

## Drugs Affecting Blood and Blood Formation

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### Questions

- 362. The treatment of choice in dicumarol poisoning is: (PGI 86, 89)**
- Heparin
  - Aminocaproic acid
  - Vit K
  - Vit C
- 363. Vitamin K is required for: (PGI 80, AIIMS 81)**
- Overdosage of Dindevan
  - Overdose of Heparin
  - Haemophilia
  - Christmas disease
- 364. Platelet aggregation is inhibited by:- (JIPMER 90)**
- Clofibrate
  - Aspirin
  - Dipyridamole
  - All of the above
- 365. Streptokinase acts by: (AIIMS 91)**
- Vasodilator action
  - Anticoagulant action
  - Fibrinolysis
  - Antiplatelet action
- 366. In dicumarol poisoning, which vit K is used: (JIPMER 98)**
- Menadione
  - Menaquinone
  - Phytonadione
  - None of the above
- 367. Heparin is:- (Rohtak 97)**
- Polysaccharide
  - Lipoprotein
  - Monosaccharide
  - Polyenoic acid
  - Ceramide

**368. Not true about heparin is: (PGI 98)**

- a. Activates antithrombin III
- b. Small unionized molecule are not absorbed orally
- c. Protamine sulphate always used to reverse its action
- d. Release lipoprotein lipase from vessel wall & tissues

**369. The tissue plasminogen activator produced by recombinant DNA technology is: (JIPMER 2002)**

- a. Anestreplase
- b. Reteplase
- c. Alteplase
- d. Abciximab

**370. Abciximab acts through: (MANIPAL 01)**

- a. TXA inhibitor
- b. ADP related inhibitor
- c. 2b/3a receptor antibody
- d. Fibrinogen degradations

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### Answers

**362. (c) Vit K**

*Ref: KDT 5th/e pg 565*

→ Bleeding as a result of extension of desired pharmacological action of Dicumarol is the most important problem : ecchymosis, epistaxis, hematuria, bleeding in GIT, intracranial or other internal haemorrhages may be fatal.

Treatment :-

- ◆ Withhold anticoagulant
- ◆ Give fresh blood transfusion : supplies clotting factors & replenishes lost blood. Alternatively fresh frozen plasma can be used
- ◆ Vit K : specific antidote, but it take 6-24 hrs for the clotting factor to be resynthesized & released in blood after vit K administration

**363. (a) Overdose of dindevan**

*Ref: KDT 5th/e pg 565*

Dindevan is a phenindione :-

- Overdosage of this drug cause bleeding as a result of extension of desired pharmacological action, the most important problem: ecchymosis, epistaxis, hematuria, bleeding in GIT; intracranial or internal haemorrhages may be total
- Vit K acts as a specific antidote in treating such pts, it takes 6-24 hrs for the clotting factors to be resynthesized & released in blood after Vit K administration.

**364. (b) Aspirin**

**(c) Dipyridamole**

*Ref: KDT 5th/e pg 572, 580*

- Aspirin at low doses, TxA<sub>2</sub> formation by platelets is selectively suppressed
- Aspirin inhibits release of ADP from platelets & their sticking to each other.
- Dipyridamole inhibits phosphodiesterase & blocks uptake of adenosine to increase platelet (ANIP which potentiates PGI<sub>2</sub> & interferes with aggregation levels of Tx A<sub>2</sub> or PGI<sub>2</sub>, are not altered but platelet survival time reduced by disease is normalized
- Dipyridamole has also been used to enhance antiplatelet action of aspirin

**365. (c) Fibrinolysis**

*Ref: KDT 5th/e pg 569*

- Streptokinase belongs to fibrinolytic group of drugs, these drugs lyse thrombi / clot to recanalise occluded blood vessels
- Streptokinase obtained from beta-haemolytic streptococci & Group C
- Combines with circulating plasminogen to form a complex which breaks plasminogen to plasmin
- Plasmin further causes fibrinolysis
- Streptokinase is antigenic, antibodies are produced against it after streptococcal infection or drug used

**366. (c) Phytonadione**

*Ref: KDT 5th/e pg 559*

- To reverse the effect of overdose of oral anticoagulants: Phytonadione (K1) is the preparation of choice, because it acts most rapidly, dose depends on the severity of hypoprothrombinemia & bleeding. Unnecessary high dose is to be avoided because it will render the patient unresponsive to oral anticoagulants for several days

Severe : 10mg i.m followed by 5mg 4 hourly, bleeding generally stops in 6-12 hrs, but normal levels of coagulation factor are restored only after 24hr. This dose of Vit K will block anticoagulant action for 7-10 days

Moderate : 10mg i.m followed by 5mg once or twice according to response

Mild : Just omit a few doses of the anticoagulant.

**367. (a) Polysaccharide**

*Ref: KDT 5th/e pg 561*

- Heparin is a non-uniform mixture of straight chain mucopolysaccharide with MW 10,000 to 20,000. It contains polymers of two sulfated disaccharide units:
  - D - Glucosamine - L-iduronic acid
  - D - Glucosamine - D - Glucuronic acid
- It carries strong electronegative charges & is the strongest organic acid present in the body
- It occurs in mast cell as a much bigger molecule, loosely bound to granular protein. Thus, heparin is present in all tissues containing mast cells, richest sources are lungs, liver & intestinal mucosa.

**368. (b) Small unionized molecule are not absorbed orally**

*Ref: KDT 5th/e pg 561 for a, 562 for b, 564 for c, 562 for d*

- Heparin acts indirectly by activating plasma antithrombin III. Heparin AT III complex then binds to clotting factors of the intrinsic

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- & common pathways & inactivates them but not factor VII a operative in the extrinsic pathway.
- The anticoagulant action is exerted mainly by inhibition of factor Xa as well as thrombin (11a) mediated conversion fibrinogen to fibrin
- Low concentrations of heparin prolong PTT without significantly prolonging PT. High concentrations prolong both.
- Heparin at higher doses inhibits platelet aggregation & prolongs bleeding time
- Heparin clears turbid post-prandial lipemic plasma
- Heparin releases a lipoprotein lipase from the vessel wall & tissues, which hydrolyses triglycerides of chylomicron & very low density lipoproteins to free fatty acids, these then pass into tissue & the plasma looks clear. This action requires lower concentration of heparin than that needed for anticoagulation.
- Heparin is a large, highly ionized molecule, therefore not absorbed orally
- Heparin does not cross blood brain barrier or placenta
- Protamine sulfate given IV neutralizes heparin weight for weight. However it is needed in frequently because the action of heparin disappears by itself in few hours

### 369. (c) Alteplase

*Ref: KDT 5th/e pg 570*

#### Alteplase

- Alteplase is a recombinant tissue plasminogen activator (rt-PA), produced by recombinant DNA technology from human tissue culture, it specifically activates gel phase plasminogen already bound to fibrin & has little action on circulating plasminogen
- It is non antigenic, but nausea, mild hypotension & fever may occur

### 370. (c) 2b/3a receptor antibody

*Ref: KDT 5th/e pg 573*

- Abciximab Fab fragment of a chimeric monoclonal antibody against GP II b/III a
- Given along with aspirin + heparin during PTCA it has markedly reduced the incidence of restenosis, subsequent MI & death
- Abciximab is nonantigenic, the main risk is haemorrhage, incidence of which can be reduced by carefully managing the concomitant heparin therapy, thrombocytopenia is another complication.
- Constipation, ileus & arrhythmias can occur