Symposium: What Is Hemophilia?

Present Concepts of Hemophilia

By Alfredo Pavlovsky, M.D.

If we consider the classical definition of hemophilia, which is described as an "hemorrhagic hereditary disease, of recessive character, linked to sex, suffered by males and transmitted by females, distinguished by a delayed clotting time and with a characteristic hemorrhagic clinical picture," we must admit that some of these concepts have recently required modification.

Hereditary Transmission

It is obvious that the number of sporadic cases of hemophilia has lately increased. The lack of hereditary antecedents must not make the diagnosis of the disease doubtful in a given case. In our experience, we have seen a large number of sporadic cases, characterized by the classical clinical and hemorrhagic picture and indications are present that once the disease has appeared in a family, it is transmitted to the next generation following the classical laws.

Sex

At present the possibility of hemophilia being present in females must be admitted, as demonstrated by Mersky,1 Israels, et al.,2 Quick and Hussey,3 and Brinkhous and Graham4 (in dogs), and lately observed in one case by us.

Clotting Time

Although a prolonged clotting time still remains as one of the principal characteristics of hemophilia, it must be admitted that there have been observed some cases with normal clotting time. For that reason the determination of prothrombin consumption constitutes a more accurate test. Nevertheless, we must admit that a defective prothrombin consumption is not seen exclusively in hemophilia, as it is also observed in thrombocytopenic purpura, although the latter can be easily differentiated from hemophilia by the decrease of the platelets and a defective clot retraction. It seems that Quick's technic to differentiate both processes using thromboplastin heated at 60 C. has given good results, as the defect of thrombocytopenic purpura is corrected, whereas that of hemophilia is not.

The determination of the coagulant activity of the antihemophilic globulin controlled with hemophilic blood has also been shown to be very useful.

However, these tests have shown great variations among the hemophilic patients, and even in the same patient at different periods. These tests, therefore, possess definite limitations, since (as will be shown later) the blood of different hemophilic patients can be complemented by other hemophilic blood.

From the Hospital Naval, Buenos Aires, Argentina.
INTERACTION OF DIFFERENT HEMOPHILIC PLASMAS

When studying the coagulant action of the mixture in different proportions of hemophilic blood, it was shown that sometimes they complement each other normalizing its clotting time. This fact has been corroborated by several authors although they gave different interpretations. Some considered that they were new hemorrhagic diseases, i.e. PTC deficiency, Christmas disease; and others have classified it as hemophilia B. To us, that fact, difficult to interpret, could be explained either by the annulment of the inhibitors of one blood by the other or because the two bloods complemented each other. Until now it has not been possible to individualize the inhibitors. However, we cannot discard them, because one of our hemophilic patients, whose blood has precisely the greatest activity in normalizing other hemophilic bloods, shows great resistance in the normalization of his own blood even with large quantities of normal plasma (more than 600 cc.).

A striking fact was observed: If we divided the hemophiliacs into A and B groups, considering their property to correct other hemophilic bloods, some of them seemed to have constant characteristics while in others (even a brother) these properties varied, giving very inconstant results which made them very difficult to classify. Other patients treated by us during many years have shown a tendency to improve their clotting time spontaneously as well as the coagulant activity of the antihemophilic globulin.

These facts show the inconstancy of the measurements to indicate the capacity of one blood to compensate another; the cause of these variations is as yet quite obscure.

We have also observed that some of these plasmas, when being adsorbed, lose their property of compensating each other (as if adsorption would eliminate the necessary factor).

It is quite evident that we do not yet know the exact nature of thromboplastin, and that is quite difficult to assert whether its synthesis takes place during the combination of amino acids with lipids or by an overcoming of the action of inhibitors. It seems that this thromboplastic synthesis does not reach the same degree in all the hemophilic patients, thus helping to explain the individual differences.

We do not know if we can really speak of two types of hemophilia, A and B, because we presume (according to our observations) that tests in other hemophiliacs may reveal new forms of the disease. That is why we do not agree to the classification of hemophilia under different denominations until the exact nature and synthesis of thromboplastin are known. With the denomination of new factors as yet not surely defined, we risk adding confusion to the scheme of coagulation. Finally, it is our opinion that, although lately some cases have been observed which differ in some aspects from the classical picture, there is only one hemophilia.

At the present moment we may define hemophilia as an hemorrhagic, hereditary disease, that can appear sporadically but is then transmitted to the descendants; of recessive character, linked to sex; suffered almost exclusively by males; characterized by a well-defined clinical symptomatology and by alterations of the thromboplastic factors of plasma, which brings about very often a
prolonged clotting time and a constant deficiency in prothrombin consumption; not correctable by addition of normal platelets, but which may be corrected with normal platelet-free plasma and tissue thromboplastin.

SUMMARIO IN INTERLINGUA

Un discusione del cognoscentias currente in re varie aspectos de hemophilia—transmision hereditari, sexo, tempore de coagulation, e interaction de differente plasmas hemophilici—suggere le sequente redefinition del morbo. Hemophilia es un morbo hemorrhagic hereditari que potre occurrere sporadicamente sed tune se transmitte al descendentes; illo es de character recessive con specificitate sexual; illo affice quasi exclusivemente masculos; illo es characterisate per un ben-definitie symptomatologia clinica e alterationes de factores thromboplastic del plasma, lo que resulta multo frequentemente in un prolongation del tempore coagulative e un constante deficientia in le consumption de prothrombina; illo non es corrigeble per le addition de plachettas normal sed potre esser corrigite per plasma normal disproviste de plachettas e per thromboplastina texital. Le datos currentemente disponibile non impoe le postulation de plure hemophilias.

REFERENCES


ALFREDO PAVLOVSKY