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CLINICAL APPLICATIONS

Screening for Alcoholism[1]

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Alcoholism is one of the largest public health problems of the nation and is a significant cofactor in such ubiquitous diseases as hypertension, developmental abnormalities, heart failure, liver failure, and many other conditions. The cost to the nation's health is immense. One strategy for reducing morbidity and cost has been to establish methods for screening in order to increase recognition rates leading to increased rates of therapeutic intervention. In this article, the rationale for two methods of alcohol screening, brief interviews and biological markers of excessive drinking, the relevant statistical issues bearing on this problem, and the current research on screening exams are reviewed and summarized. Finally, some of the newer approaches toward alcoholism screening as well as the consequences to the medical care system should alcohol screening eventuate on a large scale are briefly described.

RATIONALE

There are several reasons to screen people for alcohol addiction. The most often cited is economic: an annual cost to the nation in excess of 50 billion dollars (25) through utilization of health facilities, lost time at work, injuries and accidents, use of the legal system, and so on. At the same time, news reports regularly record the human costs of alcoholism, for example the accidental deaths among our young people that have spawned organizations such as Mothers Against Drunk Driving (MADD). More recently, the public has become aware of medical conditions more closely linked to alcohol abuse than was previously thought: widespread hypertension (14), subtle developmental changes in children whose mothers drank alcohol during pregnancy (28), heart failure and premature death in men (8), and cirrhosis of the liver among women (19). All of these and other reasons, frequently appearing in scientific, professional, and popular media, have followed a national awakening that began with the establishment of the National Institute on Alcohol Abuse and Alcoholism 15 years ago.

The fundamental justification for alcoholism screening lies in the presumed opportunity to prevent or ameliorate the economic, human, and medical costs noted above. The ultimate unproven hypothesis for those of us who work at devising and testing better screening methods for alcoholism is that by doing so we will offer the nation a method whereby it can substantially reduce the mor-

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bidity, mortality, and economic drain currently ascribed to alcohol misuse. While some early data suggest that alcohol recognition reduces medical costs substantially when persons recognized as alcoholic reach treatment, the larger question awaits the development of screening instruments that can be used systematically for large numbers of the Americans along with adequate systems of diagnosis, treatment, and follow-up for this most difficult of diseases. Surely, in the great traditions of medicine whereby we seek to limit and assuage the suffering of others, devising accurate screening tests for an illness that affects 7–10% of the population over their lifetime remains a worthy, if less than glamorous, task.

In considering this task, we must reflect on some of the attributes of alcoholism that both facilitate and impede screening processes. The greatest obstruction to screening has to do with the nature of the illness itself. Alcoholism is an addictive disease: it has four general characteristics shared with other addictions. A person suffering from alcoholism (including the synonomous terms "alcohol dependence," and "alcohol addiction") demonstrates symptoms pertaining to at least two of the four following major symptom categories. First, *tolerance* develops such that the drinking person requires greater amounts of alcohol to achieve the same subjective effect once achieved with much less alcohol. Second, *withdrawal* symptoms occur some 6 to 12 hr after a rapid drop in serum alcohol level. These include tachycardia, hypertension, tachypnea, mild hyperpyrexia, tremor, nausea (with and without vomiting), diaphoresis, and anxiety. More severe cases include withdrawal seizures and delirium tremens. Third, the person experiences a *loss of control* when drinking alcohol. After drinking begins, it cannot be stopped or limited in any consistent fashion thereafter. And fourth, the drinking patient experiences a marked *social decline* in relationships with others whether in the family, at work, with friends, with religious organizations or with legal institutions. Most accepted diagnostic criteria for alcoholism include symptoms or signs from each of these four major categories (10, 26).

Following Sir William Osler's law of parsimony, all of the symptoms and related physical complications of alcoholism stem from the inability of the drinking person to control the intake of alcohol once it has begun. The nature of this inability, in its biological, psychological, or social aspects, is currently the subject of much investigation. The only aspect germane to the present discussion, however, is that the loss of control of drinking inevitably brings about feelings of guilt and shame which in turn cause the alcoholic person to hide or greatly minimize the problem. Coexisting with this guilt and shame, there is usually a subjective perception of benefit on the part of the alcoholic for a substance that in some way, either presently or in the past, provided some effect that the individual regarded as good. In the interest of denying or avoiding shame before others or guilt in one's own mind, while simultaneously protecting a positive experience, alcoholism causes its victims to hide their illness from others. It is a disease designed to remain undiagnosed.

In its early stages, before the onset of obvious physical sequelae, alcoholism mimics a number of other diseases and syndromes for which we have specific pharmacologic treatment and toward which the clinician is inevitably biased given the common lack of awareness about treatment for alcoholism. Two of the most

common examples are major depressive disease and anxiety disorder. Alcoholism mimics the former because of the depressant characteristics of the chemical itself as well as the withdrawal symptoms that mimic the "vegetative" or "biologic" signs of major depressive disease. Similarly, alcohol withdrawal easily mimics an anxiety disorder with respect both to the presenting symptoms and to the constancy of the symptoms in a person constantly drinking. In short, neither the alcoholic patient nor the clinician unaware of alcoholism diagnosis and treatment sees much to gain by prompt recognition and referral. It is easier for the clinician to diagnose a seemingly less complicated illness for which pharmacologic treatment can be prescribed. And it is easier for the alcoholic to deny than to recognize the illness.

Faced with a disease of such ubiquity and subtlety, yet one that regularly accounts for large proportions of patients occupying hospital beds (1), clinical psychiatrists with specialized knowledge of alcoholism have historically taken the lead in attempting to find ways of suspecting and then diagnosing alcoholism. Research thrusts in this area have sought to take advantage of clinical tools, most notably the history, physical examination, and laboratory evaluation. Because physical signs generally occur late in the course of alcoholism (with the possible exception of trauma) most screening efforts have focused on the history and biochemical or hematologic signs. Similarly, most efforts at screening for alcoholism have focused on hospitalized or clinic populations rather than community samples. From a statistical point of view, this has been a serendipitous occurrence.

STATISTICAL ISSUES

Despite the difficulties in recognizing or even suspecting the presence of alcoholism in any single patient, the statistical characteristics of this problem point toward a powerful effect once adequate screening instruments have been developed. Recently a group of experts convened by the Director of National Institute of Alcohol Abuse and Alcoholism (NIAAA) to review screening methods for alcoholism in primary care settings heard a penetrating discussion of statistical issues presented by John P. Rice, Ph.D., of Washington University (21). Following a description of sensitivity and specificity, Dr. Rice focused on the relationship between the base rate in the population being screened with respect to the positive predictive value of the screening test. He pointed out that screening tests work best for conditions with a high rate of occurrence among the population being screened. We repeat an example he gave in Table 1. In this mathematical construct, in which sensitivity and specificity are held constant at 95%, the positive predictive power of any screening test—the rate at which persons suffering from the illness will be accurately recognized by the test—varies directly with the base prevalence of the illness in the population.

According to this model, a screening test with sensitivity and specificity characteristics that are significant but short of perfection can be usefully applied to populations whose disease prevalence rate is high. A screening examination whose sensitivity is in the range of 90% would be useless were it employed to screen for phenylketonuria, for example, in a large population. One-tenth of the

TABLE 1
POSITIVE PREDICTIVE POWER IN RELATION TO POPULATION FREQUENCY[a]

Population frequency	Positive predictive power
0.1%	2.0%
1.0	16.0
10.0	68.0
20.0	83.0

[a] Sensitivity and specificity are each held constant at 95%.

positive cases will have been missed—a very large proportion given the number of live births in this nation yearly. In contrast, a screening exam with the same sensitivity aimed at alcoholics in a general hospital, with a prevalence rate of approximately 25%, will have accurately detected 22.5% of that population, all of whom would be suffering from alcoholism. This is a far greater proportion of patients than we are currently able to screen accurately. As discussed below, this would be especially significant in those parts of hospital populations, such as orthopedic units, in which patients are likely to present while still in the early stages of alcoholism. Using this same screening test in an outpatient setting, where the prevalence rate is likely to be in the range of that of the general population, one still gains from a reasonably sensitive and specific screening test.

The goal of research in this area has therefore been to establish a screening test or tests that can be successfully applied to populations in whom there is a high rate of occurrence of alcoholism and in whom early diagnosis of alcoholism—that is, a diagnosis made prior to the onset of obvious or debilitating medical conditions—can be made.

EXPERIENCE TO DATE

In the mid-1960s, two groups began working on alcoholism screening devices based on the clinical history. John H. Ewing, M.D., of the University of North Carolina, recognizing a high prevalence rate of alcoholics on medical and surgical units in the general hospital, began asking a series of questions relating to alcohol and the four areas of symptom constellation noted above. From these efforts, he derived the CAGE questions presented in Table 2 (12). Their use was empirically derived and in Ewing's original work, first reported in 1970, a positive response to any one of the CAGE questions was highly indicative of an underlying alcoholism diagnosis. Ewing's work received little attention despite its having been replicated

TABLE 2
CAGE QUESTIONS

1. Have you ever felt you should cut down on your drinking?	C
2. Have people annoyed you by criticizing your drinking?	A
3. Have you ever felt bad or guilty about drinking?	G
4. Have you ever taken a drink first thing in the morning (eye opener) to steady your nerves or get rid of a hangover?	E

in a psychiatric setting by Mayfield (15). In that study, Mayfield found that positive responses to two of the CAGE questions served as the best cut-off score.

Approximately 6 years ago, our group became interested in alcoholism screening in the general hospital and began using the CAGE questions. We reported a high sensitivity and specificity for these questions among medical and surgical patients: 70 and 99%, respectively (2, 3, 4). Since that time other groups have likewise found Dr. Ewing's questions to be both valid and reliable when comparing them with an assiduously done alcoholism diagnostic interview (5, 6). We summarize the sensitivity, specificity, and positive predictive value figures in Table 3. Despite their consistency, it is important to recall that these numbers may reflect a setting-specific phenomenon. People are more likely to speak truthfully in a situation in which they believe their health and well being are at stake. This is very much the case in a hospital setting. It may not be the case in a community setting. A study by Saunders and Kirshaw for example noted a much lower degree of accuracy for the CAGE questions (20). It is difficult to assess whether this was due to their study methods or to the setting, but one must continue to regard the question of setting as an important variable. Similarly, patient subgroups whose ability to give a correct history is questionable may yield lesser accuracies of response. For example, a study by Bernadt and colleagues of psychiatric inpatients gave validity indices significantly different than those reported in a medical setting: sensitivity 91%, specificity 77%, positive predictive value 45% (15).

At about the same time as Ewing's original derivation of the CAGE questions, Melvin Selzer, M.D., then at our institution began working on a set of questions that came to be known as the MAST (Michigan Alcohol Screening Test) (22). Like Ewing, he focused on a high-prevalence population: persons suspected of driving while under the influence of alcohol. Beginning with his efforts, the 20-question MAST and several of its shorter versions and offspring have become standard screening questionnaires in many institutions as well as a standard measure of the probability of alcoholism in many research reports. One version of the MAST, the Self-Administered Alcohol Screening Test (SAAST), developed by Robert Morse and colleagues at the Mayo Clinic (24), has been well validated and reliably given in medical settings in various parts of the United States as well as in other countries (9, 13).

In a recent discussion of the SAAST (21), Dr. Morse noted that discriminant analysis revealed that nine of the items of this 35-item questionnaire accounted for most of its sensitivity and specificity characteristics. Even more interestingly, two items of the SAAST accounted for 80% of the sensitivity and 90% of the speci-

TABLE 3
VALIDITY CHARACTERISTICS OF THE CAGE QUESTIONS[a] IN MEDICAL SETTINGS (%)

	Sensitivity	Specificity	Positive predictive value
Beresford *et al.* (11, 13)	70	99	97
Bush *et al.* (15)	75	96	82

[a] Two positive responses to any of the four questions.

ficity. The two questions were: "Do close relatives ever worry and complain about your drinking?" and "Have you ever felt the need to cut down on your drinking?" These questions are all but the same as two of the CAGE questions. It seems reasonable to conclude, therefore, that similar questions derived in different settings by different groups of investigators and shown to be valid and reliable in screening for alcoholism probably reflect a universal phenomenon that is both characteristic of the disease and most easily discussed between patient and physician.

Evidence such as this has led various clinical groups and expert panels to recommend established screening exams, such as the CAGE, the MAST, and the SAAST, to primary care clinicians in screening for alcoholism. The choice of which test to use or which several tests to use simultaneously remains for further investigation. The choice of test will undoubtedly be affected by the style and practice of one clinician vs another. For example, in a busy clinical practice with a premium on personal contact with patients, such as an institutional medical or surgical clinic, the four CAGE questions are probably of the greatest use because they are brief, easy to remember, and can be quickly put in one's clinical routine. In a somewhat more leisurely outpatient practice, with sufficient nursing or other personnel to conduct a MAST interview, score a self-administered interview, or present a family version of either one of those interviews, the MAST or the SAAST may be preferable. While these instruments are available presently, and can be regarded as sound clinical devices, they do not answer some of the basic misgivings of primary clinicians when faced with the still difficult question of how to diagnose an alcoholic person and how to present that diagnosis.

NEW POSSIBILITIES

Let us consider the busy clinician, an internist for example, who faces a large outpatient practice and daily contact with a significant number of patients 1/10th of whom are alcoholic. Suppose we put the CAGE questions into the internist's hands and present him with a patient who answers three of the four questions positively. The internist tells his patient and perhaps that patient's family that based on the CAGE responses the patient has a 95% chance of suffering from alcoholism. The patient, anxious to protect the perceived good effects of the drinking as well as to staving off the shame and guilt involved with loss of control of his alcohol use, vehemently denies any alcohol use whatsoever and states that he did not understand the questions properly or he would not have given those particular answers. The doctor's dilemma is to provide some convincing "proof" that the patient was giving true responses to the CAGE questions and that the patient's problem truly is his addictive use of alcohol. The internist would be delighted to have on hand a variable which, independent of the patient's historical responses, would point overwhelmingly toward the diagnosis of alcoholism. This clinical dilemma has spurred much recent research on the so-called "biologic markers" for alcoholism. This search has been extensively reviewed recently and we refer the interested reader to that discussion (27).

From the point of view of screening, however, this same search for a biological parameter or parameters that might be used in tandem with a historical screening

mechanism would at least provide the clinician with two empirically validated methods of suspecting alcoholism. Some obvious candidates come to mind, such as the mean corpuscular volume (2), any of a series of hepatic enzymes such as γ-glutamyl transpeptidase (11), uric acid (2, 7), or, most recently, desialylated transferrin (23). The sensitivity and specificity characteristics of elevations in these tests in known alcoholic and nonalcoholic patients have been studied, with the exception of only very early data regarding desialylated transferrin. No single test, to our present knowledge, appears powerful enough, which is sensitive and specific enough, to give it credence as a screening marker for alcoholism among patients walking in the door of the internist's office. Several reasons pertain to this, some of which include the individual variation from one patient to the next on these parameters, the point at which the patient most recently began or ceased heavy drinking, the variation of laboratory measures compiled by one clinical laboratory when compared to another, and perhaps the heterogeneous nature of alcoholism. As screening tests aimed at large patient populations, the enzyme measurements present high cost to the patient or to other reimbursement parties that appears to outweigh any screening usefulness so far as present knowledge is concerned.

Faced with this kind of dilemma, Ryback and his group at the NIAAA took a novel approach (18). They hypothesized that sophisticated statistical analyses, such as the quadratic discriminant analysis they used in their original report, when applied to a series of laboratory parameters, such as the entire hematologic and biochemical screen often ordered by practicing physicians, might yield statistical patterns that identified alcoholic patients. They published a report that appeared to substantiate their hypothesis in a study of alcoholic and nonalcoholic patients seen in a Veteran's hospital. While their original enthusiasm at finding 100% accuracy in identifying known alcoholics may not have been completely warranted, they opened an avenue of investigation that may allow for a second screening mechanism, independent of the clinical history, that can be applied to large numbers of patients seeking assistance in health-care facilities.

In an effort to replicate their results, our group studied 104 patients through both historical and laboratory data methods (2). We constructed a much simpler mathematical paradigm based upon a linear discriminant analysis of some 24 hematologic and biochemical variables. Our mathematical construction came down to two equations presented in Fig. 1. These require addition of a series of products found by multiplying a constant times the patient's specific laboratory values. The variables we found to be most significant were total bilirubin, lactate

$$D_{alc} = -260.2 + 1.6(\text{MCV, M}^3) + 16.6(\log \text{BUN}) - 5.3(\text{CRE, mg/dl}) + 2.6(\log \text{TBIL), mg/dl}) - 0.15(\text{SGOT, IU/L}) - 12.0(\log \text{UA, mg/dl}) + 67.7(\log \text{LDH, IU/L})$$

$$D_{xalc} = -272.0 + 1.5(\text{MCV}) + 19.0(\log \text{BUN}) - 5.8(\text{CRE}) + 3.5(\log \text{TBIL}) - 0.17(\text{SGOT}) - 14.0(\log \text{UA}) + 70.9\log (\text{LDH})$$

FIG. 1. Linear discriminant functions (LDFs). Abbreviations used: MCV, mean corpuscular volume; BUN, blood urea nitrogen; CRE, creatinine; TBIL, total bilirubin; SGOT, serum glutamic oxaloacetate transaminase; UA, uric acid; LDH, lactate dehydrogenase.

dehydrogenase, creatinine, blood urea nitrogen, uric acid, SGOT, and the mean corpuscular volume. With the patient's laboratory data values in place, each equation results in a numerical solution. The greater of the two numbers suggests either alcoholism or its absence. In our experience, this had a sensitivity of 79%, a specificity of 80%, and a positive predictive value of 70%. While this was far short of the characteristics of the CAGE questions, in our experience, it was nonetheless approximately as effective in identifying alcoholic patients as was a more time-consuming clinical history performed by a senior medical resident. We are presently engaged in researching this finding further in order to establish its validity for larger numbers of patient subjects.

Should its clinical characteristics continue to hold up under further scrutiny and empirical evaluation, it might be a screening mechanism that could be easily translated into software procedures and used as part of the laboratory data base in any computerized clinical laboratory system. If that were the case, the office internist would have the option of asking his clinical pathology laboratory for a computer readout on the statistical likelihood of any specific patient suffering from alcoholism based on that patient's presenting constellation of laboratory parameters. Much remains to be done, however, even beyond the mere validation of this method. Should it prove to be empirically justified, we have yet to learn whether a laboratory data profile has the ability to recognize alcoholic patients early in their drinking histories or whether the profile data could serve as a significant marker of both amelioration or worsening of drinking practices. The potential gain, a widely useable independent index of alcoholism, appears at this point to justify the expense and effort of further research.

WHAT IF WE SUCCEED?

Suppose that we had a variety of valid screening tests that could be used reliably throughout medical settings in this country. Suppose that we could identify alcoholics with a frequency that approached the lifetime prevalence rate of 7% for the population. We would have a method of clinical identification that could accurately establish the high likelihood of alcoholism in some 10 to 15 million Americans. We would then be faced with two overwhelming clinical dilemmas.

First, while screening examinations may provide a statistical probability of the presence of alcoholism, diagnosis is a more stringent exercise. It requires careful interviewing of both patient and family, either in a structured interview or in the hands of a well-experienced professional. As most seasoned clinicians know, dealing with alcoholic patients and their families requires clinical sophistication in handling what is very often an angry interchange between physician and patient or family and patient as well as quiet persistence in the face of an extremely difficult disease process.

Part of the problem in taking care of a large number of people is the need for well-trained personnel. Training requires a careful understanding of and experience with patient interviews as well as one's own natural resistance to dealing with very difficult patients who both seek and reject help at the same time. While many specialized alcohol and substance abuse treatment clinics and facilities already use screening devices such as the MAST or the CAGE questions, it has

been our experience that very few medical or surgical clinics routinely use such devices. We suspect that one of the major reasons for ignoring these clinical tools has to do with the lack of training among medical personnel when faced with this dilemma. Some groups have begun to examine this area of resistance among health-care professionals. It is clearly one of many facets and one that will need to be thoroughly understood if screening procedures are to be effective in primary care settings.

We are not presently aware of any specific estimates of the numbers of medical personnel currently capable of diagnosing alcoholism. While the diagnostic and statistical manual of the American Psychiatric Association (16) (DSM III-R) is in the hands of 10,000 or more psychiatrists in this country, we do not know how many of them use or regularly consult the DSM III-R around alcohol dependence. Similarly, while the National Council on Alcoholism jointly published criteria for alcoholism in both medical and psychiatric journals many years ago (16) there are no data of which we are aware outlining the extent to which those diagnostic categories are in fact used. There is clearly a major need for education of medical personnel in this area.

What can be said of diagnosis likewise applies to treatment. The National Drug and Alcoholism Treatment Utilization Survey published in 1983 provides some numbers in estimating treatment capacity for alcoholism and other forms of drug dependency (17). This report stated that the capacity in the nation for treating alcoholism consisted of the ability to treat approximately 345,000 patients. While undoubtedly this capacity has increased over the past 5 years, if that number had tripled we would still have only a treatment capacity equal to approximately 1/10 of the lifetime prevalence of alcoholism. Further, it is worth noting that approximately two-thirds of the funding for alcoholism treatment services, according to the same survey, came from public sources. Only 26% was financed by the private health insurance industry. This is despite the fact that the overwhelming majority of Americans suffering from alcoholism continue to be employed, live with their families, and are generally ineligible for most forms of public financial assistance.

It seems clear to us that as further research on screening mechanisms unfold, as the incidence of recognition of alcoholics increases with our increased ability to screen for this disease, it will serve to highlight the training and treatment needs of the health professions in addressing this national problem. We believe that the political ramifications of this will be unavoidable and the education of our public officials and populus at large will be most important in the coming years.

CONCLUSION

Research on screening examinations for alcoholism has continued for the past 20 years. We now have valid and reliable screening interviews and questionnaires that are brief and clinically accurate. Examples such as the CAGE questions, the MAST, and the SAAST are currently available to health-care and other professionals. They are generally useful for a wide range of patients although research needs to be done with respect to specific subpopulations yielding instruments tailored to adolescents, to women, and to the elderly. Research is being done with respect to biological markers that may serve as possible screening mechanisms

for alcohol use. Efforts in this area have been directed at single tests, for example γ-glutamyl-transpeptidase, and at batteries of laboratory tests, such as the laboratory data profile. While much work remains to be done in validating these tests, they offer the possibility of wide use at low cost. The increasing use of screening tests has increased our accessibility to an underserved patient population. This in turn has pointed out the need for more education of medical and other health-treatment personnel as well as clear questioning of our current national capacities for treating alcoholic and other drug-dependent persons. As research in screening examinations moves forward, these other areas will necessarily be brought to the attention of the public and government.

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