# Founder Effect in Tay-Sachs Disease Unlikely

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The essential conditions for the founder effect and its extension, genetic drift, are that a newly established population be isolated and sufficiently small so that its gene pool soon diverges from that of the parent population because of sampling error. Unfortunately, the early migration patterns, size of communities, degree of isolation, and inbreeding of Jews in eastern Europe are not well known. From our own demographic studies we could find no evidence for the existence of conditions which would favor drift [1]. It seems unreasonable to favor the explanation of founder effect without evidence because it has the advantage "that it relieves one of the necessity to postulate a selective advantage which because of changing environmental conditions could probably never be verified" [2] over that of heterozygote advantage for which we have some evidence from both population data and a mathematical model [1].

Yet the founder-effect hypothesis is an attractive one and, assuming that all necessary conditions existed in the several newly established Ashkenazic Jewish communities of eastern Europe, it would be possible to make an estimate of and a probability statement about the effective size of the required founder population.

Casimir the Great, who ruled as king of Poland from 1333 to 1370, offered his protection to those Jews who wished to immigrate. This act, which occurred approximately 600 years or 20 generations ago, could date the hypothetical "founder" population.

Working backward from the present-day Ashkenazic Jewish gene frequency for the Tay-Sachs disease (TSD) allele of .0126, the value of $q$ after $n$ generations of complete elimination of the lethal recessive is given by $q_n = q_0/(1 + nq_0)$, where $q_0$ is the initial frequency of the gene [3]. This is calculated as .017 and the heterozygote frequency as .034, or approximately 1 in 30. We are to assume that this arose by random sampling from a population in which the carrier frequency was the Caucasian/Sephardic value of .0026. Suppose, now, that the founder population had an effective size of 90. The probability that this population contained at least three carriers would be .0019; if the founder population were larger, the probability of such a large deviation would decrease; and if the founding occurred before Casimir's time, the carrier frequency would have had to have been greater. Thus, founder effect does not seem to be a likely explanation.

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The comparison of the TSD situation among Ashkenazic Jews with that of the Ellis–van Creveld syndrome among the Old Order Amish is not appropriate. It is well known that the Amish started as an isolate, they are still an isolate, and have been practicing close inbreeding for many generations. Jewish religious law prohibits close inbreeding, and there is no evidence that the Jewish immigrants practiced inbreeding even in the early settlements. On the contrary, our studies show that there was extensive outbreeding among the Jewish communities of eastern Europe [1]. Even if inbreeding diminished over the centuries, there is no evidence that the rate of decrease among Jews was greater than that among non-Jews.

The argument may well prove to be academic. We now have data which show that pulmonary tuberculosis is virtually absent among TSD grandparents and that the concentration of places of origin of Jewish tuberculosis patients who also came from eastern Europe is highest where that of the TSD grandparents is lowest, and vice versa, suggesting that the TSD heterozygote may be resistant to pulmonary tuberculosis [4].

## REFERENCES

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