dence supporting such a disinhibitory mechanism has been obtained from studies of rats treated with 6-hydroxydopamine. After intracisternal injection of this substance, there is a specific destruction of the NE-containing terminals, as well as a complete depletion of biochemically detectable NE, in the rat cerebellar cortex (*16*). Correlated with the absence of any presumed adrenergic inhibitory input in such animals, PGE_1 accelerated firing in only 7 percent of the 28 Purkinje cells examined, as opposed to 64 percent in control animals.

Further evidence favoring disinhibition by adrenergic blockade accrues from study of the interspike interval histogram. During the slowing produced by electrophoresis of NE, the action potentials occur at the same most probable interspike interval. However, the pauses between the periods of rapid firing are markedly augmented (*10*). The complementary change is seen during the acceleration of firing produced by electrophoretic application of prostaglandin; the most probable interspike interval is unchanged, but the normally occurring pauses in spontaneous discharge, represented by the "tail" of the histogram, are reduced in duration and number (Fig. 1B).

It is difficult to define the mechanism of the reductions in spontaneous discharge seen here and observed before (*9*) with prostaglandins. They may be produced by direct effects upon the Purkinje cells, by indirect actions on presynaptic elements, or by vascular changes. Whatever the mechanisms, they do not appear to involve adrenergic presynaptic elements (*17*), as the incidence of depression of discharge by prostaglandin in animals treated with 6-hydroxydopamine is not statistically different from that in normal animals.

The prostaglandin antagonism of NE responses in the cerebellum fortifies our hypothesis that NE effects are mediated through activation of adenyl cyclase (*10*). The prostaglandins and NE may influence Purkinje cells via a reciprocal interaction with adenyl cyclase, although other possibilities cannot be excluded without biochemical determinations. Purkinje cell slowing elicited by microelectrophoretic administration of aminophylline is also antagonized by prostaglandin (*18*). However, the failure of the prostaglandins to influence responses to cyclic AMP is significant, since cyclic AMP acts beyond this postulated site of prostaglandin action. This proposed mechanism for central neurons is quite similar to that for several effector systems in the peripheral nervous system (*2–4*). In view of the presence (*7*) and spontaneous release (*19*) of prostaglandin from the cerebellum, this lipid may indeed modulate cerebellar adrenergic junctions.

BARRY J. HOFFER, GEORGE R. SIGGINS
FLOYD E. BLOOM
Laboratory of Neuropharmacology, Division of Special Mental Health Research, National Institute of Mental Health, St. Elizabeths Hospital, Washington, D.C. 20032

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Hageman Factor (Factor XII) Deficiency in Marine Mammals

Abstract. *Hematologic and coagulation studies were conducted on Atlantic bottlenose dolphins and killer whales. Hematologic values were similar to those in man. These animals differed from other mammals in that the Hageman factor (factor XII) was absent and this absence caused marked prolongation of coagulation. Levels of factors VIII and V were high and those of VII and X were low compared with levels in man.*

Interest in marine mammals has increased greatly in recent years, but information on the normal physiology of these animals is fragmentary. Recently Puppione (*1*) noted a delayed initiation of blood clotting in samples obtained from members of the cetacean order of marine mammals. This order includes dolphins, porpoises, and whales. Stimulated by this report, we studied the blood coagulation and hematology in six trained cetaceans—one female and two male Atlantic bottlenose dolphins (*Tursiops truncatus*) and one female and two male killer whales (*Orcinus orca*).

Blood for coagulation studies was obtained in plastic syringes from veins on the ventral surface of the flukes of the unanesthetized animals. After separation of plasma or serum from cells, specimens were kept frozen at −20°C in glass and plastic tubes until the laboratory tests could be carried out. Coagulation determinations were performed by standard or previously described methods for studying man (*2*); fibrinolytic studies were done according to methods of Alkjaersig *et al.* (*3*).

Hematologic values are given in Table 1. The blood cells were morphologically similar to those seen in man. An occasional nucleated red blood cell was present. The percentage of eosinophils was strikingly greater in the three dolphins than in the whales and man, but we have no reason to suspect that this was pathologic since others (*4*, *5*) have reported similar findings. However, Ridgeway suggested that this might be an indication of universal parasitism in the dolphins. By human standards, the platelet counts were within normal limits in the whales and somewhat low in the dolphins.

The results of general coagulation

tests are given in Table 2. Compared to human values, the whole-blood clotting time in siliconized tubes was within normal limits, but that in glass tubes was considerably prolonged. There was essentially no difference in results obtained by these two methods in any of the animals. The partial thromboplastin time (PTT) and activated PTT, when human brain cephalin was used as a source of phospholipid, were very prolonged. The addition of Celite, which produces maximum surface activation, failed to shorten the clotting time; in fact, in every animal it actually prolonged the time. Prothrombin consumption was markedly impaired. This test may be affected by many factors and the great variability of results is not as significant as the consistency of the abnormality.

One-stage prothrombin times, in which either human brain suspension or Russell viper venom was utilized, were slightly longer than those of human controls. The prolongation observed when human brain suspension was used may reflect the well-known species specificity of tissue thromboplastins (*6, 7*). Clot retraction was present in all samples; clot lysis was not observed in any of them. Thrombin times, determined by use of bovine thrombin and calcium, were comparable to those in man. The thromboplastin generation test, in which all animal reagents were used, was grossly abnormal, but the substitution of either human adsorbed plasma or human serum corrected the defect. The addition of "activation product," eluted by 1.7*M* sodium chloride from Celite previously exposed to normal human plasma, completely corrected the defect; a similar preparation with plasma from a human patient with Hageman factor deficiency had no effect. Similar results were obtained with these eluates in prothrombin consumption tests of recalcified whale plasma.

Limited fibrinolytic studies were also carried out. Lysis of unheated bovine fibrin plates was not observed within 24 hours. Streptokinase alone failed to activate the animal plasminogen; it was necessary to add a small amount of human plasma to initiate the reaction. After subtraction of the amount of casein hydrolysis due to this addition, the level of plasminogen ranged from 6.27 to 7.02 unit/ml in the bottlenose dolphins and from 6.37 to 6.49 unit/ml in the killer whales (the normal human range is 2 to 4 unit/ml).

Table 1. Hematologic values. RBC, red blood cells; WBC, white blood cells.

Hematologic parameters	*Tursiops truncatus*			*Orcinus orca*		
	♂ Lucky	♂ Arnie	♀ Granny	♂ Orky	♂ Snorky	♀ Corky
Hematocrit (ml/100 ml)	41.0	39.5	36.0	44	45	40
RBC ($\times 10^6$ per cubic millimeter)		3.40	3.30	3.70	3.90	3.90
Hemoglobin (g/100 ml)		15.0	14.0	15.0	16.8	16.4
WBC (per cubic millimeter)		10,500	7,500	7,300	5,600	5,400
Neutrophils (%)	51	42.5	62	49	65	64
Lymphocytes (%)	24	30.5	18	35	24	26
Eosinophils (%)	24	27	19	1	4	6
Monocytes (%)	0	4	1	7	7	4
Basophils (%)	1	0	0	0	0	0
Nucleated RBC	2/200 WBC	1/200 WBC	1/200 WBC	0	1/1000 WBC	0
Platelets ($\times 10^3$ per cubic millimeter)	160	115	142	310	240	219

Table 2. General coagulation tests.

Test	*Tursiops truncatus*			*Orcinus orca*			Normal human
	♂ Lucky	♂ Arnie	♀ Granny	♂ Orky	♂ Snorky	♀ Corky	
Clotting time (minutes)							
Glass	26	20	41	33	47	18	5–10
Silicone	25	18		31	45	25	15–35
PTT (seconds)	406	210	172	214	290	144	70–100
Activated* PTT (seconds)	427	240	240	355	568	204	35–50
Prothrombin consumption (% consumed per 24 hours)	0	0	19.0	42	58	0	>90
Prothrombin time (seconds)							
Human brain	18.6	13.7	16.4	16.3	15.7	14.8	11–13
Russell viper venom		11.6	12.4	12.6	13.8	13.0	9–11
Thrombin time (seconds)	10.5	10.2	9.0	10.0	10.4	9.9	10–12
Thromboplastin generation test [shortest clotting time (seconds)]	61.5	22.1	30.2		30.7	39.3	8–10

* Celite.

Table 3. Coagulation factors. AHF, antihemophilic factor; PTC, plasma thromboplastin component; PTA, plasma thromboplastin antecedent; and FSF, fibrin-stabilizing factor.

Factor	*Tursiops truncatus*			*Orcinus orca*			Normal human
	♂ Lucky	♂ Arnie	♀ Granny	♂ Orky	♂ Snorky	♀ Corky	
I (Fibrinogen) (mg/100 ml)	360	354	279	417	399	584	200–400
II (Prothrombin) (%)	54	110	100	80	76	84	60–130
V (Proaccelerin) (%)	125	238	145	133	208	375	60–140
VII (Proconvertin) (%)	6.8	63	25	22	23	28	70–140
VIII (AHF) (%)	407	338	650	267	343	268	50–200
IX (PTC) (%)	142	141	107	101	64	107	60–160
X (Stuart-Prower) (%)	72	47	26	20	20	14	65–140
XI (PTA) (%)	72	81	70	69	56	314	60–150
XII (Hageman) (%)	0	0	0	0	0	0	50–200
XIII (FSF) (%)	>100	>100	>100	>100	>100	>100	90–110
Antithrombin III (%)	150	148	143	112	124	140	70–140

Coagulation factors assayed in systems used for human plasma are recorded in Table 3. The high levels of factors VIII and V, compared with levels in man, are of interest because similar findings have been reported in other species of mammals (*6, 8*). The levels of factors VII and X were decreased. The significance of these variations is not known. Species specificity of the tissue thromboplastin used in the assay of factor VII (*6, 7*) may explain the apparent low level of this factor. Until species-specific thromboplastin can be obtained the activity of this clotting factor must remain in doubt. The most remarkable finding was the complete absence of factor XII (Hageman factor) in all of the animals. This finding substantiated our observation of no surface activation either in the clotting times in glass tubes or in the partial thromboplastin times. Other laboratory findings associated with factor XII deficiency in man, including a decreased prothrombin consumption and an abnormal thromboplastin generation time that can be corrected by addition of either normal human adsorbed plasma or normal human serum, were obtained from all the animals.

Hageman deficiency is a rare and curious familial disorder. Despite a marked defect in blood coagulation in vitro, patients with this syndrome do not exhibit evidences of a bleeding tendency. It is evident that Hageman factor is not essential for normal hemostasis but it is necessary for the initial stages of clotting of blood in a test tube. No explanation for this is known. One is forced to conclude that the body has some other means by which it can activate coagulation than through the intervention of activated factor XII.

This study was undertaken to compare the hematologic and coagulation profiles of two genera of marine mammals with those of man. To our knowledge, no previous reports on the coagulation mechanism in marine mammals are available. The most striking difference was the complete absence of factor XII in all animals tested. This, in turn, caused marked prolongation of tests dependent on surface activation of the intrinsic pathway of blood coagulation, such as the whole-blood clotting time in glass, the PTT and activated PTT, the prothrombin consumption, and the thromboplastin generation test. Absence of factor XII also explains why the eluate from Celite used to adsorb normal human plasma corrected the defects in the latter two tests and why a similar preparation obtained from plasma of a patient deficient in Hageman factor did not correct them.

According to Ratnoff (*9*), all other mammals studied (cattle, dogs, horses, cats, rats, guinea pigs, mice, hamsters, rabbits, gerbils, sheep, monkeys, armadillos, racoons, goats, pigs, and opossums) have Hageman factor. In submammalian species the factor is completely absent in fowl (ducks, chickens, pigeons, turkeys, and geese) and most reptiles (turtles, tiger snakes, and lizards), although 3 percent of the activity of human plasma has been found in one species of turtle (Western painted turtle). However, Hageman factor–like properties, which cannot be specifically assayed and therefore must be interpreted with caution, are present in amphibians (toads and frogs) and fish, including teleosts (carps, catfish, and trout), primitive bony fish (paddlefish), elasmobranch (dogfish sharks), and a primitive cartilagenous fish (ratfish). Thus, phylogenetically and ecologically the complete absence of factor XII activity in the two (*10*) marine mammals is of great interest.

A. JEAN ROBINSON
MONA KROPATKIN
PAUL M. AGGELER*

Hematology Research Laboratory,
San Francisco General Hospital,
San Francisco, California 94110

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Androgenesis Conditioned by a Mutation in Maize

Abstract. *A maize embryo having the nuclear constitution of a reduced gametophyte cell is produced in 3 percent of the embryo sacs of inbred strain Wisconsin-23 that carry the mutant* indeterminate gametophyte (ig). *The nucleus of most monoploid sporophytes so derived is paternal. Such androgenetic monoploids may originate from a sperm nucleus acting in conjunction with the cytoplasm of a maternal cell from which the nucleus has been functionally displaced.*

Infrequently the maize embryo develops by parthenogenesis (*1*) rather than from a zygote following syngamy. The endosperm, companion product to the embryo through double fertilization, is constituted normally in these exceptional cases by fusion of the two polar nuclei in the central cell of the female gametophyte with one sperm (*2, 3*). This type of apomictic seed formation yields embryos from which monoploid sporophytes arise. Like angiosperm haploids in general, monoploids of maize usually are matroclinous. Patroclinous monoploids, however, occasionally occur. In maize stocks of diverse origin Chase has observed an average of one patroclinous case for every 80 monoploids (*4*). The total frequency of monoploids in his experiments averaged about one per thousand seedlings but varied considerably between strains. Curiously, the monoploid frequency was strongly influenced by the paternal, as well as by the maternal, parentage. Furthermore, the parental influences proved heritable, although not according to any simple pattern (*5*). Similar influences of parentage were observed for an inbred strain described by Coe which produces up to 3 percent monoploids (*3, 6*). In the case I describe here, the monoploid tendency is associated specifically with the maternally sex-limited expression of a single gene. Moreover, the gene induces predominantly paternal (androgenetic) rather than maternal (gynogenetic) monoploids.

The gene in question, termed *indeterminate gametophyte* (*ig*), appeared in our cultures as a spontaneous mutation of the highly inbred, Wisconsin-23 (W23) strain. Through its influence on female gametophyte development, *ig* conditions various incompletely penetrant irregularities in seed formation, of