Short communications

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X-mapping in man: evidence against measurable linkage between anhidrotic ectodermal dysplasia and G6PD deficiency

SUMMARY A Sardinian kindred segregating for X-linked anhidrotic ectodermal dysplasia (AED), glucose-6-phosphate dehydrogenase (G6PD) deficiency of Mediterranean type, and Xg\(^a\) blood antigen provides evidence against a measurable linkage between the loci for AED and G6PD. Moreover, from the segregation of the combined phenotypes in four scorable sons from two triple heterozygotes with phase known, it seems highly probable that the AED locus is nearer to the centromere than is the G6PD locus.

A three generation pedigree segregating for anhidrotic ectodermal dysplasia (AED), glucose-6-phosphate dehydrogenase deficiency (G6PD) of Mediterranean type, and Xg\(^a\) blood group antigen was ascertained in Sardinia through a patient who exhibited the recessive phenotype for all three markers of the human X chromosome (Fig.). The propositus (IV.2) and the other living patient (III.7), among the five reported in the pedigree, have the classical phenotype of AED, including absence of teeth, hypotrichosis, and total absence of sweat glands as assessed through the direct count of sweat pores (Passarge and Fries, 1973). The three dead patients had all died of hyperthermia in their early infancy. One of the obligatory heterozygotes (II.3) has a reduction and malformation of teeth and a significantly low number of sweat pores/cm epidermal ridges homogeneously distributed on all of her fingertips (8.7 ± 0.28). Five control Sardinian women of the same age group had an average count of 28.5 ± 0.12 sweat pores. Subject I.1 (most probably a heterozygous carrier herself, though the pairing on of the AED gene to at least three of her children does not necessarily exclude the possibility of a fresh mutation in one of her pregential stem cells), as well as the two obligatory heterozygotes II.1 and III.1, and the potential heterozygous carriers II.8, III.4, and III.8, all have a normal phenotype and a sweat pore count within the normal range. The segregation of G6PD deficiency and Xg types is illustrated in the Fig. The classification of the heterozygotes for G6PD was performed at the level of the individual peripheral red blood cells with a modification of the methaemoglobin elution test of Gall et al. (1965) which, as is known from previous studies (Rinaldi et al., 1976), detects 95% of the Sardinian heterozygotes for the G6PD Mediterranean mutant.

Omitting the scoring of generation II, in view of

![Fig. Pedigree.](http://jmg.bmj.com/ on June 21, 2017 - Published by group.bmj.com)
the uncertainty about the segregational or mutational nature of the AED gene in I.1, the number of recombinants, with respect to the three X-linked loci mentioned above, can be directly counted among the offspring of II.3 and III.1, who are triple heterozygotes with phase known (Table). Namely, the two sons of II.3 are both recombinants with respect to the pairs of loci AED-G6PD and G6PD-Xg, but they are both non-recombinants for the AED-Xg pair. Of the two sons of III.1, one (IV.1) is recombinant and the other (IV.2) is a non-recombinant with respect to the AED-G6PD and Xg-G6PD loci, but they are both non-recombinant for AED-Xg. The children of II.1 score only for AED-Xg linkage and are both non-recombinants. Thus, the overall ratios of non-recombinants to recombinants for the various linkage comparisons are: 1nr:3r for AED-G6PD as well as for G6PD-Xg, and 6nr for AED-Xg. When the other males scoring for the G6PD-Xg linkage are added (III.9 and III.10), the ratio for this linkage comparison becomes 2nr:4r. The data bearing on the latter linkage comparison are in agreement with the absence of measurable linkage between the relevant loci established by previous studies (Siniscalco et al., 1966). The six non-recombinants between AED and Xg, when added to the ratio reported so far of 3nr:9r do not change the conclusion of an absence of measurable linkage between these loci (Race and Sanger, 1975). The greater number of recombinants among the four scorable sibs who give information for the AED-G6PD comparison hints also that these loci are at non-measurable distances from one another. When the segregation pattern of the three sets of allelic pairs in the offspring of the two triple heterozygous mothers is analysed at the same time, it becomes obvious that the most likely sequences of the loci under consideration along the X chromosome are: Xg-AED-G6PD or AED-Xg-G6PD. This conclusion stems from the fact that if the loci for G6PD were in an intermediate position, subjects III.5, III.7, and IV.1 would all have to be double recombinants. Since the locus for G6PD has been assigned to the region distal to Xq26 (Brown et al., 1976), it follows that the AED locus must necessarily be nearer to the X chromosome centromere than G6PD, though, at this time, it cannot be established whether it is on the long arm or the short arm.

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G. Filippi, Antoniettina Rinaldi, G. Crisponi, G. L. Daniels, and M. Siniscalco

1Istituto di Genetica Medica, Università di Trieste, Trieste, Italy;
2Centro di Genetica Evoluzionistica del CNR, Università di Roma, Rome, Italy;
3Istituto di Puercultura, Università di Cagliari, Cagliari, Italy;
4MRC Blood Group Unit, Wolfson House, 4 Stephenson Way, London NW1, England; and
5Sloan-Kettering Institute for Cancer Research, New York, NY 10021, USA

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Requests for reprints to Professor M. Siniscalco, Section 6108, Sloan-Kettering Institute for Cancer Research, 425 East 68th Street, New York, NY 10021, USA.

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G Filippi, A Rinaldi, G Crisponi, G L Daniels and M Siniscalco

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