ANHEMIAS - DIAGNOSIS and TREATMENT

Adorata Coman
Definition

- a pathological condition in which a significant concentration of **Hb is low** (less than 10%), Ht and the number of erythrocytes.
- lowering their number leads to decrease in the ability to **carry oxygen** to the tissues from which arises the subjective and objective symptoms.
- Anemia reveals, to a large, four groups of disorders:
  - blood loss;
  - stopping manufacturing to the end point;
  - destruction of erythrocytes or shortening the duration of their lifespan;
  - anomalies in hematopoiesis or in the synthesis of Hb.
The circumstances of a diagnosis of anemia's are:

The patient is presented to the physician just for a clinical syndrome of anemia. Decreasing ability of blood to carry oxygen causes:

- **disorders in cell function**: changes in the skin, nails, glossitis, dysphagia, asthenia, headache, vertigo, and
- **the signs and symptoms of compensatory mechanisms**: tachycardia, increased contraction of heart (fast systolic functional), low blood flow to the kidneys, the extremities, polypnea.
The circumstances of a diagnosis of anemia's are:

Anemic subclinical disorders, masked by "misleading", such as:

- congestive heart failure,
- angor pectoris - anemia reveals changes in clinical status and EKG,
- sub fever - regardless of the etiology of anemia, then a gap of the thermal curve probably by anoxia.
- brief loss of attention – especially from major anemic or sick elderly cerebral circulatory failure with pre-existing anemia.
Causes of anemia linked with Erythropoiesis

1. Missing in synthesis of folic acid, vitamin B12, iron, so on.
2. Functional deficiency of bone marrow production.
3. The inhibition of spinal hematological formation (drugs, immune influences).
4. Replacement of hematoformator bone marrow, injury of tissue (fibrosis, neoplasm).
5. Hereditary defects.
7. Idiopathic ("refractory").
8. Chronic or acute bleeding, iron deficiency secondary.
Haemolysis

- Abnormal Hemoglobin
  - Intra-corpusecular defects (S, C, D, E, unstable)
    - defects in the synthesis of globins (thalassemia)
    - defects in the synthesis of hem (porphyria)
    - enzymatic deficiencies (G-6-PD, pyruvate-kinase)
    - membrane defects (hereditary elliptocytosis, spherocytosis)
    - paroxystical nocturnal hemoglobinuria or
    - Secondary Defects.
  - Extra-corpusecular - physical agents (water, temperature, microangiopathies), chemical agents (venomous, drugs), infections (sepsis, malaria); cancer (lymphoma); connective tissues diseases (systemic lupus), splenomegaly; isoimmunisation.
History of disease

It's very important to specify the disease onset:

- **acute:**
  - acute hemorrhagies (epigastric pain accompanied by haematemesis, melena, in the case of a bleeding ulcer,
  - in malignant hematological diseases extended haemorrhagies, which can be manifested by the presence of haematomas, epistaxis, haemoptysis or haematemesis, melena, and in the case of women with menstrual cycle – meno-metrorrhagies,
  - consumption of chlorocide, butasone, oxi-phenyl-butasone,
  - hemolysis (intense abdominal pain, fever, splenomegaly).
History of disease

- chronic:
  - working in toxic environment with lead, benzene;
  - chronic medications: amydopirin, acetyl-salicylic acid, phenacetyne; antipyrine, primaquine, quinine, quinidine, sulfonamide drugs, which can cause bleeding or hemolysis even in small doses. Aplastic reversible anaemia (reversible or not) may appear.
Full clinical examination

- must determine on the one hand signs and symptoms due to anaemia itself;
- and on the other hand manifestations that might explain the etiology of anemia; such as:
  - in the oral cavity - purple, in hemopathies, acute inflammation, glossitis, and papilary atrophy.
  - Biermer dysfagic sdr. (Plummer-Vinson syndrome), in hyposideremic anemia;
  - on the skin-jaundice;
  - purple, bruising in acute and chronic haemopathies;
  - dry skin, in mixoedema;
  - fanners-anemia: hair brittle, plate, concave nails;
Full clinical examination

- haematopoietic organs - splenomegaly, with or without hypersplenism, supercilia, primitives adenopathies;
- digestive system-hepatomegaly in cyrrhosis, cancer, rectal neoplasm, haemopathies, hemorrhoids, rectorrhagies.
- abdominal mass, in Hodgkin disease, chronic leucemias;
- Genital organs - genital examination is compulsory for all women with history of anaemia.
1. **Blood count:**

- number of erythrocytes – normal values:
  - males: 4.5-5.7 million/mm³ female: 4.2-5.5 mln/mm³

- normal haemoglobin values:
  - men: 13.5-18g% female: 12-16 g%

- normal haematocrit-values:
  - males: 50-52% female: 37 – 47%

Values in the population (%)

<table>
<thead>
<tr>
<th></th>
<th>MEN</th>
<th>WOMEN'S</th>
</tr>
</thead>
<tbody>
<tr>
<td>hematocrit</td>
<td>44 (39-50)</td>
<td>39 (33-45),</td>
</tr>
<tr>
<td>hemoglobin (mg/dl)</td>
<td>15 (12-17)</td>
<td>13 (11-15)</td>
</tr>
</tbody>
</table>
Biological investigations

2. Erytrocitary-Indices

- **VEM (mean erytrocitary volume)** = \((Ht/\text{nr. E}) \times 10\); normal = 80-95 microns (Under 80 - mycrocystosis and over 100 - macrocystosis).

- **CHEM (erytrocitary average concentration of haemoglobin)** = \((Hb/Ht) \times 100\); normal = 32-34%. This is the test that indicates the character normocromic or hypocromic. No increase over normal values than sferocytosis, so we cannot talk of anaemia hypercromic. CHEM sits alongside the bubble test less faithfully, but more commonly used.

- **HEM (haemoglobin erytrocitary mean value)** = \((Hb/\text{nr.E}) \times 10\); normal = 27-31 pg.

- **IC (colour index)** = \(1/(\text{nr.E} \times 3)\); normal = 0,9-1,1.
Biological investigations

Analysis of the data above allows to affirm the existence of the **anaemic syndrome** depending on haemoglobin and classify **anaemia** in one of three groups:

- anemia mycrocytic hypochromic;
- macrocytic anaemia;
- anaemia normocytic and normochromic.
Biological investigations

3. Reticulocytes, normal values 3-8%.

Countdown will be systematically in front of an isolated anaemia. Considering that the absolute value, the number of reticulocytes is 40,000-80,000/mmc.

When reticulocytes grow over this issue we speak of a regenerative anaemia; and when the number of reticulocytes is normal or low, we are talking about non-regenerative anaemia.

Their importance is particular in normocytic and normochromic anaemia.
Biological investigations

4. Iron in plasma (sideraemia) - normal (80-120 mcg/dl). Binding of iron is associated with the determination of siderophyline which is iron-binding protein (typically 300-400 (%)) and with the determination of the two parameters:
   - the total capacity of siderophyline saturation (CTSS)-300-400 %
   - coefficient of saturation of siderophyline which is the ratio of sideraemia and CSS (normally 30-35%);

5. Bilirubinemia-normal 1 mg/dl which grows in the case of hemolysis. Normal value excludes haemolytic anaemia.
Characteristics of anaemia of reticulocytes and VEM

<table>
<thead>
<tr>
<th>AREGENERATIVE (RET &lt; 1%)</th>
<th>REGENERATIVE (RET &gt; 3%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MYCROCYTOSIS (VEM &lt; 82 µ³)</td>
<td>MACROCYTOSIS</td>
</tr>
<tr>
<td>1. Iron deficiency;</td>
<td>Acute bleeding;</td>
</tr>
<tr>
<td>2. Thalassemia;</td>
<td>Acute hemolisis;</td>
</tr>
<tr>
<td>3. Syderoblastic Anemia;</td>
<td>Postsplenectomy.</td>
</tr>
<tr>
<td>4. Chronic diseases.</td>
<td></td>
</tr>
<tr>
<td>MACROCYTOSIS (VEM &gt; 100 µ³)</td>
<td>MICROCYTOSIS</td>
</tr>
<tr>
<td>1. Deficiency of B₁₂;</td>
<td>Mycroangiopathy;</td>
</tr>
<tr>
<td>2. Deficiency of folates;</td>
<td>Some haemoglobinopathies.</td>
</tr>
<tr>
<td>3. Chronic liver dis.;</td>
<td></td>
</tr>
<tr>
<td>NORMOCYTOSIS (VEM = 82-100 µ³)</td>
<td>NORMOCYTOSIS</td>
</tr>
<tr>
<td>1. Inflammatory chronic dis.;</td>
<td>Acute bleeding;</td>
</tr>
</tbody>
</table>
Conclusions

- Diagnosis must precede the therapeutically decision.
- Questioning diagnosis is given by; the clinical examination and blood test, and a few simple biological data.
- Hypocromic mycrocytic anaemia in chronic hemorrhages is the most common in current medical practice but is not the only!
- Anaemias due to deficient products are common in third age, and they occur through different mechanisms: aplastic, non-use of vitamins and anti-eritrocytes antibodies.
- Chronic anemia which is not a simple inquiry elucidates the etiological structure are a sign of serious illnesses which will highlight clinically over time.
Treatment of iron-deficiency

- Treatment in anemia is the one which corrects entire's the anaemia.
- Conditions of a fair treatment: the treatment must be preceded by a full and correct diagnosis.
- Treatment needs to be done in good time, to rebuild the reserves of iron, vitamin B12 in the body, etc.
- **Treatment with iron.** Daily iron requirement is 1 mg/day for males and 15 mg/day for women and grows during adolescence (12-15 years) for both sexes (20 mg/day), load-second quarter-III (23-30 mg/day), as peripartum, breastfeeding.
Treatment of iron-deficiency

- The reserve of iron body lies in the liver, spleen, bone marrow (1500 mg) and Hb (2600 mg), Myoglobin (350 mg), ferritin (300 mg)-a total of 4,000-5,000 mg iron.
- Usual diet contains 10-20 mg Fe. It is absorbed approximately 1,5 mg/day.
- Losses are 1.5 to 2 mg/day on females and 1 mg/day on males.
- Iron therapy goals are normalizing Hb and recovery the deposits.
Treatment of iron-deficiency

- Medicines used: natrium ferrous (Glubifer) 100 mg/cp; ferrous sulfate (Ferogradumet) 300 mg/cp; ferrous fumarate (Ferronat) 200 mg/CP.
- Duration of treatment is 3-6 months to rebuild the reserves of iron in the body.
- Intolerance to preparations with iron is manifested by the nausea, vomiting, diarrhea or constipation, abdominal colic. It relieves by reducing the daily dose.
- If not supported, has to be administered by iv.
- Not after gastric protection, lack of absorption.
Treatment of iron-deficiency

- Parenteral iron administration is indicated only in cases where it can be administered per os.
- Medicines used: iron-polymaltozat 1f = 100 mg Fe-administered i.m. deeply. The place of injection is always changing because it can give the tattoo (not so used); Most common iv, Iron fructose 1 f = 100 mg Fe.
- Parenteral iron requirements shall be carried out by:
  - mg Fe required = (Hb 15) × G (kg) x 3
Treatment of iron-deficient

- Response to treatment with iron aims through:
- the reticulocytosis crisis to 6-7 days (5-20%);
- Hb must increase by 0.20-0.30 g/day;
- Hb should increase by 8% per week.
- If the parameters presented progressing incorrectly means that the patient still loses blood or iron is not properly used in the body, or iron intake is inadequate (too small).
- The treatment lasts for 12-24 weeks with possible extensions up to 12 months, until the sideraemia and sideroblastosis have been normalized.
Treatment of iron-deficient

- During the period of repairing, it has to be administered too ascorbic acid (200 mg/day) and folic acid (10 mg/day) to avoid macrocytosis due to the rapid recovery (hematopoiesis).

- Prophylactic treatment needs to be done especially: advising 200 mg of ferrous natrium 5 mg folic acid + 2 times/day; donor blood-1,000 mg Fe in men, 2000 mg Fe women for each 250 ml of blood donated;
Biermer anaemia treatment

- It is substitutive, parenteral way - vitamin B12, with each failure the digestive absorption (gastritis).
- The objectives are:
  - the disappearance of clinical manifestations, in particular those neurological, and
  - restoration of the vitamin B12 (5,000 mg).
- The treatment is made with vitamin B12, 100 gamma/day for 7 days, then 100gamma/day-3 days/week; in the 3rd week-100 gamma/day, 2 days/week, following both clinical and haematological remission.
Biermer anaemia treatment

- After this treatment the appeal is made by maintenance treatment (1000/monthly all his life).
- The effectiveness of the treatment must be assessed by reticulocytosis crysis on the day of the 3rd to 5th day; after that it is associated iron in treatment because it installs hypocromia of "repair".
- Anaemia disappears at 1 month (Hb increases by 1 g/dl/weeks), white blood cells and platelets altogether seven days, it relieves neurological symptoms due to remyelinisation.
Normochromic, normocytic anaemia treatment

- Seeks to eliminate specific pathogens (treatment of existing infections with antibiotics),
- Idiopathic anemias benefits of corticoides hormones administration, blood transfusions, possibly splenaectomy.
Treatment the crisis of hemolysis

- Prednisolone 40-60 mg/day (dose attack = 1 mg/kbody/day). The dose of attack can grow up to 2 mg/kbody/day, and then decrease to the minimum necessary to maintain Hb 10 g%.

- Splenectomy is possible to be applied after treatment with cortisone. Sometimes after splenectomy, maintenance dose falls considerably.

- Lymphoproliferative anemias/treatment to palliation with modest results. Prednisolone is administered in high doses (100 mg/day) and biocatalysts (vitamins).
## Drugs which affect platelets

<table>
<thead>
<tr>
<th>FUNCTION</th>
<th>NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salicylates</td>
<td>Quinidine</td>
</tr>
<tr>
<td>AINS</td>
<td>RH2 antagonists</td>
</tr>
<tr>
<td>Antidepressant tricyclic drugs</td>
<td>Sulphonamides</td>
</tr>
<tr>
<td>Clophybrates</td>
<td>Ethanol</td>
</tr>
<tr>
<td>Sulphinpirazone</td>
<td>Phenytoine</td>
</tr>
<tr>
<td>Dypiridamole</td>
<td>Valproic acide</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Barbiturates</td>
</tr>
<tr>
<td>Clemastine</td>
<td>Thiazides</td>
</tr>
</tbody>
</table>
Proliferative syndromes

- **CANCER** - is a generic term that defines a wide range of diseases characterized by alterations in the processes of growth and proliferation. It is a poligenic disease in which the progression of the tumor is the result of endless combinations of genetic and epigenetic alterations and that it is selected in a Darwinian manner malignant phenotype.

- **LEUKEMIAS** - cancer diseases are appearing through the transformation of malignant hematopoietic progenitor cells. They appear by monoclonal proliferation of a single cell, the cell lymphoid or myeloid stem cells.
Acute Leukemias

- Heterogenic group of malignant proliferation of stem cells (strain) of multipotente or unipotente. It is characterized by clonal expansion of immature cells, lymphoid or myeloid line, who had lost the ability to differentiation and maturation.

- Hematopoietic marrow invasion, suppression of growth and differentiation of cells, reduction of medullar blood cells determine the clinical and biological activities.

- **Clinic** - three main syndromes
  - anemic syndrome
  - the infectious syndrome
  - hemorrhagic syndrome

- Invasion of the peripheral lymph, lymph proliferations on organs – liver, splein, skin, CNS, testicles, can cause the tumor syndrome.
Classification

- Cell type predominant in bone marrow and its relation to normal hematopoietic system.
- Microscopic examination of the peripheral blood and froti of the sternal puncture.
- Immunocyto-chemistry techniques, electron microscopy.
- Immunological examination (monoclonal antibodies specific against structural cells at the leukemia and hematopoietic cells).
- The diagnosis of acute leukemia is if blastic cells (immature) exceed 30% of the total nucleated cells of bone marrow.
- Acute lymphoblastic leukemia-3 subtypes (L1, L2, L3).
- Acute myeloblastic leukemia – 8 subtypes (M0 – M7).

Identified and confirmed by the above techniques.
When we think of an acute leukemia?

- Signs and symptoms: altered state, fever or subfebrilitați without obvious infectious cause, sweating, inapetență, weight loss

- Signs and symptoms due to bone marrow failure:
  - sdr. anemic – physical and mental asthenia, pallor, vertigo, dyspnea, palpitations, tachycardia, angor pectoris or Cardiac decompensation in the elderly
  - sdr. infective-angina (ulcero-necrotic), secondary infections, relapsing fever in the infectious context
  - sdr. hemoragic – petechiae, bruising, hematoma, epistaxis, gingivoragii, meno-metroragii, to the digestive bleeding, bleeding in the CNS.
Signs and symptoms due to the proliferation of leukemia

- bone pain or pseudoarthritis, a migratory, accented at the compression (stern, metafize)
- sdr. tumor: adenopathies, splenomegaly, painless testicular hypertrophy, tumor mediastinal
- infiltration in CNS (1-3% of cases) – sdr. meningeal, with headache, vomiting or cranial nerve palsies (often pairs VI and VII).
- a F.O. examination (of the eye) – papilledema (mark intracranial hypertension) and/or retinal hemorrhages.
- a lumbar puncture (LP) – carry out a systematic diagnosis and highlights the leukemia cells in the CSF.
- Signs/symptoms found in LAM, as a result of the proliferation of leukemia
  - hipetrofic gingival painful
  - hematodermia or leukemia cutis-blasticae dermal-epidermal water, in the form of nodules violate anpainfull
  - Sarcoma granulocitar (cloromul) – a unique tumor extramedular, located in the paranasal sinuses, orbit, the digestive tract, genito-urinary, breast pads, mediastinum, pleura, the peritoneum.
- ATTENTION the disease can be and asymptomatic, opens with a control.
The Investigation **the most handy and binding** – complete blood count.

- Hiperleucocitosis, predominant blastic cells (granulations and body mieloblasts, the Auer body), by assigning signs of spinal cord impairment: normocitic normochromic, aregenerative anemia, neutropenia, trombopenia. Sometimes-hypo-or aleukemic form: pancytopenia with leukemia cells are rare or absent.

- During the 2, hematologist will perform the sternalpuncture and myelogram, spinal cord with rich cellularity, composed of not less than 30% blasts, diminuation of area net of other cell lines.

- The balance sheet will be completed in the hospital with cell tower-over evaluation, transcobalaminemia, uricemia), the balance of evidence, ionograms kidney, bacteriological balance.
Treatment

- It is initiated and pursued on specialized services.
- On ambulatory care we could make:
  - Prevention and treatment of infections (the patient is immunodeprimat).
  - Observation and signaling of cytotoxic treatment intolerance.
  - Diagnosis of severe cytopenia (anemia, thrombocytopenia).
  - Diagnosis and treatment in emergency of hemoragies or another lifethreatening conditions.
Emergency

- **Febrile Neutropenia** and neutropenia in a patient with axillary or oral temperature over a determination 38.3 grade C or over 38 degrees C from two determinations in less than an hour.
- Neutrophils circulating in neutropenia = absolute number as 1000/mmc.
- Neutropenia in the disease or arising as a result of cytotoxic therapy mediulotoxicității fosters the infections with trivial or opportunistic germs.

**ATTENTION**

- A patient neoplazic, or not treated with chemotherapy, which is presented to a feverish syndrome, the priority is making hemoleucograms.
- The treatment shall be set up in the hospital, where the patient is isolated or not, depending on the seriousness of the neutropeniei, and you can continue outpatient specialist if the doctor recommends it.
Emergency

- **Septic Shock** - febrile neutropenia may complicate: infectious outbreak now + hypotension (Sbp < 80 mmHg) + tachicardie with weak pulse, filiform amid general status altered with cold sweats, peripheral cyanosis. Emergency rescue call for inpatient therapy.

- **Intracranial Hypertension** by developing an expansive intracranian process (primitive tumor or metastases). The seriousness of the risk is related to his employment secondary cerebral effect of mass or hydrocephalus.
  - **Clinic** – triad: headache, vomiting, papilledema. Headache occurs at the end of the night and is exacerbated by coughing or effort. Vomiting are spontaneous or preceded by nausea. Papillary edema are decreased visual acuity (transient flu visual episodes).
Emergency

- moderate-medrol 16 mg, 4 cp/day
- severe-solumedrol intravenously slow, 120-500 mg/day associated or not with Mannitol 20% (100 cm³ every 6 hours or 250 ml – 125 ml x 2/day). The patient will be transported to the emergency hospital.

- **Pulmonary Embolism** - anxiety + anginos type chest pain or pleural, tachycardia and tahipnee with cyanosis (signs of acute respiratory failure) associated possibly with right heart failure. Transporting the patient to the hospital for an emergency investigation and treatment.
Tasks for GPs

- Neoplastic patient is a complex and vulnerable; so the basic disease, its complications, and treatment specifically ask for pathology of most diverse, including vital risk emergencies.

- Family doctor supervises the State and evolution of the patient in the territory during and after treatment is completed. Track clinical status (including in terms of nutritional or psychologist, psychiatric) and haematological and biochemical parameters, the report is communicated to the oncologist.

- After the end of treatment, the doctor will send the patient on a regular basis for evaluation in the clinic, to track the evolution of imaging and cito-biological (markers of evolutivity).

- Last but not least, the family doctor must make prevention (especially in people with high risk) and early detection of cancer in order to increase the chances of survival or cure.

- Family doctor, so an integral part of the patient care team, has as a duty to get involved actively by pursuing the patient for a correct and effective collaboration with the team.