Resistance to Antiplatelet agents: Application of 2 Platelet Function Tests

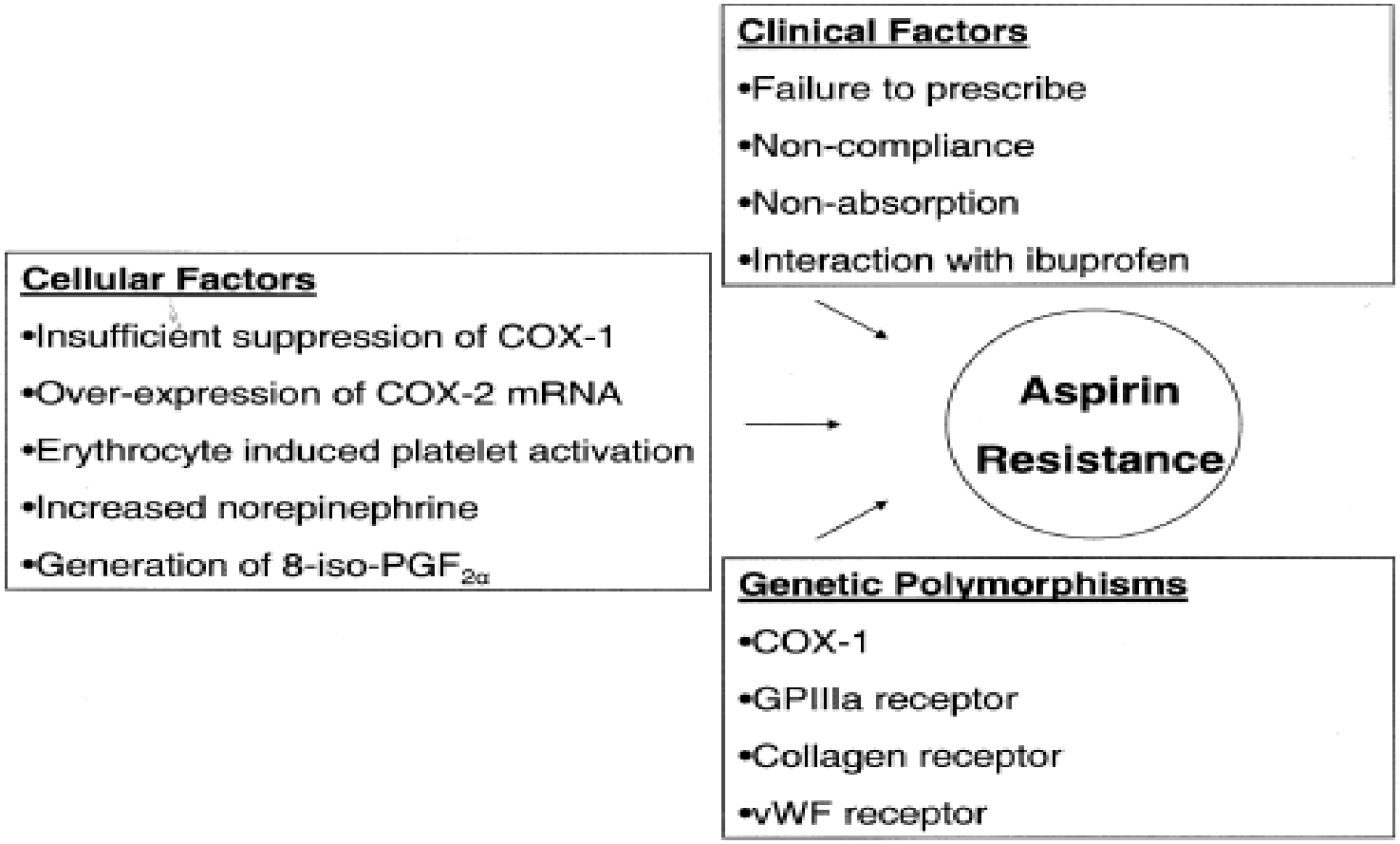
Ioannidis George

Introduction

- It seems that aspirin resistance is not that rare as doctors think.
- A similar phenomenon with clopidogrel, attracts medical attention over the last years
- Their occurrence is often associated with failure to prevent serious vascular events in patients with symptomatic atherothrombosis

Antiplatelets *treatment failure* would be a more appropriate term in this occasion

Aspirin Resistance-mechanisms proposed



Aim

To reveal or detect its presence in patients receiving antiplatelet medications, we used two different and specific assays:

1. ***Platelet aggregometry***
2. ***PFA-100 Dade Behring (Platelet Function Analyzer)***

Material

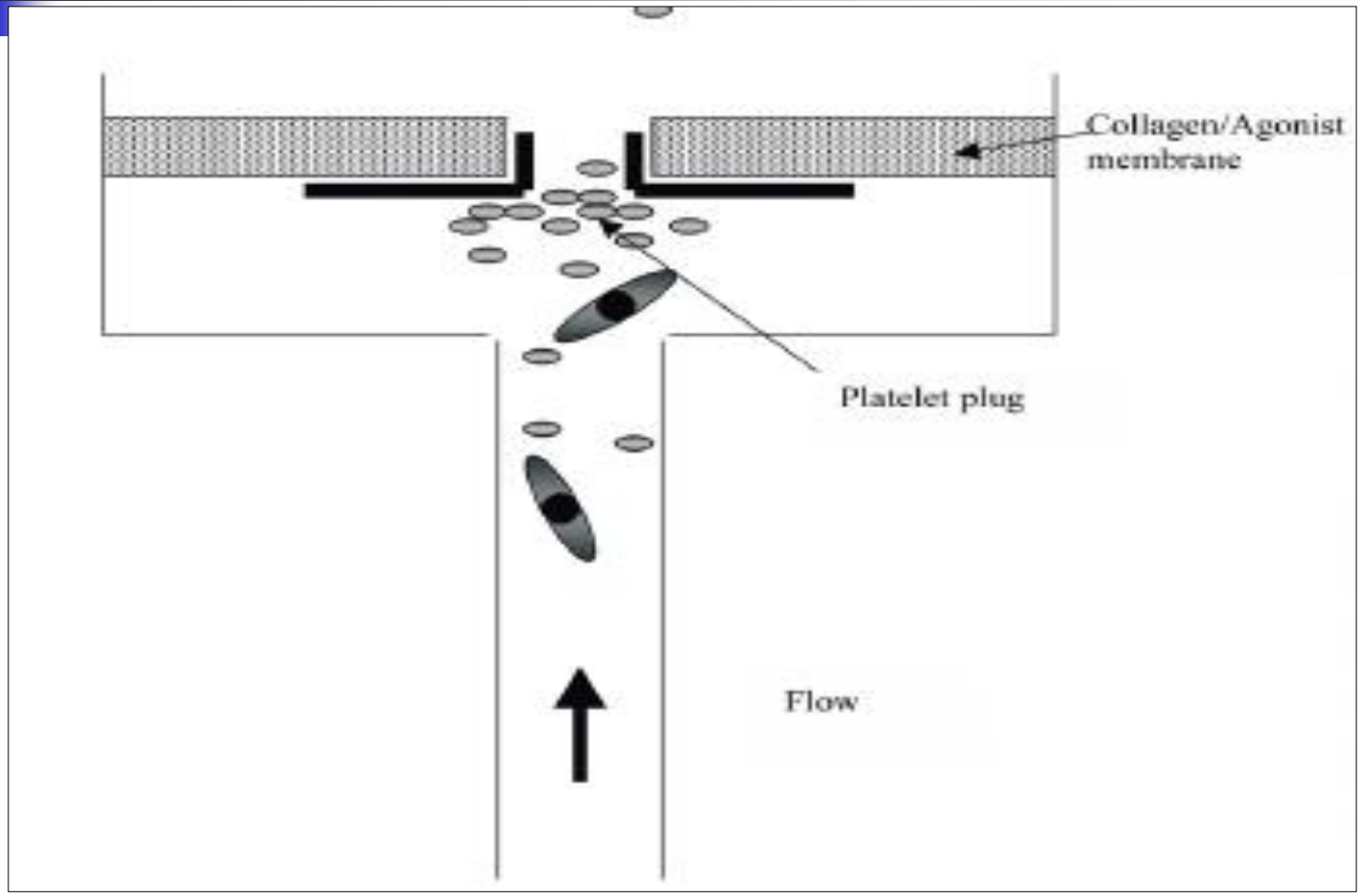
- ***29*** normal persons (medications-free)
  (14 males and 15 females with mean age of 42±12 yrs)
- ***49*** persons taking *Aspirin*
  (24 males and 25 females with mean age of 39±15yrs)
- ***8*** persons taking *Clopidogrel*
  (6 males and 2 females with mean age of 41±8 yrs)

Methods

1. Platelet aggregation (P.I.C.Aggregometer, Chronolog-Co USA), using ***ADP*** and ***collagen*** as agonists and

2. PFA-100 (DADE-Behring) with the reagents Collagen/ADP and Collagen/Epinephrine.

PFA-100 basic concept



Results

Findings from the **normal persons** group:

- Mean values for the PFA-100 results had as:
  - Colla/ADP = 86.65±15.94sec and - Colla/Epi = 105.91±15.83sec.

- Mean values for the aggregation results had as:
  - ADP = 70.34±10.63% and - Collagen = 69.29±9.42%

Adding 3 Standard Deviations (confidence limits 99%), strict limits were submitted in order to establish the cut-off value for PFA-100 Closure Time.

Results-Aspirin

13 out of 49 persons (25.5%) receiving daily aspirin and tested with aggregometry met our criteria for the ¨*ASA-non responders*¨ definition

The respective percentage for the PFA-100 was 40.8% (20 out of 49)

The difference between the two methods, was not statistically significant. ($p<0.1$)

PFA vs P.I.C.A

We assume that PFA-100 is an appropriate and highly sensitive assay, for detecting biochemical Aspirin resistance, while Platelet aggregation induced by ADP and Collagen appears to be slightly less sensitive.

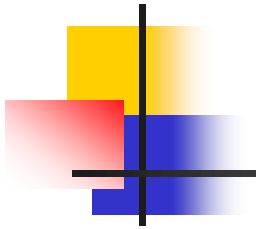
Adding Arachidonic Acid as agonist in the aggregometer might diminish the gap by increasing the sensitivity of the assay in aspirin treated PRPs

Results-Clopidogrel

- The value and the place of platelet aggregation in the monitoring of patients taking clopidogrel remains constant, as it reveals 1 non-responder for every 8 patients taking this medication.

- PFA-100 in not of the same sensitivity, because only 1 in 8 patients hardly touched the defined response levels.PFA-100 remained completely insensitive for the other 7 patients tested, mimicking results from patients not taking clopidogrel at all.

- PFA-100 can not detect clopidogrel's effects on Platelets, Therefore it should not be used for this purpose. The above results totally agree.



Review of the relevant literature and online search in MEDLINE (1995-2005)* supports the above findings

*Keywords used:aspirin,clopidogrel,resistance,PFA100,aggregometer