Linkage studies in Van der Woude syndrome¹

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SUMMARY A newly ascertained kindred segregating Van der Woude syndrome through four generations is described. Linkage studies using the methods of Ott (1974) were carried out using 19 marker loci.

Van der Woude syndrome has 3 primary manifestations: (a) bilateral lower lip pits, (b) cleft lip with or without palate, or (c) isolated cleft palate (Van der Woude, 1954; Cervenka *et al.*, 1967). The disease entity segregates as an autosomal dominant trait with 70 to 80% penetrance (Van der Woude, 1954; Gorlin and Pindborg, 1964; Cervenka *et al.*, 1967). Variable gene expression was shown by Cervenka *et al.* (1967) who observed lip pits in 69.6% of obligate gene carriers but facial clefts in only 36% of the cases. Congenital absence of second premolars has also been reported in association with Van der Woude syndrome (Schneider, 1973). A single previously published linkage study involving this syndrome observed no linkage with 13 marker loci. Unfortunately no lod scores were published (Schneider, 1973).

In the present study, linkage analysis was performed on a previously unreported family in which Van der Woude syndrome was segregating.

Subjects and methods

A phenotypic description of each family member examined is given in the Fig. Blood group phenotyping in this family involved the ABO, Rhesus, MNSs, Kidd, Kell, Duffy, and P traits. Haptoglobin was determined from serum. Erythrocytes were used in determining phosphoglucomutase, acid phosphatase, 6-phosphogluconate dehydrogenase, and adenosine deaminase. Parotid saliva was used to determine amylase₁, PA, PB, PR, and DB phenotypes. The amylase₂ phenotype was obtained from urine and the ability to taste phenylthiocarbamide (PTC) was also evaluated with PTC solutions to varying concentrations.

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Table Lod scores for linkage with Van der Woude syndrome: male and female scores combined

	0-10	0-20	0-30	0-40	0-50
ABO	-0.19	0.04	0.07	0.03	0.00
Rh	0.84	0.52	0.26	0.06	0.00
MNS	-1.16	-0.63	-0.30	-0.11	0.00
Kidd	0.22	0.13	0.07	0.02	0.00
Kell	-0.03	-0.03	-0.03	-0.02	0.00
Duffy	0.03	0.14	0.13	0.07	0.00
P	-0.12	-0.05	-0.01	0.00	0.00
Hp	0.41	0.29	0.18	0.08	0.00
PGM ₁	-0.56	-0.24	-0.11	-0.04	0.00
ACP	0.30	0.20	0.11	0.04	0.00
6GPD	0.01	0.00	0.00	0.00	0.00
ADA	0.01	0.01	0.00	0.00	0.00
AMY ₁	0.00	0.00	0.00	0.00	0.00
PA	0.05	0.07	0.04	0.01	0.00
PB	0.00	0.00	0.00	0.00	0.00
PR	0.10	0.19	0.13	0.05	0.00
DB	0.29	0.23	0.16	0.08	0.00
AMY ₂	0.01	0.01	0.00	0.00	0.00
PTC	0.31	0.22	0.13	0.06	0.00

Computation of the likelihood and lod scores for various recombination fractions was done by computer analysis for each of the marker loci using a recently available programme (Ott, 1974) which computes the likelihood of linkage recursively, as proposed by Elston and Stewart (1971), starting with the more recent generation and working back into the pedigree.

Results

The lod scores for various recombination fractions are given for each locus analysed in the Table.

Discussion

The results indicate that close linkage of Van der Woude syndrome with any of the tested marker loci is unlikely. Because of the small number of individuals involved in the present study further investigations of

these disorders for possible syntenic relationships with various loci is warranted.

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