

Hemostasis and Blood Forming Organs

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Hemostasis and Blood Forming Organs	
Recommended Curriculum Equivalent: 1.5 hr	
Drugs for Treating Anemia	
Minerals	Vitamins
FERROUS SULFATE ferrous gluconate iron dextran DEFEROXAMINE	FOLIC ACID VITAMIN B ₁₂ CYANOCOBALAMIN
Hematopoietic growth factors	
ERYTHROPOIETINS EPOETIN ALFA Darbepoetin	Myeloid Growth Factors Filgrastim Sargramostim Thrombopoietic Growth Factors Interleukin-11 Thrombopoietin
Learning Objectives	
Physiology and pathophysiology Describe/Diagram the control of normal physiological control of hematopoietic growth factors and the effect of kidney failure on erythropoiesis. Relate factors that can lead to abnormal iron balance including genetic hemochromatosis to the iron absorption and transport pathways and the. 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.	
Mechanism of action Explain the molecular mechanism of action of each drug in each drug class.	
Actions on organ systems Describe the pharmacological effects of the drugs in each class on the hematopoietic system.	
Pharmacokinetics 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. Analyze how the pharmacokinetics and therapeutic effects of epoetin alpha and darbepoetin alpha differs between normal and anemic dialysis patients. 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.	

Adverse effects, drug interactions and contraindications

Describe the principal adverse effects of the drugs in each class.

Describe the clinically important drug interactions of the drugs in each class.

Describe the principal contraindications of the drugs in each class.

Therapeutic uses

Describe the approved therapeutic indications and contraindications and pharmacokinetics for recombinant erythropoietin and the erythropoietin-like drug darbepoetin.

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?

Summarize the risks of acute iron poisoning in children and its treatment.

Describe the pharmacologic management of chronic iron overload disease (e.g. secondary to chronic blood transfusion, iron absorption disturbances, etc.).

Explain the appropriate management of the patient with a megaloblastic anemia in regards to both acute and chronic management, vitamin dosage and expected response.

Compare the possible metabolic reasons why folic acid will correct the erythropoietic lesion but not the neurologic lesion in Addisonian pernicious anemia.

What is the rationale for the use of folic acid in elevated serum levels of homocysteine and in spina bifida?

Compare the therapeutic applications for myeloid growth factors with those for thrombopoietic growth factors.

Anticoagulant Drugs		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs to consider		
Inhibition of Clotting Factors	Inhibition of Clotting Factor Synthesis	Direct Thrombin Inhibitors
HEPARIN ENOXAPARIN fondaparinux protamine Sulfate	WARFARIN SODIUM (COUMARIN) vitamin K	lepirudin bivalirudin argatroban
Learning Objectives		
<p>Physiology and pathophysiology Describe the synthesis of clotting factors Explain the regulation of hemostasis Describe the pathogenesis of thrombosis</p>		
<p>Mechanism of action Explain the molecular mechanism of action of each drug in each drug class. Identify the sites of action of heparin and direct thrombin inhibitors in the coagulation process. Describe the relationship between the chemical structure of the oral anti-coagulants and vitamin K and its importance in determining the mechanism of action of the oral anticoagulants. Describe the mechanism of action and pharmacokinetics of the following antithrombin agents: heparin, low molecular weight heparin (e.g. enoxaparin), bivalirudin.</p>		
<p>Actions on organ systems State the effects of heparin on lipolysis and its role as a growth factor. 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. Describe the role of Vitamin K for the synthesis of coagulation factors (II, VII, IX and X) and Proteins C and S.</p>		
<p>Pharmacokinetics State the appropriate routes of administration of heparin and warfarin. Compare the relationship between mechanism of action and onset of action of heparin with that of the oral anticoagulants. 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). Explain how pharmacogenomics can be used to predict the dose of warfarin in individual patients.</p>		

Adverse effects, drug interactions and contraindications

Describe the principal adverse effects and contraindications of the drugs in each class.

Describe the complications associated with heparin therapy, e.g. excessive bleeding and heparin induced thrombocytopenia with associated thrombosis.

Describe how protamine and vitamin K are used as antidotes to excessive bleeding caused by heparin and warfarin, respectively.

Discuss adverse effects, contraindications and toxicities of warfarin, including embryo and fetal toxicities.

Discuss drug-drug, drug-food, and drug-disease interactions with warfarin.

Therapeutic uses

Contrast the management of heparin therapy using standard versus low molecular weight heparin preparations.

Know how the antithrombin agents are used clinically for anticoagulation in patients with heparin-induced thrombocytopenia.

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. .

Discuss clinical uses and goals of warfarin therapy including its use in venous thromboembolic diseases, atrial fibrillation, myocardial infarction, and strokes.

Discuss the approach to the management of the patient on short term and long term oral anticoagulation.

Notes

Antiplatelet Drugs			
Recommended Curriculum Equivalent: 0.75 hr			
Drug Classes and Drugs to consider			
Cyclooxygenase Inhibitors	Phosphodiesterase Inhibitors	GPIIb/IIIa inhibitors	ADP Receptor Pathway Inhibitors
ASPIRIN (acetylsalicylic acid)	dipyridamole	EPTIFIBATIDE ABCIXIMAB tirofiban	TICLOPIDINE clopidogrel
Learning Objectives			
<p>Physiology and pathophysiology Explain the role of platelet aggregation in the regulation of hemostasis. Describe the pathogenesis of thrombosis with respect to the platelet release reaction.</p>			
<p>Mechanism of action Explain the molecular mechanism of action of each drug in each drug class. Describe how inhibition of prostaglandin synthesis affects platelet aggregation, specifically the role of COX-1 and COX-2. Compare differences and similarities in mechanism of action for antiplatelet agents: e.g. aspirin, dipyridamole, ticlopidine, clopidogrel, abciximab.</p>			
<p>Actions on organ systems Identify the site of action of each drug in the platelet aggregation process.</p>			
<p>Pharmacokinetics Contrast the effects and time course of aspirin with standard nonsteroidal anti-inflammatory agents (NSAIDs) and cyclooxygenase 2 (COX2) inhibitors on platelet function. Describe how knowledge of the pharmacokinetics of aspirin can reduce adverse effects, particularly on the GI track, by manipulation of the dosing regimen. Describe difference in routes of administration for different classes of antiplatelet drugs.</p>			
<p>Adverse effects, drug interactions and contraindications Describe the principal adverse effects and contraindications of the drugs in each class. Discuss drug-drug, drug-food, and drug-disease interactions of each drug. Explain how concomitant use of NSAIDs, e.g. ibuprofen, can interfere with the antiplatelet actions of aspirin.</p>			
<p>Therapeutic uses Discuss the approach to the management of the patient on short term and long term antiplatelet therapy. Explain the role of the platelet glycoprotein IIb/ IIIa inhibitors in the management of coronary disease. Contrast the effects of aspirin, dipyridamole, ibuprofen, and propranolol for primary post MI prophylaxis. Compare differences and similarities in appropriate clinical indications for antiplatelet agents.</p>			

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The antiinflammatory, analgesic and antipyretic effects of aspirin and NSAIDS, including COX-2 inhibitors, are discussed in Analgesics Knowledge Objectives.

Thrombolytic Drugs	
Recommended Curriculum Equivalent: 0.25 hr	
Drug Classes and Drugs to Consider	
Plasminogen Activators	Inhibitors of Fibrinolysis
STREPTOKINASE ALTEPLASE	aminocaproic acid
Learning Objectives	
Physiology and pathophysiology Explain the role of plasminogen in thrombolysis Describe the role of thrombolysis in the physiology of hemostasis	
Mechanism of action Contrast the molecular mechanism and site of action of alteplase with aminocaproic acid. Describe the differences between streptokinase and alteplase in the activation of plasminogen.	
Actions on organ systems Explain how streptokinase degrades clotting factors...	
Pharmacokinetics Compare the pharmacokinetic differences between alteplase and streptokinase.	
Adverse effects, drug interactions and contraindications Relate the major adverse effect of thrombolytic drugs to their mechanism of action. Describe the primary contraindications for thrombolytic drugs.	
Therapeutic uses Identify the major indications for thrombolytic drug therapy. Discuss 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.	
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