JSC “Medical University Astana”
Department of Internal Diseases №1

POLYCYTHEMIA

Done by: Suleymanov M.
463 GM
Checked by: Dr. scient. med.,professor
Baidurin S.A.

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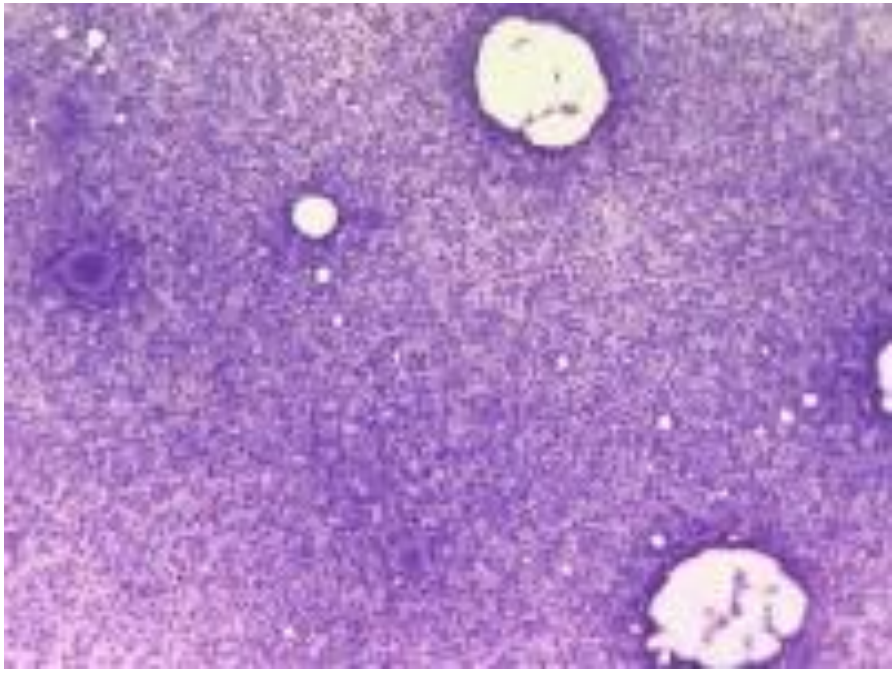
Introduction

- One of the chronic myeloproliferative disorders
  - Polycythemia Vera (PCV)
  - Essential Thrombocytopenia (ET)
  - Chronic myelogenous leukemia (CML)
  - Myelofibrosis with myeloid metaplasia
- Characterized by increased red blood cell mass or erythrocytosis

Polycythemia vera

- Bone marrow film at 100X magnification demonstrating hypercellularity and increased number of megakaryocytes

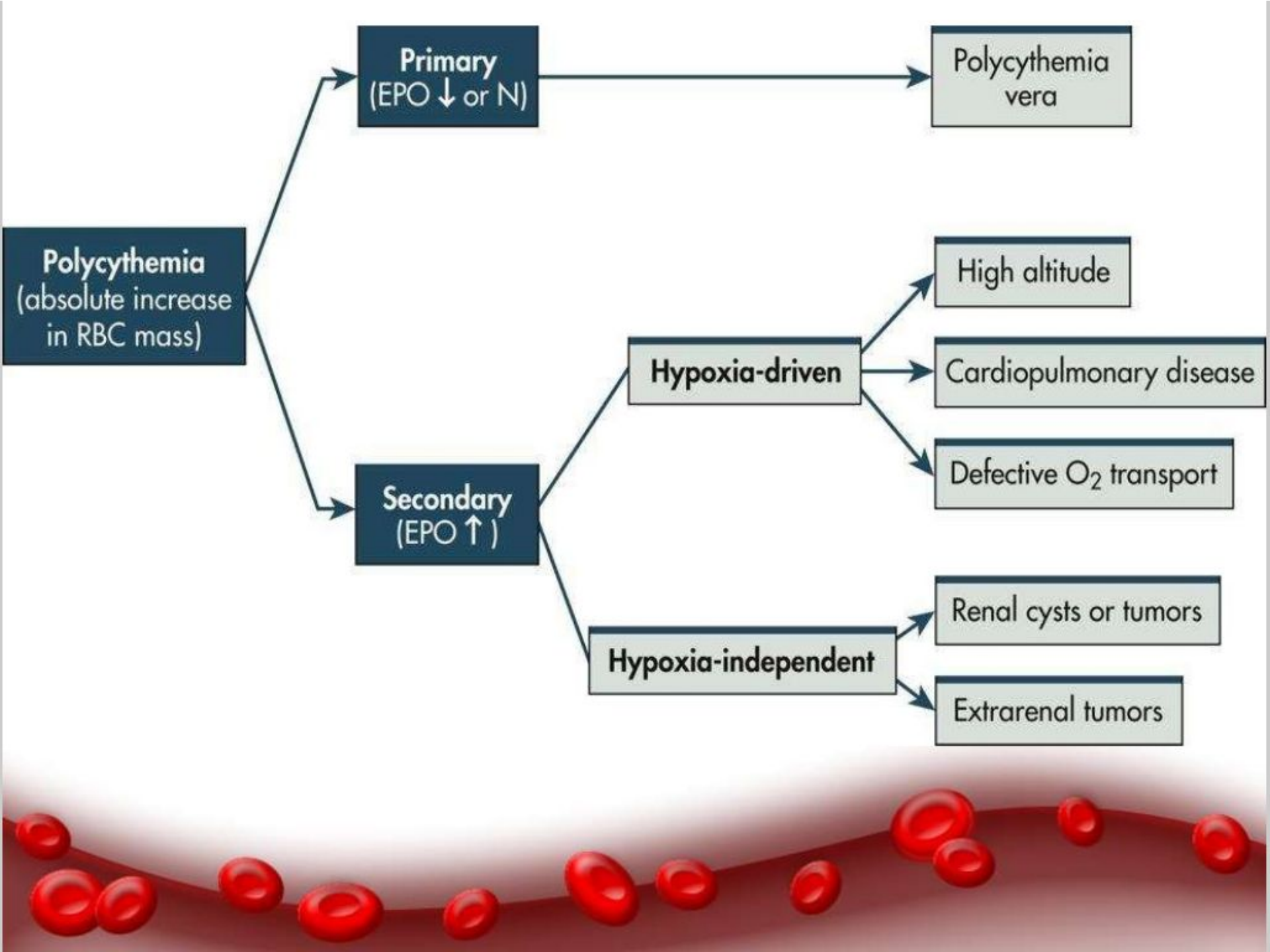


Incidence

- Median age of diagnosis is 60 but seen in wide age range between 20 and 85
- Slightly higher incidence in men than women (2.8 vs. 1.3 cases/100,000 per year, respectively)
- Survival of untreated PCV estimated between 6 to 18 months but treated patient survival is >10years

Causes of Death in PCV

- Thrombosis (29%)
- Hematologic malignancies (ie AML or MDS, 23%)
  - Rate of hematologic transformation ~1.3 episodes per 100 patient years
- Non-hematologic malignancies (16%)
- Hemorrhage (7%)
- Myeloid metaplasia with myelofibrosis (3%)

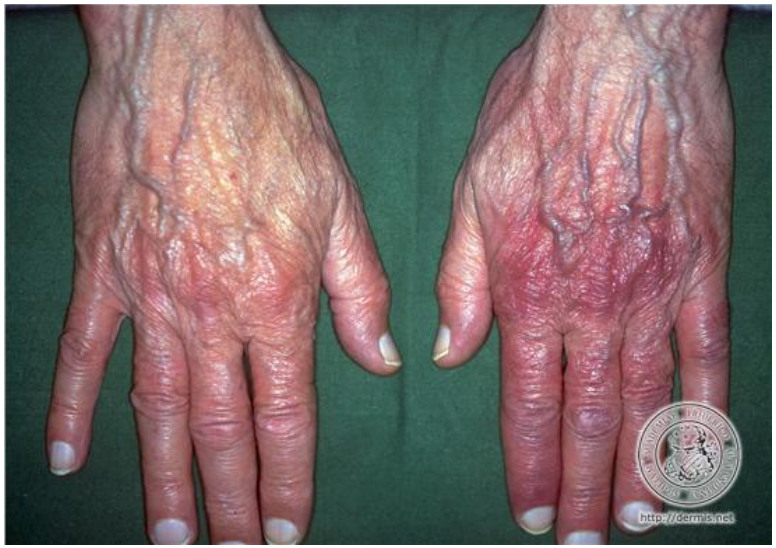

Polycythemia (absolute increase in RBC mass)
Primary (EPO ↓ or N)
Polycythemia vera
Secondary (EPO ↑)
Hypoxia-driven
High altitude
Cardiopulmonary disease
Defective O_2 transport
Hypoxia-independent
Renal cysts or tumors
Extrarenal tumors

Clinical Presentation

- Pruritus
  - Especially following vigorous rubbing of skin after warm bath or shower
  - Suggested that mast cell degranulation and release of histamine play a role
  - Also release of adenosine diphosphate from red cells or catecholamines from adrenergic vasoconstrictor nerves when skin is cooled may cause plt aggregation and local production of pruritogenic factors

Clinical Presentation

- Erythromelalgia
  - Burning pain in feet or hands accompanied by erythema, pallor, or cyanosis in presence of palpable pulses
  - Microvascular thrombotic complication in PCV and ET



Clinical Presentation

- Thrombosis
  - Secondary to increases in blood viscosity and platelet number
  - 15% of PCV pts with a prior major thrombotic complication (ie CVA, MI, thrombophlebitis, DVT, PE)
  - De novo presentation of thrombosis in pts with Budd-Chiari syndrome and portal, splenic, or mesenteric vein thrombosis
    - Suspect PCV in pts with these diagnosis under age of 45.

Clinical Presentation

- GI sxs
  - High incidence of epigastric distress, h/o PUD, and gastroduodenal erosions on upper endoscopy
  - Felt 2/2 alterations in gastric mucosal blood flow due to altered blood viscosity and/or increased histamine release from tissue basophils

Physical Exam

- Splenomegaly
- Facial plethora (ruddy cyanosis)
- Hepatomegaly
- Injection of conjunctival small vessels
- Excoriation of skin suggesting severe pruritus
- Stigmata of prior arterial or venous thrombotic event
- Gouty arthritis
- Erythromelalgia

Diagnostic Criteria
-First rule out Secondary Causes of Erythrocytosis

TABLE 2

Secondary Causes of Increased Red Cell Mass (Erythrocytosis)

Physiologically appropriate

Chronic pulmonary or cardiac disease
Decreased 2,3-diphosphoglycerate
High oxygen affinity hemoglobinopathy
Increased carboxyhemoglobin (in smokers) and methemoglobin
Residence at high altitude

Physiologically inappropriate

Adrenal cortical hypersecretion
Hydronephrosis
Tumors producing erythropoietin or anabolic steroids

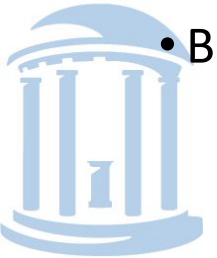
Relative (stress)

Disorders associated with decreased plasma volume (e.g., diarrhea, emesis, renal diseases)

Diagnostic Criteria

- Polycythemia Vera Study Group (1960s)
- Major Criteria
  - Increased red cell mass: Males ≥ 36ml/kg, Females ≥ 32ml/kg
  - Arterial oxygen saturation ≥ 92%
  - Splenomegaly
- Minor Criteria
  - Platelet count >400,000/microL
  - WBC >12,000/microL
  - Leukocyte alkaline phosphatase score >100
  - Vitamin B12 >900 pg/ml
- Requires all 3 major criteria or 2 major and 2 minor criteria

- BUT, there were significant limitations with these original criteria…



Problems with PVSG criteria

- Determination of red cell mass can be misleading if patient is obese as body fat is relatively avascular
  - In addition many institutions do not have ability to calculate
  - Felt that females with hgb >16.5 and males with hgb >18.5 have increased RCM making measurement not necessary
- Elevated LAP score is sensitive but not specific
- B12 studies are neither sensitive nor specific

Revised WHO criteria for PCV

- Major
  - Hgb >18.5 in men, 16.5 g/dL in women
  - Presence of JAK2 V617F or other functionally similar mutation
- Minor
  - Bone marrow bx showing hypercellularity for age with trilineage growth with prominent erythroid, granulocytic, and megakaryocytic proliferation
  - Serum erythropoietin level below nml reference range
  - Endogenous erythroid colony formation in vitro
    - Using vitro culture techniques, there is formation of erythroid colonies in absence of added erythropoietin

World Health Organization

Treatment

- Phlebotomy
  - Goal is to reduce viscosity, reduce HCT to <45.
  - Yielded best overall survival in initial PVSG trial from 1967-1987
  - But increased risk of thrombosis within 3 years leading to addition of low-dose aspirin

Treatment

- Hydroxyurea
  - Acts by non-alkalating mechanism to inhibit the enzyme ribonucleotide diphosphate reductase involved in DNA synthesis
  - Reduced incidence of thrombosis compared to phlebotomy
  - Effective in reducing blood counts although transient cytopenia may occur
  - Some question of whether this drug has potential for being leukemogenic, although not proven

Treatment

- Interferon alpha
  - Wide range of biological actions including anti-proliferative and cellular differentiating effects
  - Shown to provide relief from intractable pruritus and reduce spleen size
  - Associated with significant side effects including influenza-like syndrome, pyrexia, myalgias, and athralgias
  - Not shown to be teratogenic or cross placenta thus could be used in pregnancy

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