Z. Rechtsmedizin 80, 55–59 (1977)

Zeitschrift für
Rechtsmedizin

Polymorphism of the Third Component (C3) of Complement and of Transferrin (Tf) in Belgium

B. Hoste, J. Brocteur, J. Suys, and A. Andre

Laboratoire des Groupes Sanguins et de Transfusion de l'Universite de Liege
Rue Dos Fanchon 39, B-4020 Liege, Belgium

Summary. The phenotypes of C3 and of Tf were determined in 818 and 576, respectively, unrelated individuals living in Liege. The gene frequencies observed are:

$C3^S$:	0.811	$C3^F$:	0.186	$C3^{Var}$:	0.003
Tf^C:	0.990	Tf^B:	0.007	Tf^D:	0.003

The application to disputed paternity cases and to the study of twins is discussed.

Zusammenfassung. Die Bestimmung der C3 – und Tf – Phänotypen bei 818, beziehungsweise 576, Einwohnern von Liege (Belgien) ergab folgende Genfrequenzen:

$C3^S$:	0.811	$C3^F$:	0.186	$C3^{Var}$:	0.003
Tf^C:	0.990	Tf^B:	0.007	Tf^D:	0.003

Die Verwendung dieser Gruppen in der Vaterschaftsbegutachtung und bei Zwillingenuntersuchungen wird diskutiert.

Key words. C3 polymorphism – Tf polymorphism – paternity cases – gene frequencies, C3 and Tf

I. Introduction

The polymorphism of C3 in man was described in 1967 by Wieme and Demeulenaere [15], then by Alper and Propp [1] and by Azen and Smithies [3] in 1968. Since then, it has been intensively studied from two points of view: the population genetics and the medico-legal application. We are reporting the results obtained in Belgium.

Transferrin also shows a polymorphism, a fact long known (Smithies, 1957) [11]. As it is evidenced by the same electrophoresis as for C3, we also show the distribution of variants in Belgium.

II. Material and Methods

The 818 Belgian individuals studied were either blood donors or unrelated adults involved in disputed paternity cases.

Table 1. Frequencies of the C3 variants in Liege

Results	C3 Phenotypes						gene frequencies		
	SS	FS	FF	Var. S	Var. F	Total number	C_3^S	C_3^F	C_3^{Var}
Number	538	246	29	4	1	818	0.811	0.186	0.003
Frequency	0.658	0.301	0.035	0.005	0.001	1.000			

$\chi^2_2 = 0.02$ $p \sim 0.99$

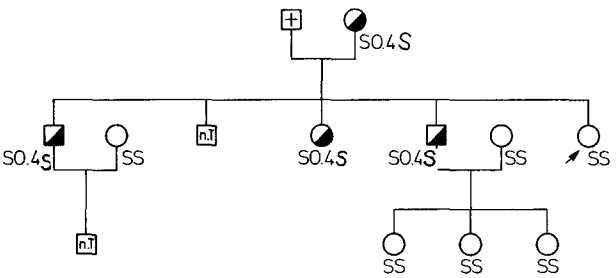

Fig. 1. Pedigree of the VAN. . . family showing the inheritance of the S0.4 variant of C3

The C3 and Tf groups were determined by high voltage electrophoresis in agarose, according to Teisberg [12], followed by fixation in a 10% solution of acetic acid and by staining with Brilliant Coomassie blue (0.125g %)

III. Results and Conclusion

a) Gene Frequencies and Inheritance

The frequency of the C3 variants in Liege is shown in Table 1.

Five rare variants were found. Two were identified as S0.5S, one as S0.4S by Prof. Rittner of the Bonn Reference Laboratory for Polymorphism of the Third Component. It had not been possible to take further samples of two F* F and S* S variants. With regard to the VAN. . . S0.4 variant, the family study confirms the supposed inheritance (Fig. 1). We must point out that this study was carried out because a very rare CDE/cd(e) Rhesus group had been detected in the propositus.

The distribution of the two main alleles of C3 is very homogeneous in Caucasian populations (see Table 2). In the black race, their frequency appears to vary more. Few populations, however, have been studied up to now.

The distribution of the Tf variants in Liege is shown in Table 3. We have classified the variants as B and D, without more precision as to their phenotype. The 11 subjects are very likely of Caucasian origin.

Table 2. Distribution of the variants of C3 in the Caucasian populations

Population	Numbers studied	Gene frequencies			References
		$C3^S$	$C3^F$	$C3^{Var}$	
U.S.A.	462	0.77	0.22 to 0.21	0.004 to 0.014	1,3
Lapland	346	0.9369 to 0.973	0.0631 to 0.027	0	4,13
Finland	1034	0.8298	0.1702	0	2
Norway	2454	0.7865	0.2082	0.0053	13
Sweden	213	0.77	0.23	0	4
Denmark	406	0.816	0.182	0.001	5
Germany	5407	0.7791 to 0.803	0.2152 to 0.193	0.0100 to 0.004	6,7,8,10
Belgium	816	0.811	0.186	0.003	present publication
Switzerland	2961	0.7924	0.2028	0.0047	9
Spain	961	0.7826	0.2113	0.0059	6

Table 3. Distribution of the transferrin variants in Liege

	Tf phenotypes					Gene frequencies		
	C	BC	CD	BD, B or D	Total	Tf^C	Tf^B	Tf^D
Number	565	8	3	0	576	0.990	0.007	0.003
Frequency	0.981	0.014	0.005		1.000			

b) Applications

Disputed Paternity Cases: The C3 system is very useful in disputed paternity cases as it yields, a priori, a 13% probability of excluding an individual who is not the father. Moreover, the C3 group can already be determined in the newborn.

Since we determined the C3 groups, in 53 expertises, the alleged father was excluded. Since the blood and serum groups we use enable us to detect "only" 94% of false fathers, it may be concluded that our 53 cases of exclusion correspond, to 56 cases in which there should be an exclusion.

Of the 53 exclusions, 8 were confirmed by the C3 groups. The results of our expertises are thus consistent with the computed exclusion probability by this system alone: 13%. (see Table 4).

Studies on Twins: The C3 group is an additional element to be added to the other blood and serum groups in order to determine the probability of twins being monozygotic. On the other hand, studies on twins can confirm the genetic inheritance of the C3 variants.

With a small series of 48 pairs of twins, we obtained the following results, which are consistent with the expected data (Table 5).

Table 4. Efficiency of C3 groups in disputed paternity cases

Number	"False fathers" excluded by C3	"False fathers" not excluded by C3	Total
Observed	8	48	56
Expected	7.28	48.72	56

$\chi^2_1 = 0.04$ $p \sim 0.84$

Table 5. Study of the C3 group in twins

	Numbers	C3 group	
		consistent	different
31 pairs of monozygotic twins	observed	31	0
	expected	31	0
17 pairs of dizygotic twins	observed	10	7
	expected	12.44	4.56

For dizygotic twins $\chi^2_1 = 0.78$ $p \sim 0.40$

Table 6. Chances of two children of a same couple, taken at random, of having different C3 groups

Possible couples			Frequency of each couple	Possible children for each couple and their frequency		
				FF	FS	SS
FF	X	FF	p^4	p^4		
FF	X	FS	$4p^3q$	$4p^3q \times 1/2$	$4p^3q \times 1/2$	
FS	X	FF				
FF	X	SS	$2p^2q^2$		$2p^2q^2$	
SS	X	FF				
FS	X	FS	$4p^2q^2$	$4p^2q^2 \times 1/4$	$4p^2q^2 \times 1/2$	$4p^2q^2 \times 1/4$
FS	X	SS	$4pq^3$		$4pq^3 \times 1/2$	$4pq^3 \times 1/2$
SS	X	FS				
SS	X	SS	q^4			q^4
Probability of a different group in the second child				$2p^3q \times 1/2$ $p^2q^2 \times 3/4$	$2p^3q \times 1/2$ $2p^2q^2 \times 2/4$ $2pq^3 \times 1/2$	$p^2q^2 \times 3/4$ $2pq^3 \times 1/2$
Sum (after algebraic transformation)				$pq\left(2 - \frac{3pq}{2}\right)$		

The expected figures were calculated as follows: The probability that dizygotic twins may have different C3 groups is the same as for brothers and sisters, and can, therefore, be calculated as shown in Table 6. p and q represent the respective frequencies of alleles F and S. When they are replaced by their numerical values 0.186 and 0.811 we obtain a discrepancy probability of 0.268, which yields, for 17 pairs of dizygotic twins, a theoretical figure of 4.56 pairs with different C3 groups.
From our studies we conclude that the alleles of C3 are very homogeneously distributed in Europe.

This group may be successfully used in disputed paternity cases and in studies on twins.

References

1. Alper, C. A., Propp, R. P.: Genetic Polymorphism of the Third Component of Human Complement (C'3). J. Clin. Invest. **47**, 2181–2191 (1968)
2. Arvilommi, H.: Genetic Polymorphism of Serum C3 in Finns. Vox Sang. **25**, 9–27 (1973)
3. Azen, E. A., Smithies, O.: Genetic Polymorphism of C'3 (B_1 C-globulin) in human serum. Science **162**, 905–907 (1968)
4. Bronnestam, R., Beckman, L., Cedergren, B.: Genetic Polymorphism of the Complement Component C3 in Swedish Lapps. Human Hered. **21**, 267–271 (1971)
5. Dissing, J., Sorensen, H.: Studies on C'3 Polymorphism in Denmark. Human Hered. **21** 272–277 (1971)
6. Goedde, H. W., Benkmann, H. G., Agarwal, D. P., Hirth, L.: Further Investigation on the Inherited Polymorphism of the Third Component of Complement (B_1 C/B_1 A-globulin). Human Hered. **22**, 488–495 (1972)
7. Kuhnl, P., Spielmann, W.: Untersuchungen zum C3-Polymorphismus (B_1 C-globulin) Genfrequenzen und Familienuntersuchungen an hessischen Blutspendern und Bantupopulation Heumangenetik **15**, 7–13 (1972)
8. Mauff, G., Potrafki, B. G., Freis, H., Pulverer, G.: Vergleichende Untersuchungen zum Polymorphismus des Posttransferrins (Pt) und der dritten Komponente des Humankomplements (C3). Humangenetik **21**, 75–80 (1974)
9. Pflugshaupt, R., Scherz, R., Steinegger, L., Butler, R.: The Frenquency of the Polymorphisms of C3 in the Swiss Population and some remarks on the identification of rare phenotypes. Protides of the Biological Fluids. 22nd Colloq. 1975
10. Rittner, C., Rittner, B.: Report 1973/1974 of the Reference Laboratory for the Polymorphism of the Third Component (C3) Vox Sang. **27**, 464–472 (1974)
11. Smithies, O.: Variations in human serum B-globulins. Nature (Lond.) **180**, 1482 (1957)
12. Teisberg: High Voltage Agarose Gel Electrophoresis in the Study of C3 Polymorphism. Vox. Sang. **19**, 47–56 (1970)
13. Teisberg, P.: The Distribution of C3 Types in Norway. Human Hered. **21**, 154–161 (1971)
14. Teisberg, P.: C3 Types of Norvegian Lapps. Human Hered. **21**, 162–167 (1971)
15. Wieme, R. J., Demeulenaere, L.: Genetically determined electrophoretic variant of the human complement component C'3. Nature (Lond.) **214**, 142 (1967)

Received January 10, 1977