Departamento de Genética,
Instituto de Ciências Naturais. Universidade do Rio Grande do Sul,
Pôrto Alegre (Brasil)

Hemophilia B in a Pair of Monozygotic Negro Twins

Israel Roisenberg *

Apparently the first reference about hemophilia in twins dates from 1857 (Bulloch and Fildes, 1911). Since that time some other cases were described (Tab. 1). But in a general way the studies were incomplete, either in relation to the diagnosis of zygosity or as to the testing methods used. For this reason I consider it important to describe in detail the results which I obtained in a pair of Negro twins, both presenting hemophilia B (Christmas disease). They were located during a research which has been going on for several years in our Laboratory, with the aim of studying all cases of hemophilia existing in the Brazilian State of Rio Grande do Sul.

Material and methods

The twins were born in 1938, separated after the third month of life and adopted by two families of different economic levels, both living in Camaquã, at a distance of 127 km from Pôrto Alegre, the Capital of the Brazilian State of Rio Grande do Sul. At the age of 16 one of the twins (V.F. 1) changed his residence to Pôrto Alegre, where he remained until this date. There exist no references of other affected people in the family (Fig. 1).

The information about the hemorrhagic symptoms shown by the twins were gathered by oral interrogation of the affected brothers and their true and adopted parents, independently and at different occasions. The system of multiple choice was choosen. For instance, it was inquired if one of the twins had presented hematomas and in the case of a positive answer if the frequency was annual, semestral, trimestral, etc. The degree of intensity of the symptoms was determined in a subjective way by the interrogator.

Coagulation tests were performed at two occasions: the first at different times and the second in parallel. The results were only compared after completion. The blood was collected without damage to the tissue by venous puncture. The anticoagulant used was 1.34 per cent sodium oxalate in the proportion of nine volumes of blood to one volume of anticoagulant. The blood was immediately centrifuged for 10 minutes at 3,000 r.p.m. Afterwards the plasma was separated and when not

* Fellow of the *Conselho Nacional de Pesquisas*.

Tab. 1. Review of the cases of hemophilia in twins reported in the literature

Author	Twin diagnosis			Type of hemophilia	Concordant	Discordant	Observations
	MZ	DZ	Not determined				
Gould, 1857			+	—	Yes		According to Bulloch and Fildes (1911).
Fischer, 1889			+	—	Yes		Since there are four women reported as affected, one of which suffered from severe bleeding; this may not be a case of true hemophilia. According to Bulloch and Fildes (1911).
Manteufel, 1893			+	—	Yes		According to Bulloch and Fildes (1911).
Sadler, 1898			+	—		Yes	According to Bulloch and Fildes (1911).
De Lacey, 1931			+	—		Yes	
Birch, 1937		+		—	?		Boy and girl. She could be a carrier. According to Quick and Conway (1949).
Birch, 1937			+	—		Yes	According to Quick and Conway (1949).
Birch, 1937	+			—	Yes		According to Quick and Conway (1949).
Sköld, 1944		+		A	?		Boy and girl. She could be a carrier. According to Nilsson et al. (1961) and Ramgren (1962). See 1.
Sköld, 1944			+	—	Yes		According to Ramgren (1962).
Sköld, 1944		+		A		?	Boy and girl. Her tests showed normal values. According to Nilsson et al. (1961 and 1962) and Ramgren (1962). See 1.
Sköld, 1944			+	A	Yes		According to Nilsson et al. (1961) and Ramgren (1962). See 1.
Sköld, 1944		+		—	?		Boy and girl. She could be a carrier. According to Ramgren (1962).
Sköld, 1944		+		B	Yes		Boy and girl. She had hemophilic sons. According to Nilsson et al. (1961) and Ramgren (1962). See 1.
Quick and Conway, 1949 (see 2)	?			A		Yes	The boy died before the development of differencial tests but his maternal first cousin married and had a hemophilic A son (Quick, 1960). See 3.
Quick, 1957 and Quick and Hussey, 1959		+		B	Yes		See 4.
Quick, 1957 and 1960	+			A	Yes		See 5.
Nilsson et al., 1961 and Ramgren, 1962 and 1964		+		B	Yes		See 1.
Geiger and Rath, 1963	+			A + von Willebrand's disease	Yes		See 6.

1. Tests performed: coagulation time, bleeding time, platelet count, AHF assay, Christmas factor assay, circulating anticoagulant, prothrombin consumption test, prothrombin and factor VII assay, factor V assay, fibrinogen assay.
2. Tests performed: coagulation time, bleeding time, platelet count, clot retraction, coagulation time of recalcified plasma, prothrombin time, prothrombin consumption test. The twins are reported as "presumably identical" on the basis of similarity in morphologic and serologic (3 systems) studies.
3. Tests performed: coagulation time, prothrombin time, prothrombin consumption test, AHF assay.
4. Tests performed: coagulation time, bleeding time, torniquet test, prothrombin consumption test, thromboplastin generation test, AHF assay.
5. Tests performed: coagulation time, bleeding time, prothrombin time, prothrombin consumption test, thromboplastin generation test, AHF assay.
6. Tests performed: bleeding time, platelet count, torniquet test, AHF assay, PTA assay, Hageman factor assay, circulating anticoagulant, recalcification time, prothrombin consumption test, prothrombin time, factor V assay, factor VII assay, prothrombin assay, Stuart factor assay, thromboplastin generation test, fibrinogen assay, fibrinolysis.

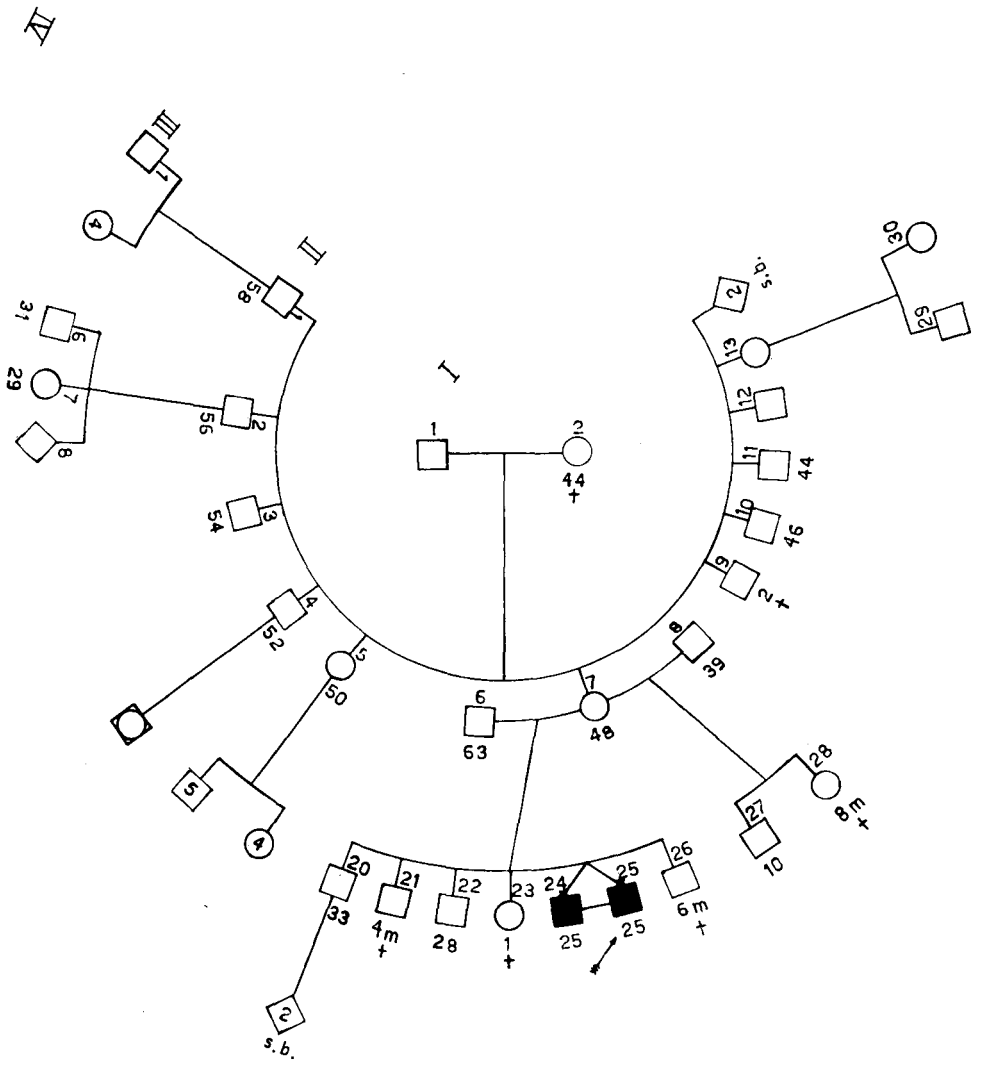

Fig. 1. Pedigree of the twins' family

in use was kept in an ice bath. When tests were performed in parallel special care was taken to assure a minimum difference of time between the collection from one twin and the other (generally 30 minutes). The coagulation tests were carried out in the following way:

Coagulation time. The technique of Lee and White (1913), was used with the whole blood in two tubes of 13 × 100 mm at 37° C.

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Bleeding time. Performed by the method of Duke (1910).

Torniquet test. As described in Biggs and MacFarlane (1957).

Platelet count. Direct method using the diluent of Rees and Ecker (Cartwright, 1958).

Clot retraction. Performed by the method of Rosenfeld (1941).

Prothrombin time. The method of Quick (1957) was used.

Prothrombin consumption test. As described in Cartwright (1958), using 2 ml of whole blood in two tubes. The test was performed at O and 60 minutes of coagulation considering the values of O minute as 100 per cent of activity.

Plasma recalcification time. Was determined by measuring the time interval between the addition of 0.1 ml of calcium chloride solution to a mixture consisting of 0.1 ml of oxalated plasma and 0.1 ml of saline 0.85 per cent at 370 C. and the appearance of a clot.

Thromboplastin generation test. According to the procedure of Biggs and Douglas (1953) with the following modifications: 1) Plasma was treated with barium sulfate rather than aluminium hydroxide; 2) chloroform extract of brain prepared according to the technique of Bell and Alton (1954) instead of the platelet suspension, and 3) eight tubes rather than six were used.

Christmas factor assay. The method of Bolton and Clarke (1959) was used with the following modifications: 1) Saline 0.85 per cent as diluent instead of the glyoxaline buffer, 2) barium sulfate as adsorvent rather than aluminium hydroxide, and 3) phospholipid prepared according Bell and Alton (1954) rather than the technique of Folch (1942). In this as well as in all tests where calcium was necessary, calcium chloride 0.02 M was used.

The twin diagnosis was performed using the characteristics presented in tables 2, 3 and 4 utilizing the usual techniques and those commonly adopted in our laboratory.

The personal history of the twins can be summarized as follows:

V.F. 1 – 25 years, male, Negro, unmarried, shoe-shiner. He was adopted by a family of inferior economic level. He had to overcome serious problems during his life, including bad nutrition and medical-hospital care. At the age of six he broke his nose by accident. Later on, he broke his left knee the welding of the bone was defective, which made him use crutches during some time. Today he moves about with some difficulty because of several hemarthroses which caused serious consequences in both legs (Fig. 2).

V.F. 2 – 25 years, male, Negro, unmarried, farmer. He had a much easier life than his twin brother since he was adopted by a family of normal economic level, with enough food and good medical-hospital care. He never suffered accidents of such intensity which could deform him in a significant way. Today he moves without difficulty in spite of having the articulations of both knees also slightly affected by multiple hemarthroses (Fig. 2).

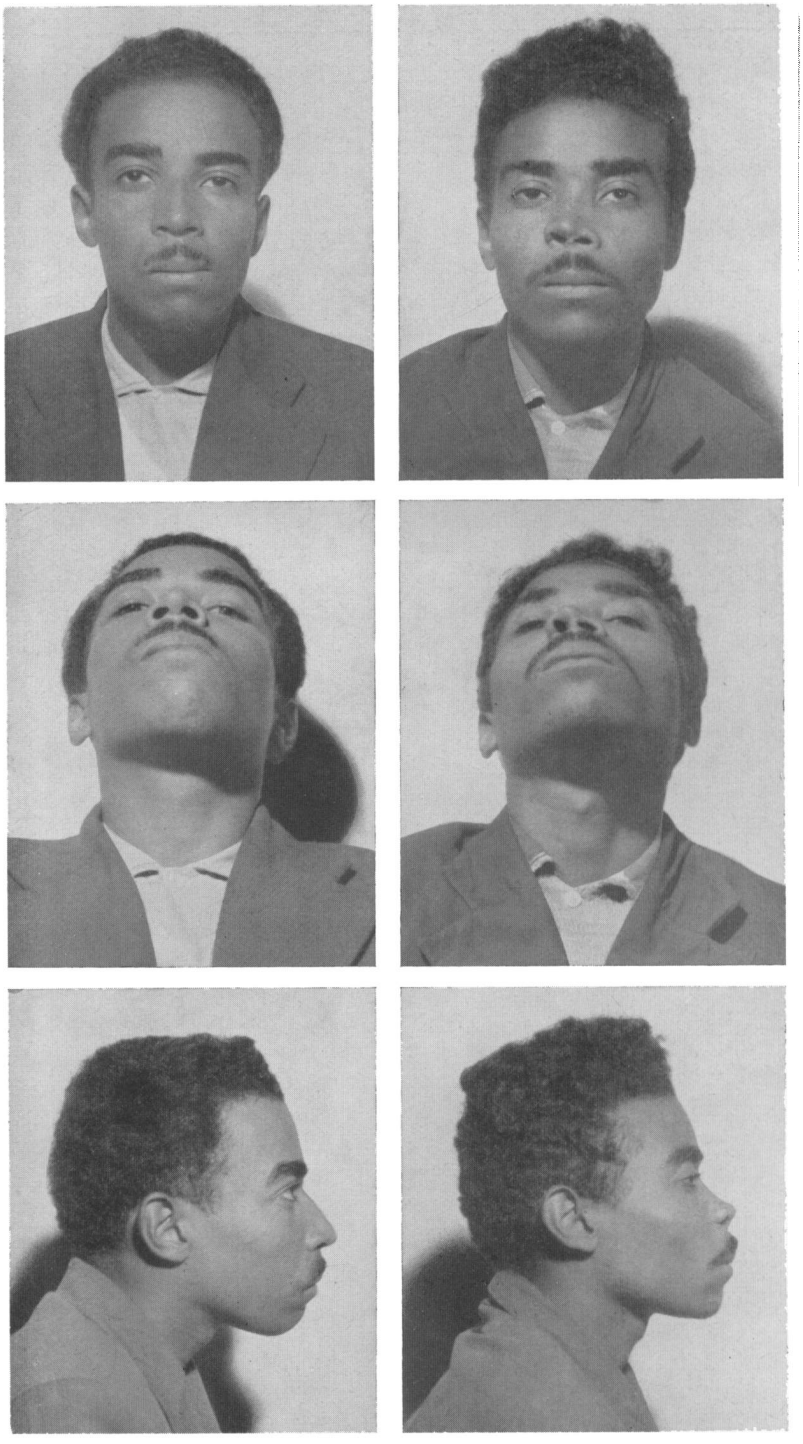

Fig. 2. The twins studied: V. F. 1 (right) and V. F. 2 (left)

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Twin diagnosis

The characteristics presented in Tables 2, 3 and 4 were utilized for the determination of zygosity.

Table 2 presents the morphological and physiological studies performed with a total of 25 measurements or observations, as well as eight calculated indices. The characteristics studied can be divided into two groups: those of anthropometric and palmar (atd angle) measurements and those of mere observation. Concerning the first group it was possible to obtain comparative results for nine anthropometric measurements from Gedda (1951) and Osato and Awano (1957). Of these four presented for our twins variations higher than those expected in monozygotic twins (weight, stature, chest circumference, head length) and five smaller variations (sitting height, vital capacity, head breadth, length and breadth of the nose). With regard to the characteristics which varied too much it was possible to have the probability calculation performed for three (weight, stature and chest circumference); of these only one presented a significant variation at the level of 5 per cent (weight). The atd angle was equal in the left hand of both, but a variation of 7° in the other hand proved enough according to Smith and Penrose (1955) to assume the probability of a dizygosity of 80 per cent. The data gathered by observation show that the twins coincide in seven points (skin color, hair color, eye color, ear lobe, middle-phalangeal hair, relative index finger length, relative 5th digit length) and that there exists a possible concordance as to distal hyperextensibility of the thumb. Photographs of both twins and results of the anthropometric measurements were sent to Dr. Friedrich Keiter, Head of the Laboratory of Legal Anthropology of Hamburg, Germany and specialist in morphologic determinations of the paternity. He belives that the twins are monozygotic and wrote as answer: « ...the morphology, with the exception of the nose, which is totally deformed in one twin, points clearly in favor of monozygosity. The smaller measurements are always obtained from the twin less favored by environment or disease. The same has a less athletic face (cfr. mandibular angles). All traits around the eyes, as well as all traits of the ears, the mouth and chin are concordant in a manner which would be extremely unlikely in dizygotic twins » (cfr. Fig. 2).

Table 3 shows the results of the twins' study and some of their relatives as to characteristics determined by simple genetic factors. Seven systems of blood groups were studied as well haptoglobin types, hemoglobin types, taste sensitivity to phenylthiourea, glucose-6-phosphate dehydrogenase and color blindness, in all of which occurred total concordance. The method of Nijenhuis (1960) can be applied to the genetic systems in which genetic segregation is expected. This method was utilized for the twins in study and showed a probability of monozygosity of 98 per cent.

Table 4 indicates the results of the twins' finger-prints. They were investigated with regard to pattern type and ridge count in each finger. The pattern types are different in two of the ten fingers. By double count, difference occurs in the number of ridges in eight fingers and the total difference is of six ridges. By single count, the

Tab. 2. Some morphologic and physiologic studies performed in twins V. F. 1 and V. F. 2 for the determination of zygosity

Characteristics	V.F. 1	V.F. 2	Differences
Weight	47 kg	54 kg	7 kg
Stature	156.4 cm	160.0 cm	3.6 cm
Sitting height	82 cm	83 cm	1 cm
Lower extremities	74.4 cm	77.0 cm	2.6 cm
Manouvrier index *a*	90.7	92.8	2.1
Nutrition coefficient of von Pirquet *b*	94.8	98.1	3.3
Rohrer index *c*	1.23	1.32	0.09
Vital capacity	2,500 cc	2,800 cc	300 cc
Pulmonary coefficient of Demeny *d*	53.19	51.85	1.34
Vital quotient of Spehl *e*	751.28	945.00	193.72
Dynamometry:			
right hand	18 kg	24 kg	6 kg
left hand	18 kg	24 kg	6 kg
Chest circumference:			
normal	82 cm	87 cm	5 cm
inspiration	88 cm	92 cm	4 cm
expiration	78 cm	80 cm	2 cm
von Brugsch index *f*	52.429	54.375	1.946
Dimensions of the head:			
length	178 mm	185 mm	7 mm
breadth	142 mm	141 mm	1 mm
Cephalic index *g*	79.8	76.2	3.6
Nose:			
length	5 cm	5 cm	—
breadth	4 cm	4 cm	—
Nasal index *h*	80	80	—
Skin color	Dark mulatto	Dark mulatto	—
Hair color	Dark	Dark	—
Eye color	Brown	Brown	—
Ear lobe	Free	Free	—
Middle-phalangeal hair	0	0	—
Relative index finger length	2 <4	2 <4	—
Relative 5th digit length	+	+	—
Distal hyperextensibility of the thumb:			
right hand	25°	25°	—
left hand	30°	25°	5°
Atd angle:			
right hand	44°	37°	7°
left hand	48°	48°	—

The signal + indicates 5th digit longer than joint between middle and distal segments of 4th digit (distal joint).

$$a\ \frac{(\text{Stature-Sitting height}) \times 100}{\text{Sitting height}} \qquad b\ \frac{\text{Weight} \times 10}{\text{Sitting height}} \qquad c\ \frac{\text{Weight (gr)} \times 100}{\text{Stature}^3\ \text{(cm)}}$$

$$d\ \frac{\text{Vital capacity (cc)}}{\text{Weight (kg)}} \qquad e\ \frac{\text{Vital capacity (cc)} \times \text{Weight (kg)}}{\text{Stature (cm)}}$$

$$f\ \frac{\text{Chest circumference} \times 100}{\text{Stature}} \qquad g\ \frac{\text{Breadth} \times 100}{\text{Length}} \qquad h\ \frac{\text{Breadth} \times 100}{\text{Length}}$$

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Tab. 3. Studies of some genetic characteristics performed in twins V. F. 1, V. F. 2 and some of their relatives

Characteristics	Twins		Father	Mother	Brothers	
	V.F. 1	V.F. 2	II-7	II-8	III-20	III-22
Blood groups:						
ABO	$I^B\ I^O$	$I^B\ I^O$	$I^B\ I^O$	$I^{A2}\ I^O$	$I^{A2}\ I^O$	$I^B\ I^O$
MN [1]	$L^M\ L^N$	$L^M\ L^N$	$L^M\ L^N$	$L^M\ L^N$	$L^M\ L^M$	$L^M\ L^N$
Rh (Tests with 5 sera) [2]	$R^1\ R^O$	$R^1\ R^O$	$R^O\ R^O$	$R^1\ R^O$	$R^1\ R^O$	$R^1\ R^O$
Kell [3]	*kk*	*kk*	*kk*	*kk*	*kk*	*kk*
Duffy	$Fy^a\ Fy^b$	$Fy^a\ Fy^b$	$Fy^b\ Fy^b$	Fy^a—	$Fy^a\ Fy^b$	$Fy^a\ Fy^b$
P	P_1—	P_1—	P_1—	P_1—	P_1—	P_1—
Wright	$wr^a\ wr^a$	$wr^a\ wr^a$	$wr^a\ wr^a$	$wr^a\ wr^a$	$wr^a\ wr^a$	$wr^a\ wr^a$
Haptoglobin types	$Hp^1\ Hp^1$	$Hp^1\ Hp^1$	$Hp^1\ Hp^1$	$Hp^2\ Hp^1$	$Hp^2\ Hp^1$	$Hp^2\ Hp^1$
Hemoglobin types	$Hb^A\ Hb^A$	$Hb^A\ Hb^A$	$Hb^A\ Hb^A$	$Hb^A\ Hb^A$	$Hb^A\ Hb^A$	$Hb^A\ Hb^A$
Taste sensitivity to phenylthiourea [4]	*T*—	*T*—	nt	nt	nt	nt
Glucose-6-phosphate dehydrogenase [5]	*Gl*	*Gl*	nt	nt	nt	nt
Color blindness [5]	*Cv*	*Cv*	*Cv*	nt	nt	nt

Observation: The — signal indicates that the other member of the gene pair could not be ascertained with certainty.

nt = not tested

[1] Tests for *Mg* performed with negative results

[2] Tests for *Cw* performed with negative results

[3] Tests for Kp^a performed with negative results

[4] Threshold: 0.63 mg/l in both twins

[5] Normal values. Since this is a sex-linked trait only one gene is represented.

Tab. 4. Finger-prints of twins V. F. 1 and V. F. 2

Hand	Digit	V.F. 1		V.F. 2		S
		Pattern type	Ridge count	Pattern type	Ridge count	
Right	1	Ulnar loop	13	Ulnar loop	14	0.02996
			—		—	—
	2	Radial loop	4	Radial loop	4	—
			—		—	—
	3	Ulnar loop	9	Ulnar loop	9	—
			—		—	—
	4	Whorl	12	Ulnar loop	12	—
			6		—	0.84510
	5	Ulnar loop	2	Ulnar loop	4	0.22185
			—		—	—
Left	1	Ulnar loop	15	Ulnar loop	13	0.05799
			—		—	—
	2	Arch	0	Radial loop	—	—
			—		2	0.47712
	3	Ulnar loop	10	Ulnar loop	8	0.08715
			—		—	—
	4	Ulnar loop	11	Ulnar loop	9	0.07918
			—		—	—
	5	Ulnar loop	3	Ulnar loop	4	0.09691
Sums			85		79	1.89526

Pattern type differences = 2. Total ridge count differences, by double count = 6, by single count = O. T = log 105 − log 99 = 0.02555. S = sum of (log 15 − log 14), etc. = 1.89526. Z = log (1.89526 + 0.76650) = 0.42517 PMZ = 0.95

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difference in the number of ridges is in seven fingers, but in the total count there is no difference in the ridge number. As to the ridge count, it was also possible to calculate the probability of monozygosity of the twins using the method of Slater (1963). The calculation is indicated in table 4 and it presents a probability of monozygosity of 95 per cent which is perfectly concordant with the evaluation obtained using the blood groups and the haptoglobin types.

Analysis of the clinical and laboratory data

Table 5 relates the fourteen hemorrhagic symptoms which were investigated in the twins. With the exception of the surgical hemorrhage shown in twin V.F. 2 when

Tab. 5. Hemorrhagic symptoms in twins V. F. 1 and V. F. 2

Symptoms	V.F. 1			V.F. 2		
	Presence	Frequency	Degree	Presence	Frequency	Degree
Hematomas	+	Four times a year	++	+	Four times a year	++
External bleeding	+	On three occasions	++	+	On three occasions	++
Ecchymoses	+	Annual	+	+	Annual	+
Hemorrhages after tooth extractions	o			o		
Hemarthrosis without impaired joint function	+	Six times a year	++	+	Two times a year	+
Hemarthrosis with impaired joint function	+	In all extremities		+	In all extremities	
Epistaxis	+	Monthly	++	+	Annual	++
Hematuria	+	On one occasion	++	+	On one occasion	++
Spontaneous bleeding from gums	—			—		
Intra-cranial bleeding	—			—		
Melena	—			—		
Intra-abdominal hemorrhage	—			—		
Hematemesis	—			—		
Surgical hemorrhage	o			+	On one occasion	+++

Presence – (+ yes) (— no) (o no information)
Degree – (+ evident) (++ moderate) (+++ intense)

the solution of hematoma was tried, concordance occurs in seven of the manifested symptoms. The frequency was equal in four of the symptoms; being the degree of intensity concordant in five. Hematomas and ecchymoses always presented normal reabsortion. External hemorrhages occurred from accidental cuts. None of the twins had extracted teeth and the fall of the milk teeth occurred without problems. Epistaxis was more frequent in both during childhood, but the frequency decreased with increasing age. Both received many transfusions.

Table 6 shows the results of coagulation tests. Ten coagulation tests were performed; with the exception of bleeding time, the torniquet test and the dosage of the Christmas factor, all were done at two occasions: first at different times and then in parallel. As expected the greatest similarity was observed when the tests were per-

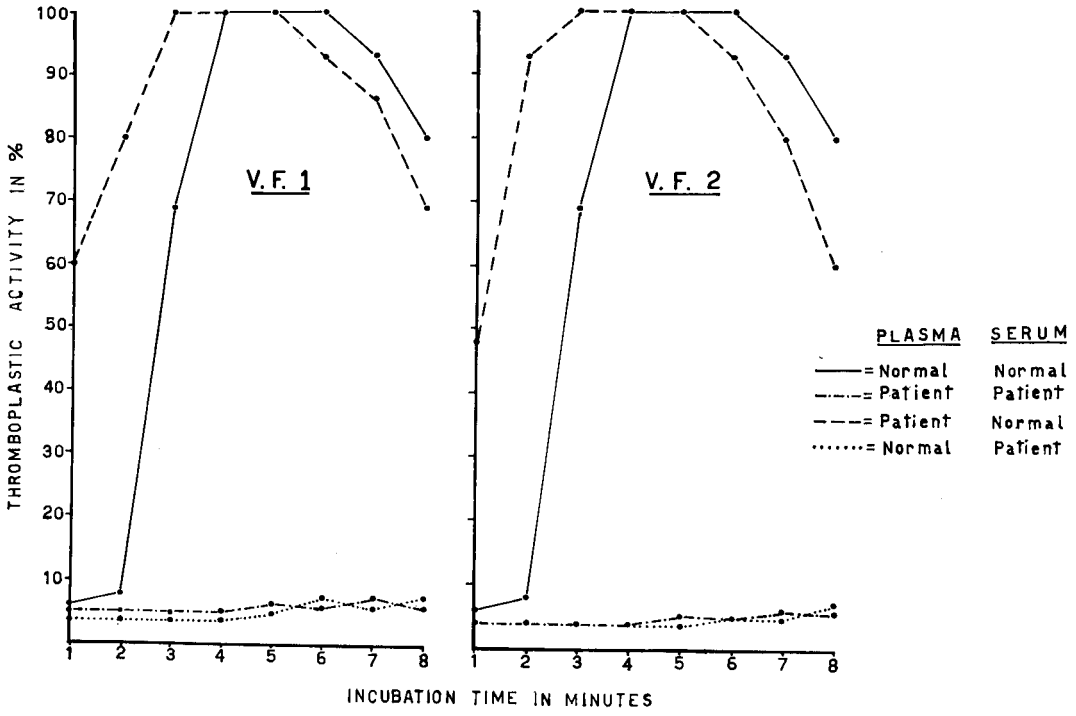

Fig. 3. Results of the thromboplastin generation test performed in the twins

formed in parallel. The results with indirect tests as the prothrombin consumption test and thromboplastin generation test (Fig. 3) already showed that the concentration of the Christmas factor could be expected to be very similar in the twins. The quantitative dosage proved this to be true.

Discussion

As can be seen from Table 1, there are only three cases of hemophilia B in twins cited in the literature. One of these (Sköld, 1944; review by Nilsson et al., 1961 and Ramgren, 1962) concerns a pair of dizygotic twins since they belong to different sexes. Quick (1957 and 1959) describes a pair referred to as dizygotic and concordant in hemophilia B, but in spite of the quoted tests having without doubt, shown

Tab. 6. Coagulation tests performed in twins V. F. 1 and V. F. 2

Tests	Normal values	Different times			Parallel		
		V.F. 1	V.F. 2	Differences	V.F. 1	V.F. 2	Differences
Bleeding time	1-3 min	1 min	1 min	—			
Clotting time	10 min	12-14 min	12-14 min	—	13-20 min	13-20 min	—
Torniquet test	negative	normal	normal	—			
Clot retraction	50%	70%	75%	5%	70%	70%	—
Platelet count/c.m.m.	150-350,000	247,500	262,500	15,000 platelets (6%)	196,500	201,000	4,500 platelets (2%)
Prothrombin time (Quick)	12-12 sec (100%)	12-12 sec	12-12 sec	—	12-12 sec	12-12 sec	—
Prothrombin consumption	84%-87%/74%	28%	31%	3%	14%	13%	1%
Plasma recalcification time	105-95/55-52/75-90 sec	255-270 sec	68-69 sec	194 sec	80-80 sec	85-85 sec	5 sec
Thromboplastin generation test (see fig. 3)		Abnormal Correction with serum	Abnormal Correction with serum		Abnormal Correction with serum	Abnormal Correction with serum	
Christmas factor assay	100%				21.1%	21.4%	0.3%

a differential diagnostic, the Christmas factor quantitative dosage was not established; but the results of the tests and the clinical histories show a great similarity. The third case (Nilsson et al., 1961 and Ramgren, 1962) is referred to as dizygotic twins (Ramgren, 1964) since they have different blood groups. They are the only pair for whom the Christmas factor dosage was established; the results showed a greater intra-pair variation (3-4 per cent) than the one observed in our case (0.3 per cent). This can be explained either by the fact that the Ramgren twins were dizygotic or by variations due to the different techniques employed.

The determination of the zygosity in our case proved to be difficult, because the twins were reared apart with different social-economic levels, suffering from a disease which can cause physical defects and with different possibilities of medical-hospital care. In relation to anthropometric and palmar data for which it was possible to get comparative data from other twin series, five provided indications of monozygosity and five of dizygosity. However, the total concordance in seven other observed characteristics and the general morphology indicate that the twins are monozygotic. Considering now the characteristics determined by simple genetic factors (blood groups and haptoglobin types) or those which having a more complex type of inheritance (ridge count of finger-prints) would not be affected by nutritional values or by disease, the probabilities of monozygosity are very high (98 and 95 per cent) and very similar. Therefore it is possible to conclude with some certainty that these twins are really monozygotic.

The clinical and laboratory data are very similar in both twins which agrees with the studies of Graham et al. (1958), Simpson and Biggs (1962) and Lewis et al. (1963) who showed that the genes causing hemophilia B have a considerable intra-familiar concordance in their consequences on the Christmas factor level. Our data also show an almost absolute concordance in the Christmas factor level for the twins. In a indirect way they also show that the diet does not necessarily disturb such levels since the twins had very different qualities of nutrition during all their lives. The consequences left by the disease, however, were different; one of the twins (V.F. 1) is in precarious physical conditions, while the other (V.F. 2) enjoys a relatively good health. This means that it is possible that no absolute direct relation between the Christmas factor levels and the consequences left by the disease exist. The differences in physical conditions of the twins studied can be interpreted as due only to differences in medical-hospital care.

Summary

A detailed description is given of the study performed in a pair of monozygotic Negro twins both suffering from hemophilia B; the bibliography is also reviewed about the occurrence of hemophilia in twins. The zygosity determination was performed utilizing anthropometric measurements, observation data, finger and palmar prints, seven systems of blood groups and five other genetic systems. The twins present a great similarity in the hemorrhagic symptoms, coagulation tests and Christ-

mas factor level, but morphologic and physical differences due to the disease. These differences are explained by the diversity in the medical-hospital care which both received.

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References

Bell W. N. and Alton H. G.: A brain extract as a substitute for platelet suspensions in the thromboplastin generation test. Nature, 174: 880-881, 1954.

Biggs R. and Douglas A. S.: The thromboplastin generation test. J. Clin. Path., 6: 23-29, 1953.

— and MacFarlane R. G.: Human blood coagulation and its disorders. 2th edition. Blackwell Scientific Publications, Oxford, 1957.

Bolton F. G. and Clarke J. E.: A method of assaying Christmas factor; its application to the study of Christmas disease (factor-IX deficiency). Brit. J. Haemat., 5: 396-412, 1959.

Bulloch W. and Fildes P.: Haemophilia. Treasury of human inheritance, Parts V and VI, Section XIVa. Galton Laboratory, University of London, 1911.

Cartwright G. E.: Diagnostic laboratory hematology. 2th edition. Grune & Stratton, New York, 1958.

De Lacey M.: Haemophilia in a twin. Lancet, 2: 1074-1075, 1931.

Duke W. W.: The relation of blood platelets to hemorrhagic disease; description of a method for determining the bleeding time and coagulation time and report of three cases of hemorrhagic disease relieved by transfusion. J. A. M. A., *55: 1185-1192, 1910.*

Folch J.: Brain cephalin, a mixture of phosphatides. Separation from it of a phosphatidyl serine, phosphatidyl ethanolamine, and a fraction containing an inositol phosphatide. J. Biol. Chem., 146: 35, 1942.

Gedda L.: Studio dei gemelli. Edizioni Orizzonte Medico, Roma, 1951.

Geiger M. T. and Rath C. E.: Occurrence of two hemorrhagic disorders with antihemophilic factor (AHF) deficiency in the same family: classical hemophilia and von Willebrand's disease. J. Lab. Clin. Med., 61: 424-436, 1963.

Graham J. G., Bullock W. R. and Barrow, E. M.: Genetic control of the hemophilioid states: characteristics of the carrier state in PTC-deficiency (Christmas disease). Proc. VIIth Intern. Cong. Internat. Soc. Hematol., Rome: 176-180, 1958.

Lee R. I. and White P. D.: A clinical study of the coagulation time of blood. Amer. J. Med. Sci., 145: 495-503, 1913.

Lewis J. H., Didisheim P., Ferguson J. H. and Li C. C.: Genetic considerations in familial hemorrhagic disease. I. The sex-linked recessive disorders, hemophilia and PTC deficiency. Amer. J. Hum. Gen., 15: 53-61, 1963.

Nijenhuis L. E.: Blood groups in twin studies. Calculation of the probability of monozygosis. A. Ge. Me. Ge., 9: 301-308, 1960.
Nilsson I. M., Blomback M. and Ramgren O.: Haemophilia in Sweden. I. Coagulation studies. Acta Med. Scand., 170: 665-682, 1961.
— — — and Francken I. V.: Haemophilia in Sweden. II. Carriers of haemophilia A and B. Acta Med. Scand., 171: 223-235, 1962.
Osato S. and Awano I.: Genetische Studien an Zwillingen. A. Ge. Me. Ge., 6: 283-366, 1957.
Quick A. J. and Conway J. P.: Hemophilia in twins. Am. J. Med., 7: 841-843, 1949.
— Hemorrhagic diseases. Lea & Febiger, Philadelphia, 1957.
— and Hussey C. V.: Hemophilia B (PTC deficiency, or Christmas disease). Arch. Int. Med., 103: 762-775, 1959.
— Sporadic hemophilia. Arch. Int. Med., 106: 335-340, 1960.
Ramgren O.: A clinical and medico-social study of haemophilia in Sweden. Acta Med. Scand., 171, suppl. 379: 111-190, 1962.
— Personal communication, 1964.
Rosenfeld G.: Retração do coágulo sanguineo. Revista Clinica de S. Paulo, 10: 43-49, 1941.
Simpson N. E. and Biggs R.: The inheritance of Christmas factor. Brit. J. Haemat., 8: 191-203, 1962.
Slater E.: Diagnosis of zygosity by finger prints. Acta Psychiat. Scand., 39: 78-84, 1963.
Smith S. M. and Penrose L. S.: Monozygotic and dizygotic twin diagnosis. Ann. Human Genet., 19: 273-289, 1955.

RIASSUNTO

Viene presentata una descrizione dettagliata dello studio condotto su di una coppia di gemelli monozigotici, negri, portatori di emofilia B, ed una rassegna bibliografica sull'incidenza dell'emofilia in gemelli. Per determinare lo zigotismo si sono usate misurazioni antropometriche, risultati di osservazioni, impronte digitali e palmari, sette sistemi di gruppi sanguigni e cinque altri sistemi genetici. I gemelli presentano grande somiglianza nei sintomi emorragici, nelle prove di coagulazione e livelli del fattore Christmas, ma differenze morfologiche e fisiche dovute alla malattia, le quali possono essere addebitate al diverso trattamento medico-ospedaliero ricevuto.

RÉSUMÉ

L'auteur présente une description détaillée de l'étude d'un couple de jumeaux monozygotes, nègres, porteurs d'hémophilie B, ainsi qu'une analyse bibliographique sur la présence d'hémophilie chez les jumeaux. La détermination du zygotisme a été faite moyennant des mesurations anthropométriques, des données d'observation, les empreintes digitales et de la paume, sept systèmes de groupes sanguins et cinq autres systèmes génétiques. Les jumeaux présentent une grande ressemblance dans les symptômes hémorragiques, les preuves de coagulation et le niveau du facteur Christmas, mais des différences morphologiques et physiques dues à la maladie, qui sont explicables par la diversité des soins médicaux hospitaliers qu'ils ont reçu.

ZUSAMMENFASSUNG

Ausführliche Beschreibung der Untersuchungsergebnisse an einem Neger-EZ-Paar, Träger einer Hämophilie B, sowie literarische Übersicht über das Vorkommen der Hämophilie bei Zwillingen. Zur Eiigkeitsbestimmung dienten Körpermaße, Beobachtungsergebnisse, Finger- und Handflächenabdrücke, sieben Blutgruppen- und fünf andere Erbsysteme. Große Ähnlichkeit weisen die Zwillinge in den hämorragischen Symptomen, in den Koagulationsproben und in dem Niveau des Christmas-Faktors auf. Hingegen unterscheiden sie sich in den krankheitsbedingten morphologischen und physischen Merkmalen, was auf die unterschiedliche ärztliche und stationäre Behandlung zurückgeführt werden kann.