The Disease of Alcoholism

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Abstract

A pharmacological view of narcotic addiction and alcoholism, or sedative addiction, serves as a basis for the further examination of these complex illnesses. The disease called alcoholism (sedativism) consists, however, of much more than just a chronic or periodic addiction to a sedative drug. The urgent need to understand the psychological and societal parameters of this illness is underscored by the likelihood that alcoholism represents the major factor in the cause of death of young adults (<45 years) in the United States today. Its further role as a carcinogen is only recently achieving adequate examination.

Although plaguing mankind since antiquity, 2 major illnesses of addiction continue to exact their terrible cost without either broad understanding of their nature or appropriate efforts directed toward their control or eradication. Perhaps the more recent of these, involving many thousands of Americans, has been accompanied by sociopathic behavior with its resultant strain upon the legal mechanisms for dealing with ethical societal problems. It has been called "drug addiction," although the illness involves addiction to only the narcotic compounds (morphine, meperidine, methadone, heroin, etc.). The other, involving millions of victims in the U. S. alone, entails addiction to any one or a combination of sedative-soporific drugs (Table 1) and has been called, also inappropriately, alcoholism. The media, perhaps because of the long social use of alcohol, have quite consistently confused the 2 addictions by referring to alcoholism on the one hand and drug addiction (grouping narcotics with solid sedatives) on the other. Of course alcohol is a drug, and, more seriously, this view obscures the basic nature of the disease of alcoholism as well as the critical relationship among sedative drugs in general. From a pharmacological standpoint, the 2 groups of drugs are quite disparate. Narcotics will classically produce analgesia without substantive sedation whereas sedative-hypnotic drugs can only produce significant analgesia after eliciting a somnifacient result. There are certain similarities to the addictive state produced by each of these groups, however. The narcotic agents can elicit a 20-fold increase in tolerance, and there is cross-tolerance among the various drugs of this group. Thus, when one has achieved considerable tolerance to methadone, there is simultaneously increased tolerance to heroin and the other drugs in the narcotic group. In the case of the sedative drugs, tolerance can be established, but it can rarely achieve more than a 2-fold increase. Cross-tolerance within the group of sedative agents also occurs, having first been observed during the 19th century when physicians attempted to anesthetize the town drunk with the then new agent, diethyl ether. The fact is, when one is tolerant to alcohol, there is simultaneously toler-

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illness come in all sizes, shapes, and colors. They may be 8 or 80 years old. The amount ingested per year might be considerably less than even the most modest social drinker’s yearly intake. Alternately, one may observe substantive tolerance and a regular daily ingestion of enormous quantities of soporific drugs. The key issue in the definition is that of ingesting a drug. The subject must have had ample opportunity to observe the untoward results on one or more previous occasions before such behavior could fall within the confines of this diagnosis. As with so many other diseases, this particular one has a spectrum of severity, that associated with the least severe aberration and function obviously being the most difficult to diagnose. In its mildest form, functional impairment might fail to appear in any area other than that of lost potential.

Many patients with this illness, in their attempts to control the difficult or even disastrous results of their drinking, turn to convoluted behavior for safety. Thus, they may switch from hard liquor to wine or beer or attempt to limit the number of their drinks as well as the day or time of day during which these may be ingested. Drinking may, under those circumstances, become dependent upon specific demands at work or the availability of a “nursemaid” at home. Such subjects will often become what is casually known as “periodics.” Their total yearly alcohol intake might be quite modest, but the functional impairment of their lives might still be and often is extreme. Since this conference deals with the relationship of alcohol and cancer, it is probably well to bear in mind that one may not make the assumption of a direct correlation between total alcohol ingestion and the diagnosis of alcoholism in any specific instance, except in those circumstances wherein the ingestion of this drug is high enough to elicit severe and consistent pharmacological problems. It is therefore entirely possible that from a public health standpoint one might observe a society in which the “social” use of ethanol is high enough to elicit untoward oncolgical problems without an overwhelming incidence of alcoholism. The difficulty in correlating total alcohol consumption and the incidence of alcoholism has been noted not only in national groups (France, Italy, and Spain) but also in subcultures within this country as well (American Jews versus American Irish). Let us nonetheless return to the primary issue at hand, an examination of the disease called alcoholism.

As we have seen, the term alcoholism is a misnomer. More technically correct would be that of “sedativism” if, only to emphasize that patients with this illness may replace alcohol with not only any one of its variant beverages but with any other soporific drug as well. Alcoholics often refer to Librium as simply “the very driest martini.” The major differences resulting from such a replacement reside only in their relative caloric content and perchance their odor. Less facetiously, we should recognize that the alcoholic who has switched from ethanol to benzodiazepines may well have leaped from the frying pan into the fire. Except among adolescents, there is little of a rewarding social milieu during pill taking, and the alcoholic, by passing this particular barrier of social acceptance, may simply have indicated something more about the severity of his compulsion and the unlikeliness with which he might respond to therapeutic efforts. Obviously, the term alcoholism is perfectly adequate as long as we all realize that nothing more than historical coincidence favored it over chloralism, barbism, or paraldehydism. Since the colorful stores, packages, and advertisements dealing with sedative use consistently limit their attention to ethanol as opposed to the other sedative drugs, let us examine this particular drug as a prototype of the group.

An understanding of the clinical pharmacology of ethanol is essential to the comprehension of the disease of alcoholism. We need concern ourselves minimally with the action of this substance upon any tissue in the body other than that of the brain. It may be facetious, but it is true that no one ingests this chemical for what it does to his liver. Fortuitously, ethanol is rapidly absorbed and achieves appreciable central nervous system levels within a short time after it is ingested. At that point, it yields its primary and major pharmacological effect, that of sedation. There is considerable popular confusion concerning this sedative effect of alcohol, since individuals vary in their psychological response to sedation. One subject will notice a surge of energy whereas another will find himself more able to sleep. Suffice it to say that the psychological response to sedation may vary, but the dominant pharmacological response of the central nervous system to ethanol during the first few hr after its ingestion is always that of sedation. If enough sedative is taken at this particular time, it will result in somnolence in all subjects. During this period, the response of animals to ethanol is one of increasing the electroconvulsive threshold (9). No matter how much ethanol one administers to a mammal, the sedative action of a nonlethal dose persists for no more than 5 hr and usually closer to 2 hr. The implication of this is that, within 2 hr of the last drink of alcohol, maintenance of the sedative action requires another dose. It has always been somewhat intriguing to realize that the blood alcohol level achieves its peak value at about the end of 2 hr, the very time at which the sedative action of the drug starts to disappear. Those very blood concentrations of ethanol associated with substantive sedation during the first hr after alcohol ingestion (during rising concentrations) may well fail to sustain any sedative action whatever 2 hr later when the blood alcohol concentrations are diminishing. Another clinical pharmacological action of ethanol becomes apparent after the sedative effect wears off. It consists of agitation, or increased psychomotor activity. The increased psychomotor activity state persists for approximately 12 hr, but its amplitude is low. We thus see that ethanol has a complex and asynchronous action upon the central nervous system: a large-amplitude, easy to observe,
short-acting sedative effect; and a low-amplitude, difficult to detect, long-acting agitating effect. Repeated use of the sedative drug on an every-other-hr basis would result after 12 hr in the disappearance of almost all of the sedative actions of 6 separate drinks, but there would be persistence of their agitating effects for many hr thereafter. This dichotomous and asynchronous effect of sedative drugs is responsible for the so-called withdrawal syndrome. Since the withdrawal syndrome starts with Dose 1 of the sedative agent and since its very appearance coincides with peak blood levels of this drug, the term withdrawal syndrome is obviously another misnomer. Quite apparently, the increased psychomotor activity level associated with the use of alcohol represents an inherent part of the pharmacological action of the drug. Indeed, animals metabolizing alcohol at rates as great as 10-fold faster than humans nonetheless demonstrate the same temporal sequence of sedation and agitation as does the human. The action of ethanol upon the brain then must be conceptualized as analogous to that of pulling a trigger on a gun: after adequate motion of the finger has taken place, the sequence of events and the firing of the projectile bear no relationship to further activity of the digit. Thus, there is little benefit to be derived from detailed studies of the metabolism of alcohol. Its zero order kinetics of catabolic degradation, pathways, or even sites of its degradation on New Year's Day and will notice a vague sense of foreboding of events one may replace the substance with some other soporific having enormous differences in its catabolism, excretion, and kinetics. Animal investigations can clearly demonstrate that it requires only extremely small amounts of sedative agents, ethanol or short-acting barbiturates, to be followed shortly by evidence of increased psychomotor activity. This agitation may be seen in the human subject if one carefully observes clinical behavior following ethanol ingestion. Although one may not notice a "hangover" the morning after the New Year's Eve party, there is little doubt that such an individual will arise relatively early on New Year's Day and will notice a vague sense of foreboding along with his modest agitation. These sensations tend to wear off early in the afternoon unless the subject chooses to take current sedation to rid himself of the agitation remaining from the previous evening's sedation: the hair of the dog. That individual unable to tolerate his own base line state of psychomotor activity may well utilize alcohol as a means of achieving a more comfortable status. Unfortunately, the cost of such a pharmacological adjustment of one's psyche is simply that of further agitation, a circumstance unlikely to be welcomed by that very subject unable to tolerate even his control level of anxiety. Thus, we hear the phrase in Alcoholics Anonymous of "one drink never being enough but always being two much." It should also be clearly appreciated that, regardless of the psychic response of the individual to sedation (be it somnolence or the hyperactivity associated with release of inhibitions), the desired central nervous system effect is that associated with sedation. No one drinks alcohol for its effect the morning after. The "reward," the desired effect, comes concomitantly with its sedative action during the first 2 hr after its ingestion.

It remained for Isbell (5) to demonstrate about 25 years ago that the intake of nutrients had little if any relationship to this pharmacological effect of ethanol upon the brain. Obviously, the continued use of ethanol in large quantities over a prolonged period of time results in a gradual increase in the psychomotor activity level of that individual. Such agitation may well be difficult for the naive observer to appreciate while current doses of sedative are being consumed. When such sedation is discontinued, however, the elevated psychomotor activity level appears in all of its florid glory, and the subject demonstrates all the phenomena associated with the withdrawal syndrome. When mild, these may consist of no more than tremulousness, ataxia, tachycardia, insomnia, hypertension, entercolitis, and minimal evidence of an organic mental syndrome. In its more extreme form, these manifestations may be joined by acute hallucinosis. Its extreme state includes a toxic psychosis known as delirium tremens. All of these states are associated with an elevated incidence of seizure activity. The degree of severity attained with this syndrome appears to vary with the age of the subject, the duration and amount of sedative ingestion, and other aspects of general physical health.

Although minor fluctuations in tolerance may stem from individual variations in metabolism or even enzyme induction, there is no question that the most significant and critical cause of tolerance is related to central nervous system adaptation. A clinical pharmacological understanding of this can best be attained if one simply considers the balance between the sedative and agitating effects of alcohol. It is quite apparent that the individual who has achieved substantive agitation due to previous alcohol ingestion might tolerate considerable current sedation (i.e., ethanol dose) without achieving that degree of sedation that is no longer compatible with maintaining life. Thus, it is not unusual to observe heavily drinking individuals with blood alcohol levels as high as 0.7%, who, at that moment, continue to maintain physical activity. Obviously, the metabolic rate affecting any of the sedative agents cannot have much to do with that type of tolerance. On the other hand, enzyme induction as well as vying for common catabolic pathways can result in an extremely complex relationship between competing sedative agents. The danger inherent in the concomitant use of ethanol with other sedatives is too well known to bear repetition at this point, especially since much of our knowledge about this stems from the efforts of one of the speakers at this conference, Dr. Charles S. Lieber (see Ref. 6).

Although Dr. Isbell's studies clearly demonstrated the responsibility of ethanol in producing the withdrawal syndrome, he failed to call upon his subjects to revolunteer for yet another drinking bout after recovering from the severe withdrawal state emanating from the original episode of alcohol ingestion. The natural hesitancy or even refusal of most subjects to comply with such a request might offer insight into the ease with which we can convert the human volunteer into an alcohol addict but not into the patient with alcoholism. To accomplish the latter requires that the subject return over and over and over again to the sequence of circumstances invariably leading to illness and distress. That compulsive return to the scene of the crime, so to speak, despite any and all costs represents the inherent difference between simple addiction in the volunteer and the disease of alcoholism. It is as though the individual with the illness is somehow unable to learn that this particular coping mechanism is repetitively and consistently followed by such adverse experiences. Since there is little doubt that there is no intellectual deficit among subjects with alcoholism, one must
look to other factors for an understanding of this phenomenon. It has been known for some time that over three-quarters (7) of any probands with alcoholism have at least one family member who also suffers from this illness. Dr. Donald W. Goodwin is at this meeting, and I am certain he will relate some of his interesting studies which have suggested a genetic predisposition to this disease. There is also more than adequate evidence that various societal and psychiatric factors must be considered in its etiology. In general, the characteristics of the alcoholic, despite a tendency to dependence, depression, and isolation, have failed to achieve a specific enough structure to permit detection of the disease prior to its clinical stages. Nonetheless, the genetic, societal, and psychiatric data which we presently possess all offer prophylactic and therapeutic possibilities for the eventual control of the illness.

It is well to bear in mind that some of the typical characteristics of alcoholism stem from the progressive loss of tolerance to sedative drugs which follows upon aging. The patient observes but often fails to appreciate that less alcohol is required for achieving drunkenness, the duration of gratification becomes shorter, and the degree of discomfort the following day is both greater and of longer duration as be becomes older. In this sense, alcoholism is a self-limited disease; there is no way to attain the tolerance of youth once lost. This mechanism may explain in part why alcoholism has been termed a "progressive disease." Such reference on the other hand might also stem from the possibility that long-term use of large quantities of ethanol might result in subtle central nervous system damage. This injury appears to be most similar to the organic mental defect associated with senility. Most patients, having lost their tolerance by their mid-40's, seek medical assistance at about the time that they have also lost normal attention span, ability to concentrate, and recent memory.

Although there is little doubt that this chronic, recidivistic illness responds to therapeutic intervention, its effective treatment at present depends upon an ethical and spiritual program rather than drug therapy. Unfortunately, a small group of behaviorists (8) has failed to understand the clinical characteristics of the illness and has therefore aimed toward the development of training programs designed to assist the alcoholic to continue so-called controlled drinking. This has been partially based upon the ludicrous assumption that the "medical model" of alcoholism implies that the first drink inevitably and invariably leads to uncontrolled drinking by the alcoholic. Of course, such a circumstance characterizes extremely few of these patients. Rather, the alcoholic can never be certain as to which first drink will eventually lead to loss of control. The fact that such an individual continues to tempt fate in such a disadvantageous manner serves as a measurement of his compulsive behavior. As with any compulsive acting out, the opportunity to resist is always greatest at the initial moment.

Many years ago, I was asked to review the records of those patients for whom my efforts failed. I was shocked to discover that the outcome for many of these individuals was sudden violent death. Their deaths varied from those associated with falls and motor vehicle accidents to purposeful or accidental suicides, as well as becoming a torch when their lit cigarette entered the couch or bed linen during their sedation. Indeed, if one were to add the 50% of motor vehicle deaths, the 60% of drownings, the 85% of deaths from hepatic cirrhosis, the burns, the suicides, and the murders, one might begin to appreciate that alcoholism represents the major cause of death of all young adults in the United States today. Certainly such a circumstance would hold true for the age category of 15 to 45 years. The Medical Examiner's Office of the City of New York recently substantiated this type of observation (4) and made a plea for a change in our documentation and record keeping of causes of death to enable us to appreciate the magnitude of this onslaught. If we now also demonstrate a relationship between alcohol ingestion and carcinogenesis, it would seem that as a nation the United States should be devoting considerably more than the precious little effort, time, and money which we have in the past decade.

References

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