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Editorial

Miths and reality of the sticky platelet syndrome

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In the 80´s Holliday and then Mammen described hereditary platelet hyperreactivity and called it Sticky Platelet Syndrome[1]. Hyperreactivity was defined in the laboratory by detection of platelet aggregation with concentrations of agonists (ADP and/or epinephrine) that are lower than those used in the routine laboratory. SPS was described as type I, II, or III, based on the agonist to which platelets overreacted (both ADP and epinephrine, ADP alone, or epinephrine alone, respectively). In his description of SPS, Mammen emphasized the distinction between acquired platelet hyperaggregability and SPS, which he considered an inherited, autosomal dominant disorder. Interestingly, he described both arterial and venous thrombosis as being associated with this platelet phenotype, and suggested that aspirin could be used to prevent further thrombosis.

There has been extensive discussion over the years of whether SPS is a real entity. This questioning is in part due to the fact that there are multiple transient or persistent acquired factors that induce a hyperreactive platelet phenotype[2]. Thus in order to make a diagnosis of hereditary SPS, one must prove that the platelet hyperreactivity persists over time and that more than one family member expresses the same phenotype. Another factor that has caused controversy in diagnosing platelet hyperreactivity is the fact that the concentrations of agonists used are not standardized, nor is the percent of platelet aggregation which is considered positive. So, for example, the usual percent of platelet aggregation which is considered normal at full concentrations of agonists is greater than 60%. If this cutoff is reduced, or if the agonists are not sufficiently diluted, then a higher percentage of individuals will be considered to have hyperreactive platelets. Figure 1 shows classical platelet aggregometry curves for platelet hyperreactivity to epinephrine.

The hyperreactive phenotype may not be restricted to ADP and or epinephrine. Yee et al. showed that in healthy individuals, there is a subset that may have hyperreactive platelets, and that hyperreactivity *in vitro* to one agonist tended to demonstrate a similar response to others, including collagen, collagen-related peptide, and ristocetin, suggesting that hyperreactivity is a global characteristic of platelets [3]. The nature of the defect or defects that cause platelet hyperreactivity is still unknown. It has been shown that human platelets exhibit both adrenergic and dopaminergic receptors that are influenced by different catecholamines, yet no defect in these receptors has been described. Recently, vitamin K-dependent protein Gas6 polymorphisms have been proposed to be implicated [4]. The fact that high fibrinogen levels correlate with this phenotype in healthy women suggests that both platelet or plasma factors may be responsible. It is noteworthy that aggregometry is carried out using platelet rich plasma, thus both patient platelets as well as patient plasma are being tested [3].

The articles published by both Kubisz *et al.* and Ruiz-Argüelles *et al*. in this issue, as well as prior work by the same groups, gives further support to the hereditary nature of this phenotype[5-7]. Independently of whether the name sticky platelet syndrome is used, there are families with both venous and arterial thromboembolic events in whom frank, persistent, platelet hyperreactivity is detected *in vitro*, either alone or in the presence of other prothrombotic risk factors. The fact that treatment with therapeutic anticoagulation may not be required if SPS is

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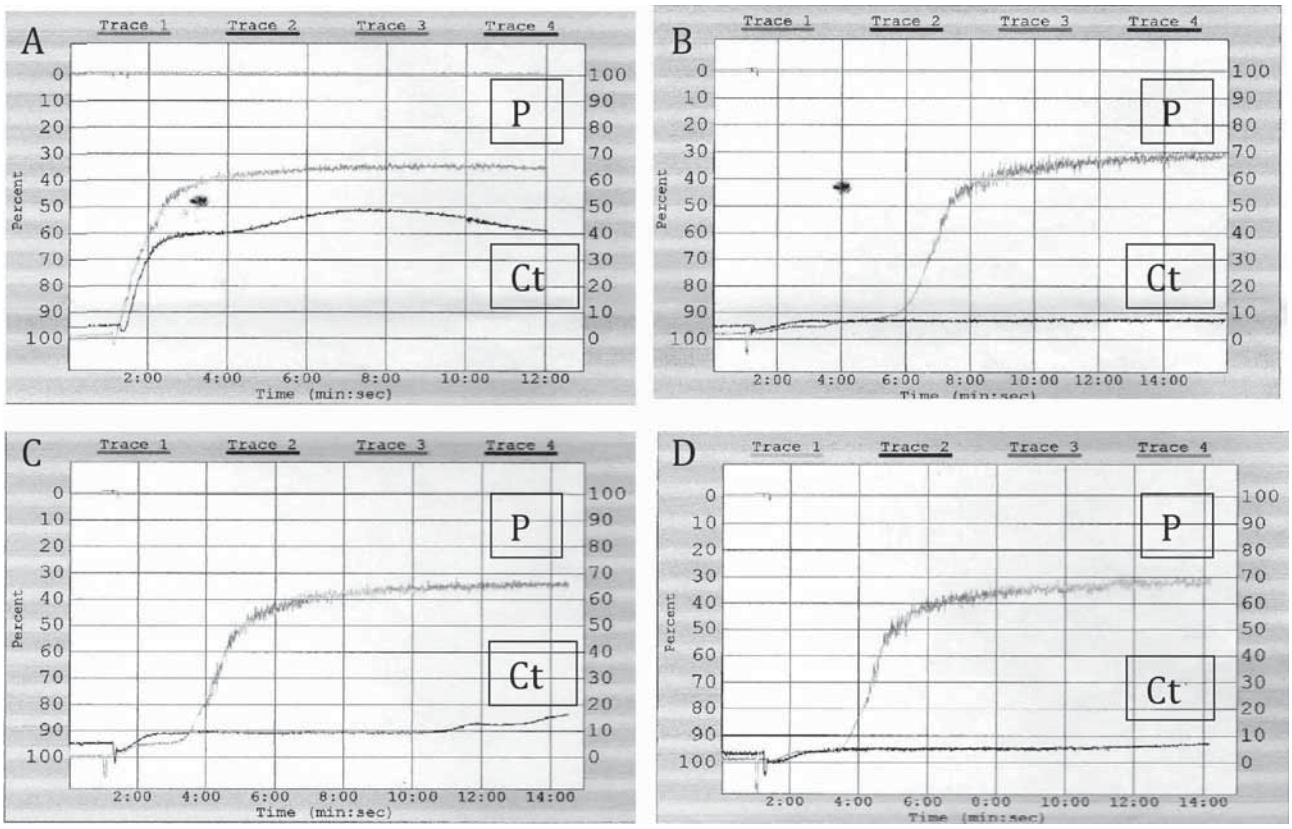

Figure 1. Platelet hyperreactivity to epinephrine.
Platelet Aggregometry using epinephrine at 1 µM (A), or with progressive dilutions 0.5 µM (B), 0.25 µM (C) and 0.125 µM (D) is shown. Curves depict percent aggregation for patient (Pt) or control (Ctr) platelet rich plasma.

diagnosed in individuals with venous thrombosis makes a strong case for thinking about this syndrome and ordering aggregometry when the diagnosis is clinically suggestive.

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