Confirmation of the multifactorial threshold model for congenital structural talipes equinovarus

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SUMMARY The first degree relatives of 174 children with congenital isolated structural talipes equinovarus were examined by an orthopaedic surgeon. The affected rate of first degree relatives was 27 times higher than the birth prevalence of Hungarian newborns. The heritability in the parents and sibs was 0.82 ± 0.15 . The multifactorial threshold model was proved by the so-called GAMT programme on the basis of the identity of the h^2 values in the different generations of first degree relatives. A relatively lower familial clustering was found in gypsies who had a higher prevalence

Familial clustering of congenital talipes equinovarus has been recognised for some time and this drew attention to the heredity patterns. Several mechanisms of inheritance were suggested, for example autosomal recessive, autosomal dominant, X linked, and polygenic.¹ Recently, various aetiological and epidemiological-clinical types, symptomatic, teratologic, secondary, postural-deformity, and structural talipes equinovarus (STEV), have been differentiated. A Hungarian genetic family study of STEV is presented here from the point of view of the multifactorial threshold model.

Materials and methods

Index patients born in Budapest from 1962 to 1967 and in Baranya County from 1970 to 1974 were ascertained during earlier surveys to determine the birth prevalence of isolated STEV.² All the first degree relatives were asked to present themselves for orthopaedic examination and personal interview. The genetic family study was complete in 174 index children and out of these 28 gypsy children were evaluated separately. Only the index patients all of whose first degree relatives had been personally examined were evaluated, and only the unequivocal diagnosis of STEV was accepted in parents and sibs.

Results and discussion

The genetic family study of the first degree relatives showed an affected rate of STEV of 34.1 per 1000

(table). This exceeds the birth prevalence of STEV by 27 times. Comparing our data with the survey of Wynne-Davies,³ the affected rate of parents is slightly higher. The affected rate of STEV was 5.5 (5/902) and 6.9 (7/1008) per 1000 in the second and third degree relatives, respectively; these values are less reliable, however, because of absence of personal examination and aetiological differentiation.

The data of the genetic family study of STEV were tested by the multifactorial threshold model⁴ with the GAMT programme.⁵ The h^2 difference between parents (0.70 ± 0.20) and sibs (0.99 ± 0.21) is not significant; their combined value is 0.82 ± 0.15 . However, the above difference may be expected to become significant as the number of cases increases, because of the slight effect of the dominant variance. The GAMT programme provides a correct description of sex distribution of affected first degree relatives. Affected girls carry a greater risk for their sibs (table). On the other hand, the increase in affection of brothers, as in the data from Scotland,³ is not observed.

The total prevalence of other so-called non-specific congenital abnormalities in first degree relatives of STEV cases is 60.6 per 1000. The registered value of total congenital abnormalities is about 40 per 1000 in Hungary.⁶ Detailed analysis of first degree relatives showed an increased occurrence (26.5 per 1000) of congenital inguinal hernia only. The birth prevalence of this in Hungarian livebirths is 11.04 per 1000. Thus, this may point to a certain overlap or linkage between STEV and the genetic system of congenital inguinal hernia: both may have

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TABLE Proportion per 1000 of relatives affected in Hungarian family studies of STEV

Index patients	p value	First degree relatives				Mother				Brother				Sister			
		Father				m	M	q	K	m	M	q	K	m	M	q	K
Males (n = 118)	1.65	118	4	33.9	20	118	3	25.4	15	61	4	65.5	38	60	1	16.7	10
Females (n = 56)	0.82	56	1	17.9	13	56	0	0.0	0	29	2	69.0	49	30	3	100.0	71
Total (n = 174)	1.25	174	5	28.6	19	174	3	17.2	11	90	6	66.6	44	90	4	44.4	30
		348				8	23.0	15		180				10	55.6	37	
						528				18	34.1	23					

p = birth prevalence per 1000 live births.

m = No of relatives.

M = affected No of relatives.

q = affected proportion per 1000 of relatives.

K = Penrose index = q/p.

a connection with anomalies of connective tissue. These data seem to prove the specific nature of the 'STEV polygenic system'.

There is a different rate of occurrence of STEV in different races.^{1 7 8} The Hungarian survey showed a greater birth prevalence of STEV in gypsies (3.4 per 1000).² According to the multifactorial threshold model, in the race with the higher birth frequency, a relatively lower risk for the relatives of affected subjects may be expected. The combined h^2 value is lower in gypsies (0.63).

Our material contained two first cousin pairs (1.15%) and four second cousin pairs (2.30%). These figures are four and eight times higher than in the normal Hungarian population, respectively.

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