Subject: HLS- Pathology

Topic: Anemia – lecture 3

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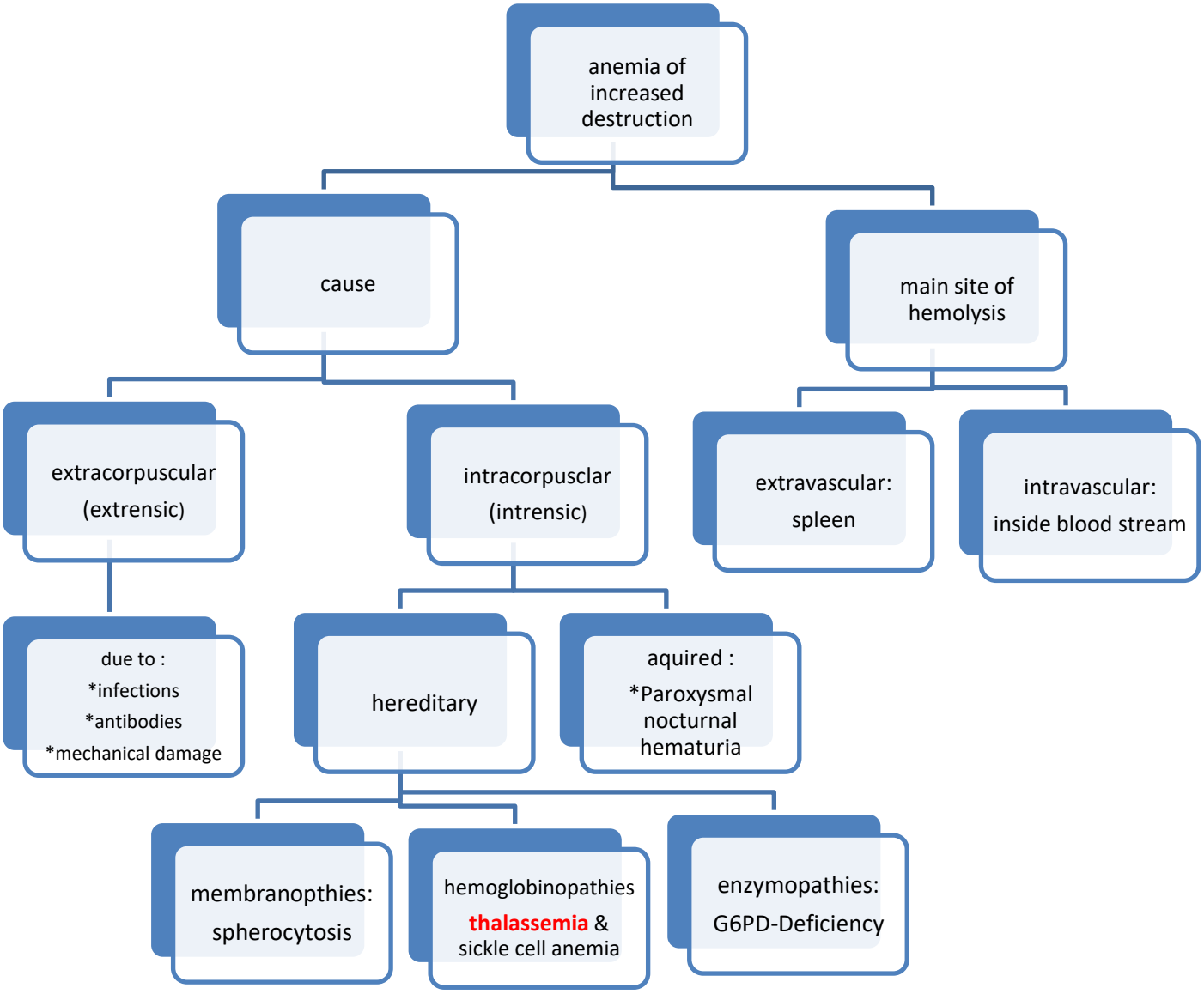
Anemia of Diminished production			
	Pathogenesis	Laboratory findings	Notes
Aplastic anemia	* **Extrinsic factor**: Activated T-lymphocytes destroy stem cells due to antigen cross reactivity * **Intrinsic factor:** inherited defects in Telomerase. - stem cells might express abnormal Antigens attracting T-cells	* decreased hematopoietic cells in BM (with residual fat) * pancytopenia (BM Failure) *normochromic or macrocyctic anemia. (Note: problems with stem cells give macrocystic anemias)	- Most cases are idiopathic - other associated factors are drugs , some viruses and pregnancy - immunosuppressive therapy restores bone marrow in 70% of cases *Special types of AA: - Fanconi anemia: rare, defect in DNA repair proteins>>>mutations. Can lead to leukemia
Myelophthisic anemia	* Infiltration of bone marrow>>>damaging hematopoietic cells (Could be Cancer, TB, Storage diseases,	* pancytopenia * Peripheral blood: Immature precursors of RBC's+ granulocytes	*patient comes with skin bleeding (Thrombocytopenia) * Neutropenia may lead to infections & death
Anemia of Renal disease	Deficiency in kidney function>> Low EPO>> Decreased RBC production	*increased serum creatinine * Low EPO * low reticulocyte count * Uremia in advanced cases (urea nitrogen in blood)	* uremia leads to abnormal platelets function (due to change in blood environment), but doesn't affect their count. *Burr cells (echinocytes) are secondary to uremia الخلايا الشوكية
Anemia of Liver Disease	***multifactorial** : - bleeding (varices, decreased synthesis of clotting factors)	*low transferrin	*morphology: spur cells (Acanthocytes) [due to abnormal lipid metabolism]
Anemia of Hypothyroidism	* Hypothyroidism>> decreased levels of thyroid hormones>> decreased erythropoiesis& EPO production	*normocytic anemia (can be macrocytic like AA)	
Myelodysplastic syndrome		* RBCs are macrocytes (Stem cells problem)	*the only neoplastic disease in this group * Acquired *relatively common *mainly old age *anemia doesn't respond to treatment (iron, folic acid,…)


anemia of increased destruction
cause
main site of hemolysis
extracorpuscular (extrensic)
intracorpusclar (intrensic)
extravascular: spleen
intravascular: inside blood stream
due to : *infections *antibodies *mechanical damage
hereditary
aquired : *Paroxysmal nocturnal hematuria
membranopthies: spherocytosis
hemoglobinopathies thalassemia & sickle cell anemia
enzymopathies: G6PD-Deficiency

Anemia of increased destruction					
	Pathogenesis	Genetics	Symptoms	Laboratory findings	Diagnosis
Thalassemia	*Genetic disorders that cause a decrease in the synthesis of α/β chains. * deficiency in one globin chain results in relative increase in the other one leading to instability and hemolysis * Most mutations in α-thalassemia are <u>deletions</u> while most mutations in β-thal are <u>point mutations</u>	**1) α-chain:** *encoded by 2 genes on chromosome 16 * deletion of 1 or 2 genes >> silent carrier * Deletion of 3 genes>> Hemoglobin H disease *Deletion of 4 genes >> hydrops fetalis **2) B-chain:** * encoded by a single gene on chromosome 11 * β 0 : no production of β-chain * β+: decreased production of β-chain Many combinations are found : ♣β/β+:silent carrier or mild anemia (thal-minor) ♣ β+/β+: thalassemia intermedia ♣ β 0 /β 0 or β 0 /β+: thalassemia major (Cooley anemia)	* Thalassemia minor>>asymptomatic * Thalassemia intermedia and HgH disease >>moderate anemia. No need for regular blood transfusions. *Thalassemia major>> symptoms begin after age of 6 months(B-chain replaces y-chain). They require blood transfusions *organ damage due to iron overload(2nd or 3rd decade of life	*low Hb >>> Hypochromic microcytic anemia * <u>Reticulocytosis</u> * poikelocytosis &nucleated RBCs in peripheral blood *hemosiderosis & ↑↑ normoblasts in BM	* Hemoglobin electrophoresis test * increase in HgA2 and HgF percentages more than 3.5%>> β-thal * absent or decreased HgA>> β-thal major β 0 /β 0 *HbH and Hb Barts bands>> HbH disease(α-thal m, severe anemia) *genetic testing is available for α-thal carrier and minor

Notes

* Mode of inheritance: autosomal recessive
* Resistant to infection by malaria falciparum
* Reticulocytosis differentiates between hemolytic anemia and anemia of diminished production