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A Population Genetic Study of Psoriasis

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In the dermatological literature, simple models for the inheritance of psoriasis have been considered invalid (1,2). This is an important question in many respects. We have therefore found it necessary to analyse further the population genetics of psoriasis.

In Sweden, we have a patient organisation with 22,000 members that has been willing to let us use its membership register. At present we have data on psoriasis from more than 12,000. In about 300 individuals, both probands and relatives, the accuracy of reporting has been checked by an experienced dermatologist. There is underreporting of very mild psoriasis amounting to a few percent only. Data on psoriasis among the children of the probands have been requested for in 1,300 families. In population genetics studies of psoriasis, the late onset of the disease is a problem as many individuals with the psoriasis genotype will be classified as not having the disease. Of those who have psoriasis and are over the age of 50 years, only about half have developed the disease before the age of 25.

As we have a very large material, we have used information from psoriasis sufferers over the age of 55 years for this presentation in order to minimise the problem of late onset of the disease. We have used data on psoriasis among parents and siblings from 5,197 families and among children from 1,195 families.

The specific question we want to discuss is whether an autosomal dominant or an autosomal recessive mode of inheritance is compatible with population genetic data.

Psoriasis among the parents of the probands is given in Table I.

Psoriasis among the siblings of probands with both or one parent having psoriasis does not distinguish between the dominant and recessive modes of inheritance.

In nearly two-thirds of the probands, no parent had psoriasis. This would exclude a dominant inheritance if we did not assume a very low penetrance of the genotype. If we had a recessive mode of inheritance, the probability of the siblings' getting psoriasis would be 25%. The number of siblings affected is determined by a binomial distribution. However, we have no families where no one got the disease, as the probands always had psoriasis, by definition. We have thus a truncated binomial distribution with one term missing, viz. the one corresponding to no one having psoriasis. There are formulae for calculating the expected number of affected individuals in sibships of differing size under these circumstances (4).

Table II shows that the observed number of affected siblings closely corresponds to the expected number for a recessive inheritance.

A penetrance slightly over 90% is obtained. If we perform the same calculations for sibships where one parent or both parents had psoriasis, a slightly lower penetrance of the genotype is obtained. Psoriasis among siblings of probands is thus compatible with an autosomal recessive inheritance for psoriasis.

Calculations of this type are dependent on random mating. What is important is that mating is random with respect to the partner having or not having psoriasis. When collecting the data about psoriasis among children, we asked if the other parent of the children also had psoriasis. It turned out that 4.9% of the female probands had children together with a partner having psoriasis and the corresponding figure for male probands was 3.7%. This is what could be expected by chance in an adult population. We thus have no indications of a selection in this respect.

With regard to psoriasis among parents, it is dependent on the gene frequency, if we have an autosomal recessive mode of inheritance. This seems not to have been taken into account by earlier investigators (1,2) when they have discarded a recessive mode of inheritance for psoriasis. We can actually calculate the gene frequency from the data on psoriasis among parents.

The gene frequency of psoriasis turns out to be about 25%, giving 6% of the population being homozygotes and thus having the genotype for psoriasis. 38% will have one gene and cannot get the disease, while nearly 60% will carry no psoriasis gene.

We should point out that the data on psoriasis among the children of the probands are compatible with an autosomal recessive mode of inheritance with a gene frequency of 25%.

As in every other material, there is a certain risk of selection error. We have compared our data with those of Lomholt from the Faroe islands (1), however, and the correspondence is very good. Lomholt seems to have overlooked the consequences of a high gene frequency and discarded the possibility of a recessive inheritance incorrectly.

Table I. *Psoriasis among parents of probands*

Both parents had psoriasis	2%
One parent had psoriasis	34%
No parent had psoriasis	64%

Table II. *Number of siblings observed to have psoriasis in sibships of differing size when no parent has psoriasis, compared with the expected number (for p = 0.25)*

Size of sibships	Male probands		Female probands	
	Obs	Exp	Obs	Exp
2	492	504	563	571
3	423	454	526	547
4	289	325	343	366
5	199	234	211	247
Sum	1403	1517	1643	1731
Penetrance	92.5%		94.9%	

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What is the effect on the population genetic data of two clinically indistinguishable types of psoriasis vulgaris with different age at onset (3)? We have made a thorough investigation of this problem, which will be described in a separate paper. However, the risk of the children getting psoriasis when both parents have the disease is less, when we have two variants of the disease than when we have just one; when one parent has the disease the risk is about the same, and when no parent has the disease but both are heterozygotes, the risk is slightly higher than for one variant.

Even though an autosomal recessive inheritance is compatible with population genetic data, this does not prove that psoriasis is inherited in this way. However, this model is useful for genetic counselling.

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