

# Myocardial Infarction

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- The acute coronary syndromes (ACS) are classified on the basis of the ECG and Plasma troponin measurements into:
  1. Pts. with ST elevation myocardial infarction (STEMI).
  2. Non- ST elevation myocardial infarction (non-STEMI) and positive troponin test.
  3. Unstable angina by ECG & –ve troponin test.

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## Initial treatment before a definite diagnosis of AMI

- Morphine or Diamorphine 2.5 – 5 mg i.v.
- Aspirin 150-300 mg orally.
- 60% oxygen.

### Immediate objective:

- Relief of pain
- Treatment to decrease mortality.

## Subsequent management of proven MI

- Treatment of complications
  1. Arrhythmias
  2. Heart failure
  3. Thromboemboli
- Secondary prevention of future MI.

# Diagnosed STEMI

- Institute myocardial reperfusion as early as possible by thrombolysis.
- Shift the patient to coronary care unit for thrombolysis.
- Non-STEMI patients may benefit those with LBBB.
- Only slight benefit to patients with Unstable Angina and pts. without ECG changes or with ST depression.

# Drugs That Produce Fibrinolysis

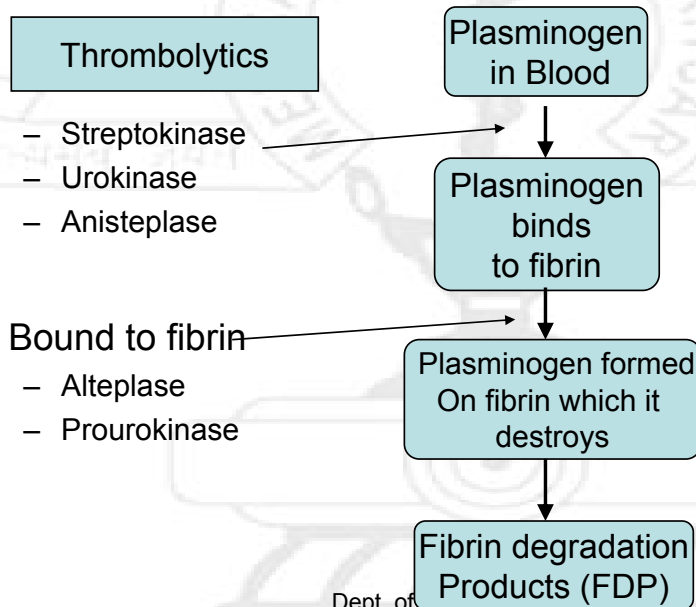
## Fibrin - selective:

- Alteplase (rt-PA)
- Reteplase
- Recombinant prourokinase

## Non-fibrin selective:

- Streptokinase
- Anistreplase (APSAC, Anisoylated plasminogen streptokinase activator complex)
- Urokinase

# Drugs That Promote Fibrinolysis



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## Thrombolytic Therapy

### First infarct patient:

- Inj. Streptokinase 15,00,000 units i.v. infusion over 1 hr.

### For subsequent infarcts:

- Recombinant tissue plasminogen activator (rt-PA or Alteplase)
- ✓ Alteplase and Stk. bind Plasminogen & convert it to Plasmin, which lyses Fibrin.
- ✓ Alteplase has much higher affinity for plasminogen bound to fibrin than in circulation.

# Streptokinase

- 47,000 dalton protein produced by  $\beta$ -haemolytic streptococci.
- Forms a stable non-covalent 1:1 complex with plasminogen.
- Converts plasminogen to plasmin.
- Loading dose 250,000 U; 2.5 mg i.v. to overcome plasma antibodies resulting from prior streptococcal infections.
- $t_{1/2}$  40-80 min.

# Recombinant Tissue Plasminogen Activator (rt-PA or Alteplase)

- Physiological conc. 5-10 ng/ml.
- Therapeutic infusion conc. 300-3000 ng/ml.
- Half life 5-10 min.
- Lysis thrombi during AMI.
- Accelerated regimen for coronary thrombolysis is 15 mg iv bolus followed by 0.75 mg/kg over 30 min. (Max 50 mg) & 0.5 mg/kg (upto 35 mg) over following hour.

# Thrombolytic Therapy

Timing of administration;

- Earlier the better
- Within 1st 3 hrs up to 12 hrs.
- Ant. MI pts. benefit most when treated within 4 hrs of onset.
- i.v. infusion over 1-3 hrs.
- Thrombolysis & Aspirin lowers the risk of stroke by limiting size of the infarct or by reducing thromboembolic episodes or by both.

Recent studies suggest that:

- Angioplasty with / without stent placement is superior to thrombolytic therapy.
- Concurrent administration of Low-dose aspirin improves the efficacy of thrombolytic therapy of MI.

# Thrombolytic Therapy

## ADRs:

- Bleeding
- Nausea, Vomiting
- Multiple micro emboli
- Cardiac arrhythmias
- Allergy – Streptokinase & Anistreplase are antigenic and anaphylactic reactions with rash, urticaria & hypotension.
- Avoid reuse b/n 5 days & 12 mths.

# Contraindications to Thrombolysis

- Haemorrhagic diathesis
- Pregnancy
- Recent symptoms of peptic ulcer / GI bleeding.
- Recent stroke (Previous 3 mths)
- Recent surgery (Previous 10-14 days)
- Prolonged CPR (currently)
- Proliferative Diabetic retinopathy.
- Severe uncontrolled hypertension.
- Aortic dissection
- Acute pancreatitis.

## Role of $\beta$ -Blockers

- Reduce mortality due to prevention of cardiac rupture.
- Inj. Atenolol 50 mg i.v.
- Tab. Atenolol 50 mg orally daily.
- Usual CIs to  $\beta$ -Blockers apply.

## Role of antiplatelet agents

- Glycoprotein IIb / IIIa receptor expression of cell surface.
- This expression is the final common pathway to platelet aggregation and thrombus formation.
- This receptor binds fibrinogen with high affinity.
- Specific monoclonal antibody – Abciximab.
- Specific antagonists – Eptifibatide.  
– Tirofiban.

- Clopidogrel – inhibits ADP-dependent platelet aggregation.
- Clopidogrel more efficacious than Aspirin for prevention of ischaemic stroke or cardiovascular death in patients at high risk.
- Clopidogrel- Thienopyridine derivative.

## Glycoprotein(GP) IIb / IIIa Antagonists

Abciximab is a *human-murine chimeric monoclonal antibody Fab fragment* that binds to GP IIb / IIIa complex with high affinity & slow dissociation rate.

It produces immediate & profound antiplatelet activity that lasts for 12-36 hrs after termination of infusion.

- Inj. Abciximab 0.25 mg/kg i.v. bolus.
- Inj. Abciximab 0.125 µg/kg/min infusion for 12hrs

- ❑ This reduces risk for death, MI or need for CABG surgery & maintains benefit upto 3yrs.
- ❑ Dose causes & maintains blockade of >80% receptors causing >80% reduction in aggregation.
- ❑ Combined with low dose of thrombolysis in AMI.
- ❑ Used as a single agent in stroke.

## Competitive inhibitors of GP IIb / IIIa

- Eptifibatid – heptapeptide
- Tirofiban ] Non-
- Lamifiban ] peptide
  - Lower affinity & Higher dissociation rates than Abciximab.
  - Platelet aggregation returns to normal 30 min to 4 hrs after discontinuation.
  - Effective in acute coronary syndromes.

# Competitive inhibitors of GP IIb / IIIa

- ADRs:
  - 1) Haemorrhage – Transfuse platelets after cessation of Abciximab necessary for life threatening or refractory bleeding.  
After transfusion, antibody redistributed to transfused platelets, reduce mean level of receptor blockade & improves platelet function.
  - 2) Thrombocytopenia – Occurs 1 hr to days after commencing treatment in 1% pts.
    - Platelet counts at 2-4 hrs.
    - Daily platelet count.
    - If severe, stop therapy. If necessary, transfuse platelets.

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# Thank You

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