Lecture 2 - Erythropoiesis

OBJECTIVES

1. List and describe the erythroid precursors in order of maturity, including the morphologic characteristics, cellular activities, normal location, and length of time in the stage for each.

2. Correlate the erythroblast, normoblast, and rubriblast nomenclatures for red blood cell (RBC) stages.

3. Name the stage of erythroid development when given a written description of the morphology of a cell in a Wright-stained bone marrow preparation.

4. List and compare the cellular organelles of immature and mature erythrocytes and describe their specific functions.

5. Name the erythrocyte progenitors and distinguish them from precursors.

6. Explain the nucleus-to-cytoplasm (N:C) ratio, describe the appearance of a cell when given the N:C ratio , and estimate the N:C ratio from the appearance of a cell.

7. Explain how reticulocytes can be recognized in a Wright-stained peripheral blood film.

8. Define and differentiate the terms *polychromasia, diffuse basophilia, punctate basophilia,* and *basophilic stippling.*

9. Discuss the differences between the reticulum of reticulocytes and punctate basophilic stippling in composition and conditions for microscopic viewing.

10. Define and differentiate *erythron* and *RBC* mass.

11. Explain how hypoxia stimulates RBC production.

12. Describe the general chemical composition of erythropoietin (EPO) and name the site of production.

13. Discuss the various mechanisms by which EPO contributes to erythropoiesis.

14. Define and explain apoptosis resulting from Fas/FasL interactions and how this regulatory mechanism applies to erythropoiesis.

15. Explain the effect of Bcl-XL (Bcl-2 like protein 1) and the general mechanism by which it is stimulated in red blood cell progenitors.

16. Describe the features of the bone marrow that contribute to establishing the microenvironment necessary for the proliferation of RBCs, including location and arrangement relative to other cells, with particular emphasis on the role of fibronectin.

17. Discuss the role of macrophages in RBC development.

18. Explain how RBCs enter the bloodstream and how premature entry is prevented and, when appropriate, promoted.

19. Describe the characteristics of senescent RBCs and explain why RBCs age.

20. Explain and differentiate the two normal mechanisms of erythrocyte destruction, including location and process.

21. List the erythrocyte metabolic processes that require energy.

22. Diagram the Embden-Meyerhof anaerobic glycolytic pathway (EMP) in the red blood cell (RBC), highlighting adenosine triphosphate (ATP) consumption and generation.

23. Name the components of the hexose-monophosphate pathway (HMP) and describe the process of detoxifying peroxide.

24. Diagram the methemoglobin reductase pathway and explain its importance in maintaining functional hemoglobin.

25. Describe the RBC metabolic pathway that generates 2,3-BPG, state the effect of its formation on ATP production, and explain its importance in oxygen transport.

26. Explain the importance of the semipermeable RBC membrane.

27. Describe the arrangement and function of lipids in the RBC membrane.

28. Explain cholesterol exchange between the RBC membrane and plasma, including factors that affect the exchange.

29. Define, locate, and explain the role of RBC transmembrane proteins in maintaining membrane stability and provide examples of these proteins.

30. Discuss how ankyrin, protein 4.2, protein 4.1, actin, adducin, tropomodulin, dematin, and band 3 interact with α- and β-spectrin and the lipid bilayer of the RBC membrane.

31. Name conditions caused by mutations in transmembrane and cytoskeletal proteins that disrupt vertical and horizontal (lateral) linkages in the RBC membrane.

32. Cite the relative concentrations of RBC cytoplasmic potassium, sodium, and calcium, and

name the structures that maintain those concentrations.

33. Describe the components and structure of hemoglobin.

34. Describe steps in heme synthesis that occur in the mitochondria and the cytoplasm.

35. Name the genes and the chromosome location and arrangement for the various polypeptide chains of hemoglobin.

36. Describe the polypeptide chains produced and the hemoglobins they form in the embryo, fetus, newborn, and adult.

37. List the three types of normal hemoglobin in adults and their reference intervals.

38. Describe mechanisms that regulate hemoglobin synthesis.

39. Describe the mechanism by which hemoglobin transports oxygen to the tissues and transports carbon dioxide to the lungs.

40. Explain the importance of maintaining hemoglobin iron in the ferrous state (Fe^{2+}).

41. Explain the significance of the sigmoid shape of the oxygen dissociation curve.

42. Correlate right and left shifts in the hemoglobin-oxygen dissociation curve with conditions that can cause shifts in the curve.

43. Differentiate T and R forms of hemoglobin and the effect of oxygen and 2,3-bisphosphoglycerate on those forms.

44. Explain the difference between adult Hb A and fetal Hb F and how that difference impacts oxygen affinity.

45. Compare and contrast the composition and the effect on oxygen binding of methemoglobin, carboxyhemoglobin, and sulfhemoglobin.