

Genetic Implications of Alcoholism

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The first question to be answered is: *what is alcoholism?* The only realistic answer to this question is that alcoholism is what it is defined to be. The delimitation of the concept is arbitrary. First of all there are in this respect great differences of opinion between different population-groups. What, in one group, may be regarded as just an innocent or even healthy habit would in a second population-group be stamped as a deplorable moral defect with disastrous consequences, and in a third group just as a pure medical problem. It is true, of course, that those members of the medical profession who are especially interested in research on alcoholism will, irrespective of the part of the world from which they come, have a tendency to converge towards a tolerably homogeneous concept of alcoholism. But even if this is the case the selection of alcoholics which come into their scope will to a high degree depend on the attitude of the population and not on the concepts of the doctor. Such selection factors must more or less unconsciously colour the view of the individual research worker. We know that not only do quantitative and qualitative properties of alcoholism differ very much from one population-group to another, but, in addition, the fraction of alcoholics which comes to medical attention is certainly not representative of alcoholism in general in that population-group. Most materials of alcoholics which have been under research must be very heterogenous, and one must necessarily differ from the other. How could it be possible to compare the genetical back-ground of such quite different and heterogenous materials?

Even within a small country differences are striking. In most countries alcoholism is much more prevalent in the cities than in the rural areas. If there is a genetical back-ground of alcoholism, is it then probable that carriers of the genes in question have drifted from the countryside to the cities? There may, of course, be a tendency at this, but it could not possibly explain the huge differences which do exist with regard to prevalence of alcoholism. If such specific genes exist, their penetrance and expression must be extremely variable. It would be quite meaningless to discuss the mode of inheritance without at the same moment taking into consideration the environmental factors which influence the manifestation of the genetical back-ground.

These differences of prevalence within a population have one more consequence: in those parts of a country where the prevalence of alcoholism is very low individuals who do nevertheless become alcoholics must have very serious reasons for it. This means that possible genetical factors will probably be present to a high degree in a material consisting of alcoholics from such population-groups. If in contrast we examine alcoholics from a population where

drinking is wide-spread and where everybody will easily come into contact with alcohol it is obvious that among these alcoholics we will find quite a lot of people who did not have specific "individual" reasons for their drinking. An investigation of the causal factors of alcoholism will, therefore, in such cases reveal a much lower incidence of genetical and pathological factors.

These elementary facts should always be born in mind when comparisons between different studies on the causal factors of alcoholism are made.

The next question is: *Is it at all possible to distinguish between genetical and environmental factors in the causation of alcoholism?* This problem has been the object of endless discussions. I think, however, that I can omit further discussion of this point if instead I just give an abstract of a case history published by professor Oedegaard of Oslo some years ago:

During a psychiatric examination the patient in question states that he is drinking because he is so nervous and needs help against his anxiety and feeling of inferiority. This might indicate that his alcoholism is caused by inborn components of his personality. But then the patient adds that he was not like this before, it started after he had been drinking for some years. Maybe, then, that his nervousness has arisen on a toxic basis? This points to an exogenous factor. But now the patient informs us that alcohol has always had an abnormal action on him, he has a low tolerance and his behaviour is definitely abnormal when he is drinking. Maybe, nevertheless, that there is a constitutional abnormal reaction to alcohol? Further on the patient states that difficulties in his marriage made him start drinking; again an environmental factor. His wife, however, is of the opinion that the problems in the marriage were caused by the fact that the husband has always been a peculiar person, even before he started drinking, extremely sensitive and jealous, with difficulties of contact except when he was a little intoxicated. Constitution again? But then we find out that his childhood environment was really very bad and might be responsible for his disharmonious character. Finally it turns out that the personality of his father was of exactly the same type as his own personality and that a number of similar types are found in the family. Perhaps genetics take the lead again? —We have all met cases like this. They are no exception and such experiences make you quite humble with regard to making positive statements concerning the causation of alcoholism in the individual patient.

Around the beginning of this century when psychiatric genetics was still in its beginning some rather primitive studies of genetical factors in alcoholism were performed. It was stated that not only was there a great number of alcoholics among the *relatives of alcoholic index cases*, but there was also a high incidence of other mental abnormalities among them. In these studies, however, no true determinations of disease expectancy were performed, and comparisons with representative materials from the general population were therefore impossible. In addition, it was of course quite naive to conclude that this accumulation of abnormal cases in the stock must be due to genetical factors. Drinking habits and the presence of abnormal personalities in the environment might as well have acted as psychogenical causes for the alcoholism in the index cases.

Later on, about 30 years ago, Brugger carried out some more systematical investigations. He did, indeed, scrutinize his materials quite carefully and his results aroused some attention. He found increased disease expectancies for different mental disorders among the relatives of alcoholics. One part of his procedure was, however, not solid, namely the statistical part. And Brugger's results have therefore been criticized seriously, especially by Amark who cal-

culated the mean errors of Brugger's figures with the result that a big part of them must be said to be without value.

The first thorough and reliable investigations concerning the genetical back-ground of alcoholism were performed about a decade ago, simultaneously by Amark in Sweden and Manfred Bleuler in Switzerland and the United States. Amark gives a comprehensive discussion of the whole problem and a survey of the material published until 1951. He stated that there was no real foundation for the belief that alcoholics should be especially tainted with regard to psychoses or oligophrenia among their relatives. Amark had a very large material at his disposal; he did not find any significant increase with regard to the expectancies for schizophrenia, manic-depressive psychosis, general paresis, senile and pre-senile psychoses, epilepsy or oligophrenia. Amark did, however, find increased risks for psychopathy and psychogenic psychoses among the siblings and parents of his index cases. The same was the case with regard to the risks for alcoholism and criminality. With regard to the accumulation of alcoholism he tried to investigate to which degree this risk was affected by the mutual environment. He found that those brothers of the index cases which had been brought up in good home conditions had a somewhat lower incidence of alcoholism than had the others who had been brought up in bad conditions, but the difference was small and of no statistical significance. The investigation of the incidence of psychopathy in the different generations and in different environments tended to show that genetical factors played a significant role in the origin of the psychopathic states.

The intellectual development of Amark's index cases did not deviate from the average. The frequency of psychopathy, however, was significantly higher than in the general population. Among the personality types especially prevalent in his alcoholics were dysphoric and depressive types, psychoinfantile, hysteric, and easily suggestible types, further so-called ixoid (epileptoid) types and he makes the conclusion that these personality types predispose the subject for alcoholism. When Amark divided his index cases into periodic and non-periodic alcoholics he found that the genetical back-ground seemed stronger in the first-named group. Amark's study gives a wealth of other information and must be regarded as a classic with regard to the study of causal factors in alcoholism.

Manfred Bleuler who performed a similarly careful study arrived at results which were in principle the same as Amark's. He studied two groups of alcoholics, each comprising 50 patients, one from Zürich and one from the New York area. The latter consisted mainly of patients admitted to the Payne-Whitney Clinic and comprised especially many patients of a superior intellectual level. The general features of the two materials were the same and the differences among them could easily be explained by differences in social and intellectual level.

Bleuler could not find any elevation of incidence of schizophrenia, manic-depressive psychosis, epilepsy and oligophrenia among the relatives of his index cases. There was, on the other hand, an accumulation of alcoholism and neurotic and psychopathic personalities. Bleuler used his unique experience in endocrinological matters also on this material and he found that more than a fourth of the cases showed clinical evidence of some endocrinological disturbance. In most of the cases he could demonstrate causal interrelationship between these disturbances and the alcoholism, but the mode of interaction varied considerably, practically all theoretical possibilities being represented. In some cases the endocrinological disturbance

was of primary importance and the alcoholism just a sequel either through direct action of the abnormal hormone balance or through secondary psychological symptoms caused by the endocrinological disorder.

In more than 40% of the cases did he — like Amark — find abnormalities of personality development before the onset of alcoholism. Only 10 out of 50 American alcoholics could be considered as clinically normal personalities before they started to drink; the rest were borderline cases. In the majority of cases sexual adjustment was unsatisfactory already before the onset of alcoholism. The home conditions during childhood were very poor in the great majority of cases. Most of the index cases had also, before the age of 20, had an intimate contact with persons with alcohol problems. Only 10 out of 50 American alcoholics could be said not to have suffered from a long-standing unhappy influence of morbid personalities before the age of 20.

Bleuler's conclusion is that it was quite impossible to separate hereditary from environmental influences. The environment seemed to form the personality and the personality formed the environment.

One more conclusion was that there was no evidence of the old hypothesis that alcoholism should cause epilepsy or oligophrenia in the offspring.

The studies mentioned until now have been based on family-investigations. But what about *twin-studies*? To my knowledge only one twin-material of a considerable size has been published, namely that of Kaij, one of Essen-Möller's collaborators. Kaij collected a material of 174 pairs, 48 of them being monozygotic. The main purpose of the investigation was to study the occurrence and structure of *chronic alcoholic deterioration*, but in addition a great amount of information was gathered concerning the etiology of abuse of alcohol. Some of the results were quite amazing. Thus it was found that so-called alcoholic deterioration was not correlated with the degree of alcohol consumption. Kaij concluded that the deterioration was not an effect of alcohol but in some cases might, on the contrary, be an etiological factor in the abuse. He also concluded that his results tended to support the "assumption that drinking habits are influenced by genetic factors and that such factors greatly determine the appearance of chronic alcoholism".

With regard to other clinical sub-types within the field of alcoholic disorders *delirium tremens* has been studied from a genetical viewpoint. It has been assumed (Brugger, Pohlsch) that there is a genetically founded predisposition to delirium tremens, probably as one expression of a more general predisposition to delirious reactions. Even if the assumption should be correct it should not be forgotten that the nature and the amount of beverage consumed are much more important factors in the etiology of delirium tremens than are the hereditary factors.

Dipsomania, clinically homogeneous as it may seem, is nevertheless undoubtedly heterogeneous in etiological respect. One subgroup has obvious relations to epilepsy; genetical studies have made this hypothesis probable, and electroencephalographic studies have confirmed it.

What about *blastophthoric effects* of alcohol? Does alcohol consumption cause defects in the offspring? Investigations on human alcoholics have not given support to any theory of this kind, and it seems improbable that the results of animal experiments, which have been performed on a large scale, can be interpreted as evidence of mutations caused by alcohol.

In conclusion I think it justified to state that in spite of the existence of excellent genetical

studies concerning alcoholism we cannot say that very much is known as to the genetic background of alcoholism. What we *can* say for certain is that investigations concerning the genetic implications of alcoholism face us with problems of a nature so intricate as we can ever hope to find within the field of human genetics.

In addition, we can just *guess* that future results will show that only a very small part of alcoholism can be attributed to specific genetic factors, whereas in the majority of those cases which have an inherited foundation the genetically determined personality disorder will turn out to constitute a starting-point for many different roads, just a part of which will lead to alcoholism.

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