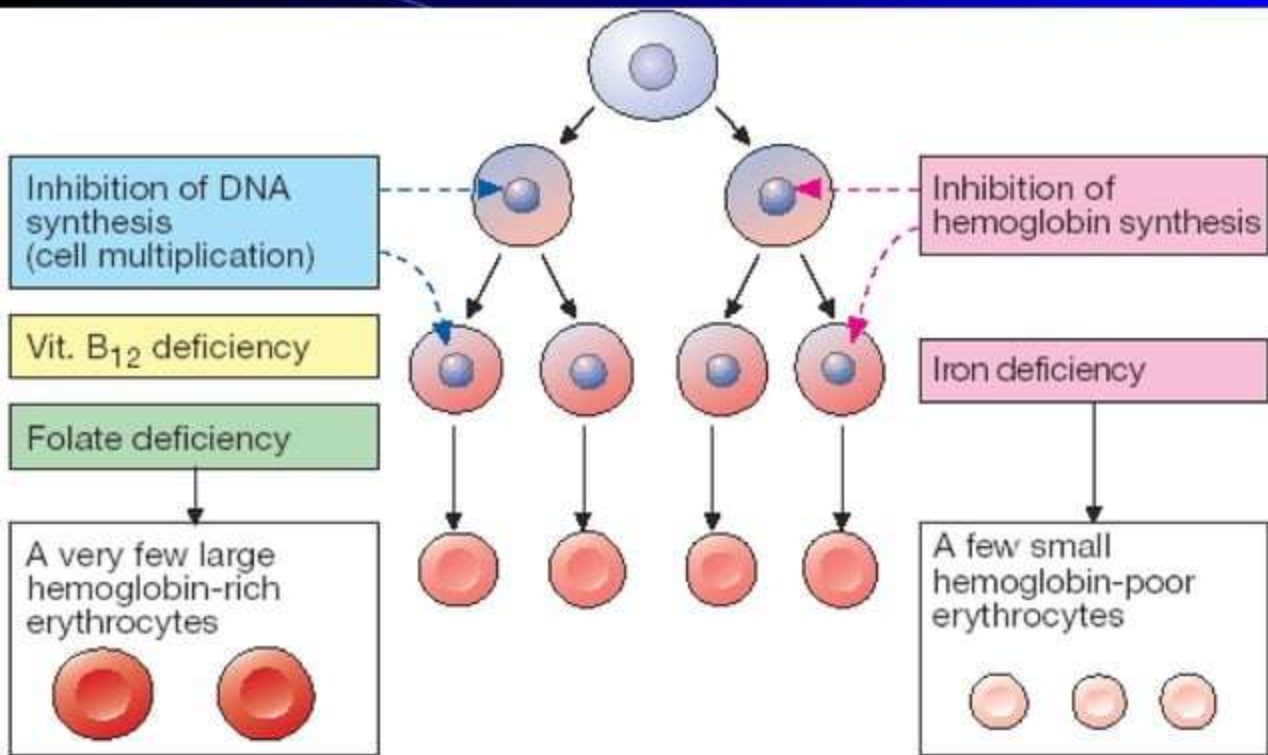


DRUGS AFFECTING BLOOD



Principal Causes of a Disturbance of Erythropoiesis :

1. **Hb** synthesis is impaired - in **Fe²⁺** deficiency
- **Microcytic Hypochromic Anemia.**
2. **Cell multiplication** is inhibited –
DNA synthesis is insufficient -
in deficiencies of *Vitamin B₁₂* or *Folic Acid*
- **Macrocytic Hyperchromic Anemia.**



Erythropoiesis in bone marrow

AGENTS AFFECTING ERYTHROPOESIS

I. AGENTS STIMULATING ERYTHROPOIESIS

1. Used in Hypochromic Anemias

A. IN IRON-DEFICIENT ANEMIAS:

a) Iron Agents:

Ferrous sulfate – caps. 0.25

Ferrous Lactate - pulv, PO 1 g

Fercoven – amp. 5 ml

Ferrum Lek - amp 5 ml

Ferrum Lek

gvožđe (II) - hidroksid polimaltozni kompleks

b) Cobalt agents: **Coamid** – amp. 1%-1 ml

B. Hematopoietic Growth Factor:

Erythropoietin - vial 2000, 4000, 10,000 IU/mL

2. In **HYPERCHROMIC** Anemias:

Vitamin B₁₂ (*Cyanocobalamin*)

amp. 0.01%, 0.05%-1 ml

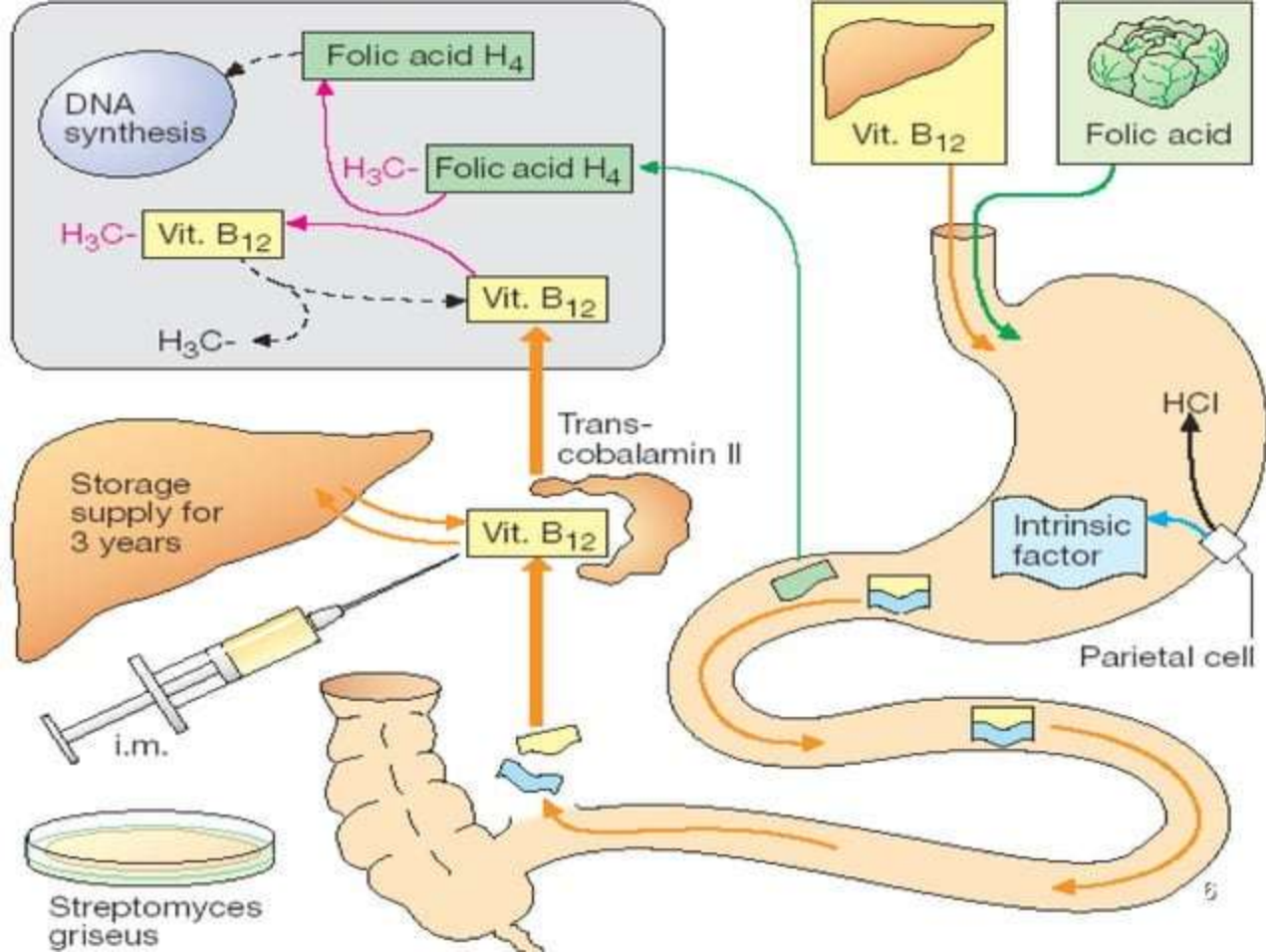
Folic Acid [Vit Bc, B9] – Tab. 1 mg



II. AGENTS INHIBITING ERYTHROPOIESIS:

Sodium Phosphate liquor labelled
Phosphor-32





OVERDOSE with Fe^{2+} COMPOUNDS

Manifestation: lethargy, nausea and vomiting green then tarry stools, weak and rapid pulse, hypotension, dehydration, acidosis, and coma.

Treatment: support of airway, respiration, and circulation. Follow gastric lavage, using a 1% *Sodium Bicarbonate solution*, to convert iron to less irritating, poorly absorbed form.

Deferoxamine (powder for injection: 0.5 g) chelates **IRON** by binding *ferric ions* to the 3 hydroxamic groups of the molecule
[1 g IM].

HEMATOPOIETIC GROWTH FACTORS:

- ▣ ERYTHROPOETIN
- ▣ Granulocyte Colony-Stimulating Factor -
G-CSF, FILGRASTIM
- ▣ Granulocyte-Macrophage Colony-Stimulating
Factor - GM-CSF, MOLGRAMOSTIM

Folate Deficiency:

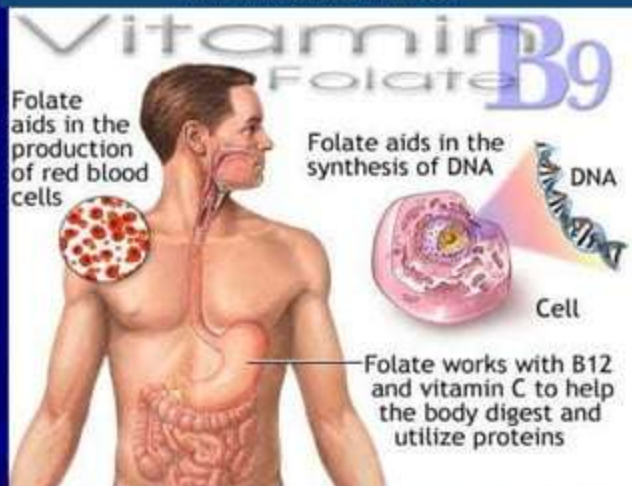
- 1) Increased Demand (pregnancy and lactation)
- 2) Poor Absorption caused by pathology of the small intestine
- 3) Alcoholism
- 4) Treatment with Drugs that are Dihydrofolate Reductase Inhibitors –
Methotrexate
Trimethoprim
Biseptol

A primary result of *folic acid* deficiency is
Megaloblastic Anemia

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Vitamin B₁₂

Food sources of
vitamin B₁₂:

Eggs, meat, poultry,
shellfish, milk and
milk products



The minimal requirement: $\approx 1 \mu\text{g}/\text{day}$.

AGENTS AFFECTING LEUCOPOIESIS

1. Agents Stimulating Leucopoiesis:

Sodium nucleinate

Pentoxyl

Methyluracil

Molgramostim

Filgrastim



2. Agents Inhibiting Leucopoiesis:

Cyclophosphamide

Dopan

Novembichin

Myelosan

Mercaptopurine

Methotrexate

FILGRASTIM (G-CSF), lineage-specific Growth Factor – supports: **Proliferation, Differentiation and**

Functional activity of Neutrophils

causing a rapid rise in **WBCs** within **2-3 days** in patients with normal bone marrow function or **7-14 days** in patients with bone marrow suppression.

Clinical use:

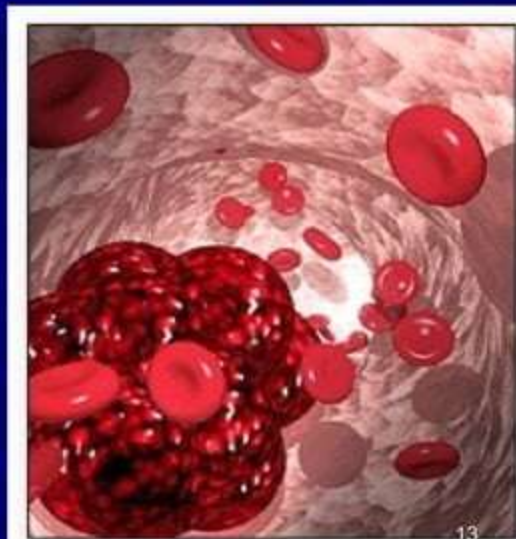
- to decrease incidence of infection after
CANCER CHEMOTHERAPY
- **Bone Marrow Transplantation** in cancer patients
- **Chronic severe Neutropenia, Agranulocytosis,**
- **Pancytopenia, Acute Leukaemia**
- **Myelodysplastic Syndrome**
- **Hematologic toxicity with drug therapy.**

AGENTS USED FOR PROPHYLAXIS AND TREATMENT OF THROMBOSIS

1. PLATELET AGGREGATION INHIBITORS

2. ANTICOAGULANTS

3. THROMBOLYTIC AGENTS



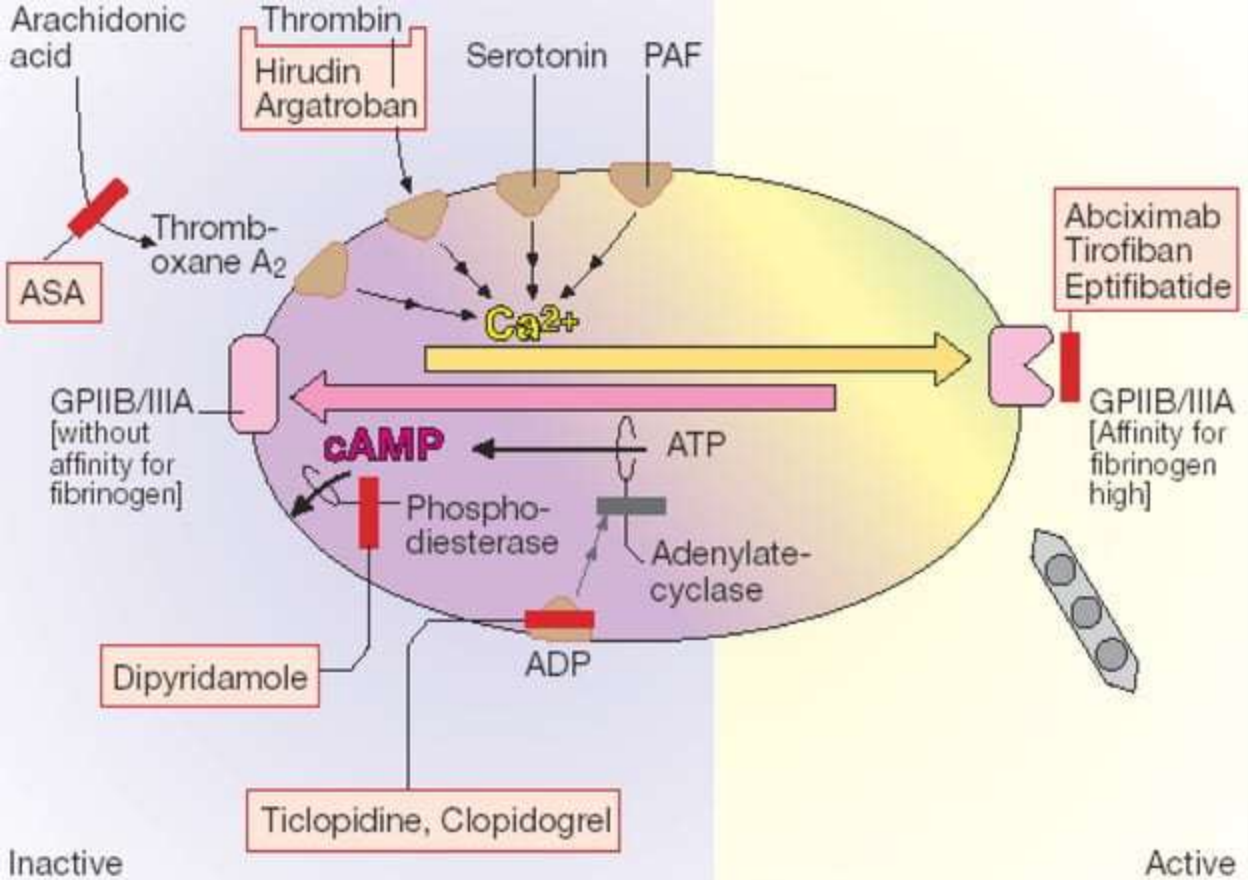
PLATELET AGGREGATION INHIBITORS (ANTIPLATELET AGENTS):

**Aspirin, Ticlopidine, Dipyridamole,
Pentoxifylline, Abciximab**

Clinical Uses:

**AMI, Prior MI,
Unstable or Stable Angina,
Stroke,
Transient Ischemic Attack,
Arterial Bypass Surgery,
Angioplasty,
Peripheral Vascular Disease.**





. Inhibitors of platelet aggregation

ASPIRIN blocks Thromboxane A_2 synthesis from *arachidonic acid* in platelets by irreversible Acetylation and Inhibition of COX – a key enzyme in PG and TxA_2 synthesis.

ASPIRIN 75 - 325 mg/day

is the Most Widely Tested Regimen.

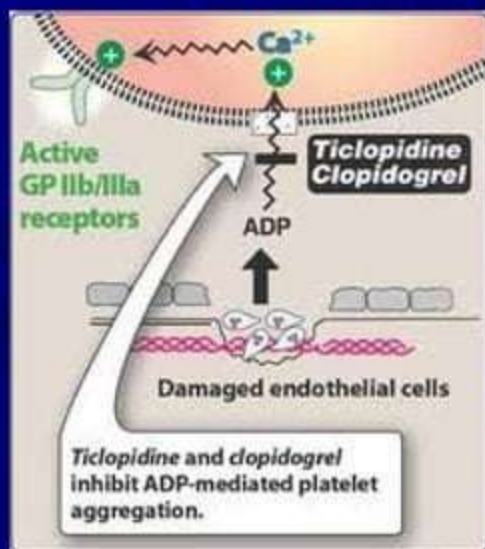


Ticlopidine and Clopidogrel inhibit the ADP pathway involved in the binding of platelets to fibrinogen and to each other.

Adverse Effects:

Prolonged Bleeding
Neutropenia

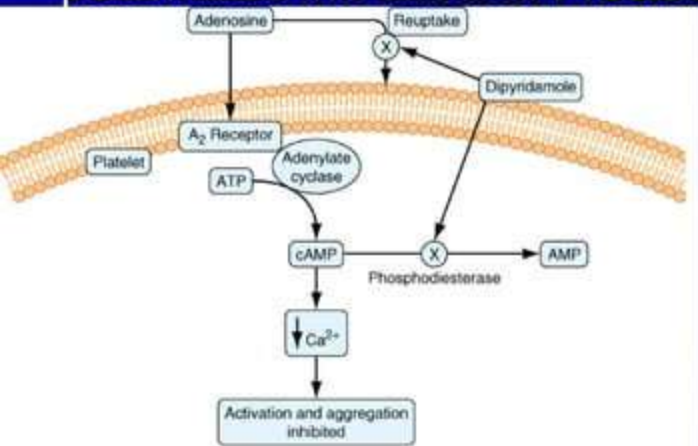
They are reserved for patients who cannot tolerate **ASPIRIN**.



Dipyridamole (*Curantil*, *Persantine*) -
a coronary vasodilator which was introduced
for Angina Pectoris.

Mechanism of action:

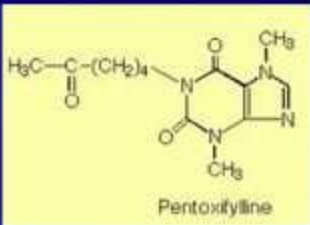
it inhibits PDE and blocks reuptake of Adenosine to increase platelet cAMP which inhibits TxA_2 synthesis and potentiates the effect of Prostacyclin (PGI_2) to



Pentoxifylline (*Trental*)

inhibits PDE, \square Platelet and Erythrocytes

Aggregation, has desaggregational properties,
enhances fibrinolysis, lowers viscosity,
IMPROVES MICROCIRCULATION.



ABCIXIMAB

ReoPro 2 mg/ml
IV injection



a Humanized Monoclonal Antibody
directed against the platelet

Glycoprotein IIb/IIIa Receptor Complex and
inhibits platelet aggregation.

II. ANTICOAGULANTS:

1. DIRECT ACTION

HEPARIN - amp 5 ml – 5000 U/ml and 10000 U/ml

FRAXAPARIN - syringe 0.3 ml, 0.5 ml, 1 ml (1 ml-9,500 IU)

ENOXAPARIN

SODIUM HYDROCITRATE

2. INDIRECT ACTION

Neodicumarin - Tab 0.05 and 0.1 g

Warfarin - Tab 2 and 10 mg

Phenylin - Tab 0.03 g

Syncumar - Tab 2 and 4 mg

Heparin



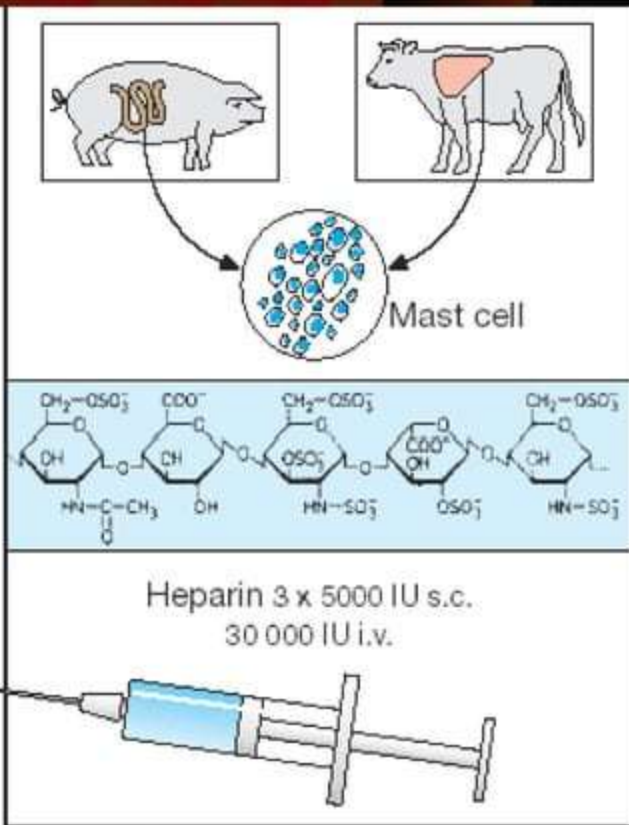
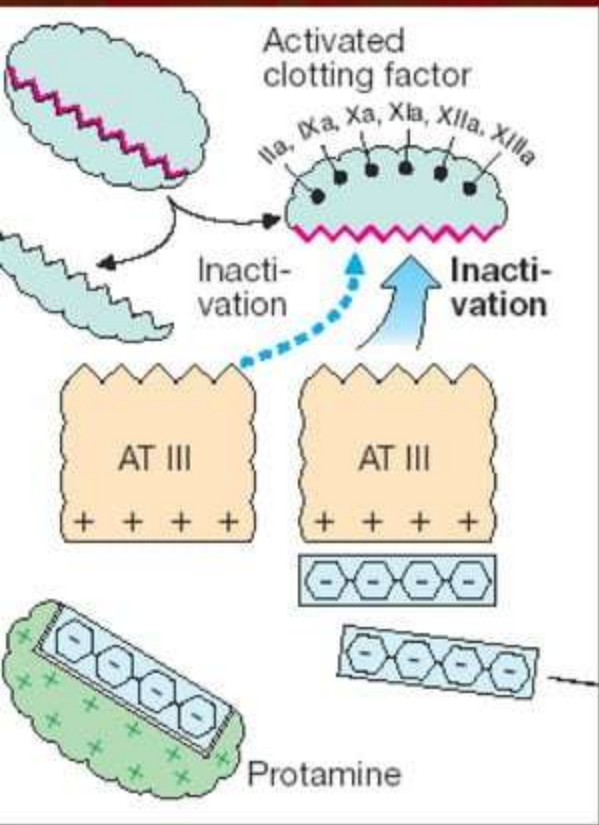
Mechanism of action:

acts indirectly by binding to **Antithrombin III**.

The **Heparin-AT III complex** binds to clotting factors of intrinsic pathways –

Ila, Xa, IXa, XIa, XIIa and XIIIa and

inactivates them.



Heparin: origin, structure, and mechanism of action

CONTRAINDICATIONS to *Heparin*:



- **Bleeding Disorders, Thrombocytopenia**
- **Hypertension, Threatened Abortion, Piles, Ulcers**
- **Subacute Bacterial Endocarditis**
- **Large Malignancies, Tuberculosis (Hemoptysis)**
- **Ocular and Neurosurgery, lumbar puncture**

ADVERSE EFFECTS of HEPARIN:

1. Bleeding complications.

Excessive bleeding may be managed by suspending the drug or treating with **PROTAMINE SULFATE**.

2. Hypersensitivity reactions: chills, fever, urticaria, Anaphylactic Shock.

3. Thrombocytopenia.

Clinical uses of *Heparin*:



- > Pulmonary Embolism and Deep Vein Thrombosis
- > Myocardial Infarction and Unstable Angina
- > Prevention of Thromboembolism
- > Intravascular Catheters
- > Disseminated Intravascular Coagulation Syndrome

Vitamin K is regenerated from the EPOXIDE by
vitamin K Epoxide Reductase.

It is the enzyme that is inhibited by:

Neodicoumarin

Syncumar

Warfarin

NEODICUMARIN (tab. 0.05 and 0.1 g) –
a coumarin derivative.

Mecahnism of action:

It inhibits the hepatic synthesis and activation of
vitamin K-dependent clotting factors II, VII, IX and X,
decreasing the blood's coagulation potential.

Clinical Uses of *Neodicumarin*:

- Thrombophlebitis
- Deep Vein Thrombosis
- Myocardial Infarction
- Artificial Heart Valves
- Atrial Arrhythmias

PRODUCTS



FIBRINOLYTIC (THROMBOLYTIC) DRUGS

I. Non-selective Activators of Profibrinolysin:

Streptokinase

Urokinase

Streptodekase

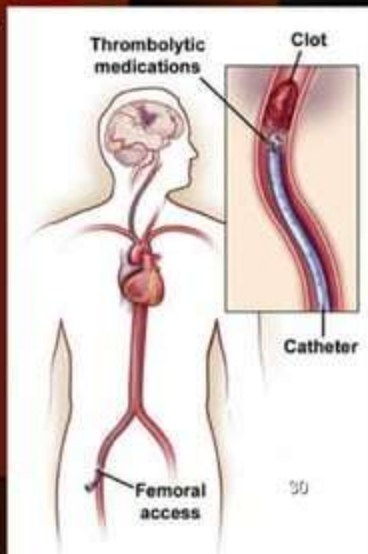
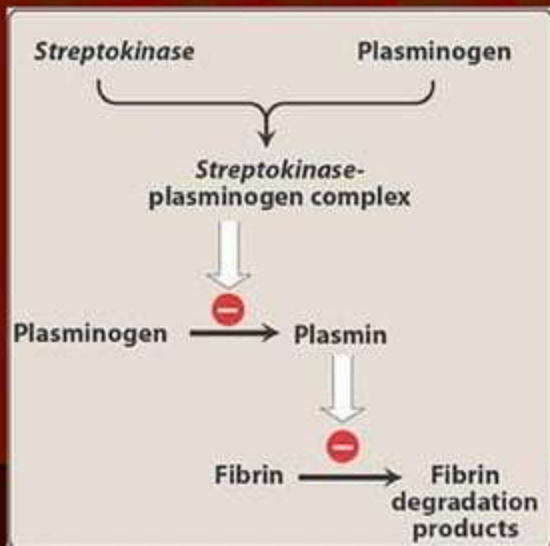
II. Selective activators of Profibrinolysin:

Alteplase

Streptokinase (amp 250,000 and 500,000 IU) -
a non-selective Activator of *Profibrinolysin*,
the enzyme extracted from cultures of
Hemolytic Streptococci.



It activates Plasminogen (Profibrinolysin) of thrombus and serum to form **Plasmin (Fibrinolysin)**, which degrades fibrin and break up thrombi.



Alteplase and *Duteplase* -
recombinant tissue-type
Plasminogen Activator (t PA) -
act selectively on plasminogen,
bound with thrombus and are
'CLOT SELECTIVE'

tissue
plasminogen
activator



Agents to Treat Bleeding (Hemostatics)

1. Agents enhancing Coagulation of blood: for Local Application:

Thrombin - amp 125 AU

Sponges hemostatic

System Action:

Gelatin

Fibrinogen

Calcium chloride, Calcium gluconate

Adroxon

Dicynon (Etamsylat)

Vitamin K

Protamine sulfate

Adroxon (*amp. 0.025% 1 ml*)

- Hemostatic action
- It is used to stop capillary and parenchymatous bleeding in traumas, during surgery and for prevention of post-operative bleeding and haematomas.

Adroxon is used:

- a) **Locally** – gauze bandage or tampon moistened with 0.025% solution;
- b) **IM or SC** 0.025% 1 ml 1–4 times during or after surgery.

Ethamsylate (Dicynone) – amp. 12.5% 2 ml IV or IM,
Caps. 0.25 g

- **Anti-hyaluronidase Action** –
improves capillary wall stability
- Inhibits PGI₂ production
- Corrects abnormal platelet function

Clinical uses: Prevention and Treatment of
Capillary Bleeding in:

- Menorrhagia
- after Abortion, Postpartum Haemorrhage
- Epistaxis (nosebleed)
- Malena (tarry stool)
- Haematuria
- after tooth extraction.



2. ANTIFIBRINOLYTIC AGENTS

Inactivation of the **Fibrinolytic System**
can be achieved by **Plasmin Inhibitors** :

Aminocaproic acid (5% sol.-100 ml)

Tranexamic acid

Amben (*Pamba* - amp. 1% sol.-5 ml)

Contrical (*Aprotinin, Trasylol*)



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