

North American Thrombosis Forum

Acute Coronary Syndromes:

Antithrombotic Therapy

Elliott M. Antman, MD

Cardiovascular Division
Brigham and Women's Hospital
Harvard Medical School

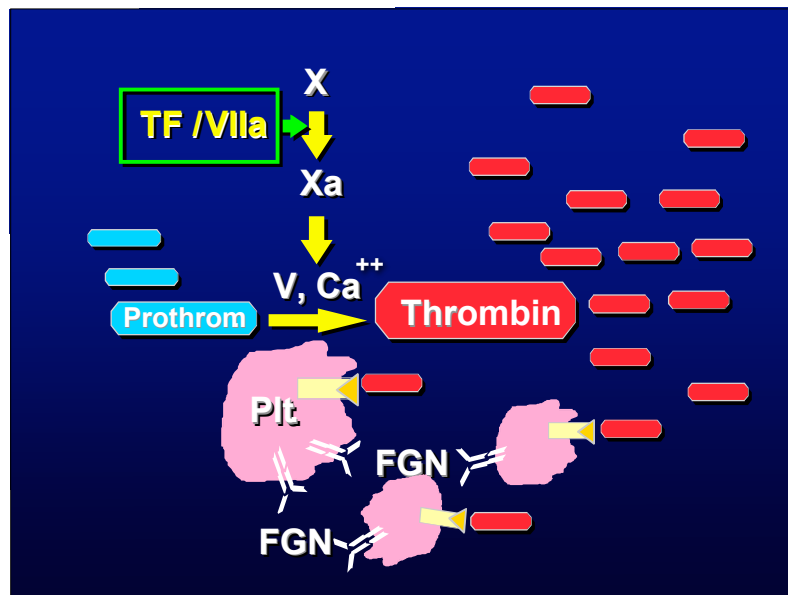


Disclosure

The TIMI Study Group has received research / grant support in the past 2 yrs through the Brigham & Women's Hospital with funding from (in alphabetical order):

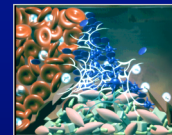
Accumetrics, Inc.
Amgen, Inc.
AstraZeneca Pharmaceuticals LP
Baxter
Bayer Healthcare LLC
Beckman Coulter, Inc.
Biosite Incorporated
Bristol-Myers Squibb
CardioKinetix
CV Therapeutics, Inc.
Daichi-Sankyo
Eli Lilly and Company
FoldRx
GlaxoSmithKline
INO Therapeutics LLC
Inotek Pharmaceuticals Corporation

The National Institutes of Health
Integrated Therapeutics Corporation
KAI Pharmaceuticals
Merck & Co., Inc.
Millennium Pharmaceuticals, Inc.
Novartis Pharmaceuticals
Nuvelo, Inc.
Ortho-Clinical Diagnostics, Inc.
Pfizer, Inc.
Roche Diagnostics Corporation
Roche Diagnostics GmbH
Sanofi-Aventis
Sanofi-Synthelabo Recherche
Schering-Plough Research Institute
St Jude Medical



Antithrombotic Goals in ACS

Medical Management



Coagulation Cascade

1. Inhibit Existing Thrombus
2. Prevent New Thrombus Formation (Acute phase of Rx)

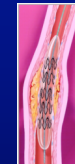
Platelets

1. Prevent Adhesion
2. Prevent Activation
3. Prevent Aggregation

Long term:

1. Prevent thrombus formation on existing plaques
2. Prevent new plaques from forming (? Role of antithrombotic Rx)

Interface with Catheter-Based Therapy



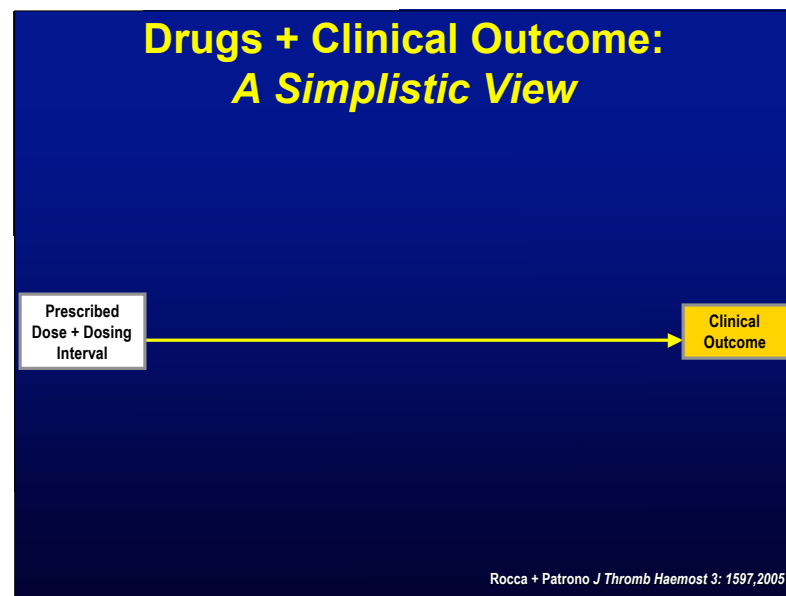
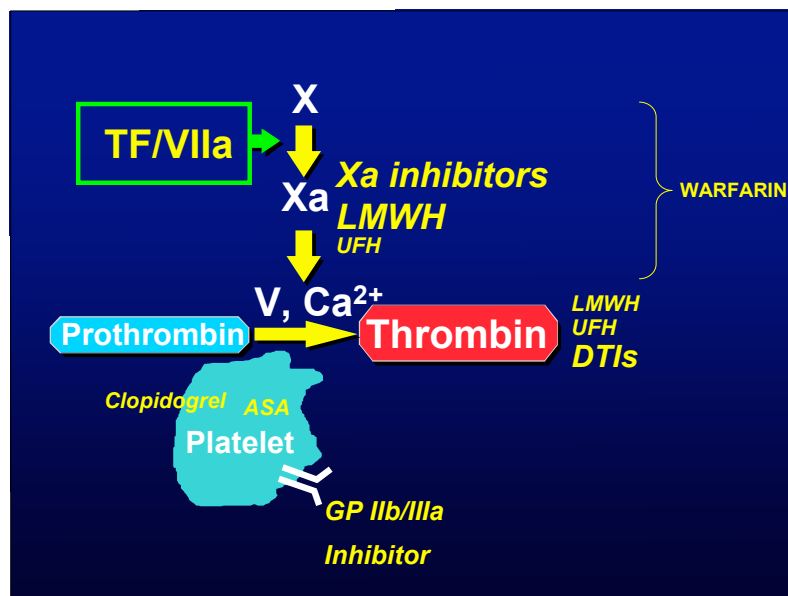
Coagulation Cascade

Prevent New Thrombus Formation:
Catheter
Stent (early)

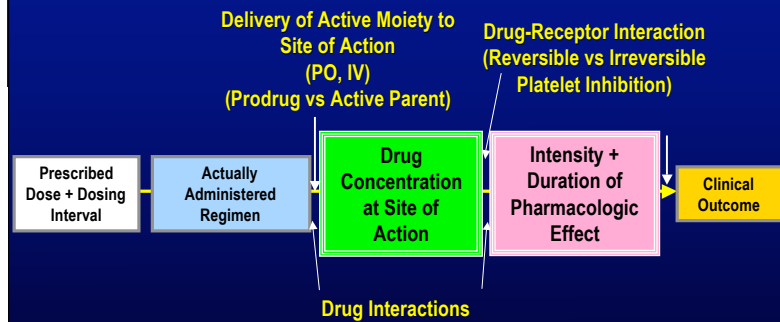
Platelets

1. Prevent Adhesion
2. Prevent Activation
3. Prevent Aggregation

} Prevent
Late Stent
Thrombosis

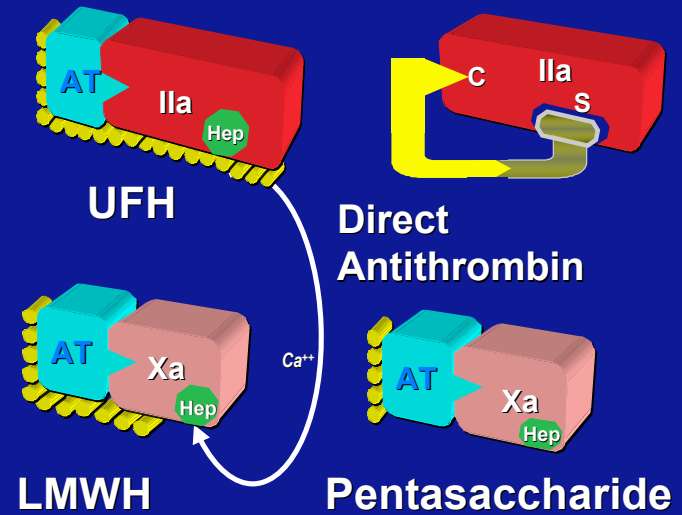


Drugs + Clinical Outcome: A Complex Relationship



Rocca + Patrono *J Thromb Haemost* 3: 1597,2005

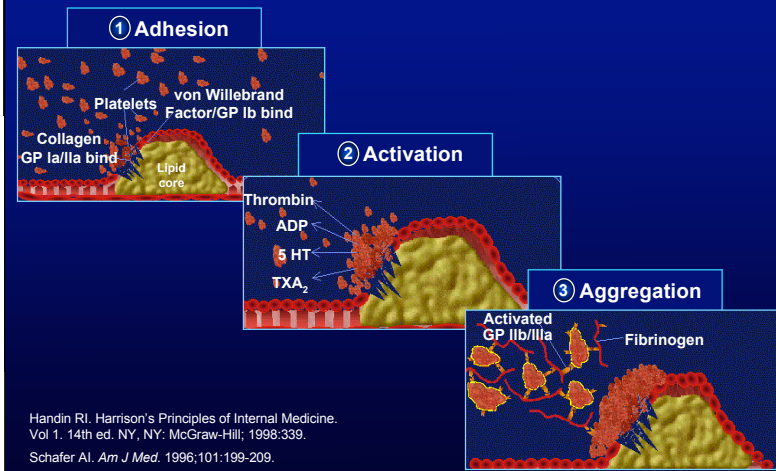
Anticoagulants for UA/NSTEMI



Anticoagulant Scorecard

	UFH	ENOX	FONDA	BIVAL
Route	IV (SC)	IV, SC	SC (IV)	IV
Monitor	aPTT, ACT	No	No	aPTT, ACT
UA/NSTEMI	Yes	Yes	Yes	Yes
STEMI_{PCI}^{Lytic}	Yes ^{Lytic PCI}	Yes ^{Lytic PCI}	Yes ^{Lytic}	Yes ^{PCI}
Bleeding	Yes	Yes	Less ?	Less
HIT	Yes	Less	None ?	None
PCI	Yes	Yes	Need anti IIa Rx	Yes
CABG	Yes	No	No	Possible
Antidote	Protamine	Protamine	None	None

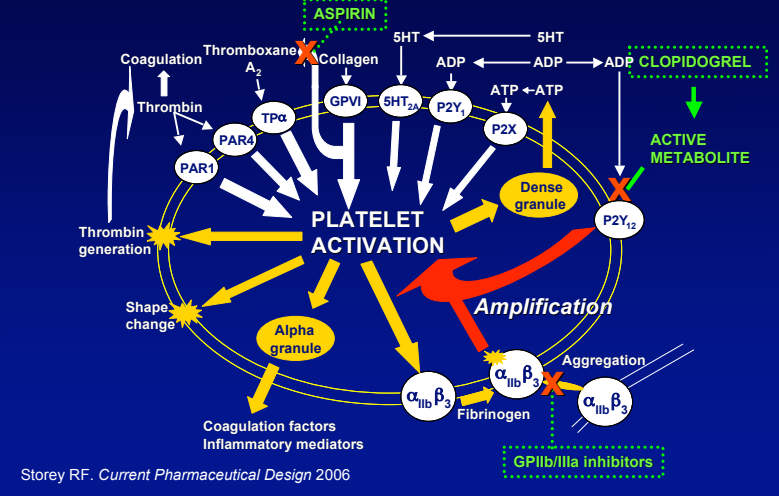
Platelet Cascade in Thrombus Formation



Antiplatelet Therapy in Ischemic Heart Disease

	Primary Prevention	UA/NSTEMI (Medical Rx)	STEMI (Medical Rx)	PCI
ASA	✓	✓	✓	✓
Thienopyridine (LD, MD)		✓	✓	✓
IV GP IIb/IIIa		✓	✓	✓

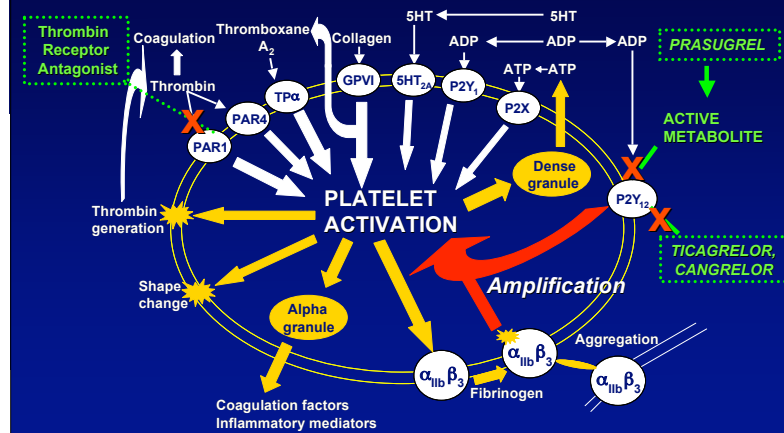
Platelet Activation + Aggregation: Current Rx Options



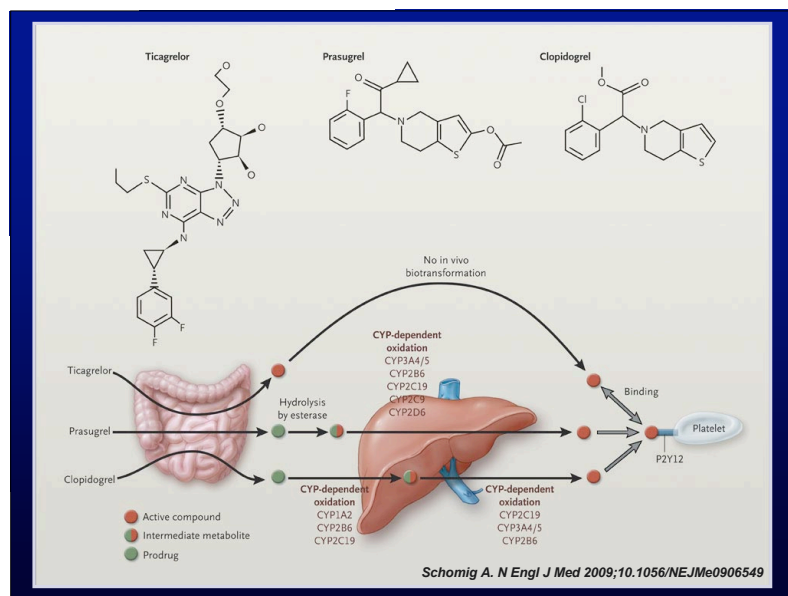
Antiplatelet Scorecard

	ASA	Clopidogrel	GP IIb/IIIa Inhib
Route	PO	PO	IV
Monitor	No (?)	Uncertain	No
Dose	325	300-600 (?)	Yes
LD MD	75-100	75 (150)	Yes (decr in renal)
UA/NSTEMI	Yes (Indef)	Yes (1 yr)	Yes
STEMI	Lytic PCI	Lytic (no LD > 75 y) PCI	PCI
Bleeding	Yes	Yes	Yes
PCI	Dual antiplatelet Rx (*DES*)		Yes
CABG	Yes	Stop prior to CABG	
Antidote	None	None	None
Issues	Variable Response (Clop >> ASA)		? Need w clopid. Not necessary pre PCI

Platelet Activation + Aggregation: New Agents



Storey RF. Current Pharmaceutical Design 2006



Antiplatelet Scorecard: New Agents

	Prasugrel	Ticagrelor
Route	PO	PO
Monitor	Not Necessary	
Dose LD MD	60 mg 10 mg daily	180 mg 90 mg BID
UA/NSTEMI	Yes	Yes
STEMI	PCI	PCI
Bleeding	Yes	Yes
PCI	Dual antiplatelet Rx w ASA	
CABG	Stop prior to CABG	
Antidote	None	None
Issues	Irreversible; Consider 5mg MD if < 60 kg and/or ≥ 75 y	Reversible (Compliance!); Dyspnea, Ventr Pauses

