Genetic Aspects of Alcoholism

By Arthur Falek, Ph.D.

It has been reported since the times of antiquity that alcohol-drinking patterns of children resemble those of their parents. The notion that alcoholism is a disease in which individuals have difficulties with or are unable to control their consumption of alcohol rather than a "mental weakness" had its origins in the medical literature of the mid 19th Century. How definitive are the findings in humans supporting the inheritance of alcoholism? Evidence of a genetic influence in alcoholism is based on family, twin and adoption studies that find that there is 1) a 25% - 50% risk of alcoholism in the lifetime of sons and brothers of men who are severely alcoholic; 2) a 55% or higher concordance rate in identical (monozygotic) twins as compared to an overall 28% concordance rate for same sex fraternal (dizygotic) twins and 3) adopted sons of alcoholic fathers and half-brothers with different fathers have rates of alcoholism more like the biological fathers rather than the foster fathers. On the other hand, existing evidence suggests a lower heritability of alcoholism in women than in men. Further support for a genetic influence of alcoholism in males is based on studies in which young men prior to alcohol use are exposed to one or another of the biochemical components of alcohol metabolism. Those at high risk for alcoholism based on family history have been found to have pleasurable responses when exposed to a moderate amount of alcohol in contrast to others with no family tendency to alcoholism who have higher frequencies of unpleasant effects when similarly exposed to alcohol. Another example of metabolic differences between high risk and control subjects is that the blood acetaldehyde levels (a biochemical component of alcohol) were found to be elevated in young men with alcoholic parents or sibs in
comparison to those in a matched control group. Furthermore, two separate types of alcoholism have been identified. Type 1 alcohol abuse is characterized by onset after age 25, occurs in both men and women, requires both genetic and environmental factors for its occurrence and results in severe psychological dependence and guilt. In contrast, Type 2 alcohol abuse has onset before age 25, rarely occurs in women, is much more heritable and is characterized by an inability to abstain from alcohol along with frequent aggressive and antisocial behaviors. At the molecular genetic level, research studies have found that transmission through a single gene (Mendelian transmission) has been rejected as has a proposed relationship between the candidate genes responsible for the oxidative pathway in ethanol metabolism or neurotransmitter genes like dopamine and serotonin receptor genes long thought to be associated with alcoholism. What is more likely is that there are several genes accounting for the different family risks for alcoholism. Collaborative studies incorporating both the biological and the environmental influences on the risk of alcoholism in families are being conducted to provide source material for detecting and mapping specific genes as well as the critical gene-environmental interactions associated with this complex disease.

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