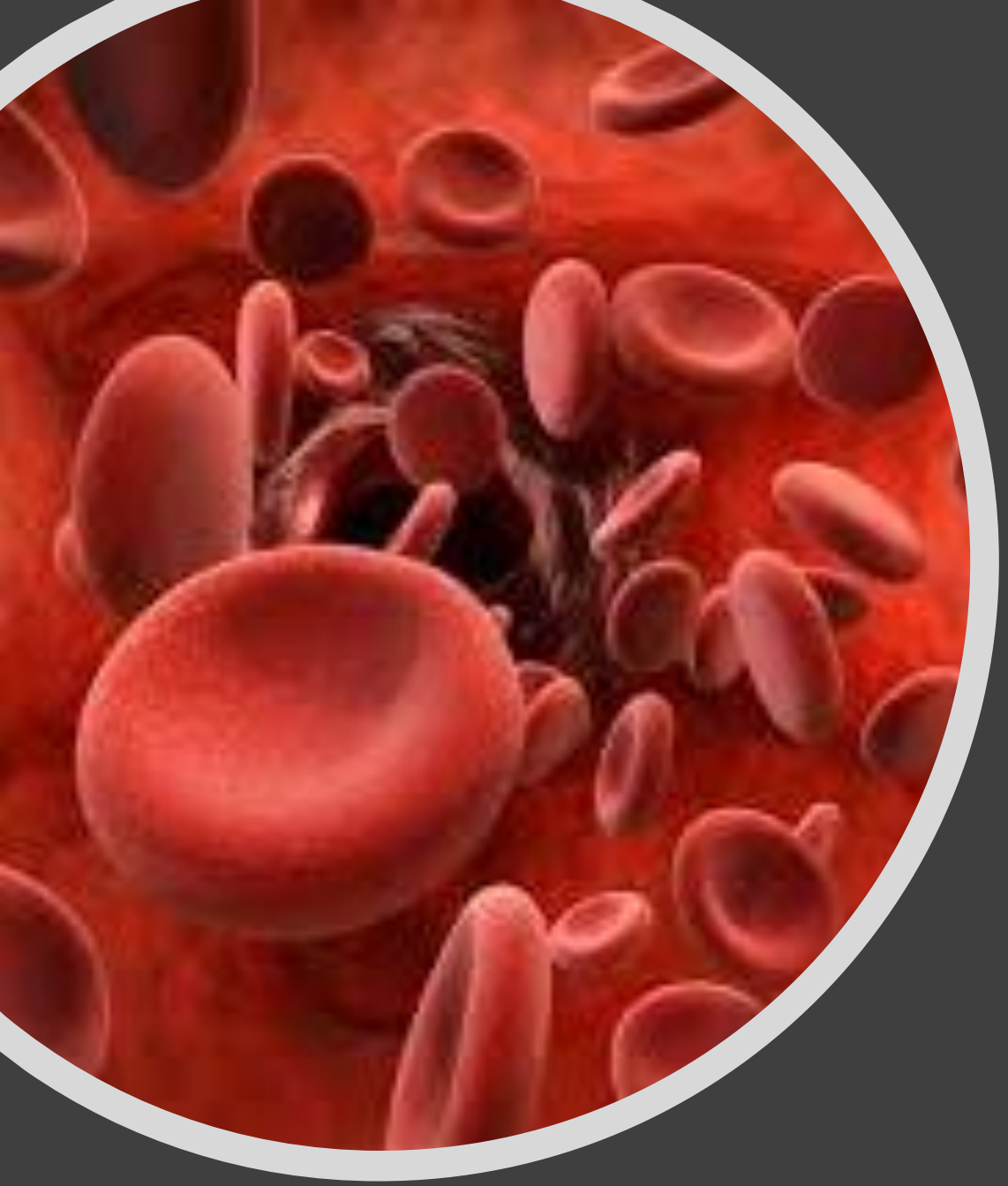

Lecture_2

Polycythemia

fourth year students

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13th/December/2018

Red blood cells (erythrocytes)

Red cell precursors formed in the bone marrow from the erythroid

(CFU–E) progenitor cells are called erythroblasts or normoblasts

These divide and acquire haemoglobin, which turns the cytoplasm pink; the nucleus condenses and is extruded from the cell.

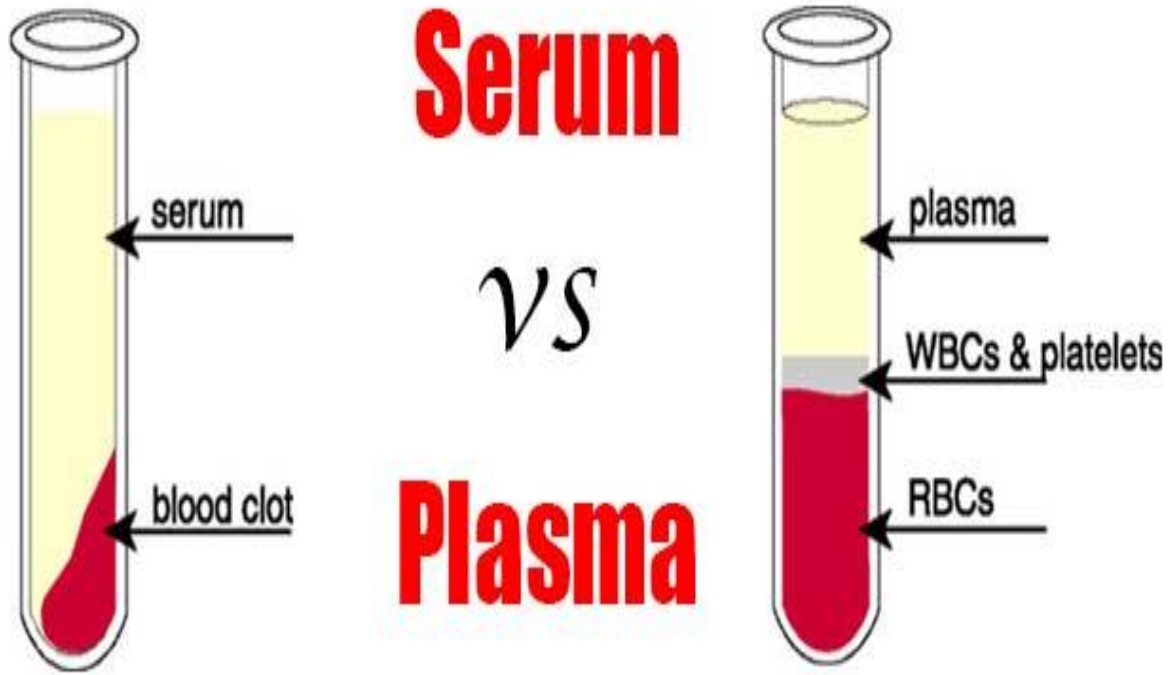
Proliferation and differentiation of red cell precursors is stimulated by erythropoietin, a polypeptidem hormone produced by renal interstitial peritubular cells in response to hypoxia

- Normal mature red cells circulate for about 120 days
- They are 8 μm biconcave discs lacking a nucleus but filled with
- Haemoglobin is a protein which delivers oxygen to the tissues

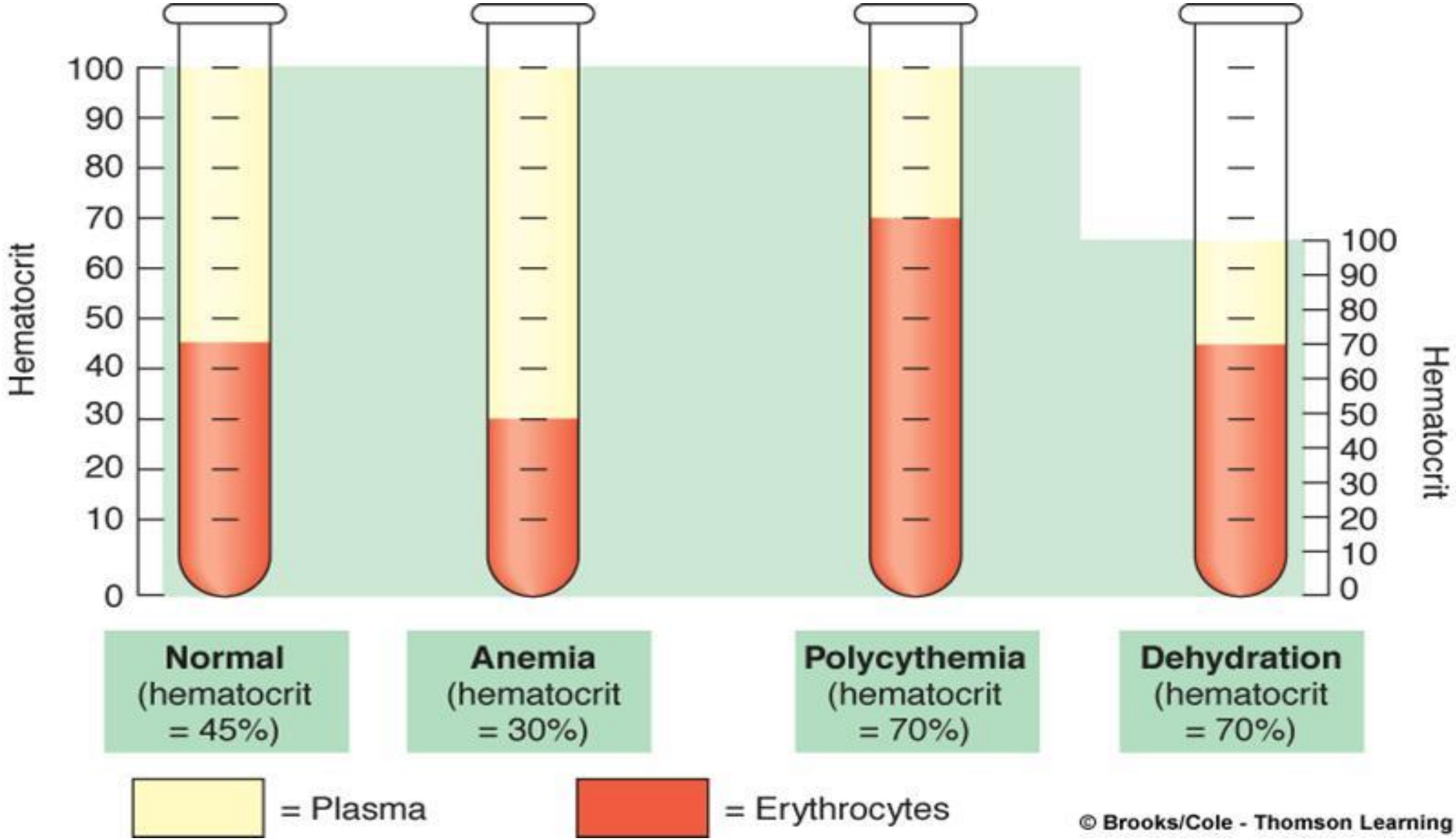
- The reference ranges for Hb concentration in adults are:
  - Men: **14.0 -17.5** (mean 15.7) g/dL
  - Women: **12.3 -15.3** (mean 13.8) g/dL

- **Hematocrit** is the fraction of whole blood composed of red blood cells
- Reference ranges of hematocrit (SI units/conventional units) are:
  - Males - **0.40-0.54 / 40-54%**
  - Females - **0.36-0.46 / 36-46%**

- **Serum** is the liquid portion of the blood after it has been allowed to clot , while,
- **Plasma** is the liquid portion of blood that has been prevented from clotting and is more reflective of the blood as it circulates in the body



Serum = Plasma – Clotting Factors


Hematocrit
100
90
80
70
60
50
40
30
20
10
0
Hematocrit
100
90
80
70
60
50
40
30
20
10
0
Normal (hematocrit = 45%)
Anemia (hematocrit = 30%)
Polycythemia (hematocrit = 70%)
Dehydration (hematocrit = 70%)
= Plasma
= Erythrocytes
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Polycythaemia

- is a disease state in which the haematocrit (the volume percentage of red blood cells in the blood) is elevated

- It can be due to an increase in the number of red blood cells 'True polycythaemia' (or absolute erythrocytosis) or to a decrease in the volume of plasma 'relative', 'apparent' or 'low-volume'

Classification and causes of erythrocytosis

	Absolute erythrocytosis	Relative erythrocytosis
Haematocrit	High	High
RBC mass	High	Normal
Plasma	volume	Low
Causes	<u>Primary</u> Polycythaemia rubra vera (primary proliferative polycythaemia) <u>Secondary</u> 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

Absolute polycythaemia

- The overproduction of red blood cells may be due to a primary process in the bone marrow (a so-called myeloproliferative syndrome), or it may be a reaction to chronically low oxygen levels or, rarely, a malignancy

It divided into:

1. Primary polycythaemia PRV
2. Secondary polycythaemia
3. Altered oxygen sensing

1. Polycythemia vera (PCV), polycythemia rubra vera (PRV)

- is a myeloproliferative disease occurs due to excess production of RBCs as a result of BM disorder, with excess WBCs and platelets
- Median age of diagnosis is 60 but seen in wide age range 20 - 85
- Slightly higher incidence in men > women
- Survival of untreated cases between 6 -18 months but treated patient survival is >10years
- Mutation testing: **JAK2 V617F-positive**

Clinical features:

- Asymptomatic
- Pruritus especially vigorous rubbing of skin after warm bath or shower
- Erythromelalgia burning pain in feet or hands accompanied by erythema, pallor, or cyanosis in presence of palpable pulses
- Facial plethora (ruddy cyanosis)
- Symptoms of hyperviscosity, such as lassitude, loss of concentration, headaches, dizziness, blackouts, pruritus and Epistaxis
- splenomegaly +/- hepatomegaly
- In some patients high blood pressure , Venous thromboembolism
- A hallmark of polycythaemia is an elevated ith Hct > **55%** in **83%** of cases

Treatment

1. Aspirin reduces the risk of thrombosis
2. Venesection 400 - 500 mL of blood, and can be repeated every 5–7 days until the haematocrit is <45%
3. Suppression of marrow proliferation with hydroxycarbamide or interferon-alfa may reduce the risk of vascular occlusion control spleen size and reduce transformation to myelofibrosis
4. Imatinib (Gleevec) Tyrosine kinase inhibitor which inhibits tyrosine kinase activity of BCR-ABL

2. Secondary polycythaemia

- is caused by either natural or artificial increases in the production of erythropoietin
- Secondary polycythaemia resolves when the underlying cause is treated
- It could be classified into physiological and non physiological polycythaemia

Causes of secondary polycythemia

Physiological increase in EPO	Inappropriate increase in EPO
Chronic obstructive pulmonary disease	Renal cell carcinoma
Cyanotic heart disease	Haemangioblastoma
Obstructive sleep apnoea	Hepatocellular carcinoma
Restrictive lung disease (e.g., obesity)	Uterine fibroids
Carbon monoxide poisoning (e.g., smoking)	Cerebellar tumours

Relative polycythaemia

- is an apparent rise of the RBCs level in the blood; however, the underlying cause is reduced blood plasma (hypovolemia ex: dehydration).
- Relative polycythemia is often caused by loss of body fluids, such as through burns, dehydration, and stress.
- A specific type of relative polycythemia is Gaisböck syndrome, and is typically seen in obese middle-aged men who are receiving a diuretic for treatment of hypertension causes a reduction in plasma volume

Case History

August 2014

- A 67-year-old female is diagnosed PV after complaining of fatigue
- Physical Exam was unremarkable
- CBC:
  - HCT, 48%
  - WBC, 12,100/μL
  - Platelets, 603,000/μL
- Mutation testing: JAK2 V617F-positive
- The patient was started on treatment with low-dose aspirin and hydroxyurea 500 mg/day
- Her symptoms resolved within 3 months

February 2016

- She now complains of left upper quadrant pain
- For 1.5 years, the patient was maintained on treatment; however, for the past 9 months her hematocrit has risen to 48% and she has required 4 phlebotomies in last 6 months
- Hydroxyurea was increased from 500 mg to 1,000 mg daily
- Physical Exam: remarkable for splenomegaly

August 2016

- Physical Exam: still remarkable for splenomegaly, slightly smaller
- HCT 47.5%

Thank you