

# Use of Anti-Platelet Agents In Patients with Acute Coronary Syndromes

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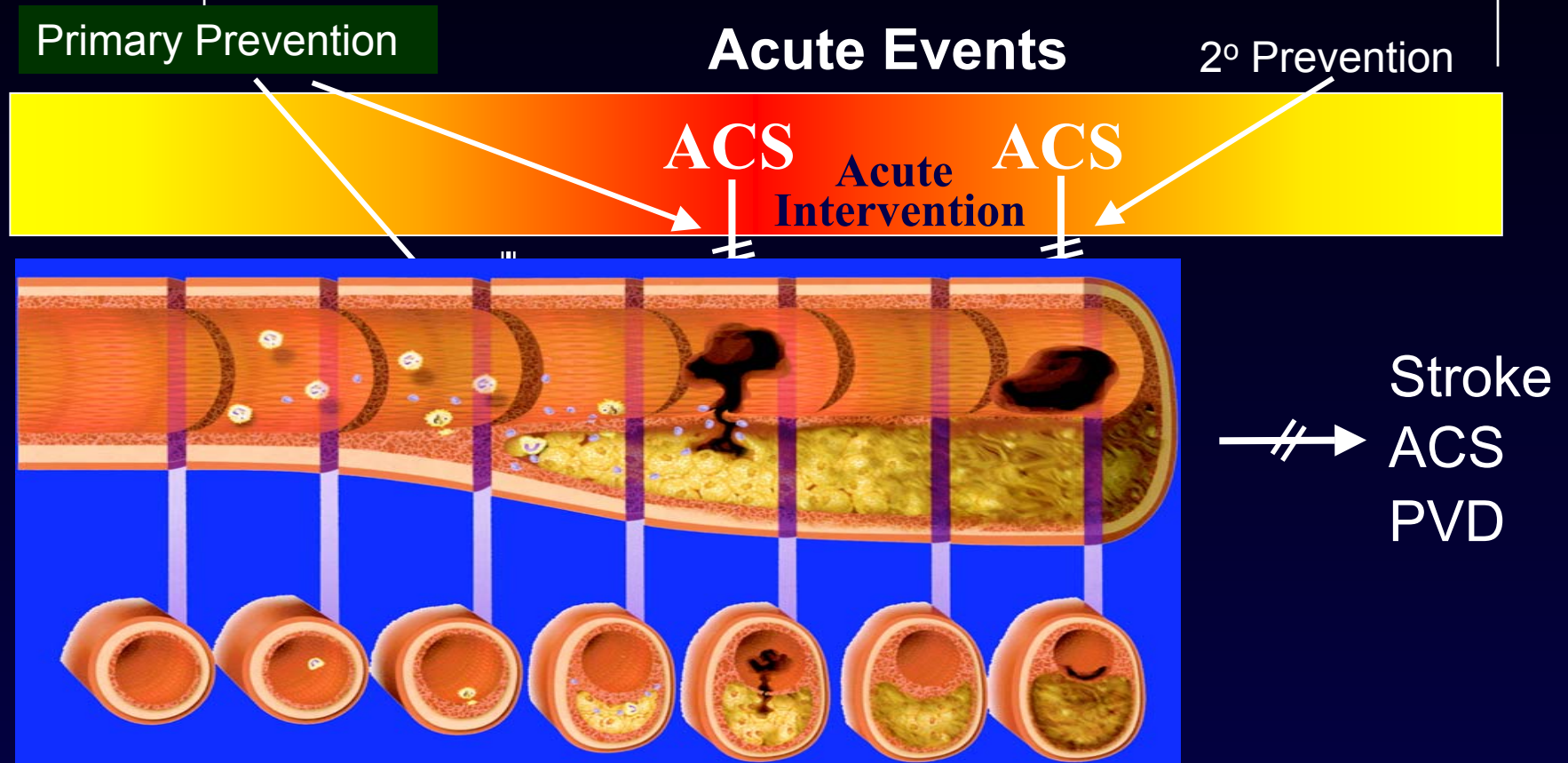


# Role for Anti-Platelet Agents

- \* Prevention
- \* Acute treatment
- \* Reduce recurrence

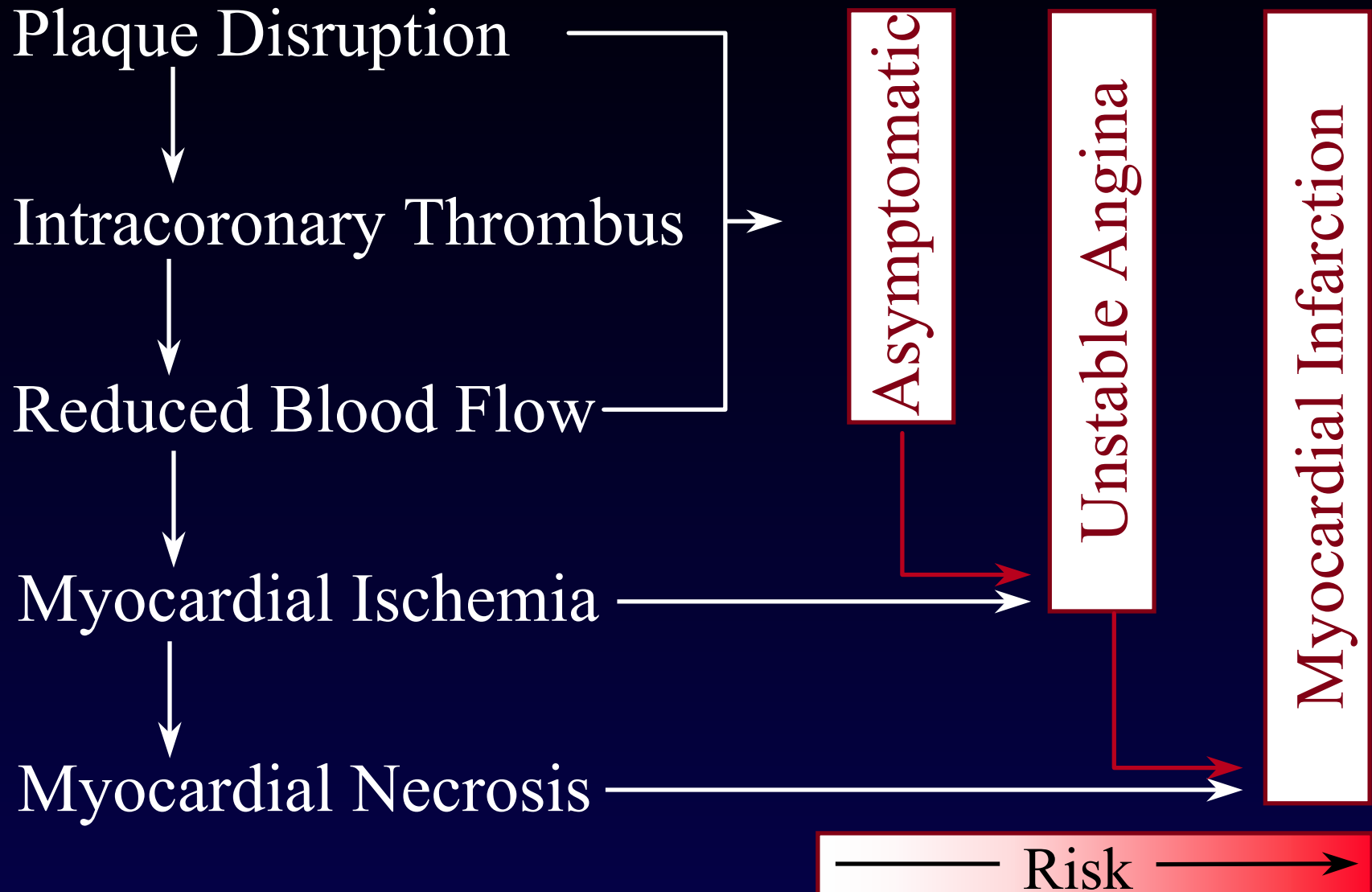
# Athero-thrombotic Coronary Artery Disease

## Anti Platelet Therapy



## Pathophysiology

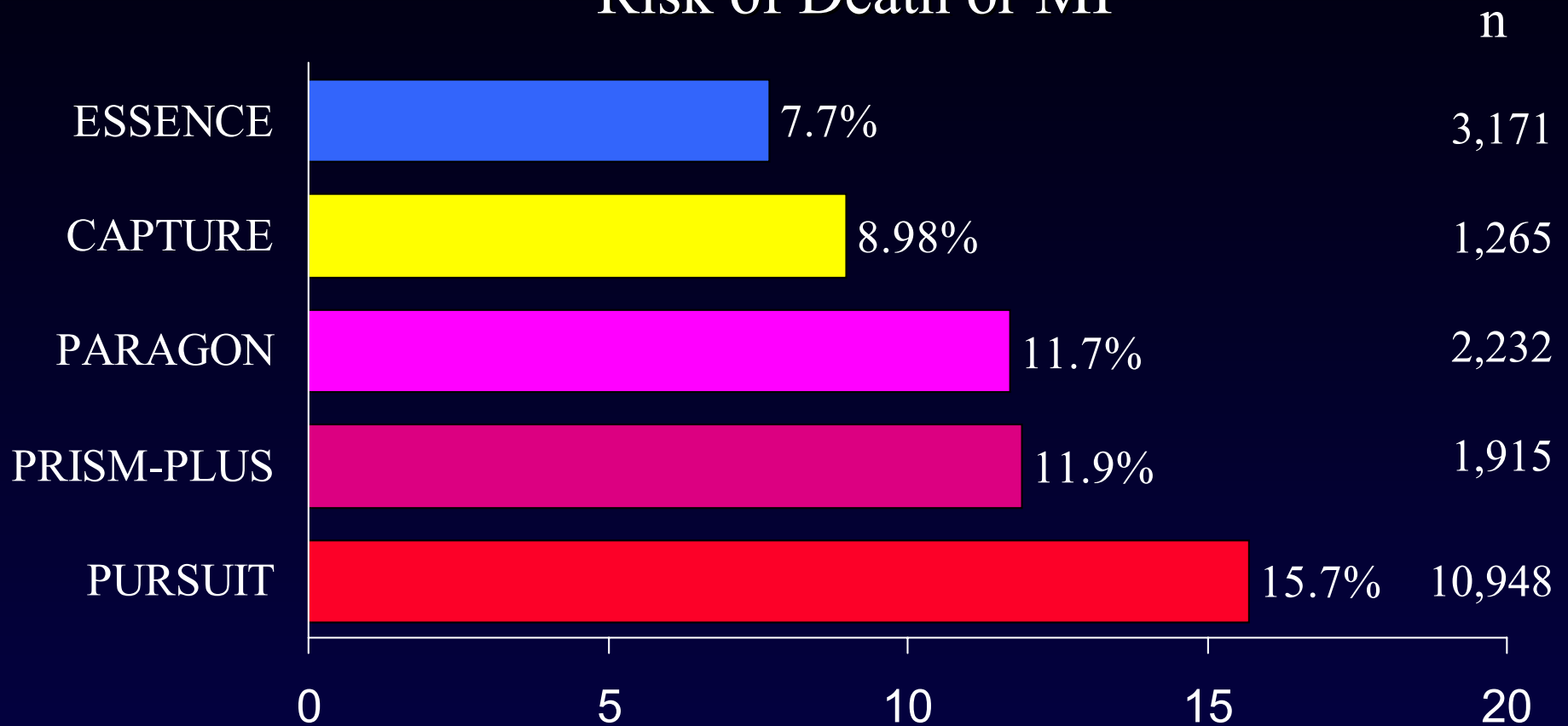
## Clinical Diagnosis



# Risk of ACS

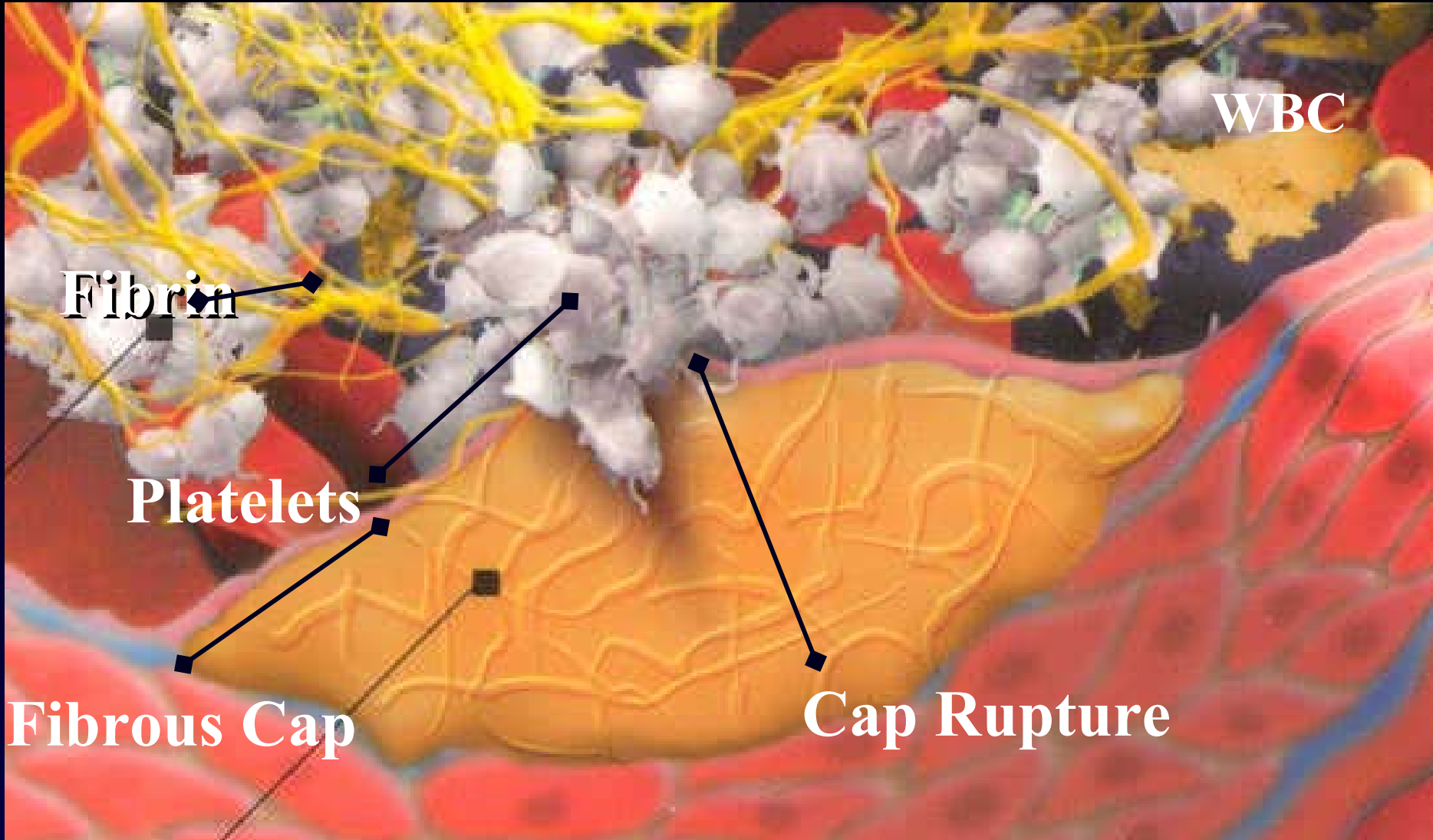
## Clinical Outcomes at 30 Days in **Standard Care Arm**

### Risk of Death or MI



Cohen et al. *N Engl J Med.* 1997;337:447-452.

Kong et al. *Circulation.* 1998;98:2829-2835.



WBC

Fibrin

Platelets

Fibrous Cap

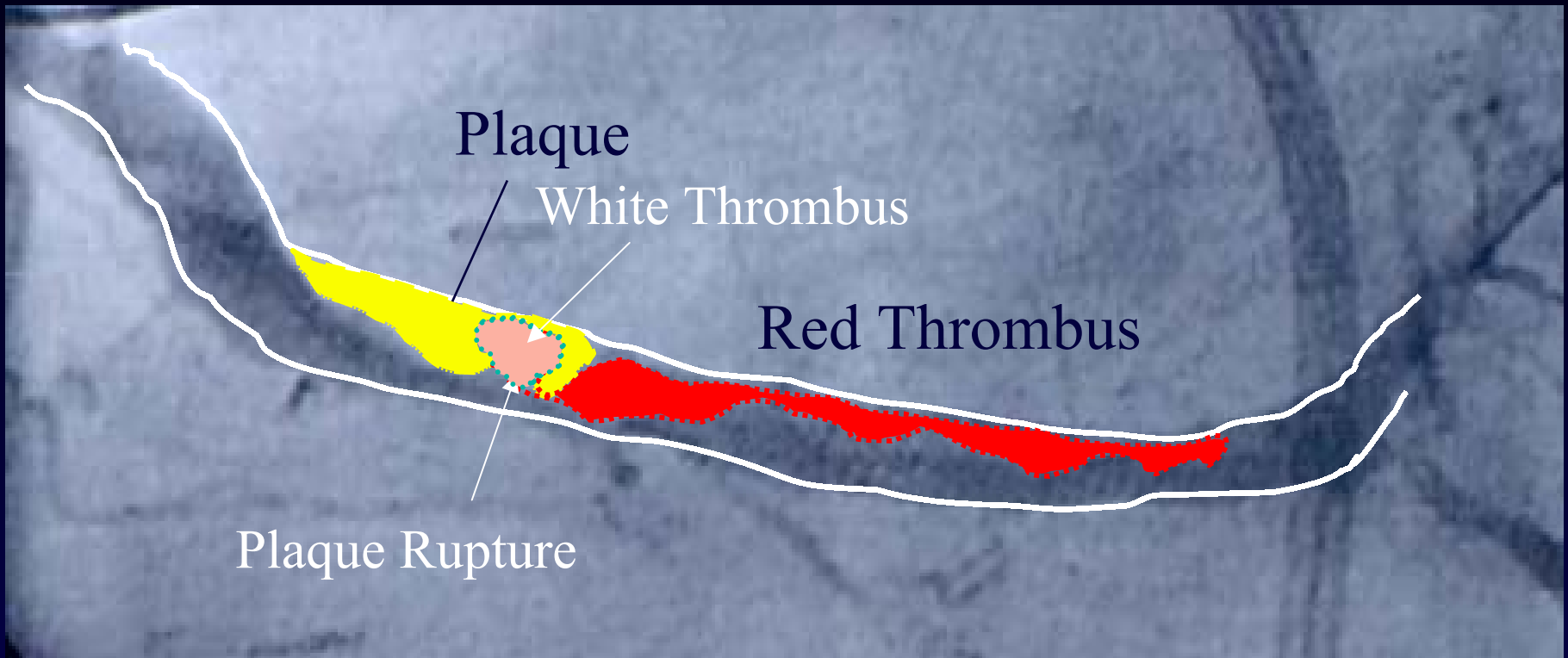
Cap Rupture

Lipid Core

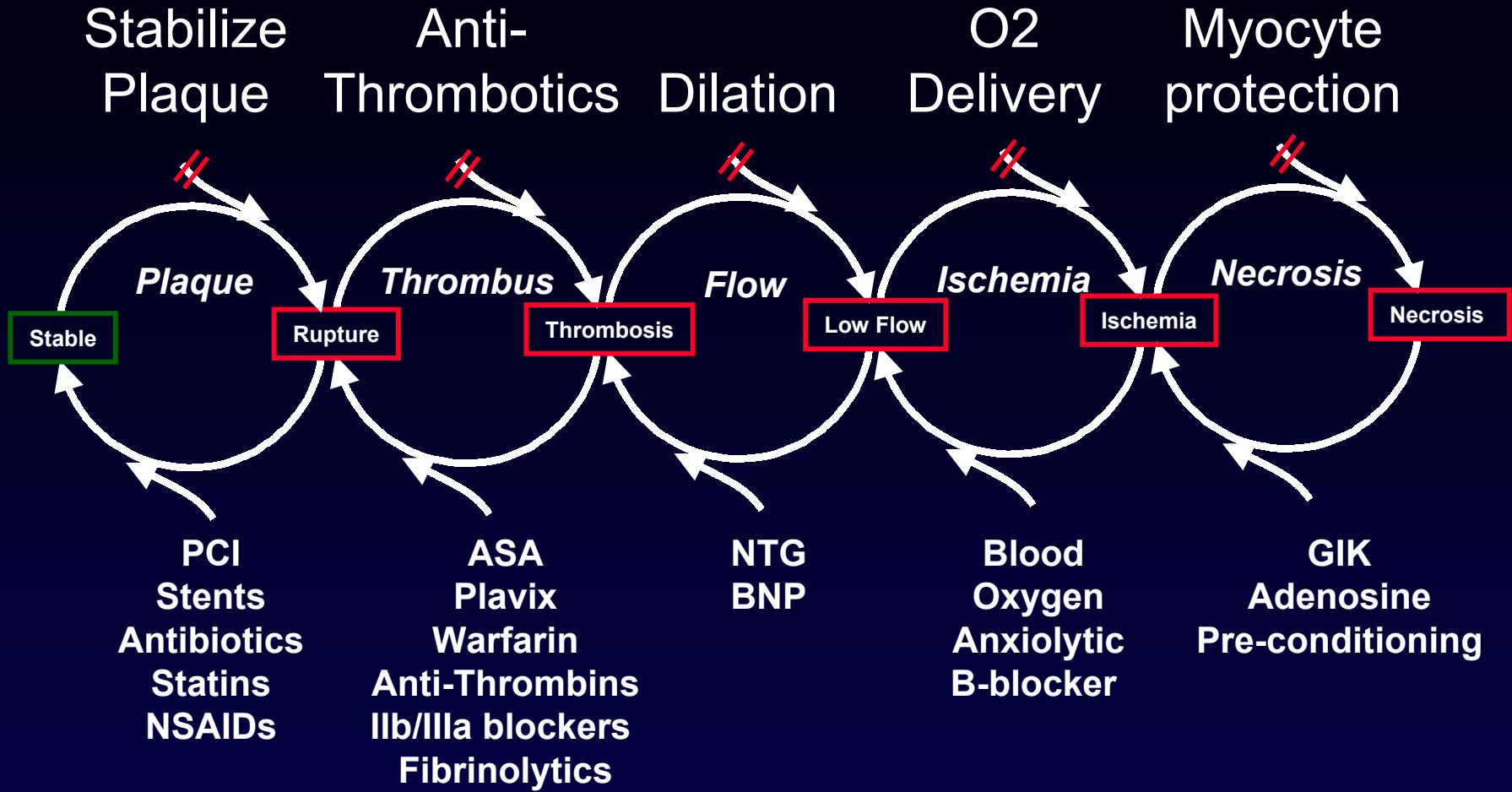
# ACS

## Pathophysiology

### Plaque Disruption



# Treatment Strategies for ACS



**Disease State Markers**

*Chronic treatments ameliorate the negative inputs*

Destabilizing inputs

**Event Markers**

**Chronic Treatment**

**Stable**

**Unstable**

Outputs

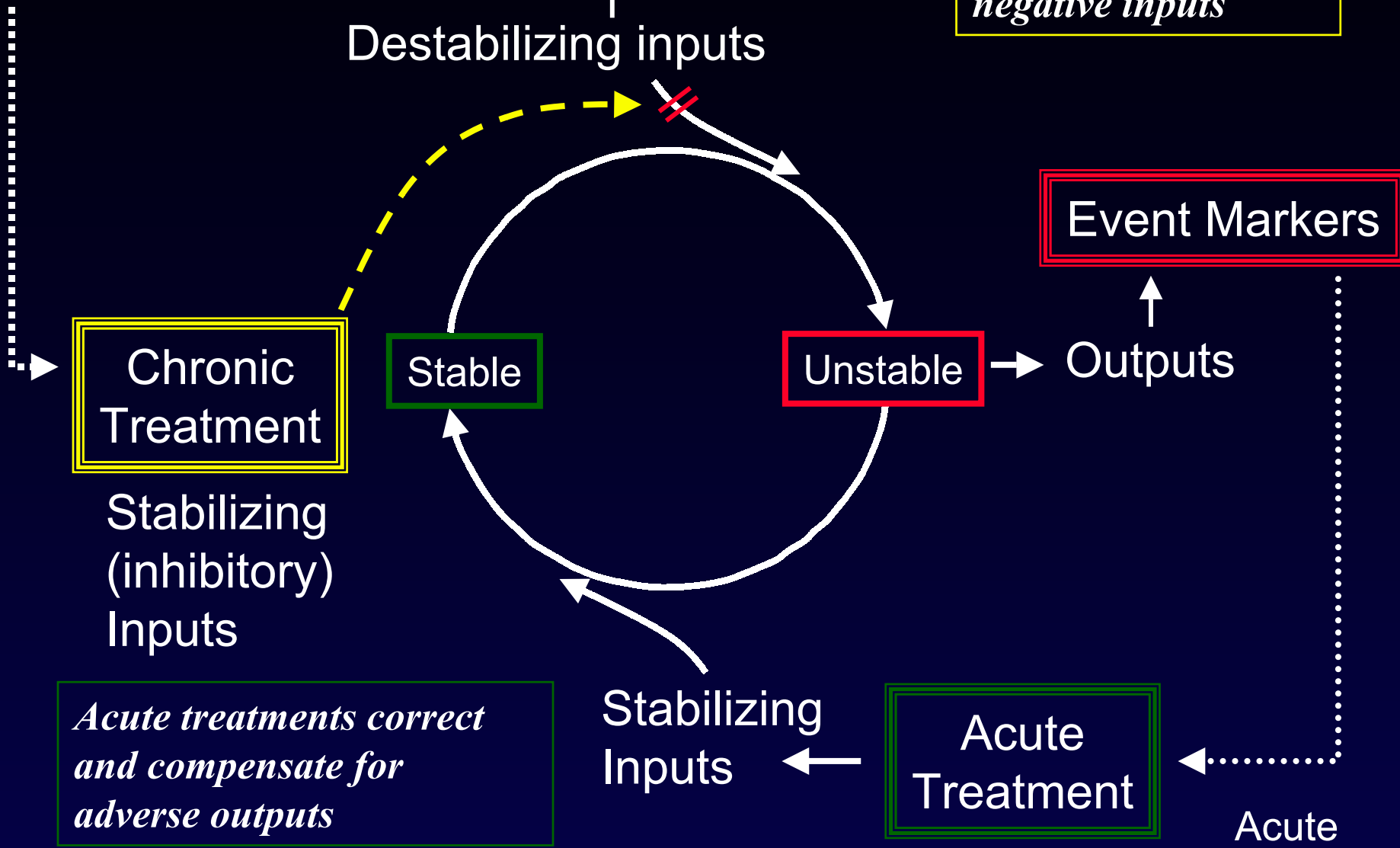
Stabilizing (inhibitory) Inputs

*Acute treatments correct and compensate for adverse outputs*

Stabilizing Inputs

**Acute Treatment**

Acute



# Disease State Markers

CRP / IL-6  
Lipid profile  
MDA-LDL  
HbA1c

Smoking / Oxidation  
Diabetes / Lipids / Drugs  
Hormones / t-PA:PAI-1  
Vasculopathies / Aging

Plavix  
ASA

## Thrombus

No-clot

Clot

### Event Markers

ST-depression  
P-selectin  
TPP  
D-dimer, FDPs

### Chronic Treatment

Clopidogrel  
Anti-thrombins  
ASA  
Warfarin  
Fibrinolytics

### Acute Treatment

Acute

# Disease State Markers

Smoking / Oxidation  
Diabetes / Lipids / Drugs  
Hormones / t-PA:PAI-1  
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CRP / IL-6  
Lipid profile  
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Plavix  
ASA

## Thrombus

No-clot

Clot

### Event Markers

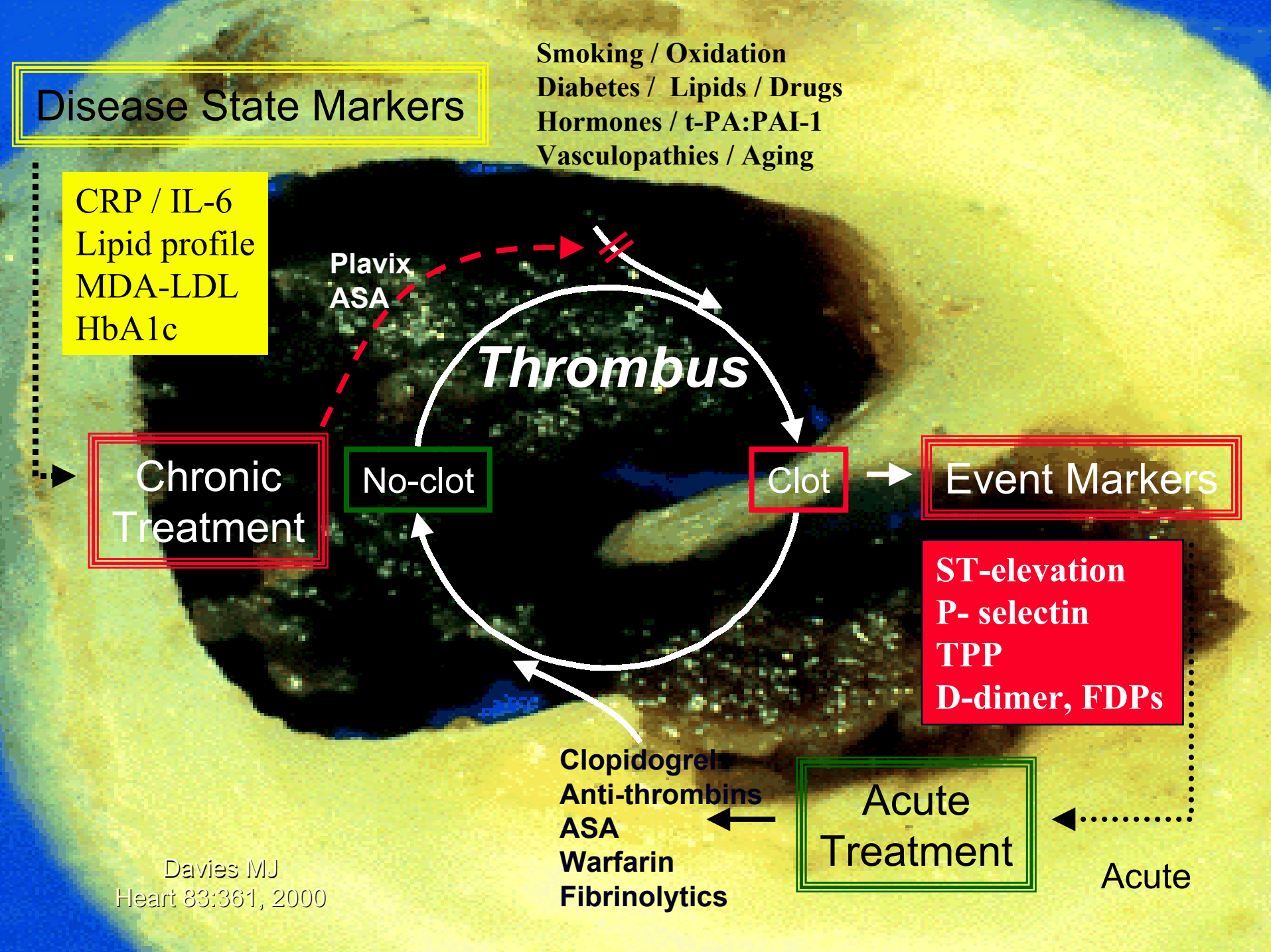
ST-elevation  
P-selectin  
TPP  
D-dimer, FDPs

### Chronic Treatment

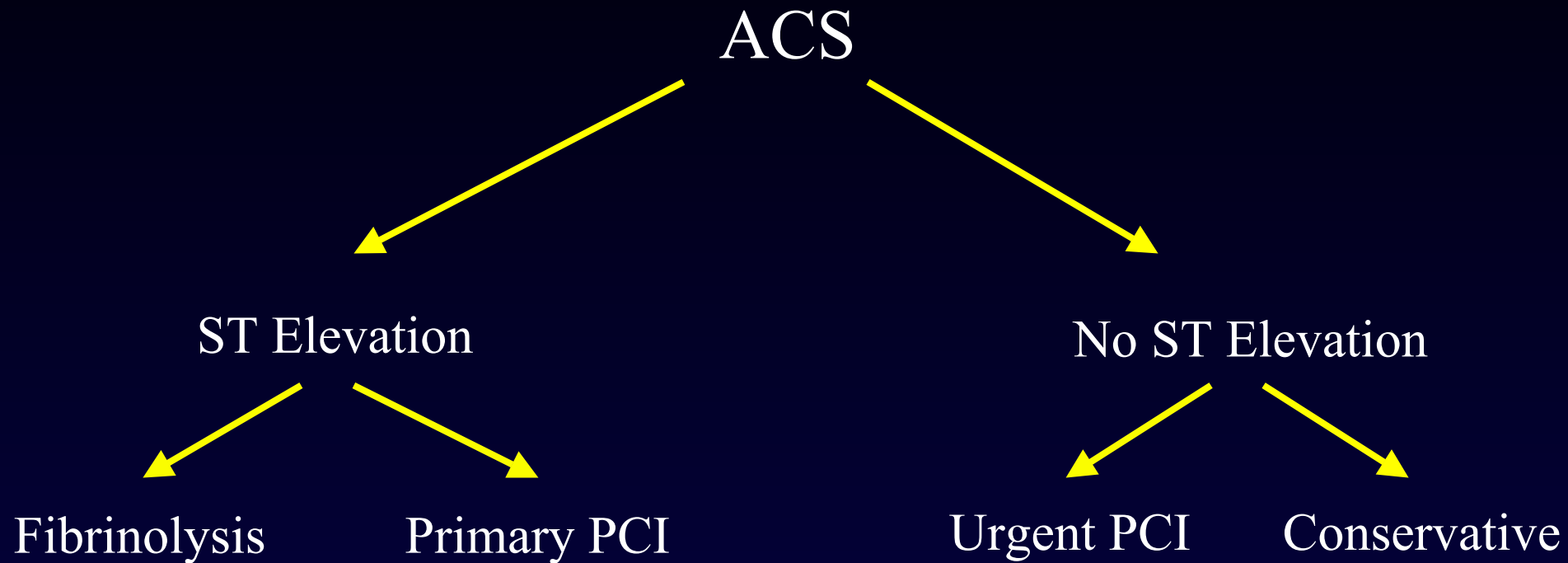
### Acute Treatment

Clopidogrel  
Anti-thrombins  
ASA  
Warfarin  
Fibrinolytics

Acute

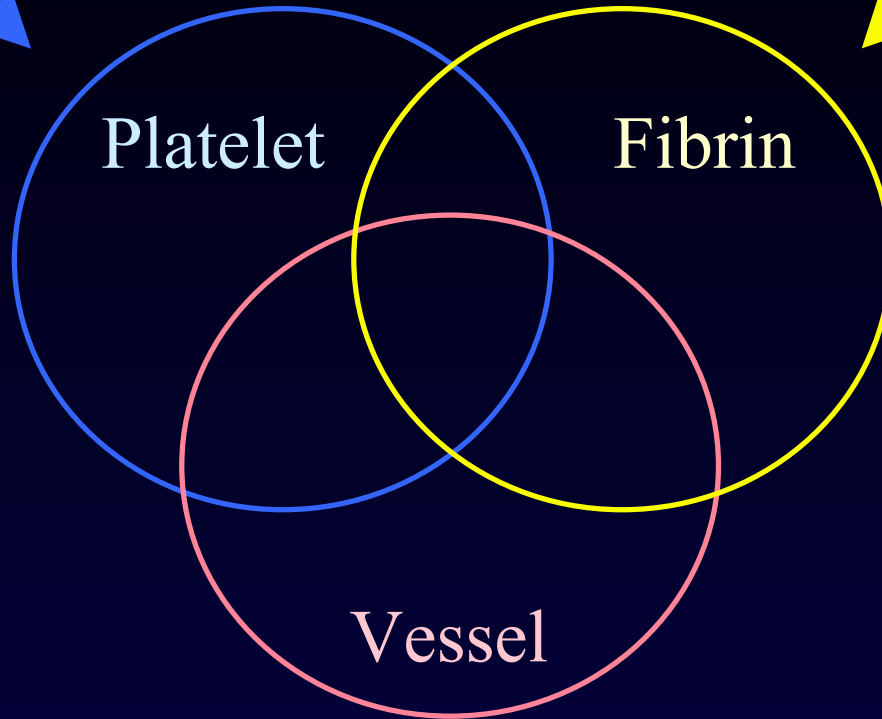


# Current Management Strategies for ACS



**Dethrombosis**

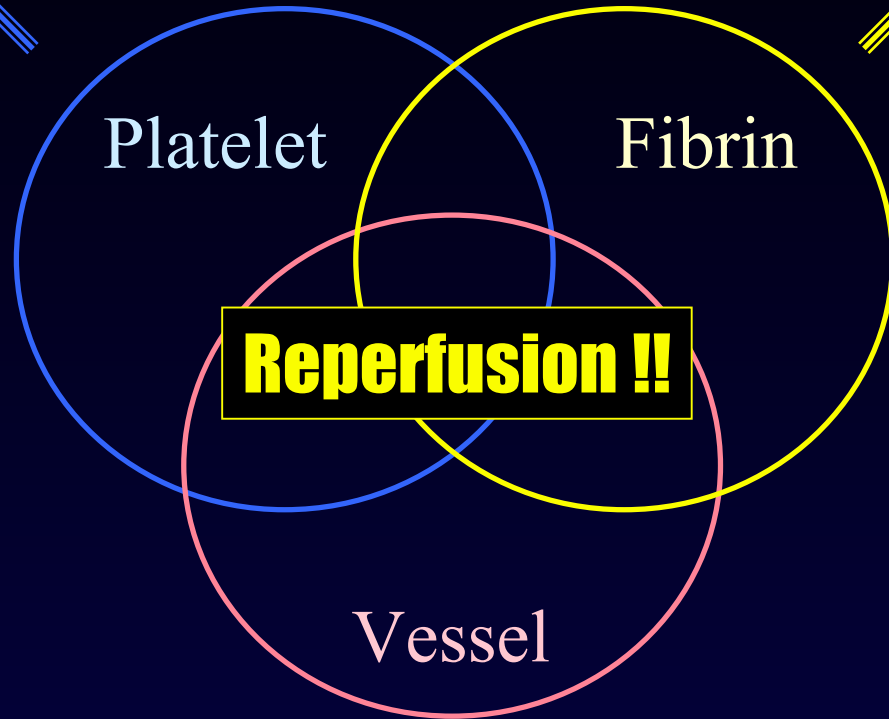
**Fibrinolysis**



**Passivation**

**Dethrombosis**

**Fibrinolysis**



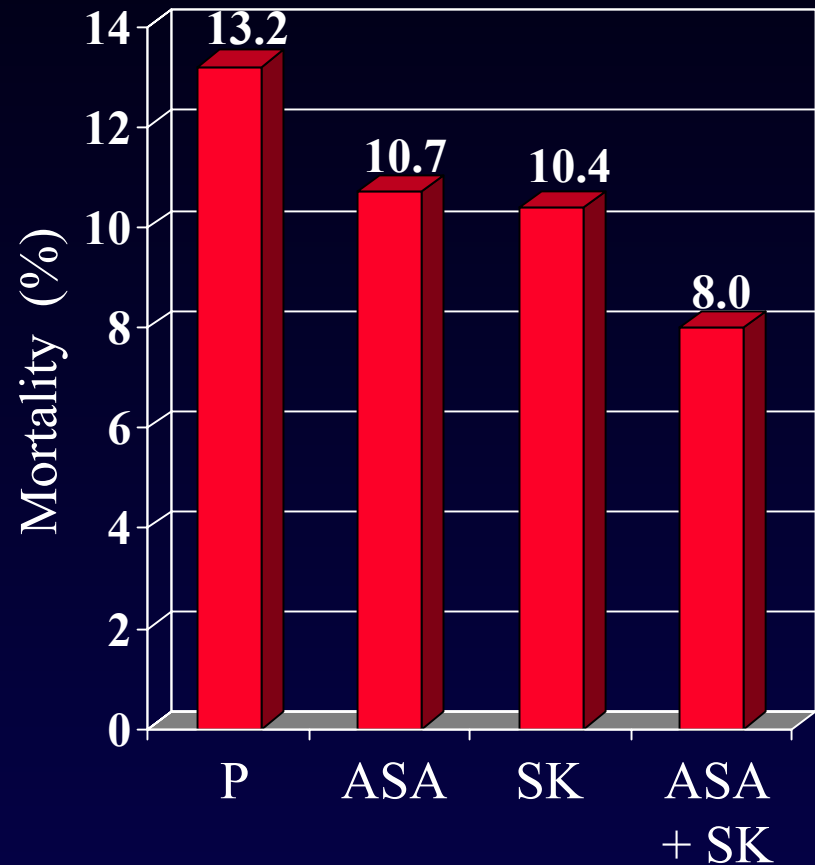
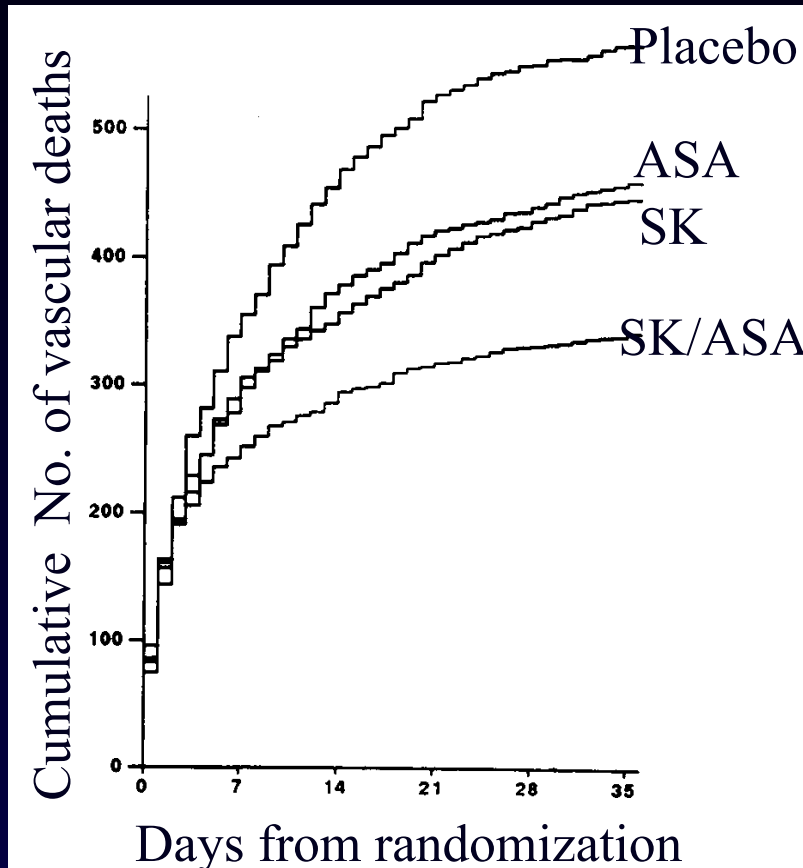
**Reperfusion !!**

Vessel

**Passivation**

# Combination Therapy for AMI

## Anti-Platelet With Lytic - ISIS



# Coagulation Cascade

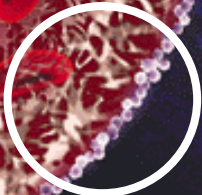
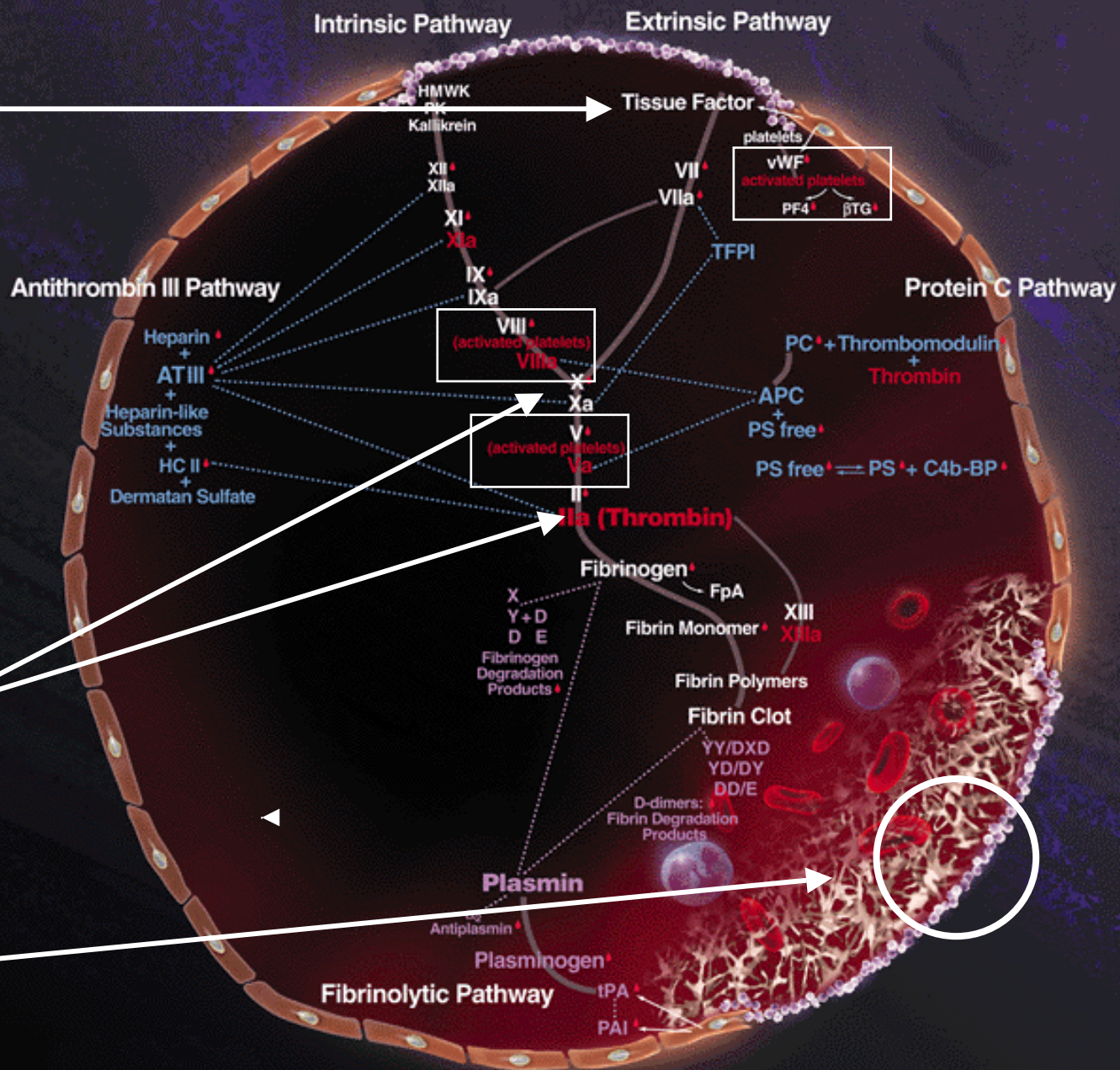
TFPI



Platelet Inhibition

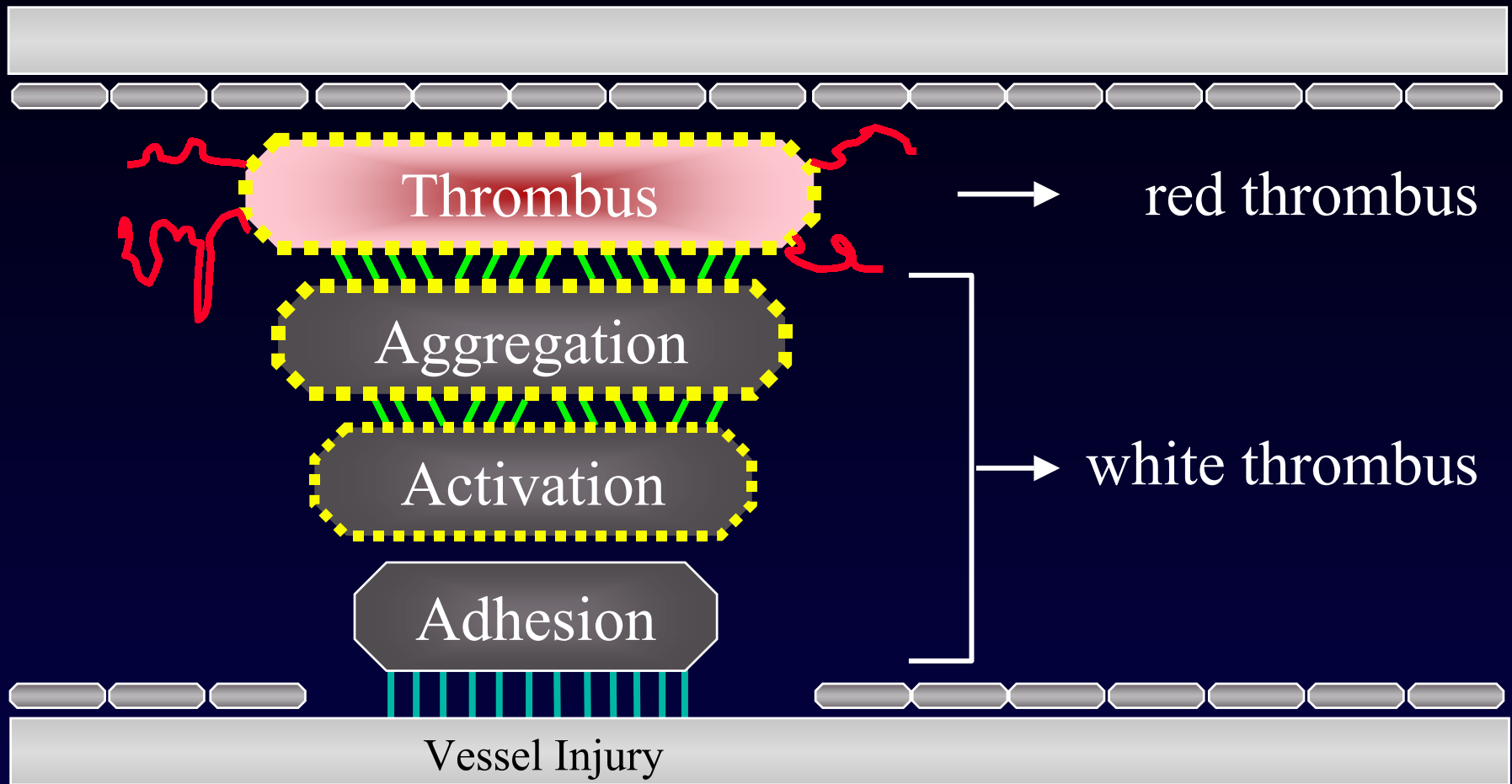
Anti-Thrombins

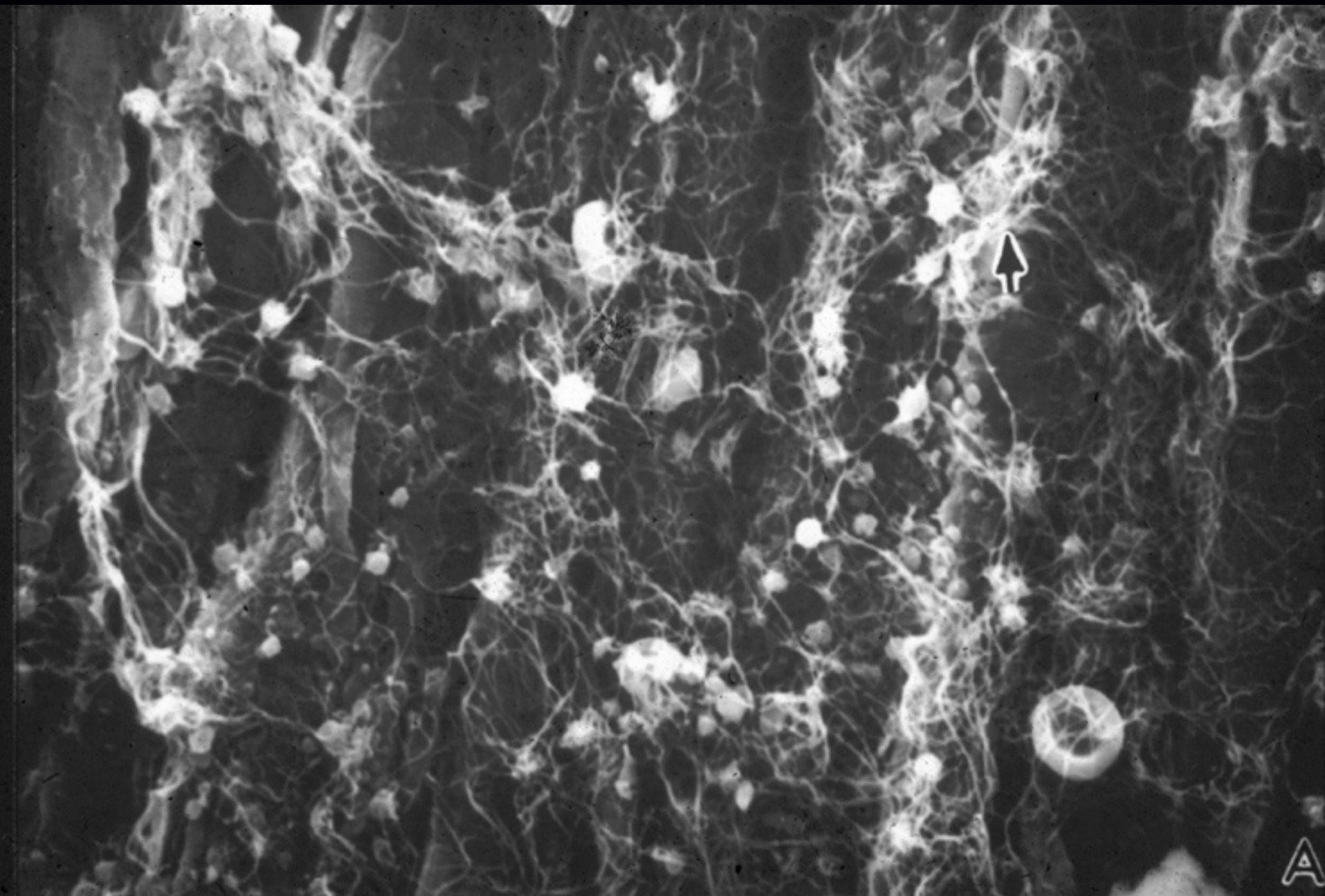
Anti-aggregants



# Overview of Platelet Function

## Specific Components of Thrombosis





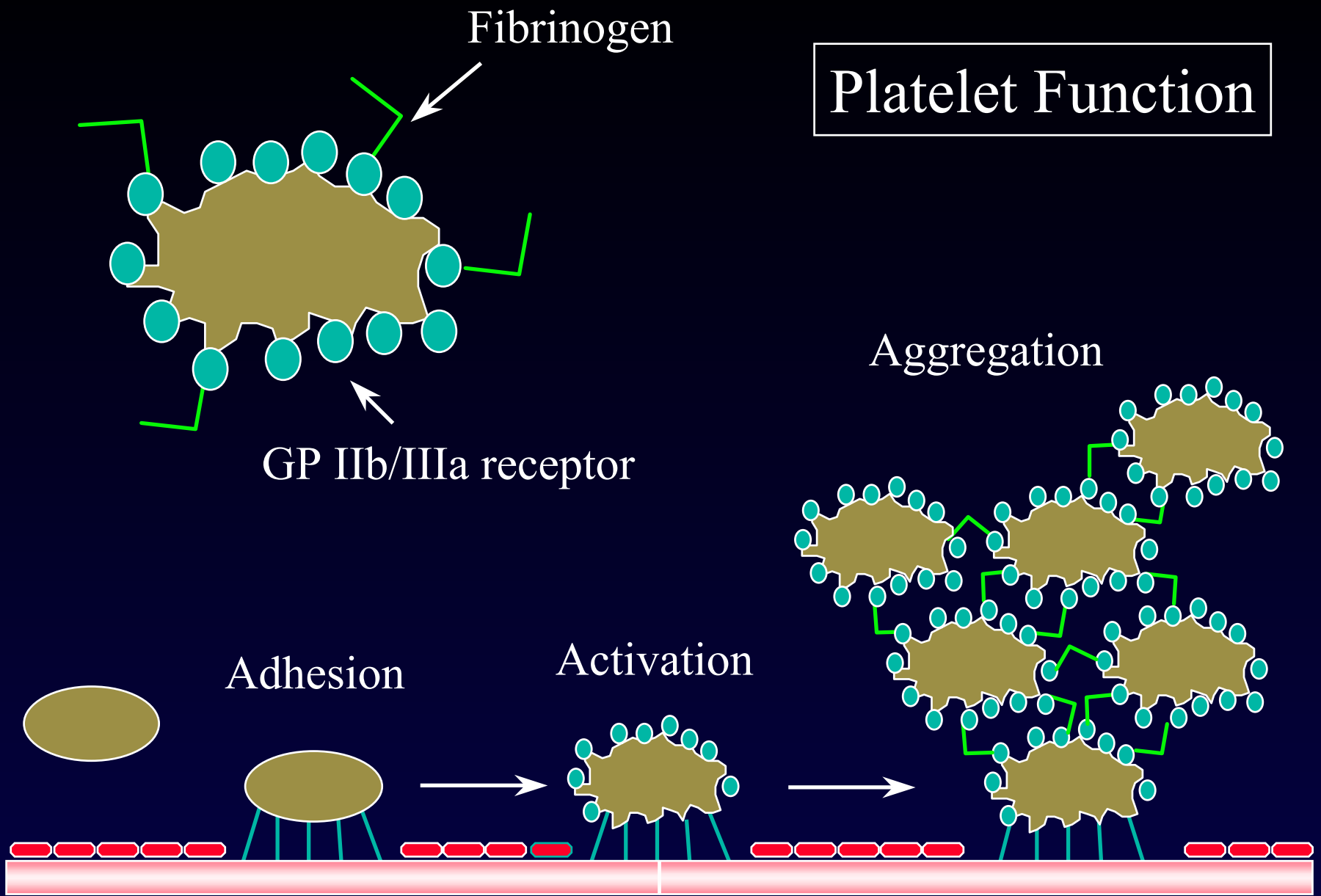


A black and white micrograph showing a dense field of small, rounded, light-colored structures, possibly spores or cells, against a dark background. A prominent, elongated, and somewhat irregularly shaped structure is visible on the left side. A diagonal line or boundary runs across the center-right of the image. In the top right corner, there is a scale bar consisting of two parallel horizontal lines, with the text "10 μm" positioned below it. The letter "B" is located in the bottom right corner.

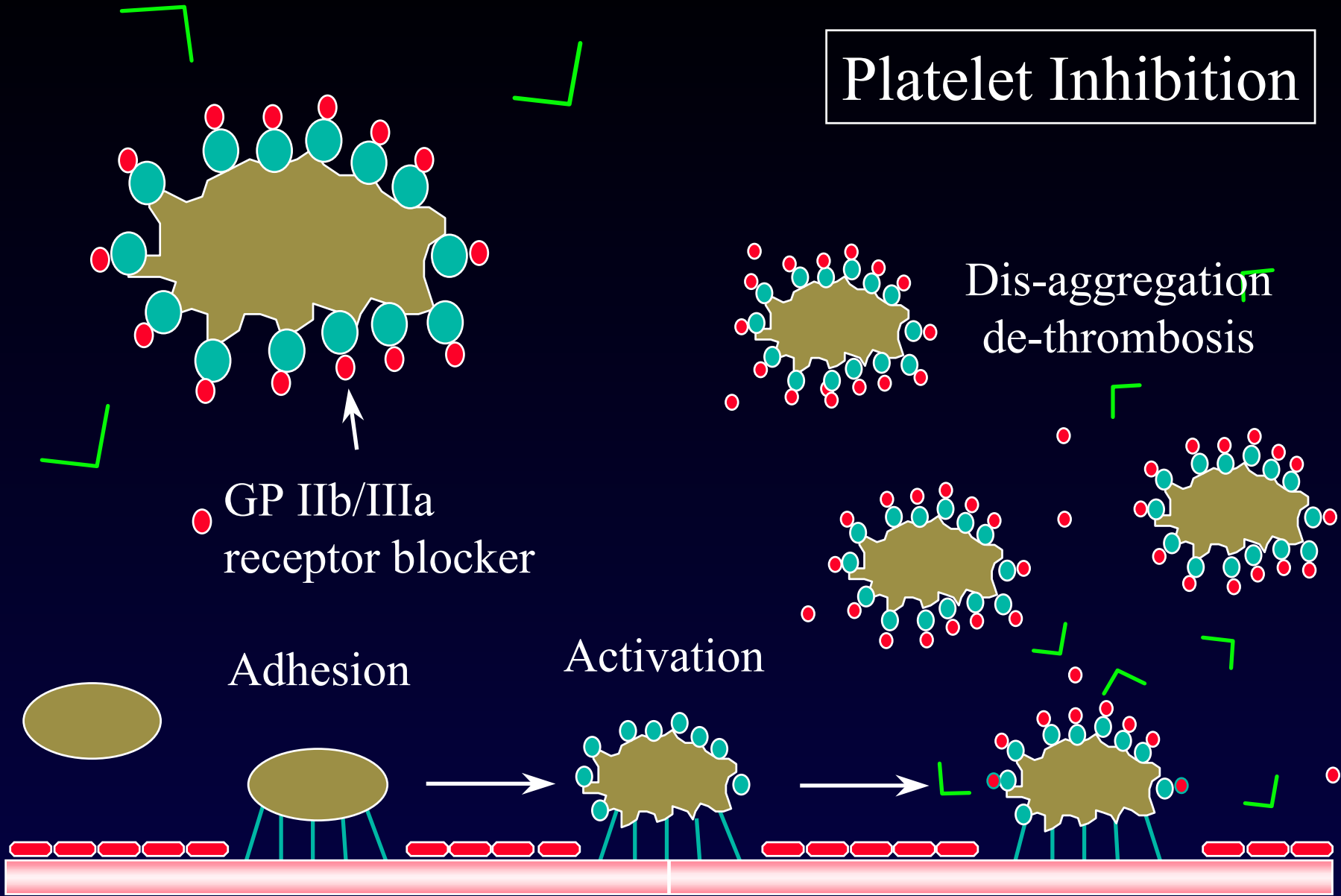
10  $\mu\text{m}$

B

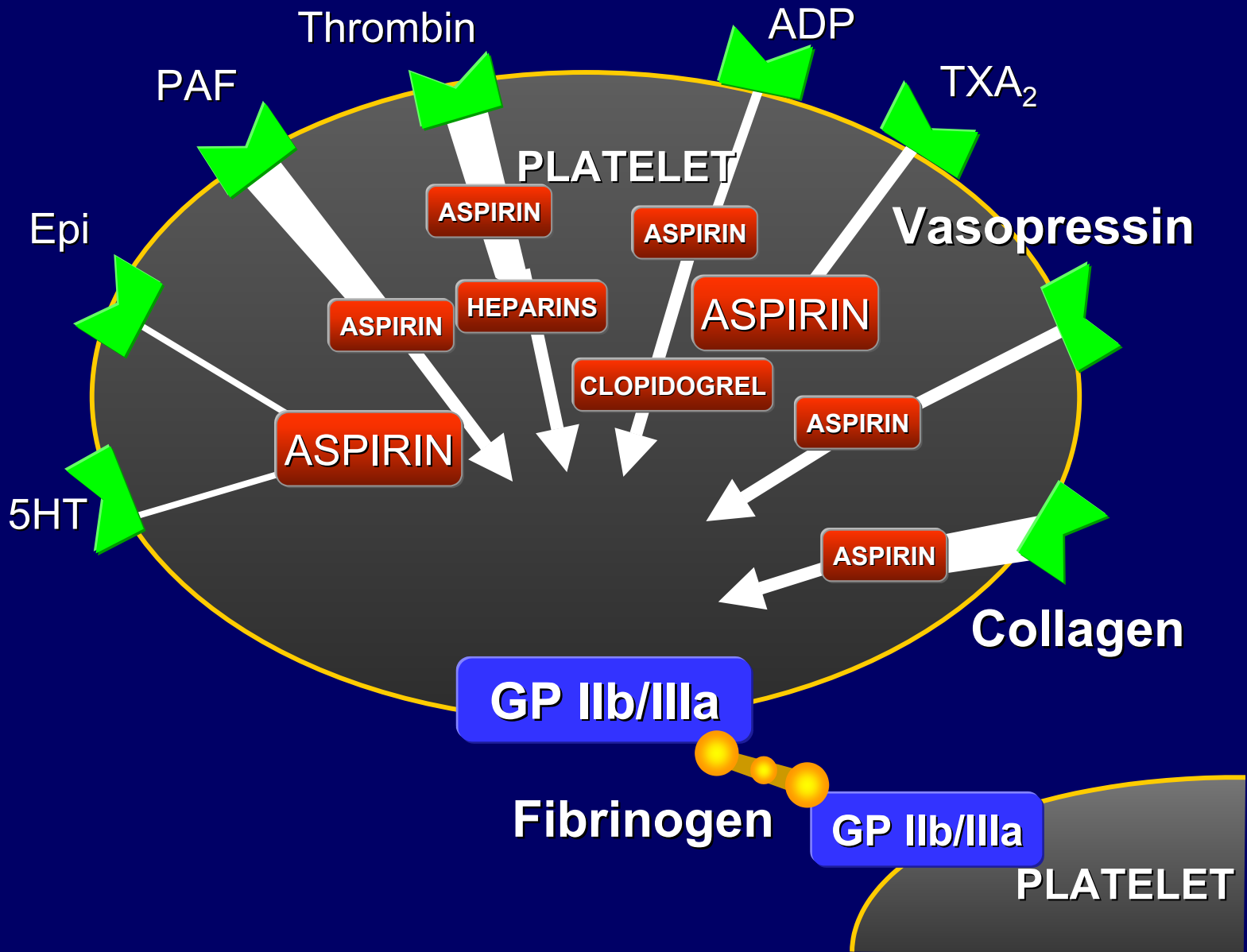
# Platelet Function



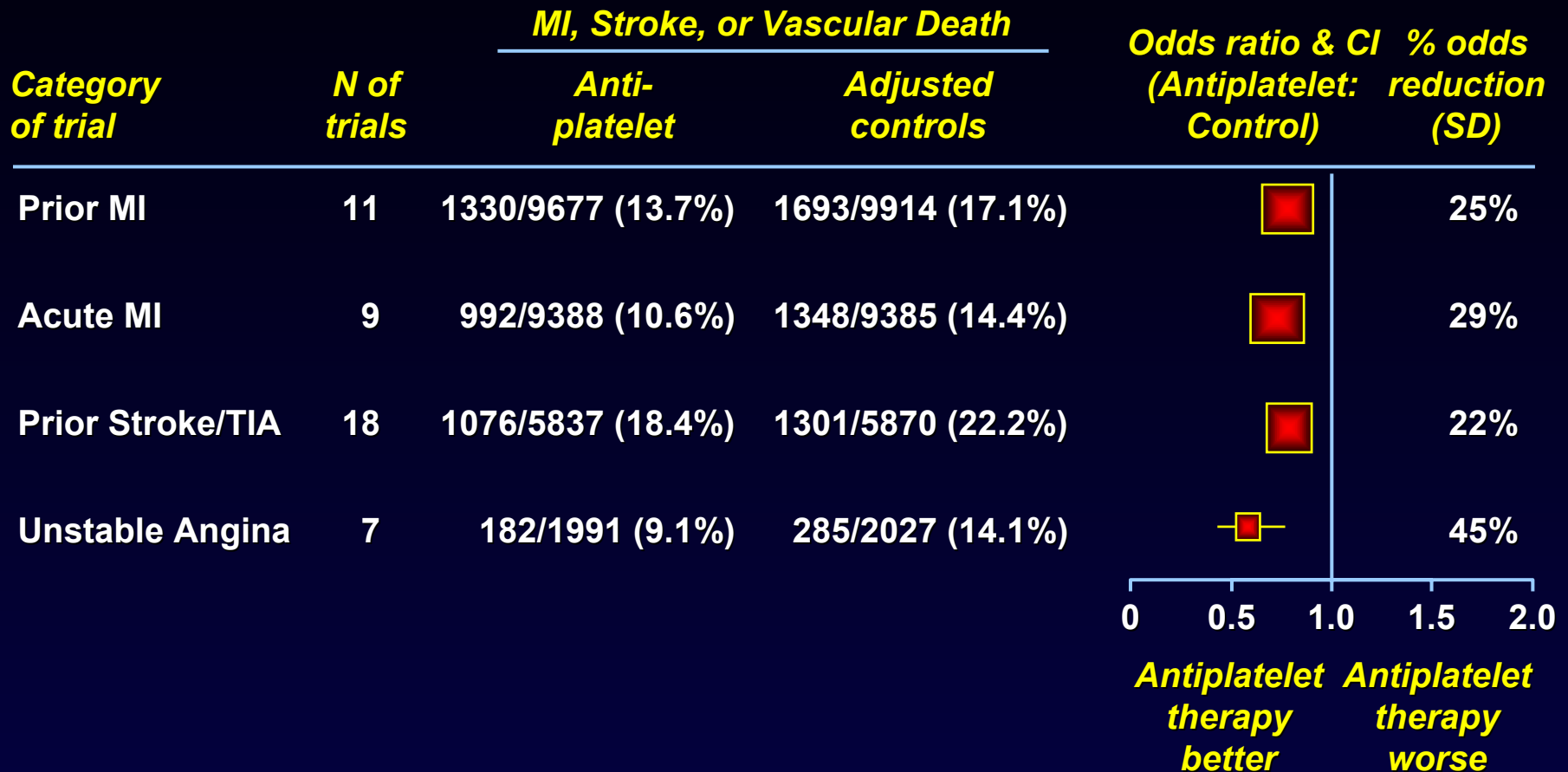
# Platelet Inhibition



# GP IIb/IIIa Receptor Activation Pathway

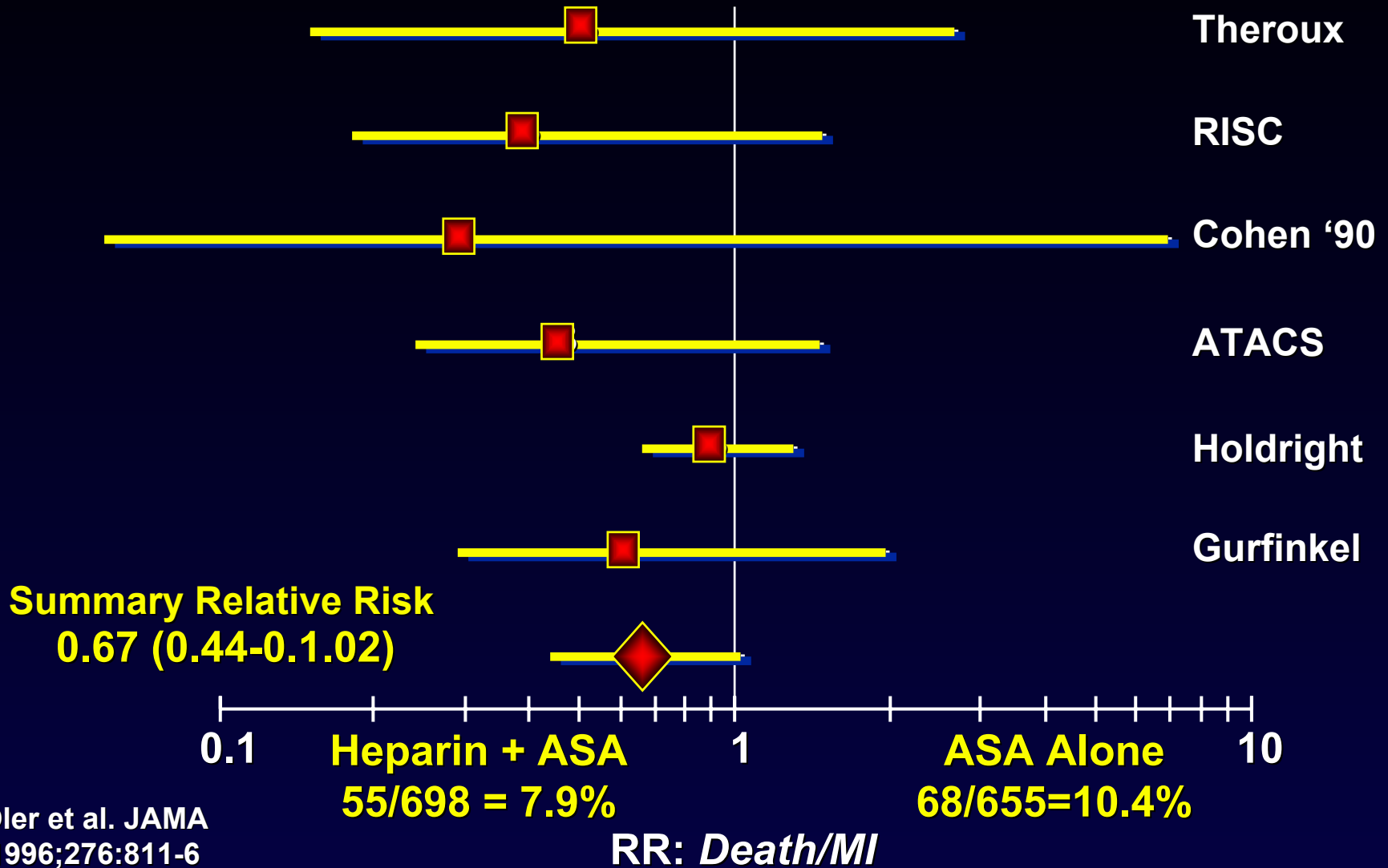


# Anti-Platelet Therapy in ACS



Antiplatelet Trialists' Collaboration. BMJ 1994;308:81-106

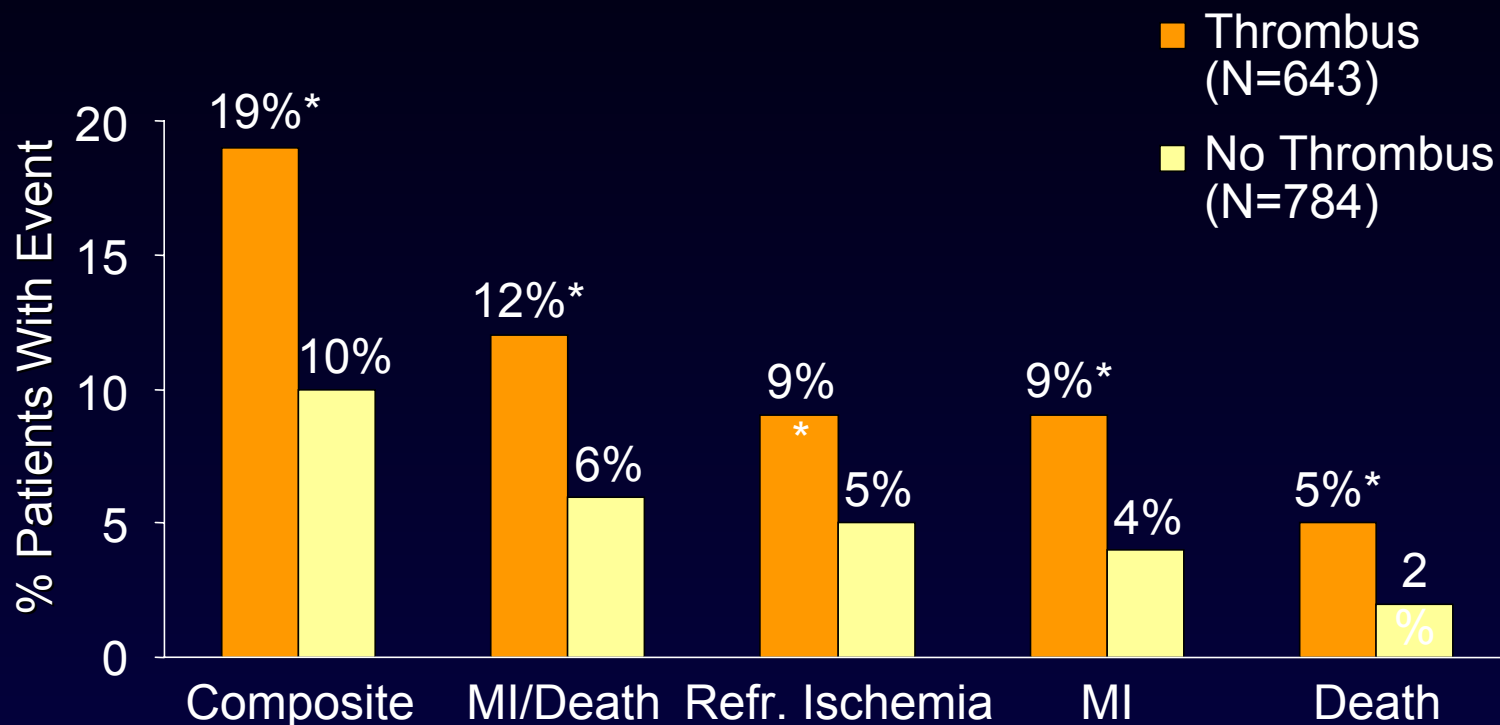
# Heparin + ASA vs. ASA in ACS



Oler et al. JAMA  
1996;276:811-6

# Intracoronary Thrombus as a Predictor of Clinical Outcomes in Unstable Angina/NQWMI

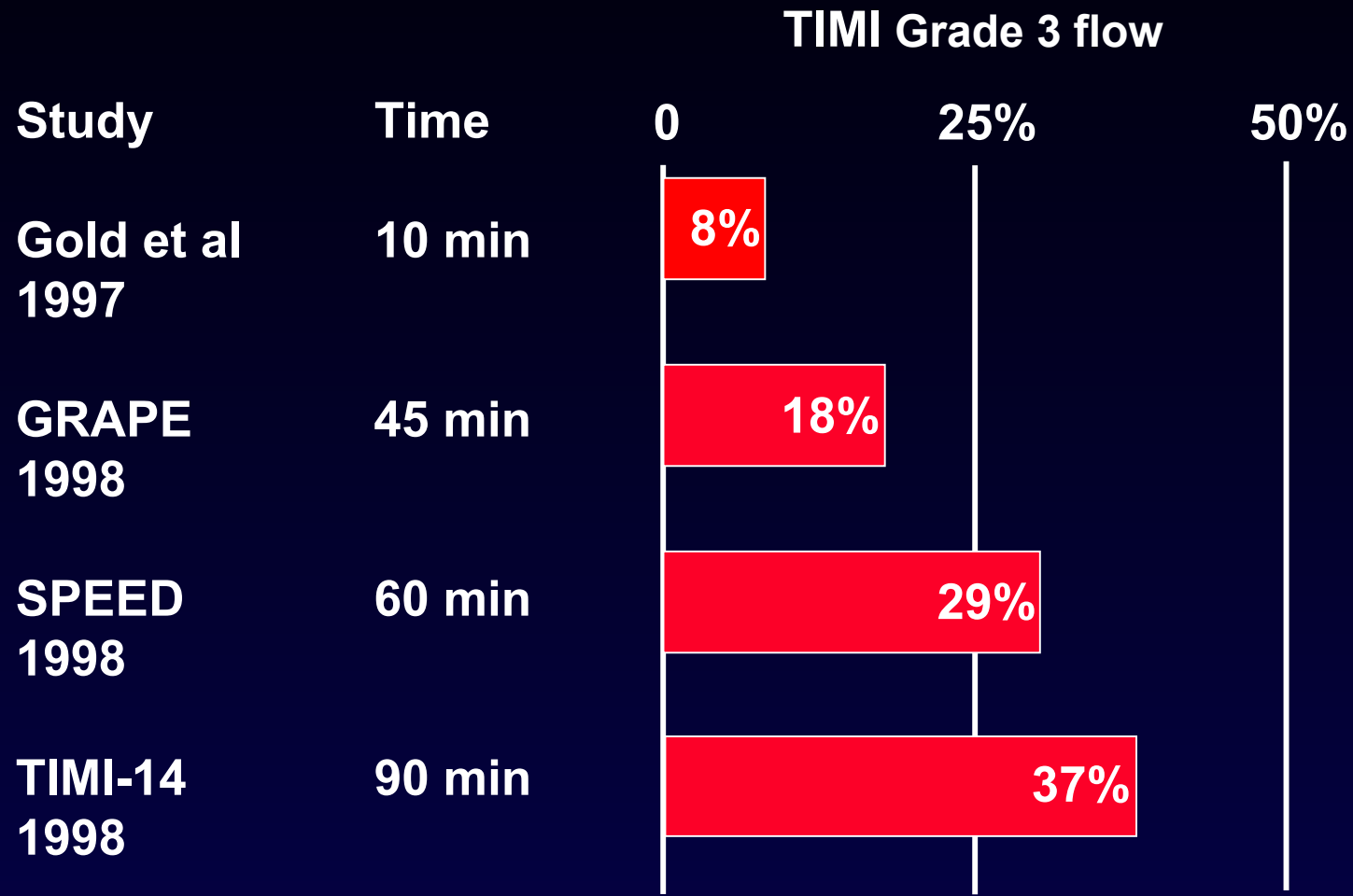
## Events at 30 Days



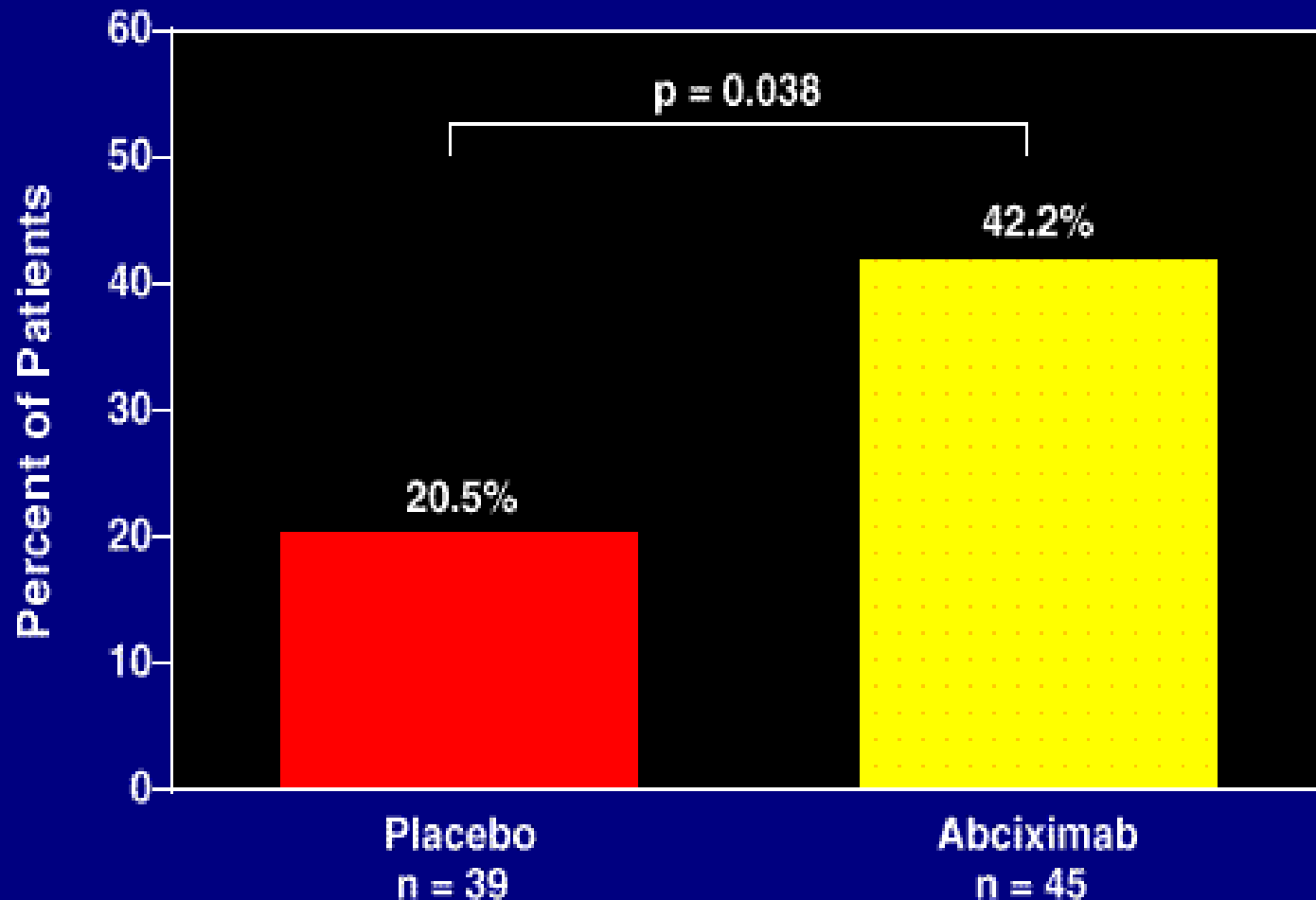
\*  $P < 0.005$ .

Zhao et al. *Circulation*. 1999;100:1609-1615.

# Ability of Abciximab to Cause Dethrombosis



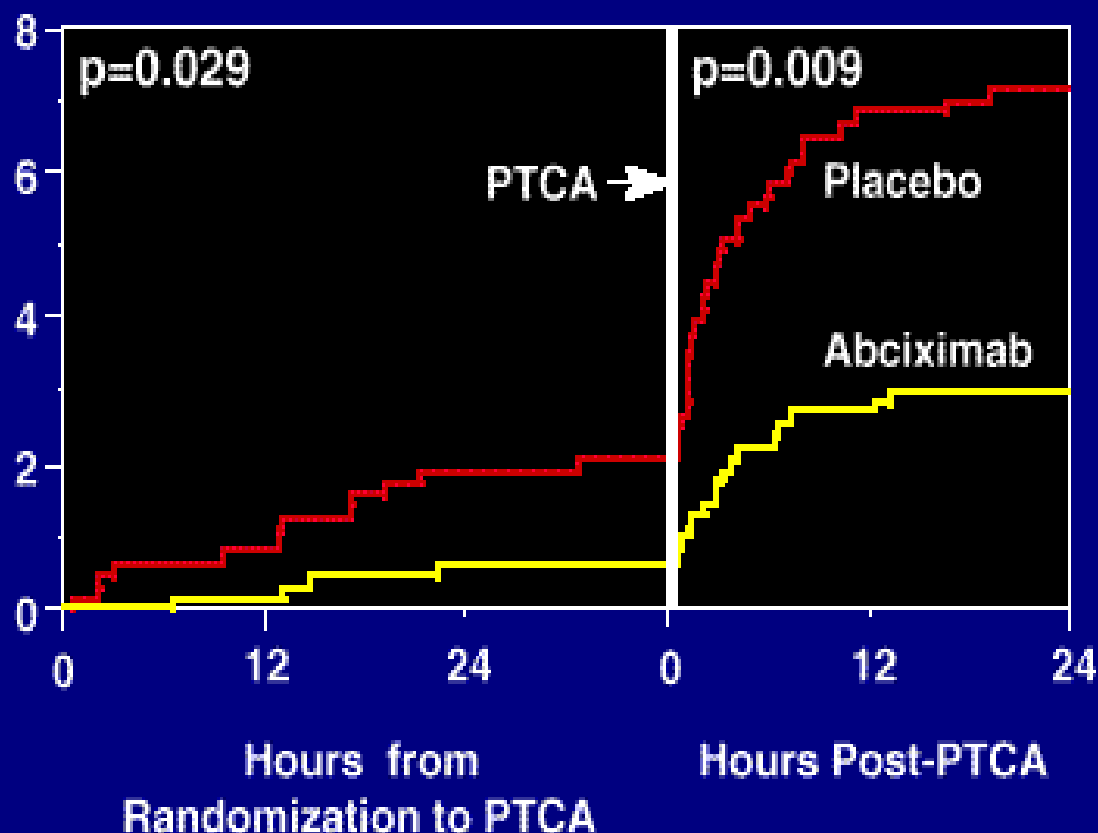
# CAPTURE: Thrombus Resolution Pre PTCA



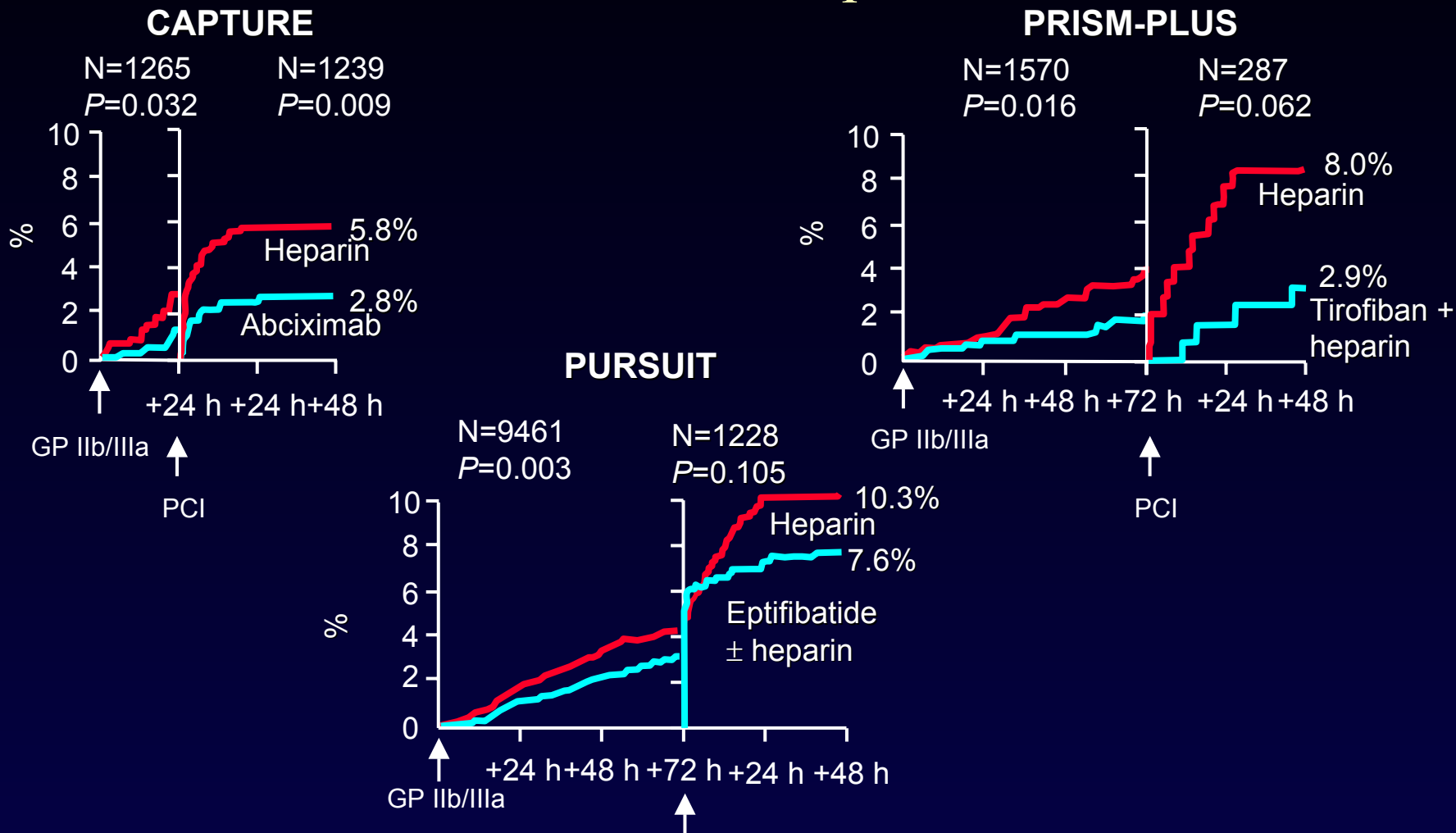
# CAPTURE: Myocardial Infarction

## Incidence Before and After PTCA

% of Patients with MI



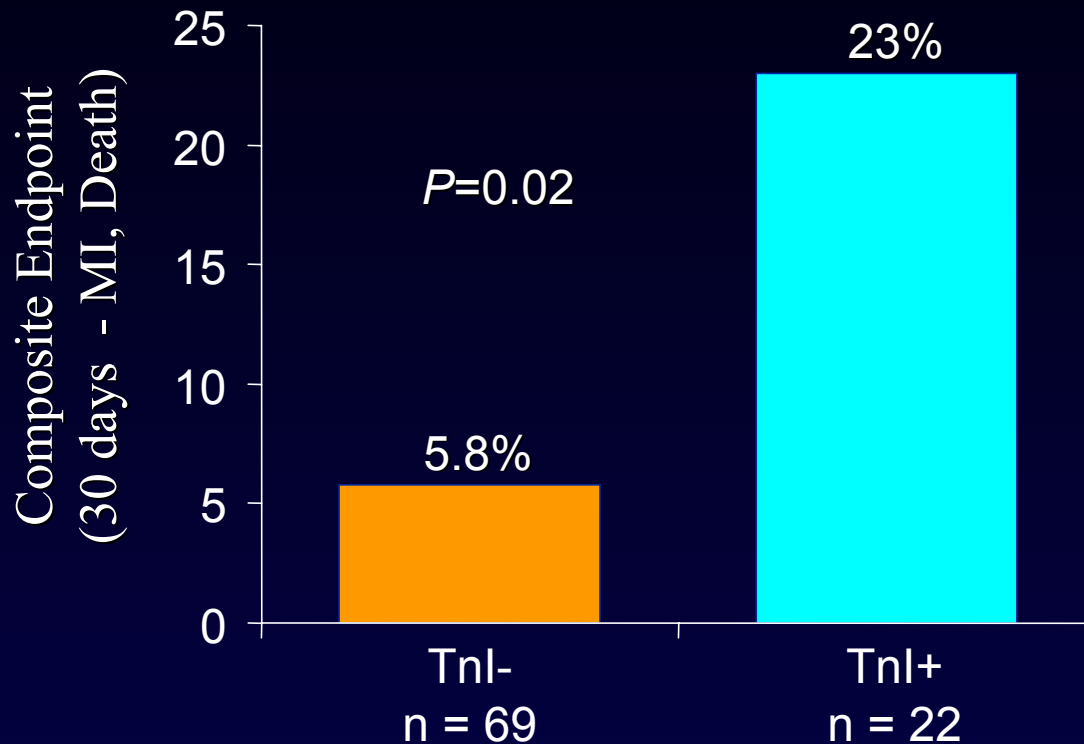
# GP IIb/IIIa Inhibitors in ACS Trials: Death/MI in All Patients and Postprocedure in PCI Groups



# Cardiac Endpoints in Unstable Angina

## Value of Troponin in CK-MB Negative Patients

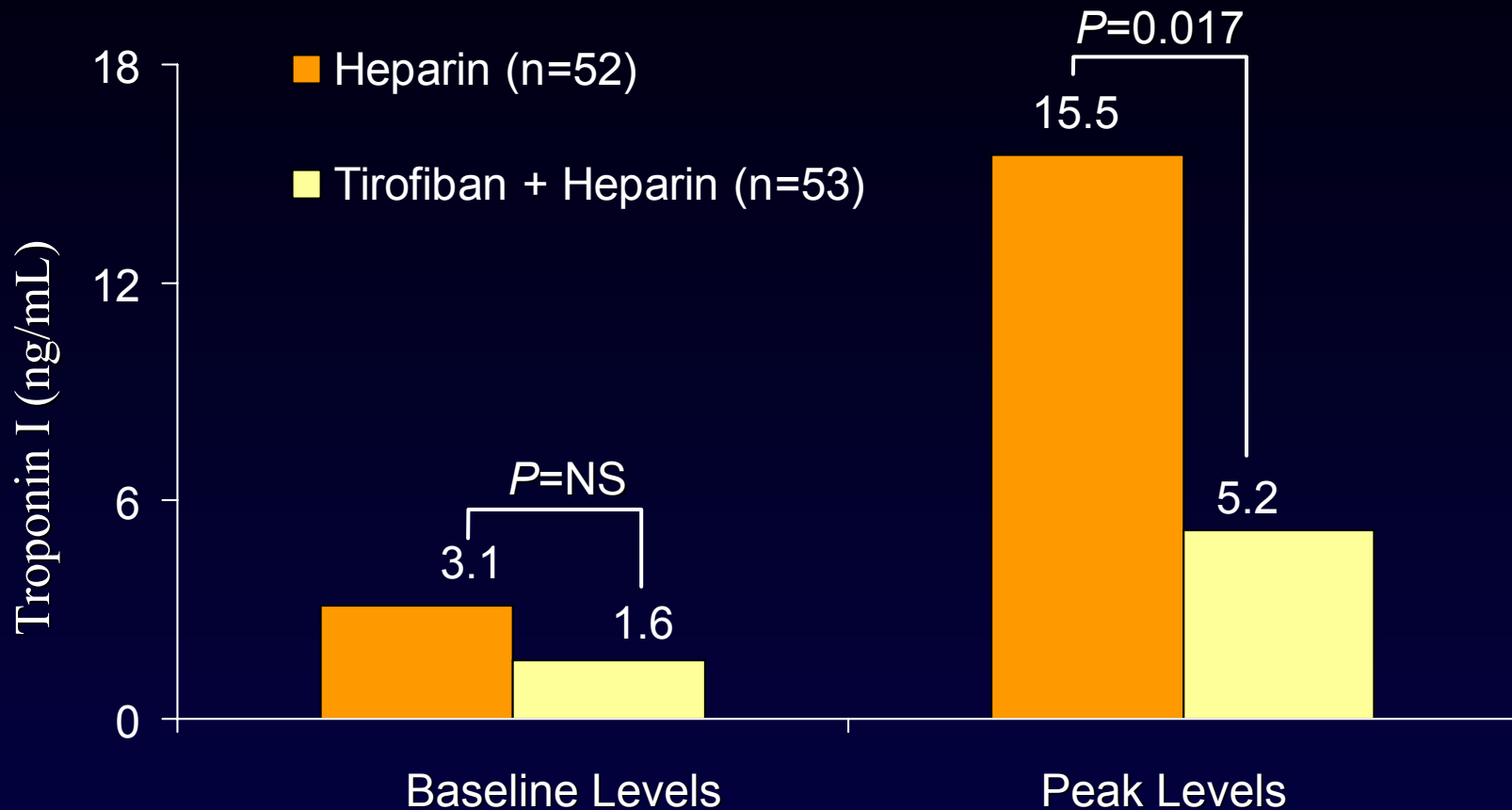
Braunwald Class III Patients With Pos ECG  
AMI Ruled Out by CK-MB at 16 Hours



**Conclusion: TnI has important prognostic value for patients with unstable angina**  
Galvani. *Circulation*. 1997; 95:2053-2059.

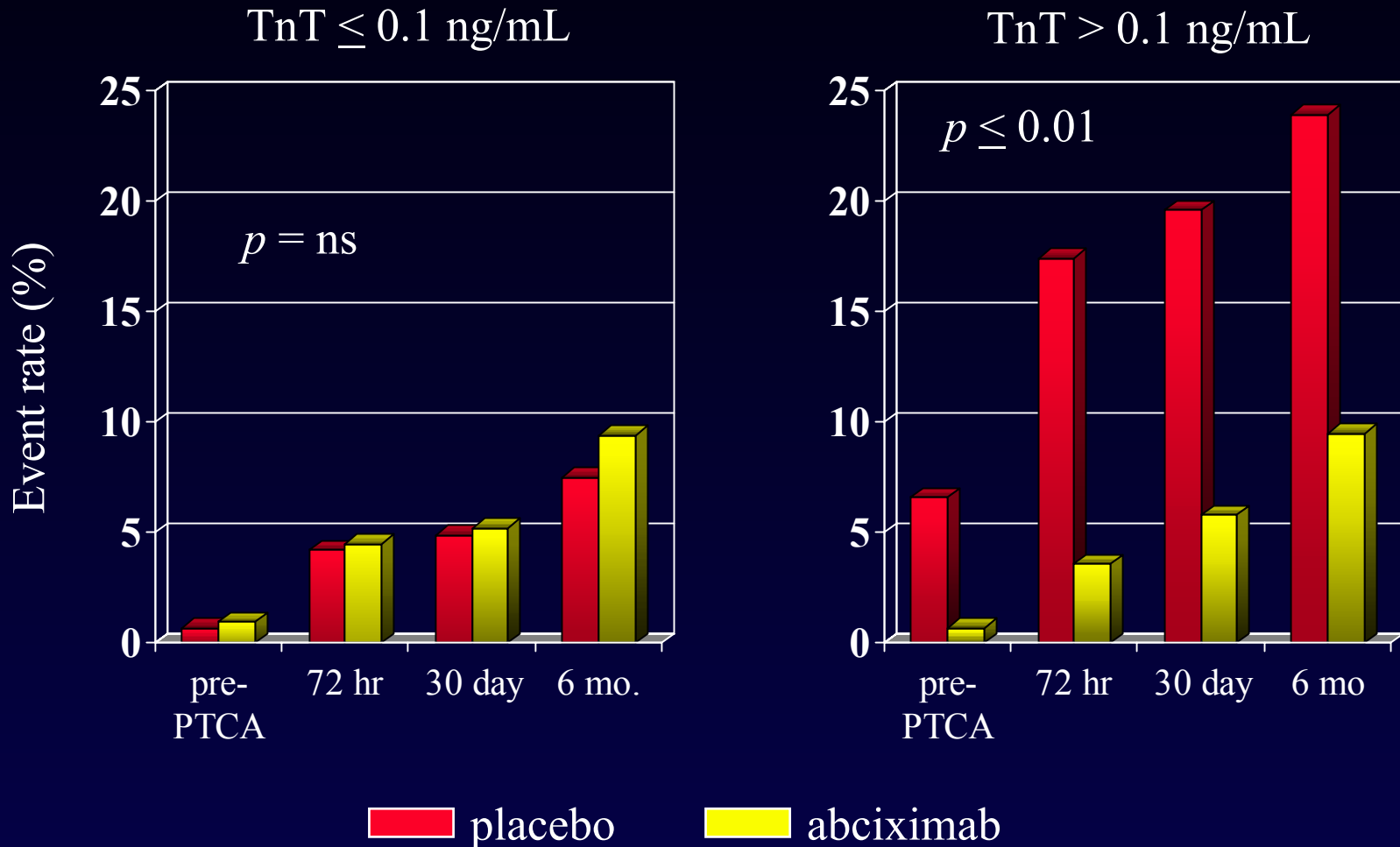
# TnI Levels in UA/NQWMI

## Patients Treated With Tirofiban: PRISM-PLUS

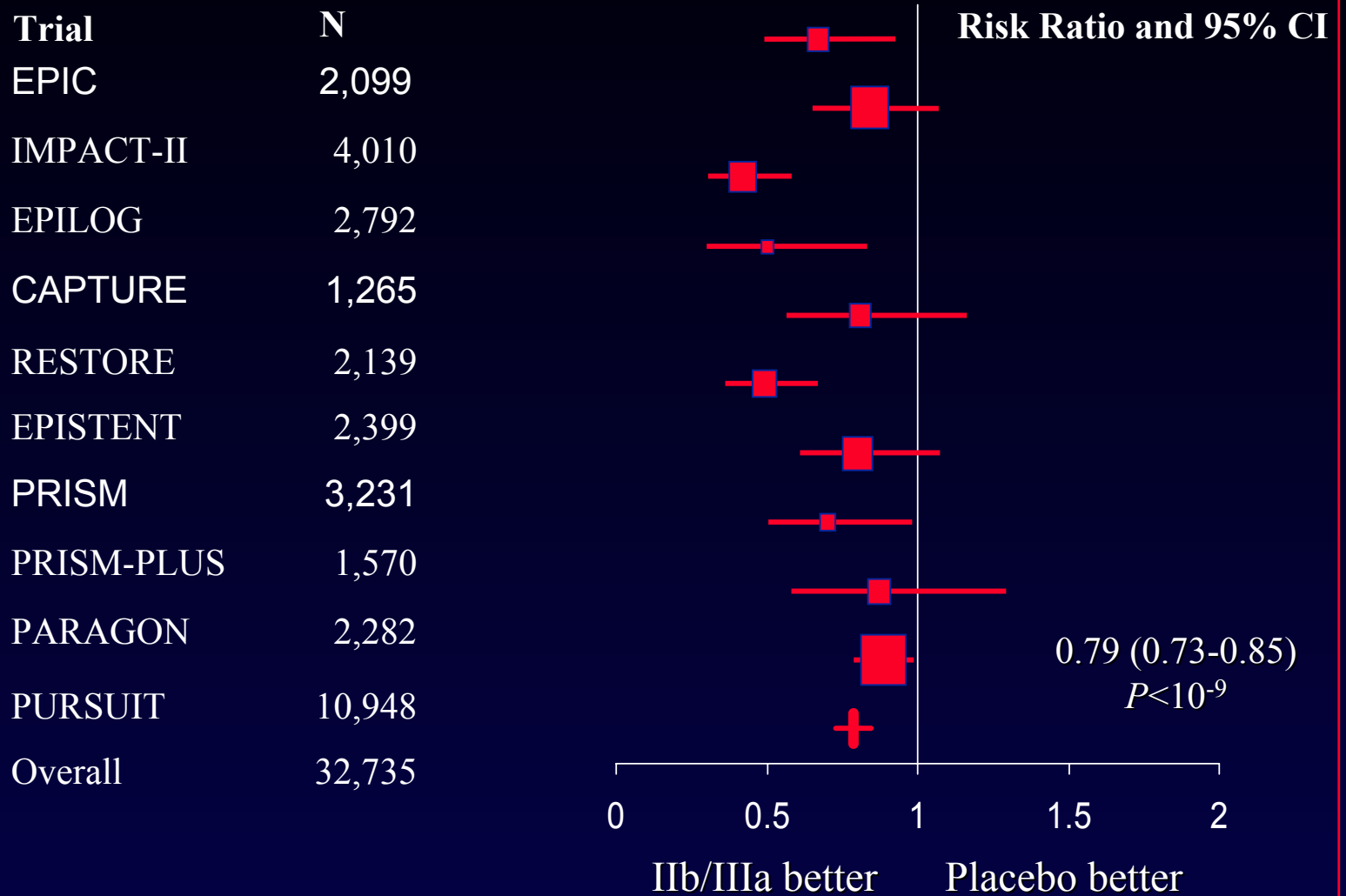


# CAPTURE – Outcomes by Troponin Status

## Death and MI at 72 Hours

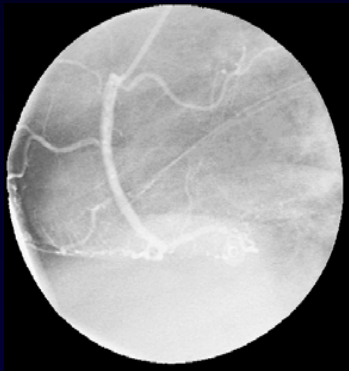


# Clinical Trials of GP IIb/IIIa Inhibitors: Meta-Analysis Death/MI at 30 days



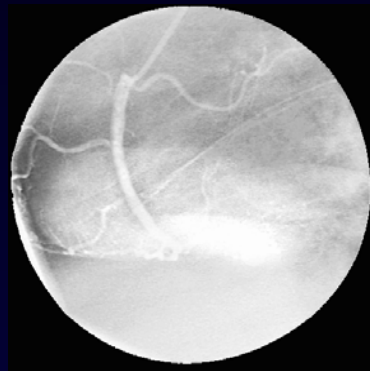
# Evaluation of Myocardial Perfusion

## TIMI Myocardial Perfusion Grading



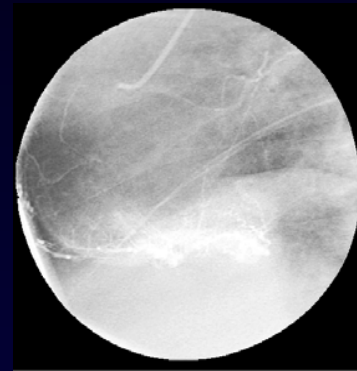
### TMP Grade 3

Normal ground glass  
appearance of blush  
Dye mildly persistent  
at end of washout



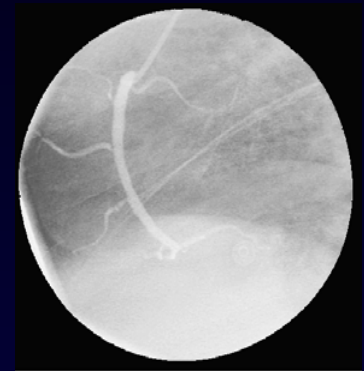
### TMP Grade 2

Dye strongly persistent  
at end of washout  
Gone by next injection



### TMP Grade 1

Stain present  
Blush persists  
on next injection

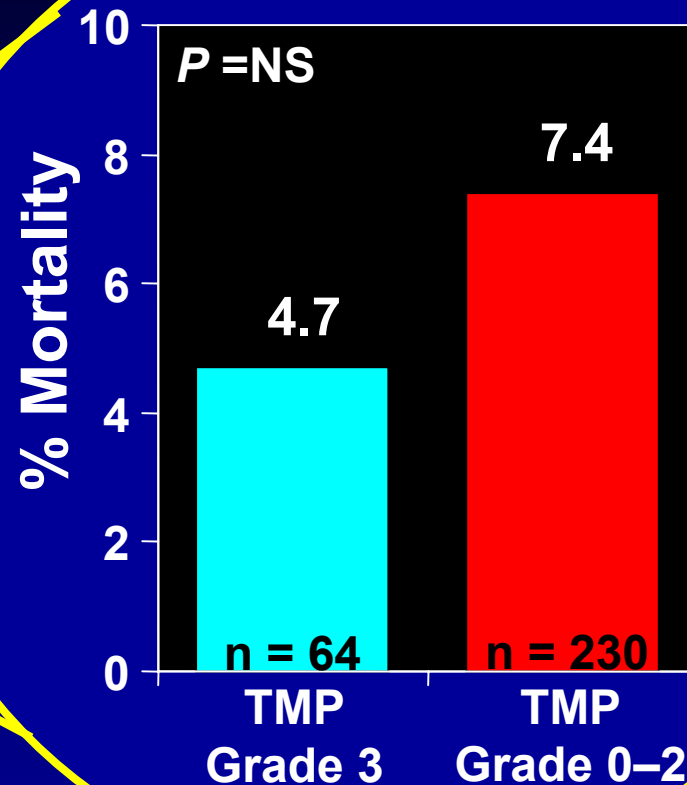
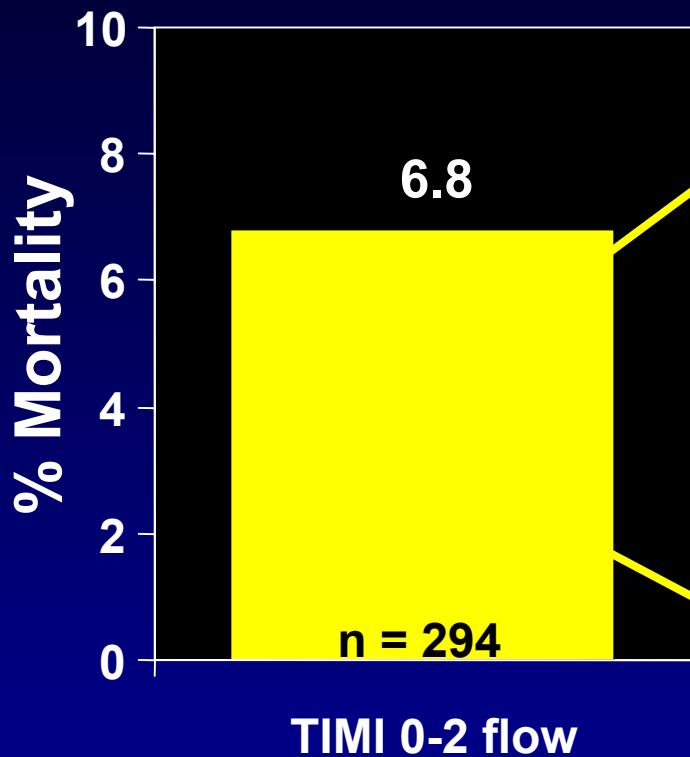


### TMP Grade 0

No or minimal blush

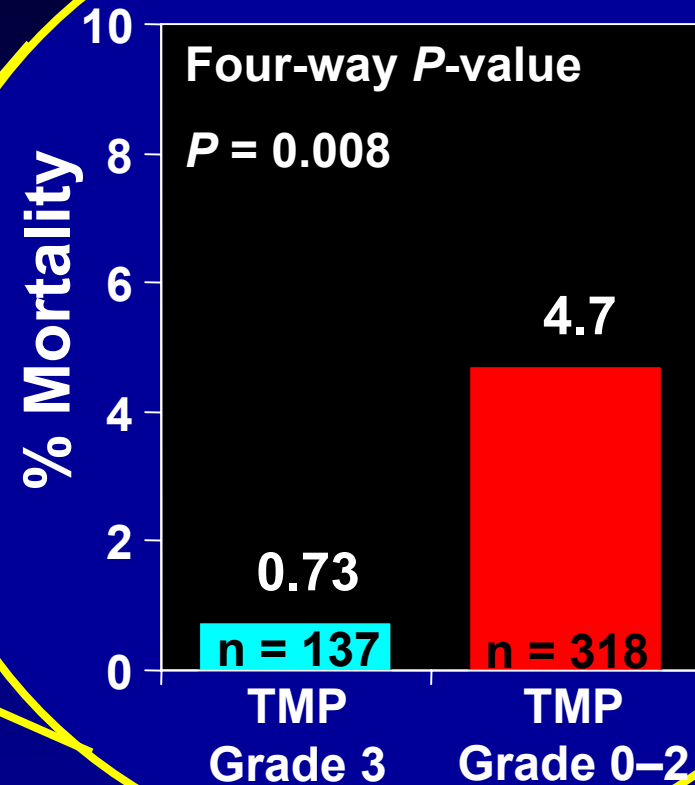
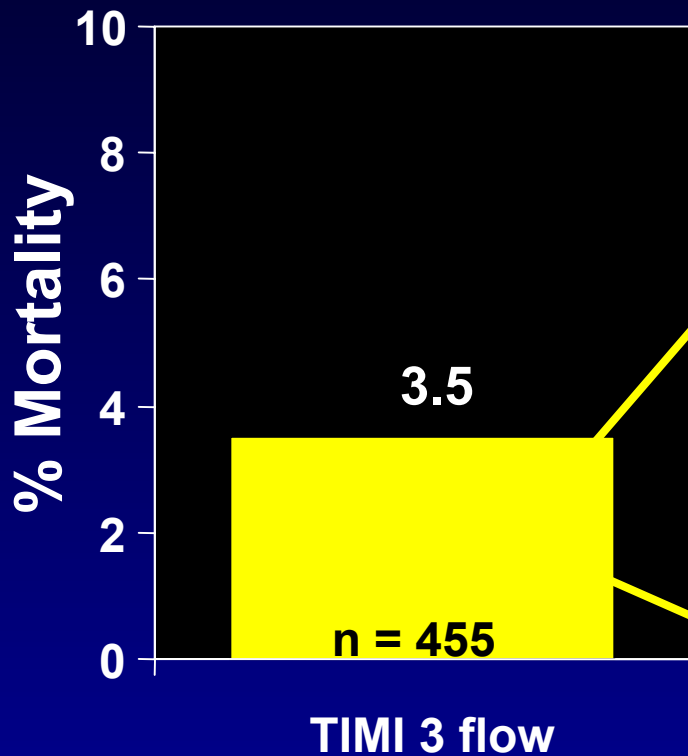
## Mortality Based on TMP Grade Patients With 90-Minute TIMI 0–2 flow

### TIMI Myocardial Perfusion Grade (TMP Grade)



## Mortality Based on TMP Grade in Patients With 90-Minute TIMI 3 Flow

### TIMI Myocardial Perfusion Grade (TMP Grade)



# CURE

## Cardiovascular death/MI/stroke

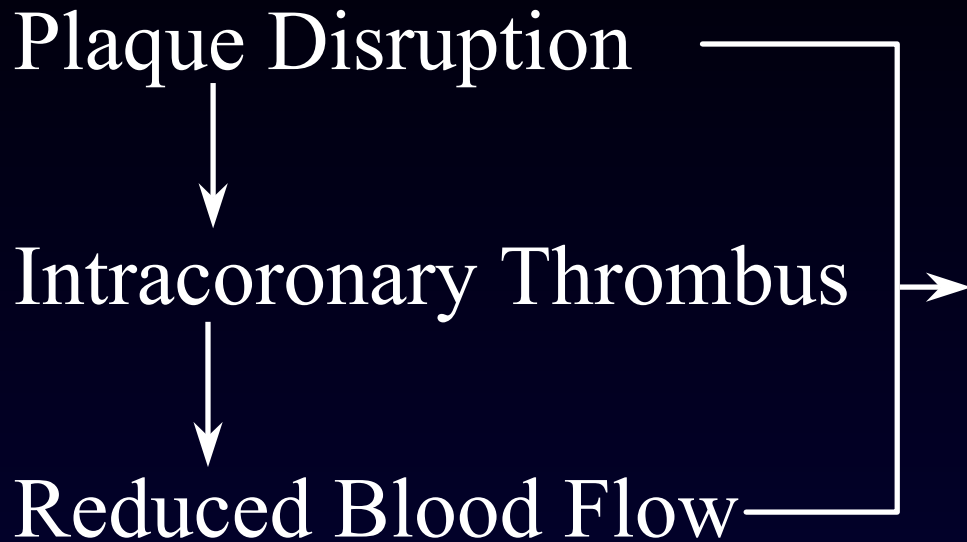
Time period	Placebo	Clopidogrel	Relative risk (95% CI)
0-30 days	5.4 %	4.3 %	0.79 (0.67-0.92)
30 days-1 year	6.3 %	5.2 %	0.82 (0.70-0.95)

# CURE

## Outcome Stratified by TIMI Risk Score

Risk group	Clopidogrel	Placebo	Relative risk (95% CI)	p
Low (TIMI 1 to 2)	4.1%	5.7%	0.71 (0.52- 0.97)	0.04
<b>Intermediate</b> (TIMI 3 to 4)	9.8%	11.4%	0.85 (0.74- 0.98)	0.03
<b>High</b> (TIMI 5 to 7)	15.9%	20.7%	0.73 (0.60- 0.90)	0.004

# Pathophysiology



# Clinical Diagnosis

Asymptomatic

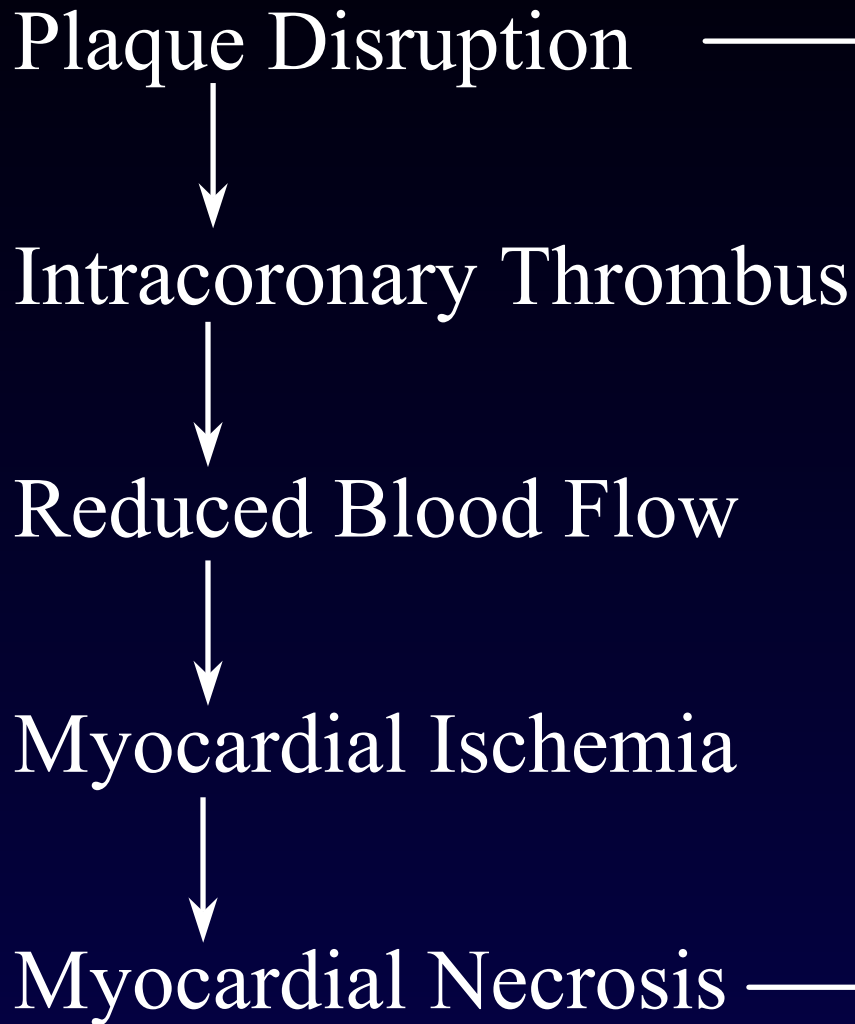
**Disease State**

- HTN
- DM
- Smoking
- Genes
- Age
- lifestyle

Lipids  
CRP

———— Risk —————>

## Pathophysiology



## Clinical Diagnosis

Symptomatic

Acute  
Event

ACI  
AMI

Risk

# Management of Acute Coronary Syndromes

- **Cornerstones of therapy**

- \* ASA, Statins, B-blockers

- **Issues for 2003**

- \* Protecting the microcirculation

- \* Acute: IIb/IIIa inhibitors vs clopidogrel

- \* Plaque passivation: ↓ thrombogenicity

- \* Long-term: anti-platelet +/- anti-thrombin