A Pair of Twins, One of whom has Chronic Granulocytic Leukaemia

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The finding that one of our patients with chronic granulocytic leukaemia had an apparently identical twin brother led us to undertake genetic studies to establish zygoty, and to study carefully their history for any possible leukaemogenic factors. Bone-marrow cells of the affected twin contained the Ph¹ chromosome whereas those of his brother did not (Woodliff and Dougan, 1965).

Material and Methods

Blood was collected from the twins, one sib, and their parents by venepuncture (Fig.).

Blood groups were determined by standard methods at the Human Genetics Unit, University of Western Australia. The antisera used were anti-A, anti-A₁, anti-B, anti-AB, anti-C, anti-c, anti-D, anti-E, anti-e, anti-C^W, anti-E^W, anti-E^T, anti-V, anti-M, anti-N, anti-S, anti-s, anti-Mi^a, anti-Vw, anti-Mg, anti-P₁, anti-K, anti-k, anti-Kp^b, anti-Kp^a, anti-Le^a, anti-Le^b, anti-Fy^b, anti-Lu^b, anti-Xg^a, anti-Vel, anti-Wr^a, anti-Di^a, anti-Js^a, anti-Jk^a, anti-Jk^b, and anti-Fy^a. The Gm and Inv types were done by courtesy of Dr. Arthur G. Steinberg. Transferrin and haptoglobin types were determined by vertical starch gel electrophoresis by the method of Smithies (1959). Serum alkaline phosphatase types were examined by a modification of the method of Arfors, Beckman, and Lundin (1963), as previously described (I. D. Scott and M. K. Scott, 1966, unpublished observations).

The parents, the twins, and the younger sister were carefully interviewed concerning their family history, and a standard questionnaire was completed for the twins.

Results

Genetic Study. The detailed findings of the blood grouping investigation and the examination of the serum genetic markers are given in Table I. In addition, all subjects were found to be C^W(-), E^W(-), V(-), Mg(-), V^W(-), Vel(-), Di(a-), Wr(a-), and Js(a-). Results of the Gm typing showed that I.2 was homozygous for the factors

Gm^{3, 5, 13, 14}, and that the subjects I.1, II.3, II.4, and II.5 were heterozygous Gm¹/Gm^{3, 5, 13, 14}. All subjects were of the Inv phenotype Inv(1-). The nomenclature is that proposed by a committee of W.H.O. (1965).

From the results of the Gm typing and the findings set out in Table I, the probability that this pair of twins was monozygotic was calculated as suggested by Dr. C. W. Cotterman (Race and Sanger, 1962), and is as shown in Table II.

It was calculated that the probability that the twins were monozygotic was 0.995.

Personal and Family Histories

The twins E.F. and F.F. were born at King Edward Memorial Hospital for Women, Subiaco, Western Australia, on March 30, 1928; the parents were Roman Catholics who had recently migrated to Australia from Italy. This was the mother's third pregnancy and it continued to term. She had no recollection of any antenatal X-ray examinations. F. was born first as a vertex presentation and E. within the next few minutes by the breech. Their early development was quite normal and the first 10 years were spent in an inner suburb of metropolitan Perth. In 1938, when the twins

FIG. Pedigree chart.

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TABLE I
DATA BEARING ON ZYGOSITY

	I.1	I.2	II.3	II.4	II.5
<i>Blood groups</i>					
ABO	OO	A ₁ O	A ₁ O	A ₁ O	OO
Rhesus	R ₁ r	R ₁ r	rr	rr	R ₁ r
MNSs	MsMs	NsNs	MsNs	MsNs	MsNs
P	P ₁ (w)	P ₁	P ₁ (w)	P ₁ (w)	P ₁
Kell	k _B k _B	k _B k _B	k _B k _B	k _B k _B	k _B k _B
Lewis	Le(a-b+)	Le(a-b+)	Le(a-b+)	Le(a-b+)	Le(a-b+)
Duffy	Fy(a-b+)	Fy(a-b+)	Fy(a-b+)	Fy(a-b+)	Fy(a-b+)
Kidd	Jk(a+b+)	Jk(a+b+)	Jk(a+b+)	Jk(a+b+)	Jk(a+b+)
Lutheran	Lu(a-b+)	Lu(a+b+)	Lu(a+b+)	Lu(a+b+)	Lu(a-b+)
Mia	Mi(a-)	NT	NT	NT	Mi(a-)
Xg ^a	NT	NT	Xg(a+)	Xg(a+)	NT
<i>Serum factors</i>					
Transferrins	CC	CC	CC	CC	CC
Haptoglobins	2-2	2-2	2-2	2-2	2-2
Alkaline phosphatase	Pp1	Pp1	Pp1	Pp1	Pp1

TABLE II
CALCULATION OF ZYGOSITY

Initial chance of being dizygotic	0.70	monozygotic	0.30
Likeness of sex	0.50	"	1.00
Likeness of blood group:			
ABO	0.50	"	1.00
Rhesus	0.25	"	1.00
MMSs	1.00	"	1.00
P	0.50	"	1.00
Kell	1.00	"	1.00
Duffy	0.50	"	1.00
Lewis	1.00	"	1.00
Lutheran	0.50	"	1.00
Kidd	0.50	"	1.00
Likeness of serum factors:			
Haptoglobins	1.00	"	1.00
Transferrins	1.00	"	1.00
Alkaline phosphatase	1.00	"	1.00
Gm factors	0.50	"	1.00
Inv factors	1.00	"	1.00
	0.0014		0.30
Relative chance of this pair of twins being dizygotic	0.30	0.0014 : 0.30	
Probability of being monozygotic		= 0.995	
Probability of being dizygotic	1.0 - 0.995 = 0.005		

Note: NT, not tested, either unavailable or antisera not suitable.
Kell genotypes are notated as proposed by Allen, Lewis, and Fudenberg (1958).

were 10 years of age, the family moved back to Europe and lived there for the next 11 years in Bergamo, Northern Italy. There the boys went to school together and most of their activities were shared. They took up the same sport of cycling.

Returning to Australia in 1949, they went to work for a Perth firm engaged in galvanizing iron, and stayed in this occupation for two years. Following this both joined the government railway service, E. as a shunter, and F. as a signalman, and they have continued in these occupations.

E. married in 1955 and set up house in an inner metropolitan suburb, his twin married two years later and lived in the same area, two streets from E. The parents' home and those of both twins are all within a radius of one mile.

Neither twin had been exposed to radiological procedures apart from routine chest clinic surveys and neither had a significant drug history. E. suffered from otitis media and sinusitis during the two years before the diagnosis of his blood dyscrasia in 1963. At the time of the earlier mild illness he was found to be allergic to milk and kapok. Family members described personality differences, F. having been always the more dominant and E. having a more gentle nature.

E. and his father both suffered from moderate deafness. In the case of E. this was due to otosclerosis and this was probably also the case with his father. F. had normal hearing.

The living sibs are two sisters, born in 1922 and in 1931, both of whom are in good health but only one was available for testing and interview. Another female sib,

born in 1921, died at the age of 6 months from respiratory tract infection. There was no family history of other serious blood dyscrasias, malignancy, congenital malformations, major allergic state, or parental consanguinity.

Discussion

The aetiology of chronic granulocytic leukaemia is unknown but it is considered unlikely that hereditary factors are important, since there is no familial incidence of the disease. The role of the Ph¹ chromosome is uncertain, but since it is present only in the haemopoietic cells the abnormality cannot be hereditary, a deduction confirmed by the finding in the present twins and in another pair of twins reported by Goh and Swisher (1965) that the Ph¹ chromosome occurs only in the affected twin (Woodliff, Dougan, and Onesti, 1966). Irradiation is the only generally accepted aetiological agent in leukaemia. Other possible leukaemic agents include certain drugs and chemicals, viruses and other infective agents, and dietary deficiencies. It was, therefore, important to seek out any possible differences in the environmental history of the twins. In spite of diligent questioning we were unable to detect any differences that might reasonably be thought to be leukaemogenic.

Summary

Monozygosity was established with reasonable certainty in a pair of twins, one of whom had chronic granulocytic leukaemia. No apparent environmental stimulus to leukaemogenesis was found. Nevertheless it must be concluded that nurture rather than nature is the more important in the development of this form of leukaemia.

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