Camitta criteria

23.60 Camitta criteria

Severe AA (SAA)

- Marrow cellularity < 25% (or 25–50% with < 30% residual haematopoietic cells), plus at least two of:
  - Neutrophils $< 0.5 \times 10^9$/L
  - Platelets $< 20 \times 10^9$/L
  - Reticulocyte count $< 20 \times 10^9$/L

Very severe AA (VSAA)

- As for SAA but neutrophils $< 0.2 \times 10^9$/L

Non-severe AA (NSAA)

- AA not fulfilling the criteria for SAA or VSAA

Treatment:

The treatment of aplastic anemia can be divided into two phases: supportive care and definitive therapy.

1.Supportive care includes red cell transfusions for symptomatic anemia and platelet transfusions for bleeding due to thrombocytopenia. Prophylactic platelet transfusions should be considered for patients with severe thrombocytopenia (5,000–10,000) even in the absence of bleeding. It is desirable to use single donor platelets as much as possible to avoid alloimmunization and the patient becoming refractory to future platelet transfusions. Transfusions from relatives or potential bone marrow donors should be avoided to decrease the chance of later marrow transplant rejection. Antibiotics should also be given for fever or infection in the presence of neutropenia (absolute neutrophil count 500–1,000). Initially, broad-spectrum antibiotics should be used for fever, with specific antibiotics chosen based on results of the cultures.

2.Definitive Therapy:

Immunosuppressive therapy includes antithymocyte globulin (ATG) and cyclosporine. A definitive therapy for aplastic anemia include bone marrow transplantation and immunosuppressive therapy. Bone marrow transplantation is considered the treatment of choice in young, otherwise healthy patients with severe aplastic anemia who have a related histocompatible donor. Long-term survival rates for patients less than 40 years of age transplanted from HLA-identical siblings are currently approximately 75%

Mortality/morbidity:

Infection and bleeding are major causes of morbidity and mortality from aplastic anemia. Patients who undergo bone marrow transplantation have additional issues related to acute and chronic toxicity from the conditioning regimen and graft versus host disease (GVHD), as well as a potential for graft failure.

In approximately 30% of patients with aplastic anemia, the condition does not respond to immunosuppression.

In cases with a treatment response, relapse and late-onset clonal disease, such as paroxysmal nocturnal hemoglobinuria (PNH), myelodysplastic syndrome (MDS), and leukemia, are risks—regardless of the treatment response or degree of response.

Polycythemia

A hemoglobin level greater than the upper limit of normal (adult females 165 g/L or hematocrit > 0.48; adult males 180 g/L or hematocrit > 0.52) for more than 2 months should be investigated.

It may be due to an increase in the number of red blood cells (true polycythemia) or a reduction in the plasma volume (relative or apparent polycythemia.

Relative polycythemia with a reduction in plasma volume is usually a consequence of dehydration, diuretic use or alcohol consumption .Direct measurement of red blood cell mass is necessary to differentiate these conditions.

Classification of polycythemia :

Primary polycythemia (POLYCYTHEMIA RUBRA VERA): due to JAK 2 gene mutation characterized by splenomegaly and itchy skin after hot shower. It will be covered in the lecture on myeloproliferative disorders.

Secondary polycythemia: True polycythemia and Relative polycythemia

Due to secondary causes most commonly are COPD , Hypoxia and congenital heart diseases. Males with Hct values of over 0.52 and females over 0.48 can be assumed to have polycythemia . Apparent erythrocytosis with a raised Hct, normal red cell mass (RCM) and reduced plasma volume may be associated with hypertension, smoking, alcohol and diuretic use which is called (Gaisböck'ssyndrome).

23.8 Classification and causes of erythrocytosis

	Absolute erythrocytosis	Relative (low-volume) erythrocytosis
Haematocrit	High	High
Red cell mass	High	Normal
Plasma volume	Normal	Low
Causes	*Primary* Myeloproliferative disorder Polycythaemia rubra vera (primary proliferative polycythaemia) *Secondary* High erythropoietin due to tissue hypoxia: High altitude Cardiorespiratory disease High-affinity haemoglobins Inappropriately increased erythropoietin: Renal disease (hydronephrosis, cysts, carcinoma) Other tumours (hepatoma, bronchogenic carcinoma, uterine fibroids, phaeochromocytoma, cerebellar haemangioblastoma) Exogenous testosterone therapy Exogenous erythropoietin administration: Performance-enhancing drug-taking in athletes	Diuretics Smoking Obesity Alcohol excess Gaisböck's syndrome

CLINICAL FEATURES OF POLYCYTHEMIA:

A clinical history and examination will provide clues as to the etiology of polycythemia .
decreased mentation, headache dizziness ,fatigue, generalized weakness, and poor exercise tolerance.
plethora or a ruddy complexion .
The cardiovascular and respiratory systems should be assessed for evidence and causes of hypoxemia
The presence of splenomegaly supports a diagnosis of polycythemia Vera rather than secondary polycythemia.
Cardiac murmurs and clubbing of the fingers may suggest a congenital heart disease.
Those with PRV may have arterial thromboses, pruritus worse after a hot bath, hepatosplenomegaly and gout (due to high red cell turnover) . If no other cause is identified, further investigations to exclude inappropriate erythropoietin secretion should be performed.
A clinical history and examination will identify most patients with polycythemia secondary to hypoxia.

Management :

No medications are available to treat secondary polycythemia. Treat the underlying causes.
Provide oxygen supplementation to patients with chronic obstructive pulmonary disease.
Recommend weight loss in patients with obesity and hypoventilation.
Recommend smoking cessation for patients with carboxyhemoglobin.
Surgically correct arteriovenous shunts.
To restore viscosity and maintain circulation at its optimal level, phlebotomy to ameliorate the symptoms of polycythemia and also decrease the risk of thrombosis, strokes, myocardial infarction, and DVT.