Platelet Malondialdehyde Production and Aggregation Responses Induced by Arachidonate, Prostaglandin-G2, Collagen, and Epinephrine in 12 Patients With Storage Pool Deficiency

By Harvey J. Weiss and Bruce Lages

We assessed the integrity of the prostaglandin synthetic pathway by measuring malondialdehyde (MDA) production and studied platelet aggregation responses to arachidonic acid and PGG2 in 12 patients with storage pool deficiency (SPD). Eight patients were deficient only in dense granules (δ-SPD) and four were deficient in both dense and α-granules (αδ-SPD). Production of MDA in response to arachidonic acid (AA), epinephrine, and collagen suggested that the transformation of AA to prostaglandin metabolites was normal in δ-SPD but abnormal in αδ-SPD and that the liberation of AA from phospholipids was abnormal in the majority of patients with SPD. Since the content of secretable adenosine diphosphate (ADP) is diminished in SPD platelets, the aggregation responses of these platelets to AA and PGG2 were studied to help answer the question whether these agents aggregate platelets directly or through release of endogenous ADP. Among patients with δ-SPD, aggregation by both AA and PGG2 was decreased in four albinos whose platelets were markedly deficient in ADP. In contrast, normal, or less strikingly abnormal, responses were observed in patients whose platelets either contained higher levels of platelet ADP or showed increased sensitivity to ADP. The more markedly impaired responses to AA and PGG2 in patients with αδ-SPD suggest that substances derived from α-granules may also play a role in platelet aggregation by these agents. The aggregation responses in these patients with various types of SPD is consistent with a theory that granule-derived ADP mediates platelet aggregation by AA and PGG2.

STIMULATION of platelets by aggregation and secretion-inducing agents results in the release of granule-bound substances, including adenosine diphosphate (ADP) and the enzymatic liberation of arachidonic acid from platelet phospholipids. Arachidonic acid is subsequently converted to the prostaglandin (PG) endoperoxides PGG2 and PGH2 and to thromboxane A2. It is generally held that thromboxane A2 and released ADP are responsible for collagen-induced platelet aggregation and, in part, for the augmented (secondary) aggregation responses to ADP and epinephrine. Presently unanswered is the question whether thromboxane A2 or arachidonic acid and PGG2(H2) that are converted to thromboxane A2 aggregates platelets directly or through an effect of released ADP. The latter theory is consistent with our previous findings of impaired arachidonate and endoperoxide-induced platelet aggregation in five patients with storage pool deficiency (SPD), a disease characterized by diminished amounts of granule-bound, secretable ADP. In contrast, however, Ingerman et al. and Minkes et al. have reported normal aggregation responses to arachidonic acid in a family and patient with this disorder.

Our recent studies have demonstrated considerable heterogeneity of the platelet defects in SPD. Decreased dense granule substances (including ADP), but normal α-granule substances, were found in 14 patients who were designated as having δ-SPD. The magnitude of the dense granule defect was variable; the greatest deficiencies of ADP and other dense granule substances were observed in albino patients with the Hermansky-Pudlak syndrome. Four other patients had diminished amounts of both α and dense granule substances, and were designated as having αδ-SPD. In addition, we have recently reported 2 patients with δ-SPD who show normal second-phase aggregation responses with epinephrine despite markedly diminished stores of platelet ADP.

Thus, in an attempt to clarify the conflicting observations on arachidonate and endoperoxide-induced aggregation of SPD platelets, and hence the role of dense granule ADP in mediating these aggregation responses, we have measured platelet aggregation by these agents in 12 patients whose storage pool defect has been previously characterized. In addition, because other studies have suggested that the pathway for synthesizing prostaglandins and thromboxane A2 may be abnormal in some SPD patients, we also measured the production of malondialdehyde, which is formed during the enzymatic breakdown of PGH2, in response to various aggregating agents including arachidonic acid. Parallel studies were performed in patients with thrombasthenia and in normal subjects who had ingested aspirin.

MATERIALS AND METHODS

Collection of Blood

After obtaining informed consent, blood was obtained by venipuncture and 9 parts were added to 1 part of 3.2% sodium citrate.
(dihydrate) in plastic tubes. Platelet-rich plasma (PRP) was obtained by centrifugation at 1500 g for 3 min at 20°C. Platelets were counted with an electronic particle counter (Coulter Model ZBI).

Platelet Aggregation

Platelet aggregation was measured with a Payton Dual Channel Aggregation Module and Riken-Denshi SP-5 recorder (Payton Associates, Buffalo, N.Y.). The lower and upper limits were set with PRP and with platelet-poor plasma (PPP) obtained by centrifugation of PRP at 12,000 g for 2 min in an Eppendorf microcentrifuge. Aggregating agents, added to PRP in 1/40 volume or less, and their final concentration included a standardized suspension of human connective tissue (collagen) in 0.15 M NaCl and the same suspension diluted 1:3 in saline, epinephrine (adrenaline-hydrochloride, Parke-Davis, Detroit, Mich.), 5 μM in 0.15 M saline, and arachidonic acid (Nu-check Prep, Inc., Elysian, Minn.), 125 and 250 μg/ml in DMSO. Platelet aggregation was quantified as previously described.16 Studies of platelet aggregation by PGG2 were performed by adding to 1 ml of PRP 2 μl of indomethacin (final concentration 24 μM), 10 μl of 0.25 M CaCl2, and 0.2–2 μl of PGG2 (final concentrations 100–1000 ng/ml). The PGG2, prepared from sheep vesicular glands,21 was a generous gift of DRS. Curt L. Malmsten and Bengt Samuelsson, and some of these studies were performed in collaboration with Dr. Malmsten.

Malondialdehyde Production

Malondialdehyde production was measured according to the method of MacFarlane et al.24 modified from that of Smith et al.25 Briefly, aliquots of PRP (4 ml) were aggregated for 10 min following addition of collagen or epinephrine and for 5 min following addition of arachidonic acid, after which 1.5 ml of 40% trichloroacetic acid in 0.1 N HCl was added. The samples were vortex-mixed and then centrifuged at 17,500 g for 10 min at 4°C. Aliquots of the clear supernates were mixed with 1/5 volume of 0.1 M thiobarbituric acid in 0.26 M Tris, pH 7.0, heated to 70°C for 30 min, cooled in an ice bath, and applied to DEAE-cellulose columns containing 1 ml of a 4%–8% DEAE cellulose slurry. After rinsing with distilled water, the pink color band was eluted in 1/3 the original volume with 6 N KOH and the absorbance peak at approximately 548 nm measured by scanning the 500–600 nm region. For each experiment, a standard curve was obtained from samples of PPP, containing known concentrations of malondialdehyde, carried through the same procedure; malondialdehyde was produced by hydrolysis of tetraethoxypropane.

Platelet ADP

Platelet ADP was determined by a firefly-luciferase method.12,15 In most patients the values are from a previously published study.15 Two other patients, J.D. and an 'atypical' albino patient, W.A., are unique in showing normal second-phase aggregation responses with epinephrine on multiple testing despite diminished aggregation with collagen. A detailed report on the findings in these patients has been published.16 αδ-SPD. Patients deficient in both dense granules and α-granules have been designated as having αδ-SPD.15 One patient, J.C., has a marked deficiency of α-granules, and three members of family C (R.C., S.C., and D.C.) have a partial deficiency of α-granules; the latter have been previously designated as having αδ-SPD.15

Thrombasthenia

Patient M.C. is a previously reported patient whose platelets do not aggregate with collagen, epinephrine (50 μM), or ADP (50 μM), and have decreased amounts of glycoproteins II and III.26 Patient C.G. is a previously unreported 15-yr-old girl with similar abnormalities of platelet aggregation and glycoproteins (the latter studies kindly performed by Dr. Graham Jamieson). A third patient, MaMo, with these types of defects27 was studied through the courtesy of Dr. Margaret Johnson.

Normal Subjects

Twenty-two control subjects (ages 20–50) were normal hospital personnel. Three of these subjects were also studied within 18 hr after ingesting 1.3 g of aspirin.

RESULTS

Platelet Aggregation (Table 1)

Thrombasthenia and Aspirin Ingestion

The characteristic absence or impairment of platelet aggregation in response to epinephrine, collagen, and arachidonic acid was observed in these subjects.

Storage Pool Deficiency

Epinephrine. The decreased aggregation responses observed in 10 of the 12 patients were due to an absence of second-phase aggregation. The secondary aggregation responses obtained in patients J.D. and W.A. were similar to those obtained in previous studies on these subjects.16

Collagen. The characteristic impairment of collagen-induced aggregation was observed in all subjects. This defect was most striking in patients deficient in both α and dense granules (αδ-SPD).

Arachidonic acid. The platelets of patients with αδ-SPD showed little or no aggregation responses to 0.4 and 0.8 mM arachidonic acid. The aggregation tracings obtained in patients J.C. and R.C. with αδ-SPD are shown in Fig. 1.

The findings in patients deficient in dense granules only (δ-SPD) were more variable. Consistently decreased aggregation responses to 0.8 and 0.4 mM arachidonic acid were observed in the four typical Hermansky-Pudlak albinos, in whom platelet aggregation responses were about 25% of that in normal subjects (for patient M.V., see also Fig. 1). In the two
Table 1. Platelet Aggregation

<table>
<thead>
<tr>
<th>Subjects</th>
<th>No.</th>
<th>Studies/</th>
<th>Platelet ADP</th>
<th>Platelet Aggregation (%)</th>
<th>Collagen</th>
<th>Epinephrine</th>
<th>Arachidonic Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Subject</td>
<td>(nmole/10⁶)</td>
<td></td>
<td>Undiluted</td>
<td>5 μM</td>
<td>0.8 mM</td>
</tr>
<tr>
<td>Controls</td>
<td>22</td>
<td>1</td>
<td>23 ± 1</td>
<td>71 ± 1</td>
<td>70 ± 2</td>
<td>71 ± 1</td>
<td>72 ± 2</td>
</tr>
<tr>
<td>δ-SPD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albinos</td>
<td>4</td>
<td>1</td>
<td>2 ± 0.5</td>
<td>34 ± 7</td>
<td>7 ± 5</td>
<td>4 ± 2</td>
<td>18 ± 2</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L.G.</td>
<td>1</td>
<td>1</td>
<td>9</td>
<td>75</td>
<td>50†</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>E.P.</td>
<td>1</td>
<td>1</td>
<td>9</td>
<td>58</td>
<td>3</td>
<td>5</td>
<td>15</td>
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<td>Second-phase aggregation*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J.D.</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>67</td>
<td>44†</td>
<td>70</td>
<td>51</td>
</tr>
<tr>
<td>W.A.</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>48</td>
<td>6</td>
<td>60</td>
<td>40</td>
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<tr>
<td>α-SPD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family C</td>
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<td>3</td>
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<td>20 ± 5</td>
<td>2 ± 2</td>
<td>4 ± 2</td>
<td>7 ± 4</td>
</tr>
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<td>J.C.</td>
<td>1</td>
<td>3</td>
<td>10</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Thrombasthenia</td>
<td>3</td>
<td>1</td>
<td>23 ± 2</td>
<td>1 ± 1</td>
<td>1 ± 1</td>
<td>2 ± 2</td>
<td></td>
</tr>
<tr>
<td>Aspirin ingestion</td>
<td>3</td>
<td>1</td>
<td>—</td>
<td>12 ± 6</td>
<td>2 ± 1</td>
<td>13 ± 5</td>
<td>5 ± 1</td>
</tr>
</tbody>
</table>

*Patients who consistently show normal second-phase aggregation with epinephrine; patient W.A. is an albino, J.D. is not.
†Patients are more clearly abnormal with higher dilutions of collagen.
Values for groups of subjects are mean ± SE.

miscellaneous (nonalbino) patients L.G. and E.P., platelet aggregation by 0.8 mM arachidonic acid was markedly decreased. Paradoxically, either normal (E.P.) or only slightly decreased (L.G.) responses were observed with 0.4 mM arachidonic acid (see also Fig. 1 for E.P.). The reason for this phenomenon in these two patients (whose plasma albumin concentrations were normal) is not clear, but could be related to similar findings observed with normal platelets at much higher concentrations (5–7.5 mM) of arachidonic acid.28 In the two patients (J.D. and W.A.) whose platelets aggregated normally in response to epinephrine, arachidonic-acid-induced aggregation was either normal or only slightly reduced (see Fig. 1).

PGG₂. In normal subjects, strong and irreversible aggregation responses were obtained with PGG₂ at concentrations of 250–1000 ng/ml (Fig. 2). Among 6 patients tested, abnormal aggregation responses to PGG₂ were observed in each type of storage pool deficiency (Fig. 2). In two albinos (M.V. and L.V.) with δ-SPD, minimal aggregation was obtained with 500 ng/ml PGG₂, and aggregation followed by disaggregation was observed with 1000 ng/ml PGG₂. Strikingly decreased aggregation responses with all concentrations of PGG₂ were also observed in three patients...
with αδ-SPD. In contrast, PGG$_2$-induced aggregation was more nearly normal in patient J.D. (δ-SPD), in whom second-phase aggregation responses to epinephrine have been consistently observed. In this patient, the initial platelet aggregation response was normal with all concentrations of PGG$_2$, but the platelets rapidly disaggregated.

Malondialdehyde Production (Table 2)

**Thrombasthenia and Aspirin Ingestion**

Although thrombasthenic platelets did not aggregate with arachidonic acid (Table 1), they produced normal amounts of malondialdehyde. Malondialdehyde production was somewhat decreased ($p < 0.05$) in response to collagen and was virtually absent in response to epinephrine. As anticipated, malondialdehyde production in response to these three agonists was markedly reduced or absent in normal subjects who had ingested aspirin.

**Storage Pool Deficiency**

**Epinephrine.** Normal platelets produced 48 ± 4 nmole of malondialdehyde/10$^{11}$ platelets in response to 5 μM epinephrine. Malondialdehyde production was either undetectable or <3 nmole in all subjects with storage pool deficiency, except for two patients (J.D. and W.A.) showing second-phase aggregation responses.

<table>
<thead>
<tr>
<th>Subject</th>
<th>No.</th>
<th>Studies per Subject</th>
<th>Collagen</th>
<th>Epinephrine</th>
<th>Arachidonic Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>22</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>δ-SPD</td>
<td>4</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albinos</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L.G.</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E.P.</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second-phase aggregation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J.D.</td>
<td>1</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W.A.</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>αδ-SPD</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family C</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J.C.</td>
<td>1</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombasthenia</td>
<td>3</td>
<td>1</td>
<td>97 ± 7</td>
<td>37 ± 2</td>
<td>1 ± 1</td>
</tr>
<tr>
<td>Aspirin ingestion</td>
<td>3</td>
<td>1</td>
<td>5 ± 3</td>
<td>2 ± 1</td>
<td>3 ± 2</td>
</tr>
</tbody>
</table>

Values for groups are mean ± SE.
**Collagen and arachidonic acid.** Several patterns were observed in patients. Production of malondialdehyde was decreased by approximately 50% in response to collagen, but normal in response to arachidonic acid in patients with δ-SPD. This pattern was obtained in the four typical Hermansky-Pudlak albino and in E.P. A similar trend was also observed in the four other δ-SPD patients, but the results were more variable.

Malondialdehyde production in response to both collagen and arachidonic acid was decreased in patients with αδ-SPD. This pattern was observed with both concentrations of collagen and of arachidonic acid in the three members of family C. Patient J.C. also showed strikingly decreased malondialdehyde production with both concentrations of collagen and with 0.4 mM arachidonic acid, but normal production was obtained with 0.8 mM arachidonic acid.

**DISCUSSION**

In the present study we examined the platelets of 12 patients with various types of storage pool deficiency for possible defects in the prostaglandin synthetic pathway and also measured the aggregation responses of these ADP-deficient platelets to arachidonic acid and PGG2.

We monitored the prostaglandin pathway by measuring the production of malondialdehyde (MDA) induced by arachidonic acid, epinephrine, and collagen. Recent studies29 have shown the MDA and I of these ADP-deficient platelets to arachidonic acid and PGG2.

Of these ADP-deficient platelets to arachidonic acid and PGG2. Hence, MDA production induced by arachidonate should reflect cyclooxygenase activity and possibly thromboxane synthetase activity as well, while that induced by epinephrine and collagen should also reflect the phospholipase activities that liberate endogenous arachidonate from phospholipids,29,30 as well as the coupling of the initial stimulus to these activities. While the thiobarbituric acid reaction may be influenced by other lipid and nonlipid substances, and hence is not completely specific for MDA, it has been suggested that only the MDA complex absorbs in the 450–550 nm range;24 thus, we used this region for the MDA measurements.

Two types of abnormalities of MDA formation were observed in SPD patients. In 8 patients with dense granule deficiencies only (δ-SPD), MDA production was normal in response to 0.8 and 0.4 mM arachidonic acid, but diminished to varying degrees in response to epinephrine and collagen. The most consistent defects were observed in the 4 albino patients with typical Hermansky-Pudlak syndrome. These results suggest that δ-SPD platelets convert arachidonate to thromboxane A2 normally, but are defective in phospholipase activity or in stimulus–phospholipase coupling. This conclusion is in accord with our previous studies on the synthesis of PGE2 and PGF2α in SPD platelets11,12 and with those of Rendu et al.18 and Malmsten et al.19 on a patient with Hermansky-Pudlak syndrome.

In patients with αδ-SPD, MDA production induced by collagen was diminished to an even greater extent than in δ-SPD, and in addition, an abnormality in the conversion of arachidonic acid to MDA was found. Hence, although phospholipase activity could be abnormal in these patients also, interpretation of the data is complicated by this impairment in arachidonate metabolism. The nature of this impairment, and its possible relationship to the more severe aggregation defects in the αδ-SPD patients (see below), remains to be determined. However, it is unlikely that this abnormality of arachidonate metabolism is a direct result of the impaired aggregation responses, since conversion of arachidonate to MDA (Table 2), and to thromboxane A2 and PGE2 and PGF2α,11,17 as well, was normal in thrombasthenic platelets, despite an absence of aggregation.

A second purpose of this study was to examine the aggregation responses of ADP-deficient SPD platelets to arachidonic acid and PGG2 in an attempt to clarify the question whether platelet ADP mediates endoperoxide or thromboxane-induced aggregation. Ingerman et al.13 and Minkes et al.14 reported normal aggregation responses to 0.5 mM arachidonic acid in a family13 and in a patient14 with SPD and suggested that these findings argued against an obligatory role for platelet ADP. In contrast, Malmsten et al.19 found impaired arachidonate-induced aggregation in a Hermansky-Pudlak patient. The aggregation responses to arachidonic acid and PGG2 obtained in 12 patients with various types of SPD are summarized in Table 3. Both normal and abnormal responses were observed, illustrating in yet another way the heterogeneous nature of this disorder13 and the need to take this into account in interpreting studies in SPD platelets.

Despite this heterogeneity in aggregation responses, our findings clearly indicate that arachidonate- and PGG2-induced aggregation is abnormal in many SPD patients. Table 3 also presents some other findings in these patients that could be relevant in accounting for the varied aggregation responses. Taken together, these results suggest that ADP does play a role in endoperoxide- and thromboxane-induced aggregation. Thus, among patients with δ-SPD, very low values of endogenous ADP (2 ± 0.3 nmole/109) and impaired arachidonate- and PGG2-induced aggregation were observed in typical Hermansky-Pudlak patients. In contrast, aggregation with 0.4 mM arachidonic acid was normal in platelets from E.P. and L.G., which
Table 3. Summary of Platelet Findings

<table>
<thead>
<tr>
<th>Patients With Storage Pool Deficiency</th>
<th>Platelet ADP Content</th>
<th>α-Granules and Substances Sensitivity</th>
<th>Platelet Aggregation</th>
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</thead>
<tbody>
<tr>
<td>δ-SPD Albino M.V., L.V., P.E., R.Z.</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
</tr>
<tr>
<td>E.P., L.G.</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
</tr>
<tr>
<td>J.D.</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
</tr>
<tr>
<td>Albino W.A.</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
</tr>
<tr>
<td>αδ-SPD J.C.</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
</tr>
<tr>
<td>Family C (R.C., D.C., S.C.)</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
<td>↓↓↓↓</td>
</tr>
</tbody>
</table>

*Second-phase aggregation. Degree of abnormalities (arrows) for platelet ADP content and arachidonic acid aggregation are from Table 1, for PGG₂ aggregation from Fig. 2, for α-granule substances from reference 15, and for platelet sensitivity to ADP (where determined) from reference 16.

N, normal; ND, not determined.

contain 9 nmole ADP/10⁹ cells. Of interest, the average ADP content reported in the family of Ingerman et al. was 11.5 nmole/10⁹, and in the patient of Minkes et al. was 12 nmole/10⁹. (This latter patient also had a normal number of platelet dense granules, whereas these have been consistently absent in other SPD patients.) Hence, in these patients and in those with δ-SPD described above, aggregation responses to 0.4–0.5 mM arachidonic acid correlated with the amount of endogenous ADP. The normal aggregation responses in the platelets of J.D. and W.A., despite their very low levels of ADP, could be related to their previously described enhanced sensitivity to ADP.

While our results support the view that endogenous ADP plays a role in arachidonate- and endoperoxide-induced aggregation responses, they do not resolve the conflicting evidence from other studies. As suggested previously for epinephrine-induced aggregation, it is possible that the contribution of endogenous ADP to aggregation induced by arachidonate and PGG₂ occurs, in part, within the microenvironment of the platelet, perhaps thereby activating it and enabling it to attach to similarly activated platelets. In this way, very small amounts of granule-derived ADP could mediate aggregation responses even in the absence of measurable “secreted” ADP. Such a theory would incorporate and perhaps explain many of the conflicting findings in previous studies.

Finally, the most severe abnormalities of arachidonate- and PGG₂-induced aggregation were observed in patients with αδ-SPD even though the ADP contents of their platelets were actually higher than in many patients with δ-SPD. Thus, it is possible that α-granule substances (possibly fibrinogen) also play a role in endoperoxide- and thromboxane-induced aggregation. Gerrard et al. have recently reported normal aggregation responses to 0.8 mM arachidonic acid in two patients with α-SPD deficient in α-granules only. Since their results suggest that α-granule substances do not play a primary role in these aggregation responses, our findings in the αδ-SPD patients could reflect an enhancement of the effects of endogenous ADP by α-granule substances. However, because SPD may include platelet defects other than granule deficiencies, which could also contribute to the observed aggregation defects, further studies will be necessary to clearly establish the involvement of granule-bound substances in endoperoxide- and thromboxane-induced aggregation responses.

REFERENCES

PLATELET MALONDIALDEHYDE PRODUCTION


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HJ Weiss and B Lages