# Molecular testing for Huntington disease and the risk of disclosure of unsolicited pre-symptomatic status: a recurring theme

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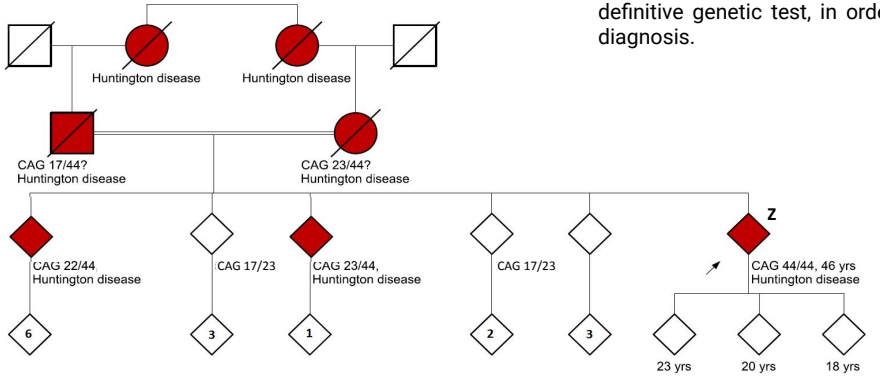
## CASE HISTORY

Z, a person with 46 years of age (yrs) and motor symptoms for seven years, was seen by a neurologist who requested a *HTT* molecular test. After that, the subject was referred for genetic counseling (GC) with us. Our laboratory detected 44/44 CAG repeats – i.e., Z was homozygous for *HTT*. The lab team became concerned that there might be children at risk who had not yet been heard about their interest in discovering their genetic status. To overcome this, our lab decided to report that "a technical problem had occurred and that a new blood sample should be collected to repeat the test, after consultation".

At our first evaluation, we learned that Z had consanguineous parents and two siblings with Huntington's Disease (HD) symptoms and three healthy children aged between 18 and 23 yo. All the children were asked to come for individual follow-up visits: they were informed that Z might have a 33% chance of being homozygous, given that his/her parents were both affected; and that if it was in fact the case, a standard molecular report would simultaneously reveal that all three were obligate carriers. To solve the tangled situation, two choices were proposed: (a) the usual DNA report would be delivered if all children chose to know their own genetic status; or (b) Z report would only mention the final diagnosis without including the *HTT* genotype. Since two children decided not to know their genetic status, the chosen one was (b). A second blood collection was taken, DNA result was the same and reported as (b). Four of Z's siblings were genotyped after GC, the symptomatic ones were both heterozygotes. The child who wanted to know his/her genetic status left the predictive testing process.

## DISCUSSION

We report this case because the molecular diagnosis performed before the GC placed three sibs at high risk of stress. To reveal the Z genotype would be to disrespect their children's right to decision-making autonomy (1, 2, 3). Given the potential harm that revealing the genotype could bring, we judged that not releasing the genotype result would be less harm. However, to choose the lesser evil, we were forced to invent a technical problem. By making an apparently autocratic decision, we only partially protect this family. After all, they just don't know about Z homozygosity - but we do. Therefore, the autonomy of what to know about their own lives has been hurt anyway (1).




## CONCLUSION

Molecular diagnosis of HD can bring challenges sometimes overlooked, as when the molecular diagnosis of a symptomatic person can reveal the pre-symptomatic status of other family members. The usual procedure for the present molecular diagnosis would disclose unsolicited pre-symptomatic status of all children. The "merciful lie" presented at the first molecular test allowed the postponement of disclosure and the autonomous decision of these relatives. However, we would like to discuss with the scientific community about other alternatives for action against this scenario.

Cases like this remind health professionals about the importance of analyzing the family history before asking for a definitive genetic test, in order to avoid unwanted predictive diagnosis.

**Image 1.** Family Pedigree. The sex of the individuals from the 3rd and 4th generations were hidden to avoid the possibility of identification. The individuals of the 2nd generation weren't genotyped, the CAG repeats were inferred.

**References:**

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