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HEREDITARY PLATELET FUNCTION DISORDERS IN JAPAN. K. Yasunaga. The First Department of Internal Medicine, Kansai Medcal University, Osaka, Japan.

Nationwide surveys of hereditary platelet function disorders in Japan were carried out in 1976, 1981, and 1986. Information on 271 cases received in the 1986 survey was analyzed with that for 103 other cases reported in earlier surveys but not in 1986, making a total of 374 cases. The mortality rate was 6.8% of 162 cases in 1976, 6.6% of 213 cases in 1981, and 5.9% of 374 cases in 1986. Bleeding symptoms appeared at age 12 years in 56.8% of patients and the most common were epistaxis and purpura. Of the 295 cases 49.5% were isolated cases, 20.3% had siblings with confirmed bleeding tendencies, and 30.2% had other kin with bleeding tendencies. suggestings autosomal tnansmission. Consanguineous marriage was reported by 11.9% of patients.

Of the 374 cases in 1986, 59.4% were thrombasthenia (TA), 11.5% Bernard-Soulier symdrome (BSS), 22.5% release abnormalities (PRA), 1.3% other, and 5.3% unclassified. Of the 84 cases of PRA, 60 were storage pool deficiency, 18 release mechanism abnormalities, and 6 undecided between the two types. The results of laboratory tests were as follows.

Tests	TA Type I		TA Type II		BSS		PRA	
	N	A	N	A	N	A	N	A
Bleeding time	2	121	6	64	3	36	18	54
Platelet count	123	3	70	2	12	30	54	25
Platelet morphology	98	9	61	3	3	39	37	30
Clot retraction	5	101	51	18	18	4	34	1
Platelet retention	1	73	11	51	8	14	17	47
Platelet aggregation								
ADP	0	99	1	71	25	5	16	54
Collagen	2	89	3	63	24	6	17	57
Ristocetin	4	15	6	12	1	19	10	5
Bovine fibrinogen	1	2	2	6	2	10	8	0
Thrombin	0	5	1	11	0	0	0	1
Epinephrine	0	62	0	45	10	4	10	38

N: normal A: abnormal

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PLATELET DYSFUNCTION INDUCED BY TETRAHYDROCANNABINOL. R. Patel, R. Bick. Regional Cancer & Blood Disease Center of Kern, Bakersfield, California, and UCLA Center for the Health Sciences (Dept. of Medicine), Los Angeles, Calif., USA.

Many drugs and other agents have been reported to induce platelet dysfunction and clinical bleedability; however, tetrahydrocannabinol (marijuana) has thus far not been reported. The patient herein described is a 28-year-old Caucasian female who was referred for evaluation of easy and spontaneous bruising. On history, the patient related that for a three-month period she had been developing spontaneous ecchymoses of the extremities and torso. She denied any medication other than heavy marijuana use. Hemostasis evaluation revealed her to have a normal prothrombin time, partial thromboplastin time (PTT), Factor VIII coagulant activity (Factor VIII:C), Factor VIII related antigen (Factor VIII:RAg), and ristocetin cofactor activity. Platelet aggregation was performed which revealed abnormal aggregation to epinephrine, adenosine diphosphate (ADP) and abnormal release but normal aggregation to ristocetin. She was asked to refrain from marijuana and was reaggregated revealing normal aggregation and release to epinephrine, ADP, collagen and arachidonic acid; however, ADP release induced by ristocetin remained moderately abnormal, even though aggregation was normal. In addition, with cessation of marijuana use, her clinical bruising abated.

Following this, she again indulged in marijuana and she was reaggregated, revealing delayed aggregation and release to epinephrine with abnormal aggregation to ADP. Additionally, ristocetin release and adenosine triphosphate (ATP) release remained abnormal but aggregation remained normal and arachidonic acid aggregation remained normal.

In summary, we herein describe a young female who demonstrated aggregation abnormalities and clinically significant spontaneous bruising during periods of using marijuana; the defect disappeared upon cessation of marijuana and reappeared upon resumption of marijuana use. The defect at present appears to be that of a membrane-type defect with no evidence that marijuana interferes with the prostaglandin pathway.

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FURTHER CHARACTERIZATION OF PLATELET RELEASE MECHANISM DEFECT WITH DEFECTIVE A23187 AGGREGATION. A. Hattori, R. Nagayama, I. Fuse, T. Takeshige, S. Takizawa and A. Shibata. The First Department of Internal Medicine, Niigata University School of Medicine, Niigata 951, Japan.

In order to clarify the basic abnormality of patients with release mechanism abnormality with defective response to A23187 (A23) (Hattori et al. Acta Haematol. Jap. 44:969, 1981), the proband (female) showing a life long mild hemorrhagic tendency was further examined. Her platelet (plt) count, morphology, storage pool was normal. Bleeding time (Duke) was more than 15 min.

PRP-aggregation (Ag) was normal when induced by PMA, whereas decreased (only primary Ag) by ADP, adrenalin, arachidonate (AA) (-2mM), Tx analog STA2 (-4μM), PAF (-10μM). Ag was defective in response to A23 (-40μM). Ag using washed plts was decreased slightly in response to thrombin or considerably to ionomycin. Adrenalin potentiation was observed in Ag and ATP release (R) by either AA or A23. Ca replacement (over 2mM) with heparinization normalized both Ag and R to those agonists, but Ca agonists did not improve the abnormality. Ca, Na and Cl contents were within normal range. Ca mobilization by Quin-2AM method occurred normally in response to thrombin (0.1, 0.5U/ml), and that by Aequorin method was also normal, but retarded with normal peak values in response to A23 and decreased to STA2. Shape change response to various agonists including A23 was normal. AA metabolite analysis by HPLC was normal, but Tx production was low by low dose of A23 but normal by high dose A23 and thrombin (serum). 20 and 40 K protein phosphorylation occured normally when challenged by high and low concentrations of A23 or thrombin. Clot retraction was normal.

These results suggest that the abnormality do not exsist in agonist-receptor reactions, enzymes related to production of Tx, Ca slow channel (if it exists), c-Kinase system, Ca content and amount of mobilizable Ca, actomyosin system, protein phosphorylation and reactions after Ca mobilization, but may exsist in activation of phospholipases and an early stage of Ca mobilization based on unknown defect(s).

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NORMAL URINARY PROSTAGLANDIN E_2 EXCRETION IN THE PATIENT WITH PLATELET CYCLO-OXYGENASE DEFICIENCY. T. Takeshige (1), I. Fuse (1), A. Hattori (1), T. Momotsu (1), A. Shibata (1) and K. Abe (2). The First Department of internal medicine, Niigata University School of Medicine, Niigata, Japan (1) and The Second department of Internal Medicine, Tohoku University School of Medicine, Japan (2).

Platelet (P) Cyclo-oxygenase (CO) deficiency is characterized by bleeding tendency due to platelet release mechanism defect. Pareti et al. have reported a patient with PCO deficiency whose CO activity was defective not only in platelets but also in vessel walls. But it has not been demonstrated whether other cells than platelets do have this enzyme in other patients with PCO deficiency. Recent data suggest taht hemorrhagic or thrombotic diathesis is dependent on the site(s) (platelet, vassel wall or others) or CO deficiency. In order to determine the CO activity in kidney in a patient with PCO deficiency (Scand. J. Haematol., 32; 167 - 174, 1984), We studied the urinary PGE_2 excretion and renal function at basal state and before and after intravenous administration of angiotensin II (ANG II). Before ANG II infusion to the patient, 600 ml H_2O was orally intaked, and then AGN II (5, 10, 18 ng/min. each dose for 10 min.) was infused intravenously. Urine samples were collected before (20 min.) AGN II infusion. Urinary PGE_2 was measured by RIA. Urine osmorality was determined by Fiske osmometer. To measure basal daily excretion of urinary PGE_2, daily total urine was collected into ice box for 2 days, and then stocked at -80°C until PGE_2 measurement by RIA.

Basal PGE_2 excretion
145.5 ng/day (normal range : 36-216, mean 132)

	Basal	ANG II	Recovery
$UPGE_2$ (pg/mg creatinine)	undetect	124	126
Uosm (m osm/kg)	65.5	550.7	435.0

A reduction of Uosm following the intravenous infusion of ANG II to normal humans has been reported by Usberti et al. (Am. J. Physiol. 248; 254-259, 1985), and it also reported that Uosm increased after aspirin administration.

It was concluded that CO activity in the kidney of this patient was not al least defective, but endogenous PGE_2 synthesis stumulated by ANG II may be decreased.

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