

HICC 2007 – St. Gallen

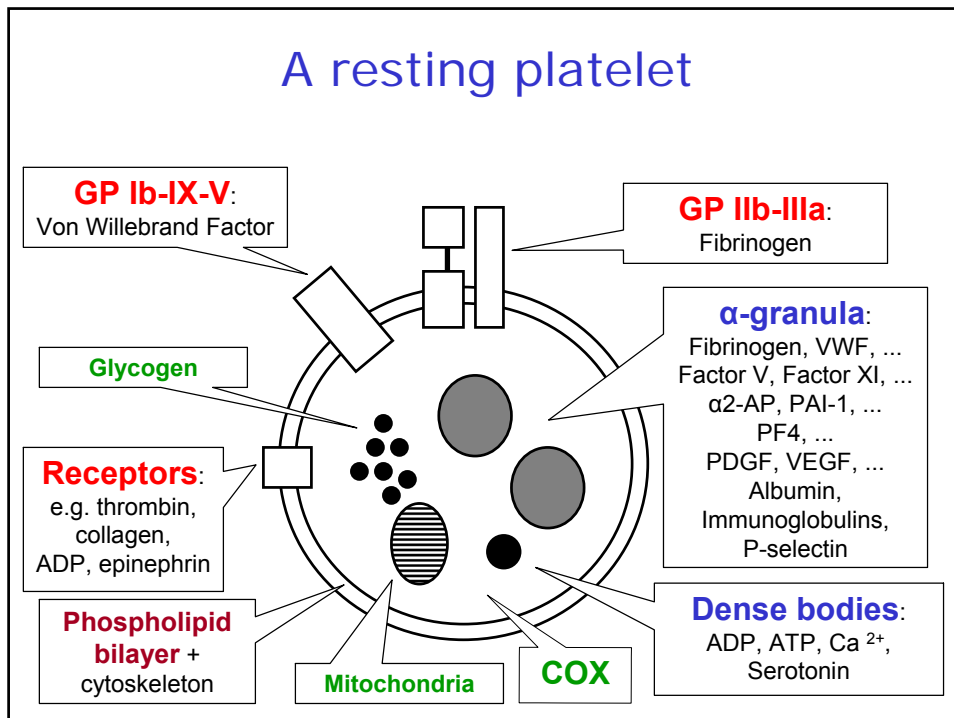
14. September 2007

Platelets
*how they work and
what we do to make them stall*

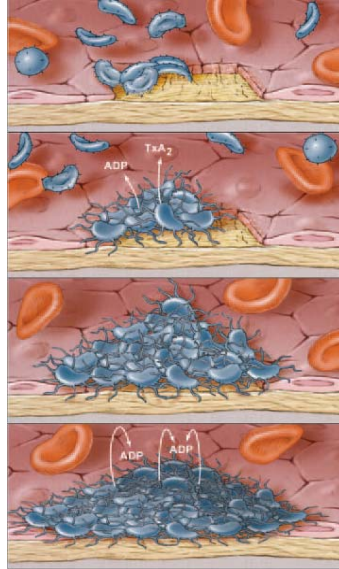
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A resting platelet

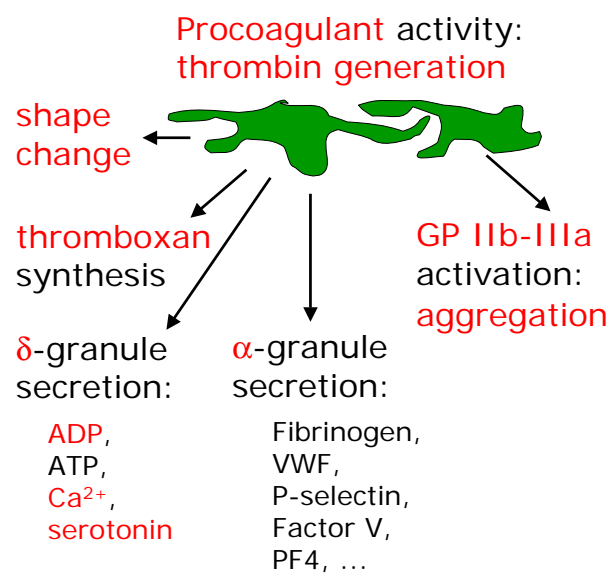


Platelet function

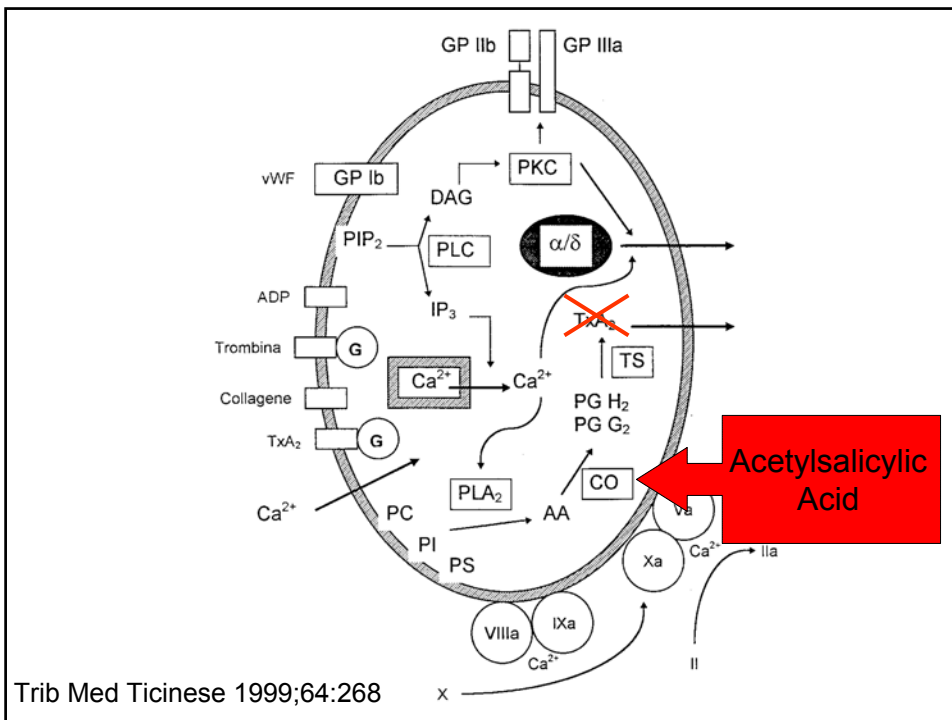


Blood 2006;108:2883

Platelet activation

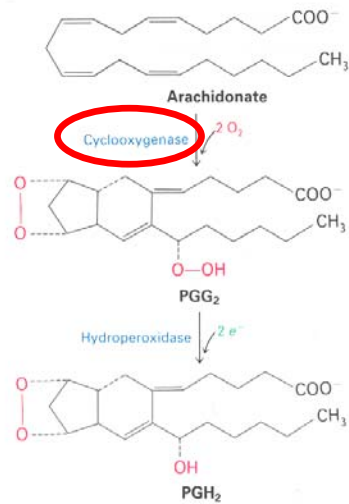


Anti-platelet Drugs



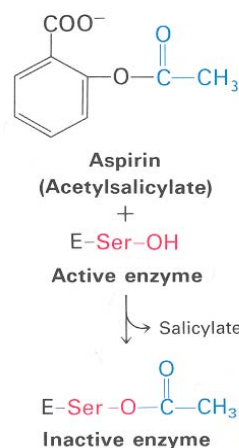
Acetylsalicylic Acid

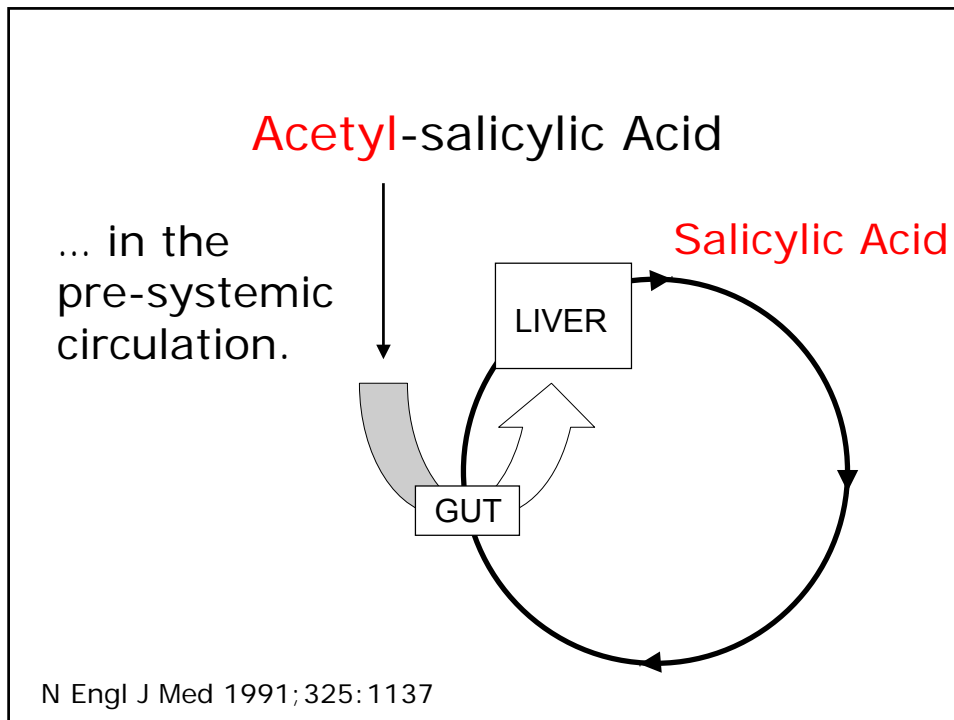
... inhibits the synthesis of prostaglandins ...



Acetylsalicylic Acid

... by irreversibly acetylating a specific serine hydroxyl group (Ser 529) of the cyclooxygenase ...





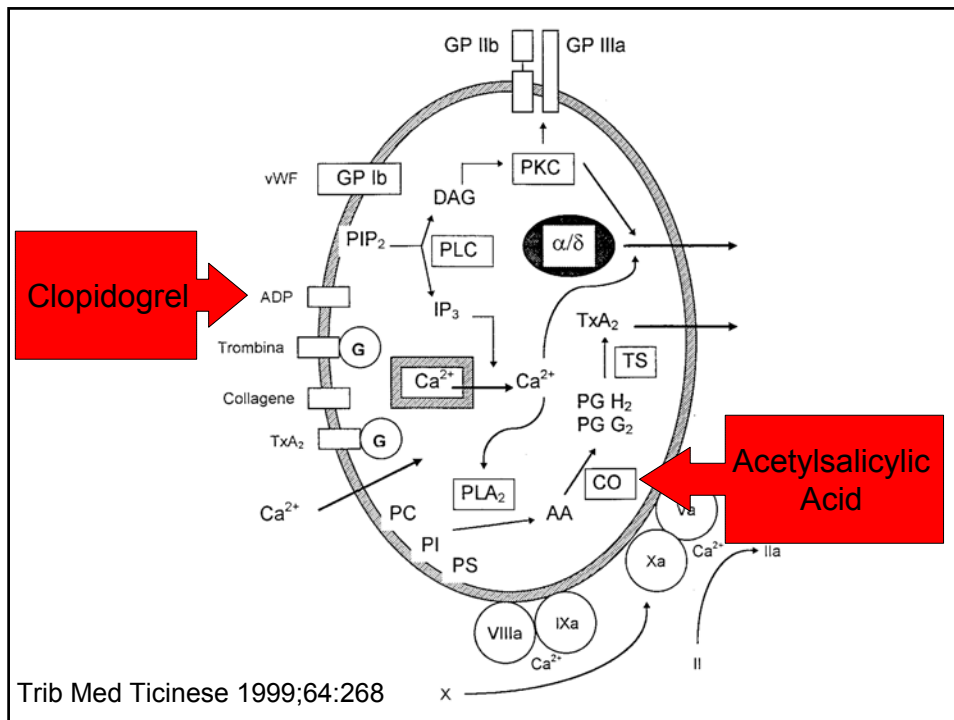
Acetylsalicylic Acid

Irreversible COX inhibition (TxA₂)

RRR ≈ **25 %** (Placebo)

Cheap

► Standard



Clopidogrel

Thienopyridine derivative

Irreversible inhibition of ADP-mediated platelet activation

Hepatic metabolism

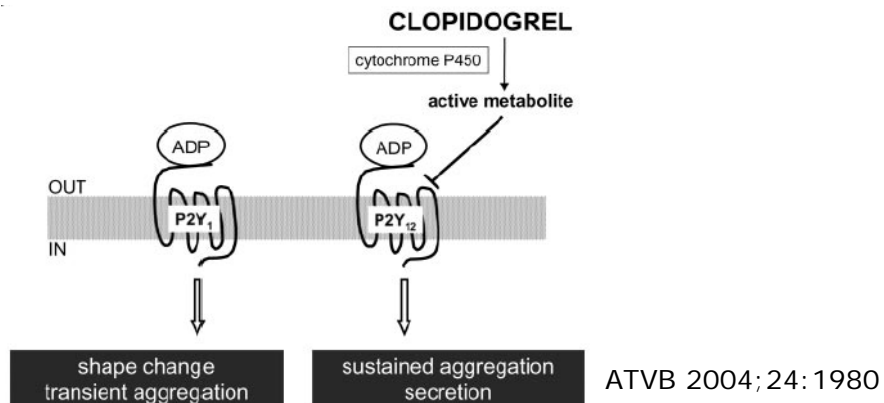
Maximal **action is delayed**

after 75 mg/d p.os: 3-5 days

after 300 mg p.os: 4-6 hours

Clopidogrel

The **active metabolites** of clopidogrel **inhibit** the $P2Y_{12}$ receptor for **ADP**



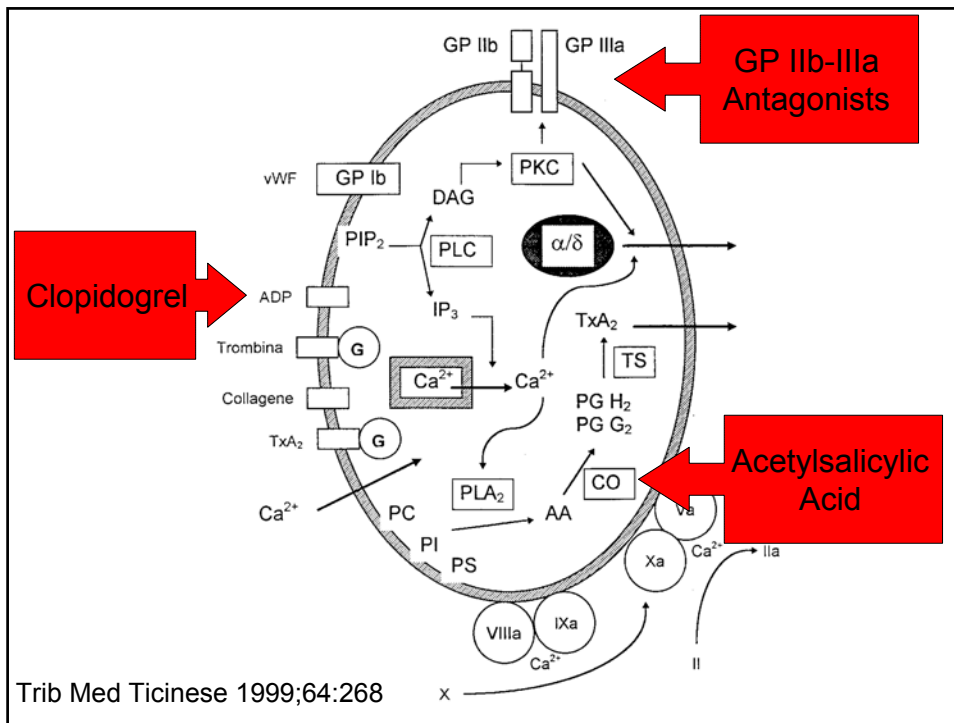
Clopidogrel

Irreversible inhibition of the $P2Y_{12}$ **ADP** receptor

RRR \approx **8 %** (Aspirin)

Expensive

► **Combination with ASA**



GPIIb-IIIa Antagonists

Table 63.1. Structures and uses for the three approved GP IIb-IIIa antagonists

Generic name	Epitifibatide	Tirofiban	Abciximab
Brand name	INTEGRILIN®	AGGRASTAT®	ReoPro®
Structure			Fab fragment of the chimeric human-murine monoclonal antibody 7E3
Affinity (K_D) for GP IIb-IIIa	120 nmol/l	15 nmol/l	5 nmol/l
Approved for use	PCI and unstable angina/ non Q-wave MI	unstable angina/non Q-wave MI	PCI

P. Gresele et al. (eds) Platelets. Cambridge University Press, 2002; 943

GPIIb-IIIa Antagonists

Reversible inhibition of the
Fibrinogen receptor

Very Expensive

- ▶ interventional cardiology
and only high risk patients?

The D&G - connection

Dextrans

Garlic

Ginger

Ginko

Green tea

Ginseng

The D&G - connection

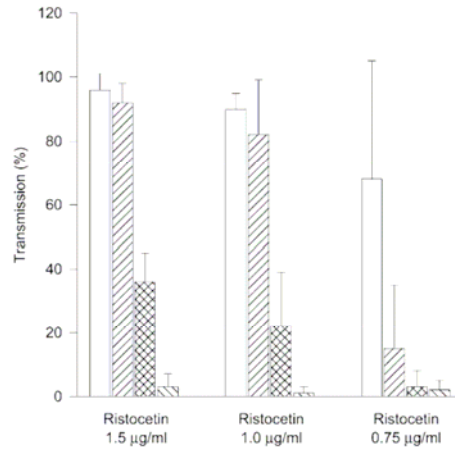
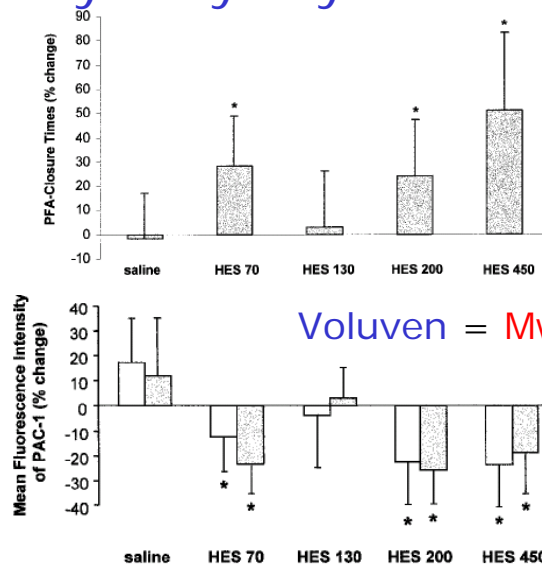


Fig. 3. Influence of DXS 5000 on platelet aggregation with ristocetin. Results are given as mean \pm S.D. of five separate experiments. \square 0, ▨ 100, ▩ 200, and ■ 1000 $\mu\text{g/ml}$ DXS 5000.

Macrodex = Mw 70'000

Thromb Res. 2002; 105: 441

hydroxyethyl starch



Voluven = Mw 130 kD

Anesth Analg 2001; 92: 1402