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ARACHIDONIC ACID-INDUCED PLATELET AGGREGATION AND THROMBOXANE PRODUCTION IN WASHED HUMAN PLATELETS

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Enhanced platelet aggregation has been implicated in the pathogenesis of many thromboembolic-related diseases. Though it's a rather complex process; as many platelet and tissue 'mediators' are involved, platelet function seems to have a pivotal role on the initial microthrombus formation. Conventionally platelet rich plasma has been successfully used for the assessment of platelet function so far, while the method suffers the insensitivity to detect the fine controlling mechanism of the involved mediators. We anticipate to see a better insight into the roles of the platelets in a well defined medium and delineate further the relationship of those mediators with platelet aggregatability to various related diseases.

Washed human platelet suspension (adjusted to 0.2 million/microliter) in isotonic tris-buffer, pH 7.4, was prepared from citrate treated blood of human volunteers. Platelet derived thromboxane A-2, a known potent mediator taking part in the aggregatory process was followed in the medium by a radioimmunoassay method for thromboxane B-2 (the representative stable metabolite of thromboxane A-2). Platelet aggregation was monitored by a turbidometric method. Incubation of arachidonic acid with platelet suspension was carried out for five minutes at room temperature. Arachidonic acid caused platelete aggregation and thromboxane production in a dose dependent manner. The dose-response curve of arachidonic acid on thromboxane production appeared to be of characteristic bell-shape; i.e., up to 100 micromolars arachidonic acid progressively increased thromboxane production, while the inverse response was shown in higher doses. The aggregatory response of the platelets to arachidonic acid ran parallel to the bell-shape curve of thromboxane, except that the former peaked at 1000 micromolars while the levels of the latter were declining.

The data clearly indicates that arachidonic acid can induce platelet aggregation in a dose dependent manner and presumably thromboxane is its mediator. The suppressive effect of arachidonic acid on the platelet thromboxane production preceeds its supressive effect on platelet aggregation reemphasizing the closely mediating role of thromboxane in the aggregatory process. These findings further suggest that arachidonic acid metabolism in the platelets involves not only in the pro-aggregatory pathway but a more complex modulating role could be foreseen.