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Inherited Deafness Studies May Affect Genetic Counseling

Researchers have confirmed that one type of genetic mutation causes inherited profound deafness, while another mutation thought to cause deafness does not. These results, say the investigators, emphasize the value of basing genetic counseling on data derived from detailed genetic studies.

Writing in the June 16, 1999 issue of the *Journal of the American Medical Association*, the team, which included HHMI investigator Val Sheffield of the University of Iowa College of Medicine, reported that about three percent of their sample population carried a mutant form of the gene *GJB2*. The lead author of the study was Glenn Green at the University of Iowa College of Medicine.

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Genetic tests on 52 young people with moderate to profound congenital deafness showed that 42 percent had mutations in the *GJB2* gene. This finding confirms earlier studies by Sheffield's team and others which suggest that mutations in *GJB2* contribute to inherited deafness. The Iowa team found that the majority of those people with a defective *GJB2* gene had a specific mutation, which researchers call 35delG.

Studies of 560 randomly selected healthy infants showed that about 2.5 percent of these children are "carriers" of the 35delG mutation. These infants were not deaf because they carried only one copy of the defective gene. (Two mutant copies of such a "recessive" gene are required to cause genetic disease.) Overall, however, the researchers found that about 3 percent of the infants had some type of mutation in the *GJB2* gene.

But the incidence of a second type of mutation in *GJB2* (which researchers call M34T) was found to be very low in the group with profound deafness. An earlier study by other investigators suggested that the M34T mutation is a

"dominant mutation," which means that inheriting only one copy of the mutant gene would be enough to cause deafness.

"Initially, based on a very small sample, it had been suggested that the M34T variant was a dominant gene for deafness," Sheffield explained. "But our subsequent screening studies found that it was not uncommon for normal individuals to carry this variant, and we do not believe that it causes deafness. Based on this latest study, we don't find this mutation in deaf people at the level you would predict based on how prevalent it is in non-deaf people."

Sheffield says that it is important for researchers to do these types of carrier-rate studies "so that good genetic counseling can be given based on solid scientific information. This finding means that a test for 35delG, which thanks to advances in molecular genetics can be done in a couple of hours, is a good place to start in determining the cause of congenital deafness."

Sheffield also advises that genetic counselors and physicians use caution when advising parents on the possibility that a child's illness or disability may have genetic roots. "The take-home message from the findings on both 35delG and M34T is that mutations really need to be proven deleterious before giving genetic counseling that is based on their presence. We don't want people doing genetic screening and basing counseling on any genetic mutation they might find until it's been more carefully characterized."