

10 - Hemostasis and Blood Forming Organs

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1. Drugs for Treating Anemia

- a. Describe/Diagram the sites of action of the hematopoietic growth factors in the differentiation and maturation of marrow cell lines.
- b. Describe the approved therapeutic indications and pharmacokinetics for recombinant erythropoietin and darbepoetin.
- c. Describe the possible etiologies, which should be considered if a delayed or diminished response to doses of recombinant erythropoietin within the recommended dose range occurs.
- d. Analyze the pharmacokinetics and therapeutic effects of darbepoetin alpha (novel erythropoiesis stimulating protein, NESP) and epoetin alpha (erythropoietin) in anemic dialysis patients.
- e. Relate factors that can lead to abnormal iron balance including genetic hemochromatosis to the iron absorption and transport pathways and the.
- f. State the criteria used for the diagnosis of iron deficiency anemia and criteria for oral therapy versus parenteral iron therapy. What are the associated side effects and the predicted rates of response to the two therapies?
- g. Summarize the risks of acute iron poisoning in children and its treatment.
- h. Describe the pharmacologic management of chronic iron overload disease (e.g. secondary to chronic blood transfusion, iron absorption disturbances, etc.).
- i. Describe the sources, transport, metabolism, storage, and excretion of vitamin B-12 and folic acid. State the factors, which influence the bioavailability of vitamin B-12 and folic acid.

- j. Describe the biochemical systems, which are impaired in B-12 and folic acid deficiency, and the role of cyanocobalamin and folic acid in correcting the metabolic defect in DNA thymine and methionine synthesis.
- k. Explain the appropriate management of the patient with a megaloblastic anemia in regards to both acute and chronic management, vitamin dosage and expected response.
- l. Compare the possible metabolic reasons why folic acid will correct the erythropoietic lesion but not the neurologic lesion in Addisonian pernicious anemia.
- m. What is the rationale for the use of folic acid in elevated serum levels of homocysteine and in spina bifida?
- n. Know the advantages and disadvantages of pegfilgrastim vs. G-CSF (filgrastim) in the management of neutropenia.

2. Anticoagulant, Antithrombotic and Thrombolytic Drugs

- a. Identify the sites of action of anticoagulant, antithrombotic and thrombolytic drugs in the coagulation process.
- b. Contrast the effects and time course of acetylsalicylic acid, standard nonsteroidal anti-inflammatory agents (NSAIDs) and cyclooxygenase 2 (COX2) inhibitors on platelet function.
- c. Compare differences and similarities in mechanism of action, pharmacokinetics, adverse effects and appropriate clinical indications for antiplatelet agents: e.g. acetylsalicylic acid, dipyridamole, ticlopidine, clopidogrel, abciximab.
- d. Explain the role of the platelet glycoprotein IIb/ IIIa inhibitors in the management of coronary disease.
- e. Describe the mechanism of action and pharmacokinetics of the following antithrombin agents: heparin, low molecular weight heparin, lepirudin, danaparoid.
- f. Describe the complications associated with heparin therapy, e.g. excessive bleeding and heparin induced thrombocytopenia with associated thrombosis, and the management of heparin toxicity including protamine to reverse the effects of heparin and hirudin.
- g. Contrast the management of heparin therapy using standard versus low molecular weight heparin preparations.

- h. Among the antithrombin agents, know how argatroban and fondaparinux, are used clinically for anticoagulation in patients with heparin-induced thrombocytopenia.
- i. Describe the effect of Vitamin K on the coagulation factors (II, VII, IX and X) and Proteins C and S.
- j. Discuss the onset of action and duration of action of warfarin effect in relationship to half-life of clotting factors and their production in the human.
- k. Discuss the consequences of warfarin inhibition of Vitamin K dependent clotting factors and the procoagulant effects in the presence of protein C or Protein S deficiencies.
- l. Relate how the monitoring of warfarin therapy using PT, INR and the indications for measuring warfarin levels is affected by the pharmacokinetics of warfarin (absorption, distribution, metabolism and excretion).
- m. Discuss adverse effects, contraindications and toxicities of warfarin, including embryo and fetal toxicities.
- n. Discuss drug-drug, drug-food, and drug-disease interactions with warfarin.
- o. Discuss clinical uses and goals of warfarin therapy including its use in venous thromboembolic diseases, atrial fibrillation, myocardial infarction, and strokes.
- p. Discuss the approach to the management of the patient on short term and long term oral anticoagulation.
- q. Relate the major adverse effect of thrombolytic drugs to their mechanism of action.
- r. Describe the pharmacokinetics of the thrombolytic agents and their use in thrombolytic therapy.
- s. Consider the problems associated with thrombolytic therapy e.g. streptokinase in primary post MI.
- t. Identify the major indications for and contraindications to thrombolytic drug therapy.
- u. Discuss epsilon-aminocaproic acid (EACA), a fibrinolytic inhibitor, which is used routinely along with desmopressin and factor

replacement in dental procedures in patients with hemophilia and von Willebrand's disease and for non-dental bleeding episodes in both diseases.