

## ARE NORTH AMERICAN INDIANS BIOCHEMICALLY MORE SUSCEPTIBLE TO THE EFFECTS OF ALCOHOL?

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The abusive use of alcohol is a problem experienced by many different nations and their respective peoples, and it is well known that North American Indians are no exception.<sup>1</sup> The rates of alcoholism among some Indian tribes are high, especially when compared to national, state or provincial statistics. As a consequence, an increased incidence of social, judicial and health problems is commonly experienced by Indian people. Because of high rates of alcohol abuse and because Indians are a visible minority, the general public has developed a vivid, stereotyped image of a drunken Indian, one which is racially defined and seldom applied to people of European descent.

The image is one of an Indian male who drinks to such excesses that he loses control and becomes aggressive--sexually and otherwise. The drunken Indian becomes crazed, may enter into physical fights with other Indians or Whites, may throw-up, defecate or urinate in public, and eventually pass out in the street or other inappropriate place.<sup>2</sup> What many people in the general public seem to ignore or be unaware of, however, is that such behaviour has become associated with Indians because of their visibility. In White urban areas, Indians look different, are a minority and, therefore, are noticed and remembered. A Caucasian drunk who behaves in the same way will not be noticed to the same extent because he is not expected to behave in this manner and because he is considered to be the exception rather than the rule. Consequently, we do not mentally tally up the number of Caucasian drunks we see, but we do note and remember the drunken Indians we encounter. Even Indians themselves are likely to practice such selective perception; however, in this case, the underlying reason is not because they expect their kin to be unruly drunkards but because they feel a sense of shame

and are keenly aware that such behaviour is what the White culture expects of them. So every example of drunken behaviour by their kin is a noteworthy event to them, too. We do not lump all of the 'Whites' together and expect them to behave the same way. Nor do we expect the members of the dominant European-derived cultures to be a heterogeneous group from a socio-economic point of view, and therefore, some of them can behave quite poorly according to social norms. Yet paradoxically, we expect the members of the Indian culture to be a homogeneous lot who all act the same way.

Associated with the idea of a typical Indian drunk is the concept that Indians are somehow innately predisposed to the effects of alcohol. They are believed to be more sensitive to the euphoriant effects of alcohol and to be less able to control their behaviour while under its influence. In essence, Indians are thought to have a hereditary biochemical predisposition that accounts for their high level of drinking. The idea of genetic predisposition is mentioned frequently as one of the possible factors contributing to drinking levels displayed by Indian peoples. Although this explanation has been dismissed as unlikely by some, it has not been discounted in a significant volume of published research on the topic. This paper is addressed to such research.

Alcoholism is a problem experienced world-wide, and despite a vast number of studies, no consensus exists as to what factors cause an individual to become a problem drinker or addicted. Nor does a universal definition of alcoholism exist. The factors which can influence drinking behaviour may be divided into three broad categories: psychological, physiological and sociological factors. This paper focuses on the physiological or biochemical dimensions.

A plethora of hypotheses as to why people become problem or abusive drinkers has been proposed. These range from defects in sugar metabolism to the formation of narcotic-like compounds in susceptible individuals. However, two avenues of approach seem most promising: first, studies concerned with the role of

heredity in the expression of alcoholism, and second, studies centering on genetic or racial differences in alcohol metabolism.

While it is difficult to separate genetic and environmental factors when analyzing the aetiology of alcoholism, a number of studies have concluded that a genetic predisposition to alcoholism can occur.<sup>3</sup> When children of alcoholic parentage are raised away from the home environment, their frequency of alcoholism drops compared to those raised in the home (alcoholic) environment. Thus, environmental factors influence the development of alcoholism. However, in a Danish study, male adoptees separated from their alcoholic parents were four times more likely to become alcoholic than adoptees from non-alcoholic parentage.<sup>4</sup> Similar findings were reported in Sweden. There, adopted-out sons of alcoholic parentage were more likely to be registered in the record of the Swedish Temperance Board for alcoholism than adopted-out sons of non-alcoholic parents.<sup>5</sup> Despite the problems of adoption studies, such as illegitimacy of the adopted children or the possibility of prenatal damage with alcoholic mothers, other studies have borne out the findings. Independent studies in Sweden and the United States comparing the rates of alcoholism among monozygotic (genetically identical, one fertilized egg split to produce twins) and dizygotic (non-identical, two different eggs fertilized to produce twins) twins have shown that the monozygotic twins were more likely to be similar with respect to a measure of alcoholism than were dizygotic twins.<sup>6</sup> Therefore, development of alcoholism does appear to have a genetic component.

A related area of research is concerned with racial differences in alcohol metabolism. In the body, alcohol is broken down or metabolized by specific enzymes whose production is genetically programmed. It has been found that the pattern of alcohol metabolizing enzymes is different in Orientals and Caucasians;<sup>7</sup> thus, these two races are genetically divergent with respect to these enzymes. Interestingly, these enzyme differences have been deemed responsible for the increased

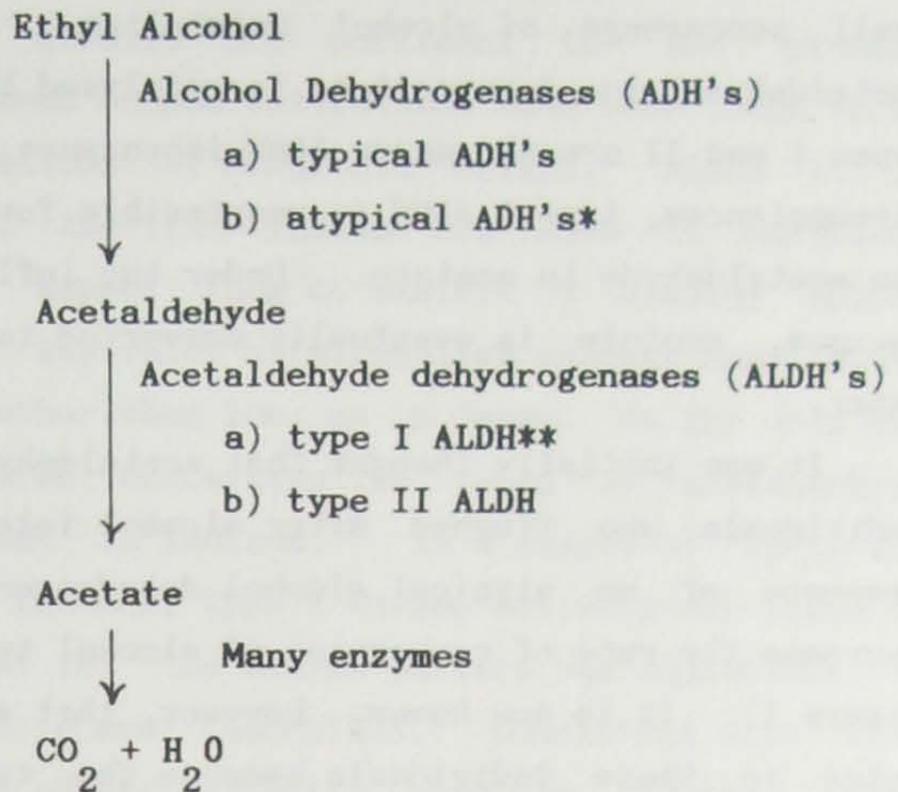
susceptibility of the Japanese to the dysphoric or unpleasant effects of alcohol. Similarly, more recent studies have suggested that because the North American Indians may be derived from the same gene pool as the Japanese and other Oriental races, they too should have a greater sensitivity to the dysphoric effects of alcohol. Sensitivity to these effects (measured by facial flushing) was absent in a sample of Tarahumara Indians from New Mexico, but was present in a large percentage of Eastern Cree Algonkian Indians.<sup>8</sup> An individual who is susceptible to the dysphoric effects of alcohol may appear to be unable "to hold his/her liquor" and thus might be thought to be at risk in terms of becoming a problem drinker or an alcoholic. However, quite the opposite phenomenon has been observed. It was clearly demonstrated that those Japanese who are sensitive to the dysphoric effects of alcohol do not become alcoholics.<sup>9</sup>

In studies comparing Orientals and Caucasians, it has been found that alcohol intake causes significant physical discomfort for about half of the Oriental subjects, but very little or no discomfort in most Caucasians. Such discomfort following alcohol intake acts as a deterrent to further alcohol intake and ultimately inhibits the development of alcoholism. This discomfort is characterized by marked facial flushing, dizziness, increased heart rate and decreased blood pressure. These effects are due to an accumulation of acetaldehyde. In ninety to ninety-five per cent of the European population and in about half of the Japanese population, little or no acetaldehyde accumulates in the body because it is readily broken down or effectively eliminated. In contrast, in those individuals who experience an adverse physical reaction to alcohol intake (i.e., in about half of the Japanese population and five to ten per cent of the European populations), acetaldehyde does accumulate in the body.

The metabolism of alcohol in the body is catalysed by a number of enzymes acting sequentially (see Figure 1). Alcohol metabolism occurs mainly in the liver. The conversion of

FIGURE 1

## SIMPLIFIED SCHEME OF ALCOHOL METABOLISM




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Acetaldehyde accumulation causes dysphoric effects in humans.

\*At one time it was thought that the presence of an atypical ADH (there are several types) caused an accumulation of acetaldehyde by increasing the rate of conversion of alcohol to acetaldehyde.

\*\*Now it has been found that type I ALDH is inactive, or functionally absent, in individuals who have an adverse flushing response after alcohol intake. Acetaldehyde accumulates in these individuals because its degradation to acetate has been significantly retarded by the absence of type I ALDH.

alcohol to acetaldehyde is catalyzed by alcohol dehydrogenase (ADH). This enzyme exists in a number of physically distinct forms, or isoenzymes, which vary in their ability to catalyse the conversion of alcohol to acetaldehyde. The ADH isoenzymes are the major enzymes involved in the first stage of alcohol metabolism. Two other enzymes, catalase and the mitochondrial ethanol oxidizing system (MEOS), can also catalyse the conversion of alcohol to acetaldehyde, but they account for only a small percentage of alcohol metabolism. The metabolism of acetaldehyde to form acetate is catalysed by ALDH isoenzymes. Types I and II are the major ALDH isoenzymes, and under normal circumstances, type I ALDH is responsible for converting most of the acetaldehyde to acetate. Under the influence of many other enzymes, acetate is eventually converted to carbon dioxide and water.

It was initially thought that acetaldehyde accumulation in individuals who flushed after alcohol intake was due to the presence of an atypical alcohol dehydrogenase,<sup>10</sup> which would increase the rate of conversion of alcohol to acetaldehyde (see Figure 1). It is now known, however, that acetaldehyde accumulates in these individuals because the type I acetaldehyde dehydrogenase which metabolizes, or gets rid of most of the<sup>11</sup> acetaldehyde, is inactive or deficient in these individuals. So, in most Europeans and in non-flushing Orientals, alcohol is metabolized to produce acetaldehyde, which in turn is metabolized mainly by type I acetaldehyde dehydrogenase. The type II enzyme is present, but the properties of these enzymes are such that the type I rather than the type II enzyme, degrades most of the acetaldehyde produced from alcohol. In those individuals who flush adversely after alcohol intake, the type I enzyme is inactive. If the inactivity or functional absence of type I enzyme acts as a deterrent to alcohol intake, one would not expect this enzyme to be absent in alcoholics. This is precisely<sup>12</sup> what has been found. This enzyme was absent in only three out of 150 Japanese alcoholics. This contrasts significantly from a control sample of the Japanese population in which the

enzyme would be absent in about 75 of 150 subjects. Therefore, it appears that those Japanese with a type I enzyme deficiency are protected from becoming alcoholic because of the dysphoric effects that alcohol causes in them. Having said this, however, one must keep in mind that the incidence of alcoholism in Japan, which traditionally has had very low rates of alcoholism, has risen over the last forty years.<sup>13</sup> Apparently other factors can override this genetic deterrent to alcohol intake.

These enzyme studies are pertinent to the present discussion because such enzyme alterations have been found to be confined to populations of Mongoloid origin. Since it is thought that North American Indians are also of Mongoloid origin, one might expect them to exhibit a similar enzyme pattern. However, the rates of alcoholism amongst many Indian peoples are high, rather than low, as in Japan. So far only two reports have appeared concerning the types of acetaldehyde dehydrogenase present in Indians.<sup>14</sup> In a sample of forty-six northern New Mexico Indians, type I enzyme activity was found in all forty-six; that is, the enzyme pattern was equivalent to what has been found in most Caucasians. Consistent with this enzyme pattern, no adverse effects, such as flushing, were observed. Similarly, in a study of sixty-three full blood Indians from Oklahoma, only sixteen percent were found to be deficient in type I enzyme, and were seen to drink less than those Indians who had the enzyme, though they drank more than the Caucasian subjects. Overall then, from these two studies one can conclude that most of the Indian peoples studied so far metabolize alcohol in the same fashion as most Caucasians rather than like the portion of Oriental races who are sensitive to the adverse effects of alcohol, and hence, rarely become alcoholic.

The idea that North American Indians are more susceptible to the effects of alcohol may have arisen from some of the early work comparing rates of alcohol metabolism in Caucasians and in Indians. While one study showed a slower rate of alcohol metabolism in Eskimo and Indian males compared to White males, all subsequent studies reported either no differences or an

increased rate of alcohol metabolism in the Indian subjects.<sup>15</sup> Thus, it seems highly unlikely that the presumed susceptibility of Indians to the inebriating effects of alcohol is due to their diminished ability to metabolize or get rid of alcohol.

Many factors make it difficult to compare rates of alcohol metabolism between individuals of the same or different races.<sup>16</sup> In some of these studies, differences in body weight, body composition and previous drinking history were not taken into account. Because there are a number of different types of alcohol and acetaldehyde metabolizing enzymes and because their degree of expression varies from one person to the next, widely different rates of alcohol metabolism are observed between individuals. Moreover, while moderate alcohol intake can induce, or stimulate, the formation of other alcohol metabolizing enzymes, chronic abusive alcohol intake can have the opposite effect. In addition, the nutritional status of the individual plays an important role. Some of the acetaldehyde metabolizing enzymes are lost after periods of poor nutrition, but can be regained with the resumption of proper nutrition. Thus, measurements of the rate of alcohol metabolism are subject to many variables whose presence or absence may artifactually cause differences in alcohol metabolism compared to a so-called control group.

If it does turn out that some Indian peoples have a genetic aversion to becoming alcoholic, as does a large percentage of the Japanese race, and if the rates of alcoholism are higher amongst such Indians than in the Caucasian population, then one could speculate that these Indians are over-exposed to other factors which lead to alcoholism. Though a particular group of Indians may be resistant to developing alcoholism, perhaps they can still become alcoholic because of the presence of unusually high levels of environmental stress.

Overall, with respect to physiological or biochemical factors that contribute to the development of alcoholism, it can be concluded that genetic factors do play a role as evidenced by the adoption studies and by the alcohol metabolizing enzyme studies. The former studies have revealed an undefined genetic

predisposition, while the latter have revealed a well-defined genetic aversion. While we know that an aversion is expressed primarily in people of Mongoloid origin, we do not know whether a predisposition also occurs in these people because the adoption studies which revealed this tendency were done in Europe. The biochemical studies reported so far do not support any presumed susceptibility of North American Indians to the aversive effects of alcohol that can be attributed to differences in their metabolism of this drug compared to that of Caucasians.

The development of alcoholism is probably polygenic and influenced by many other interacting factors. By using a simplistic approach, we can continue to find single factors that vary from one culture to another and that appear to explain differing abuse rates, but these factors are not universally significant. Such approaches tend to emphasize the differences between cultures, while it may be that the similarities are more important. Perhaps we are unconsciously attempting to find a psychological or physiological deficiency in the alcoholic (Indian and non-Indian) so that we as a society do not have to accept responsibility for the problem. The alcoholic is forced to accept all of the blame. Similarly, from a cross-cultural perspective, perhaps we are saying that cultural factors inherent in Indian society are to blame. This approach is irrational because it ignores the fact that alcohol problems are not confined to Indian society. It is time we accepted the fact that people of all races and cultures are more likely to become problem drinkers or alcoholics when they live in conditions of social deprivation and extreme poverty.

#### NOTES

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