Fibrinolytic Drugs & Fibrinolytic Inhibitors

Sources:

- **Bertram G. katzung Basic & Clinical Pharmacology 15th Edition**
- **Goodman and Gilman's The Pharmacological Basis of Therapeutics13th edition. Laurence Brunton, Bjorn Knollmann, Randa Hilal-Dandan - (2017)**

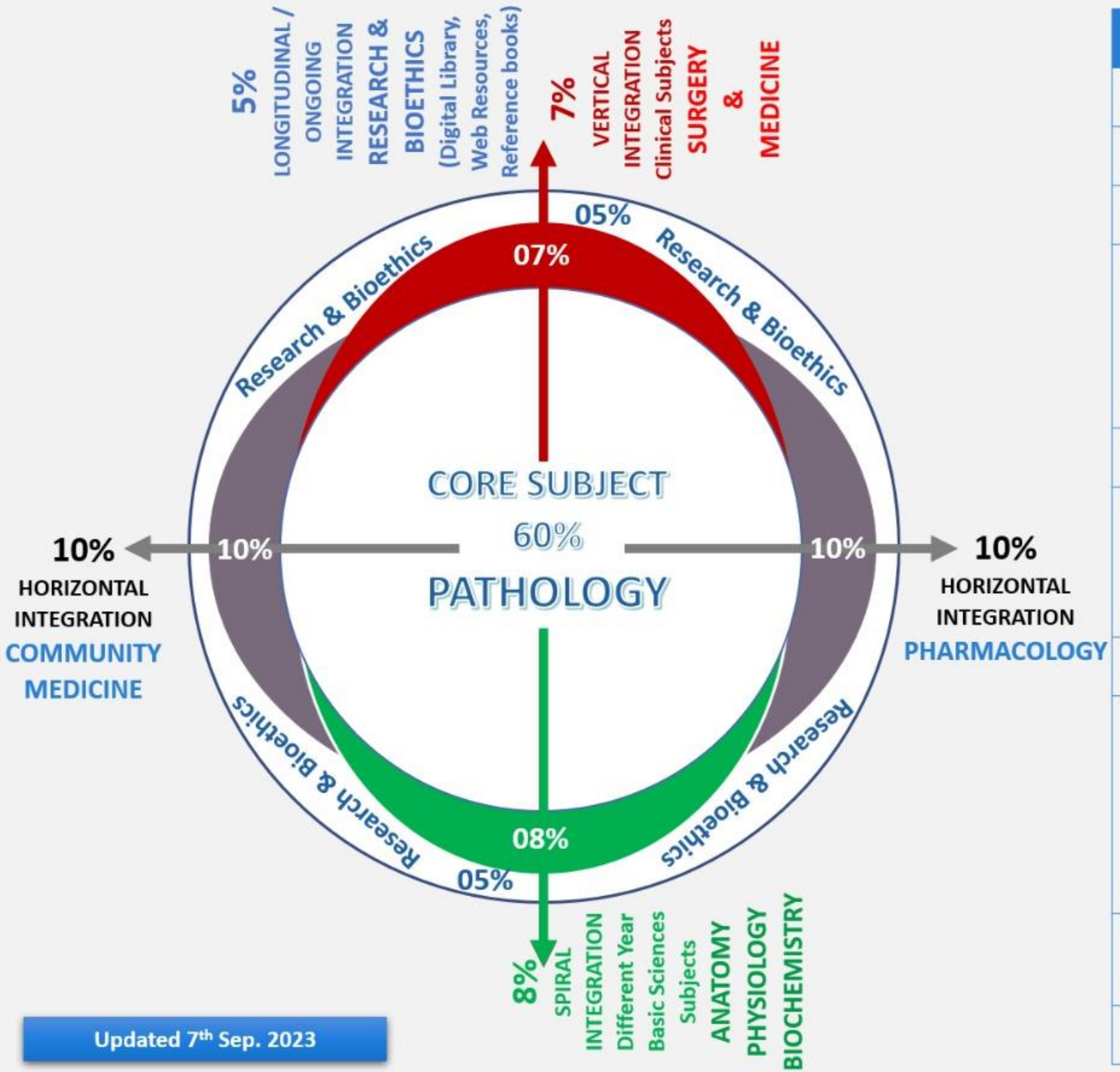
Motto And Vision

To impart evidence based research oriented medical education

To provide best possible patient care

To inculcate the values of mutual respect and ethical practice of medicine

Prof. Umar's Clinically Oriented Integration Model
For Basic Sciences Interactive Lectures

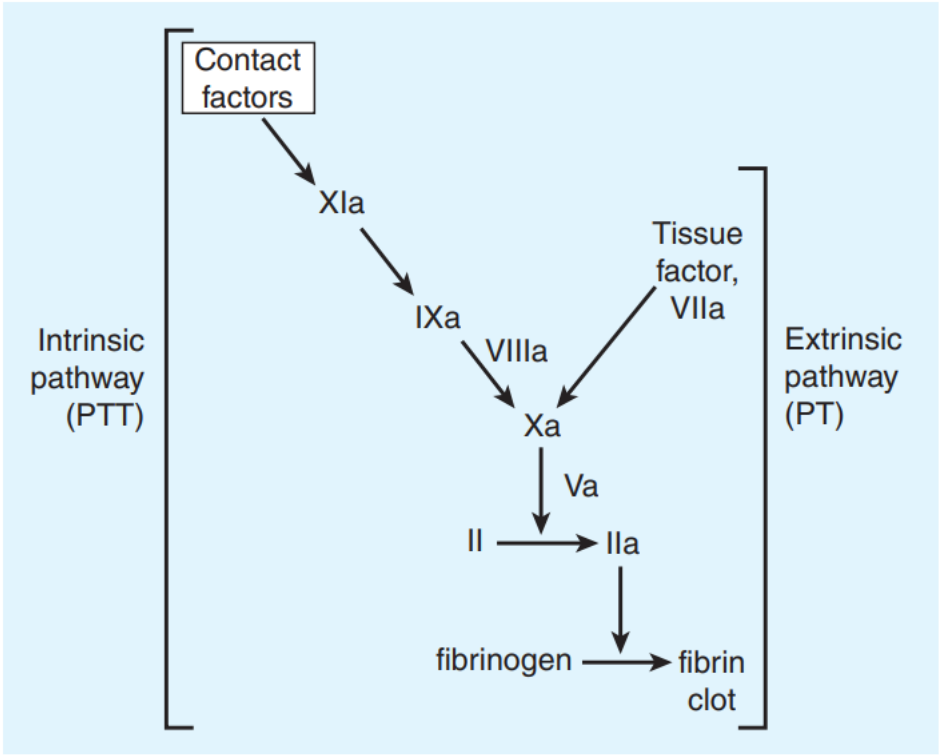


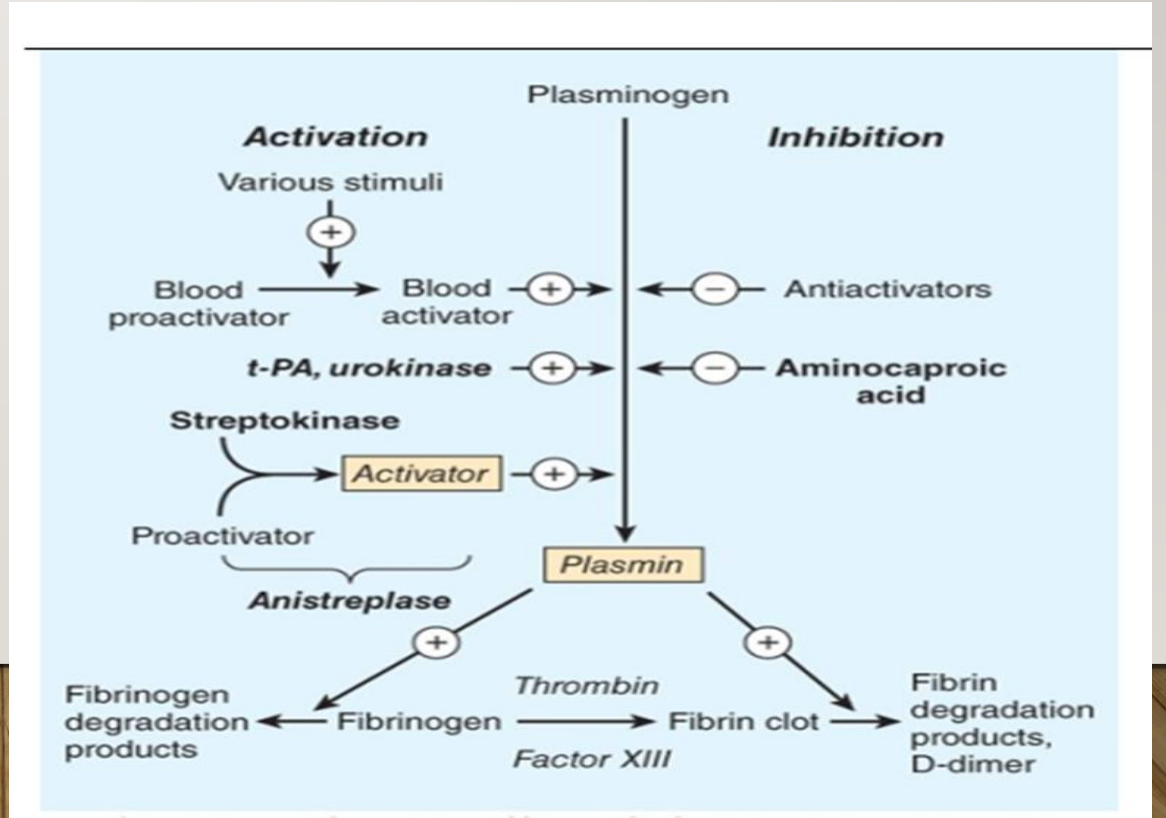
Updated 7th Sep. 2023

Model 3rd Year Pathology LGIS (≈30 slides)	
Core Subject – 60% (≈ 18-20 slides)	
Pathology (≈ 18-20 slides)	
Horizontal Integration – 20% (≈ 5-6 slides)	
Same Year Subjects	• Pharmacology (10%) (≈ 2-3 slides) • Community Medicine (10%) (≈ 2-3 slides)
Vertical Integration – 07% (≈ 2-3 slides)	
Clinical Subjects	• Medicine (3-5%) (≈ 1-2 slides) • Surgery (3-5%) (≈ 1-2 slides)
Spiral Integration – 08% (≈ 2-3 slides)	
Different Year Basic Sciences Subjects	• Anatomy (1-3%) (≈ 1-2 slides) • Physiology (1-3%) (≈ 1-2 slides) • Biochemistry (1-3%) (≈ 1-2 slides)
Longitudinal / Ongoing Integration – 05% (≈ 1-2 slides)	
Research & Bioethics (≈ 1-2 slides)	

Fibrinolysis

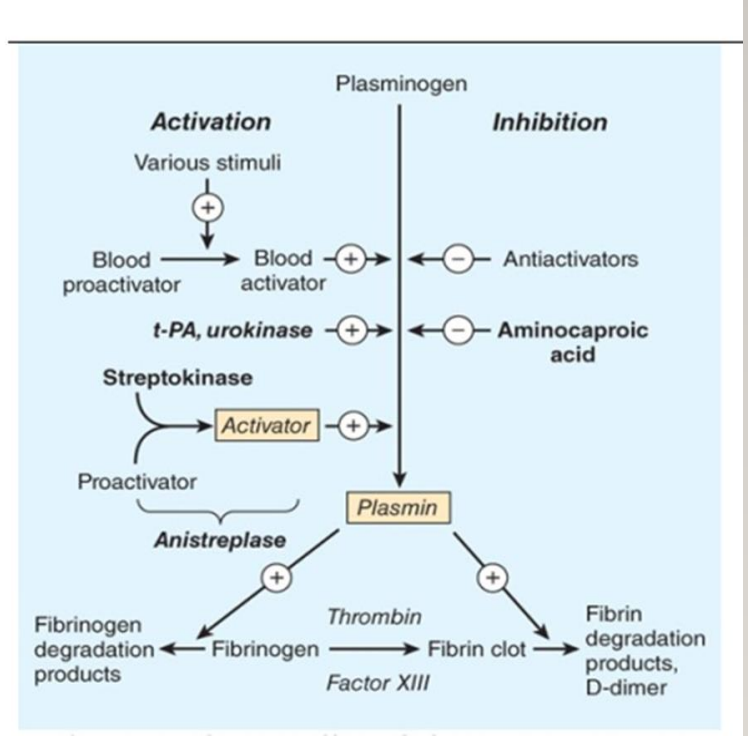
- Fibrinolysis refers to the process of fibrin digestion by the fibrins specific protease, plasmin





Fibrinolytic Drugs & Fibrinolytic Inhibitors

- Increased fibrinolysis….effective for thrombotic disease
  - Tissue plasminogen activator
  - Urokinase
  - Streptokinase
- Decreased fibrinolysis…reduces the bleeding of hemostatic failure
- Aminocaproic acid…useful inhibitor of fibrinolysis



Fibrinolytic Drugs

- **Streptokinase**…..a Protein…not an enzyme…..by Streptococci combines with the proactivator plasminogen… catalyzes the conversion of inactive plasminogen to active plasmin
- **Urokinase** a human enzyme synthesized by the kidney converts plasminogen to active plasmin
- **Plasmin** cannot be used…..naturally occurring inhibitors (antiplasmins)

Fibrinolytic Drugs

- Endogenous by **tissue plasminogen activators** (t-PAs)
  Activate plasminogen…..bound to fibrin
- **Alteplase**…recombinant human t-PA
- **Reteplase**….recombinant human t-PA
- **Tenecteplase**….mutant form of t-PA
  - A longer half life…..an intravenous bolus
- Reteplase and tenecteplase
  - Simpler dosing schemes
  - Their longer half-lives

Fibrinolytic Drugs..Indication & Dosage

- Intravenous route
  - Pulmonary embolism with hemodynamic Instability
  - Severe deep venous thrombosis
  - Ascending thrombophlebitis
- Intra-arterially….Peripheral vascular disease

Fibrinolytic Drugs…Acute MI

Acute Myocardial Infarction

- **Streptokinase** I/V of a loading dose of 250,000 units,….followed by 100,000 units/h for 24–72 hours
  - Antistreptococcal antibodies…Fever, allergic reactions, and therapeutic resistance
- **Urokinase**…..a loading dose of 300,000 units given over 10 minutes……a maintenance dose of 300,000 units/h for 12 hours

Fibrinolytic Drugs…Acute MI & Ischemic Stroke

- Acute MI:
  - Alteplase (t-PA)….15-mg bolus….. by 0.75 mg/kg (up to 50 mg) over 30
  - minutes …..0.5 mg/kg (up to 35 mg) over 60 minutes
  - Reteplase…..two 10-unit bolus injections, the second administered 30
  - minutes after the first injection
  - Tenecteplase …..a single intravenous bolus ranging from 30 to 50 mg
- Ischemic Stroke:
  - Recombinant t-PA….Within 3 hours of symptom onset

recommended dose is 0.9 mg/kg, not to exceed 90 mg, with 10% given as a bolus and the remainder during a 1-hour infusion.

Streptokinase NOT RECOMMENDED IN ISCHEMIC STROKE

Contraindications to thrombolytic therapy

1. H/o intracranial haemorrhage
2. H/o ischaemic stroke in past 3 months
3. H/o head injury in past 3 months
4. Intracranial tumour/vascular abnormality/ aneurysms
5. Active bleeding/bleeding disorders
6. Patients receiving anticoagulants
7. Peptic ulcer, esophageal varices
8. Any wound or recent fracture or tooth extraction
9. H/o major surgery within 3 weeks
10. Uncontrolled hypertension
11. Pregnancy

Fibrinolytic Inhibitors

- Aminocaproic acid (EACA)….Chemically similar to the amino acid
  - Rapidly oral absorption
  - Cleared by kidney
  - Oral dosage of EACA is 6 g four times a day.
  - Intravenously, a 5-g loading dose should be infused over 30 minutes to avoid hypotension
- Tranexamic acid…analog of aminocaproic acid
  - Administered orally with a 15-mg/kg loading dose followed by 30 mg/kg every 6 hours.

Fibrinolytic Inhibitors

- Clinical uses
  - Adjunctive therapy in hemophilia
  - Therapy for bleeding from fibrinolytic therapy
  - Prophylaxis for re bleeding from intracranial aneurysms
  - Postsurgical gastrointestinal bleeding and post prostatectomy bleeding
  - Bladder hemorrhage secondary to radiation- and drug-induced Cystitis
- Adverse effects
  - Intravascular thrombosis from inhibition of plasminogen activator
  - Hypotension, myopathy, abdominal discomfort, diarrhea, nasal stuffiness
- Contraindication:
  - Disseminated intravascular coagulation
  - Genitourinary bleeding of the upper tract, eg, kidney and ureters

Research, Bioethics, Artificial Intelligence, Family Medicine

- Barrett, C.D., Moore, H.B., Moore, E.E., McIntyre, R.C., Moore, P.K., Burke, J., Hua, F., Apgar, J., Talmor, D.S., Sauaia, A. and Liptzin, D.R., 2020. Fibrinolytic therapy for refractory COVID-19 acute respiratory distress syndrome: scientific rationale and review. Research and Practice in Thrombosis and Haemostasis, 4(4), p.e12357.
- Zhang, K., Jiang, Y., Zeng, H. and Zhu, H., 2023. Application and risk prediction of thrombolytic therapy in cardio-cerebrovascular diseases: a review. *Thrombosis Journal*, *21*(1), p.90.

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