

Letters to the Editor

Limits of Detection and Quantitation of Ethanol in Specimens of Whole Blood from Drinking Drivers Analyzed by Headspace Gas Chromatography

Dear Sir:

The concentrations of ethanol permitted in the blood of motorists differ between countries and also within regions of the same country [1]. Legislative bodies are aiming towards setting lower permitted levels of blood-ethanol concentration (BEC). By the year 2000, 0.05 g% w/v has been suggested as a goal for most European countries. The statutory BEC limit for driving in Sweden was recently lowered from 0.053 g% w/v to 0.021 g% w/v BEC *per se*. The decision to lower the legal limit to 0.021 g% w/v was made without any consideration of the methods of blood-alcohol analysis available and their reliability at low BECs. The notion of enforcing a zero BEC has emerged for novice drivers who are especially prone to involvement in road-traffic accidents [2-4]. A recent report entitled "Zero Alcohol and Other Options" looked at BEC limits for truck and bus drivers and other individuals engaged in public transport services [5]. Although the feasibility of detecting and measuring impairment at low BECs was mentioned, the accuracy, precision, and limit of detection (LOD) of evidential methods of alcohol analysis in blood and breath received only scant attention.

The official method of blood-alcohol analysis in Sweden involves the use of computer-aided headspace gas chromatography. The exact details of the procedure were recently described in this journal [6]. In brief, three different laboratory technicians each make a single determination of BEC using a different set of equipment. Three 10- μ L aliquots of blood are removed from two different Vacutainer tubes. These are filled in rapid succession from a single stick in a cubital vein of the person suspected of driving under the influence (DUI). The headspace gas chromatography is performed with three different stationary phases and this furnishes a high specificity for ethanol. The standard deviation (SD) of blood-alcohol analysis by this method is more or less constant until a BEC of 0.08 g% w/v is reached. Thereafter, the SD increases linearly as the BEC increases towards 0.35 g% w/v. This implies that the analytical precision is less at higher concentrations of ethanol in the blood specimen. When the limits of detection (LOD) and limits of quantitation (LOQ) are being discussed, the uncertainty (SD) at zero BEC is a primary concern. The LOD may be defined as the lowest concentration of analyte that can be statistically distinguished from a blank [7].

The LOD of a method of chemical analysis can be determined either from the precision of repeated measurements of a blank or from the scatter of data points around a calibration plot for the method [8-10]. Figure 1 is the SD of a single determination plotted against the concentration of ethanol in the blood specimen. The SD values were derived from triplicate measurements made on each blood specimen submitted to our laboratory for routine analysis of ethanol. A total of 15 288 blood specimens were analyzed and the results were grouped into concentration intervals of 0.1 mg/g (0.01 g% w/v). The pooled SD was computed from the sums of squares of each triplicate assay within the relevant

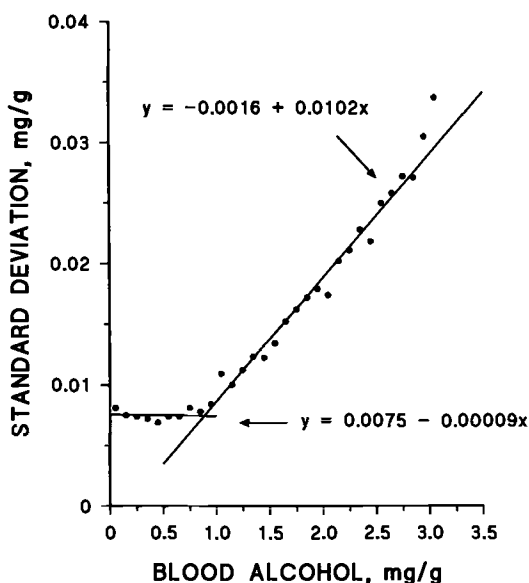


FIG. 1—Relationship between the standard deviation of a single determination of ethanol in blood from drinking drivers, and the concentration of ethanol in the specimens analyzed. All determinations were made by headspace gas chromatography [6].

concentration intervals. Regression relationships were calculated by the method of least squares. Over the BEC range of 0.00 to 0.80 mg/g, the equation was $y = 0.0075 - 0.00009x$. Over the BEC range of 0.80 to 3.5 mg/g, the equation was $y = -0.0016 + 0.0102x$. The y -intercept of the regression line at the lower range of BEC has important implications when the LOD and LOQ are assigned to the method [11]. When BEC is zero, the SD_0 is 0.0075 mg/g. The LOD of this method in routine use with 95% confidence is given by 3×0.0075 , which is 0.0225 mg/g. The LOQ for 95% confidence is given by 10×0.0075 , which is 0.075 mg/g. These values of LOD and LOQ might be different if the operating conditions were modified, for example, by renewing the chromatographic columns. The experience of the technician responsible for the analysis might also influence the LOD and LOQ for the method. Both the LOD and LOQ should be reestablished whenever the method undergoes any significant modifications.

Gas chromatographic (GC) methods of blood-alcohol analysis with a flame ionization detector have the potential to analyze concentrations of ethanol very much lower than the LOD cited above. Note that the LOD for the instrument is not the same as the LOD of the method. The latter depends on the particular analyte and the sample matrix available. The concentrations of endogenous ethanol in blood have been determined by GC analysis and are within the range 0.00025 to 0.0001 g% w/v [12,13]. But, in routine forensic science work, such as day-to-day analysis of BEC, the GC instruments are not finely tuned for trace analysis. Note that the LOD and LOQ for determinations made at clinical laboratories are not necessarily the same as those made at forensic science laboratories, depending on, among other things, the sample matrix (whole blood or plasma serum) and the method of analysis used (gas chromatography as opposed to

enzymatic batch analyzers). If low concentrations of blood alcohol have medicolegal significance, the analytical report should also include the LOD and LOQ of the method used.

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Discussion of "Dangerous Mentally Disordered Criminals: Unresolvable Societal Fear?"

Sir:

In the January 1991 issue of this journal, Drs. Leong, Silva, and Weinstock reviewed some of the legal and clinical literature concerning mentally disordered offenders [1]. They concluded, "Given the lack of efficacious treatment outcomes and the recidivism rate for NGI [not guilty by reason of insanity] acquittees, a similar pessimistic forecast seems likely for the non-NGI dangerous mentally disordered criminal" (p. 215).

I strongly disagree. The difficulty with these authors' conclusions is the limitation of their empirical data. The one study of California insanity acquittees which they cited [2]—although, admittedly, there have been only a few published [3]—drew from a sample

that was released to the community in 1979. Since 1 Jan. 1986, California has had an intensive and comprehensive involuntary outpatient program for insanity acquittees similar to that of the Psychiatric Security Review Board in Oregon. Each county in California administers this Mental Health Conditional Release Program through contracts with the state's Department of Mental Health, and the jurisdiction of the patients remains with the local Superior Court.

Since the inception of the Conditional Release Program, 710 individuals have been admitted to the program. The rearrest rate was 8.3% after one year in the community, 13.2% after two years, and 16.7% after three years [4]. The rehospitalization rate was 21% for the first two years of operation. Less than half of those who reoffended were charged with violent crimes. Most of these patients are clinically and demographically similar to other NGI populations, modally described as typically a Caucasian male with a diagnosis of schizophrenia who committed a violent felony for which he was found legally insane. In San Diego County, California, the second most populated area of the state, 64 individuals have been treated through the local Conditional Release Program for from one to five years (1986–1990, inclusive) after being released from the state hospital. There have been 2 reoffenses, both nonviolent, for a rate of 3% (one patient was absent without leave (AWOL) from the program and was later rearrested in Vermont; another patient was revoked for possession of a controlled substance).

The remarkable success of this statewide program is attributed to the low patient-to-staff ratio (10:1) and the mandated core standards of treatment, which include weekly individual and group psychotherapy, random urine toxicology screens, and active case management in the field by clinicians [5]. Although the annual costs per patient have averaged \$15 000 to \$20 000, this is only one quarter of the costs of state hospitalization. I remain hopeful that the mentally disordered offender population [6], the non-NGI group mentioned by the authors [1], will have the same quality and quantity of treatment, at least in California. I am less optimistic about this population's outcome, however, since they clinically appear to be quite different from the NGI population. They display more psychopathic, or antisocial, personality traits and have been conditioned to a prison, rather than a hospital, environment.

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Authors' Response

Dear Sir:

We commend Dr. Meloy on the success his program has attained in treating or monitoring acquittees judged not guilty by reason of insanity (NGI) on conditional release status in San Diego County. It would appear that Dr. Meloy's program is an exception, rather than the rule, as our review of the literature indicates. Moreover, Dr. Meloy does not address the intense competition for public sector mental health funds in California at a time when budgetary constraints are forcing severe cutbacks in psychiatric services for all. While his program costs appear modest compared with state hospitalization costs, the funding may have been provided at the expense of non-criminally related public sector psychiatric services. Other California counties, however, may actually allocate less funding per patient than San Diego County for treatment (monitoring) of NGI Conditional Release Program patients and thereby increase the likelihood of revocation of their outpatient status.

Our review of insanity acquittee studies suggests that the non-NGI mentally disordered offenders and NGI mentally disordered are similar enough to make at least preliminary conclusions in terms of clinical and ethical problems. If, however, Dr. Meloy's assertion that the non-NGI group is indeed qualitatively different from the NGI group in terms of psychopathy or antisocial traits, then our clinical and ethical concerns take on heightened significance as the alleged treatability of the non-NGI group becomes a very difficult goal to attain and clinicians are therefore being used solely to perform an essentially social control function.

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Discussion of "Relationship of Ischemic Heart Disease to Sudden Death"

Dear Sir:

I read the excellent article "Relationship of Ischemic Heart Disease to Sudden Death," appearing in this journal (Vol. 36, No. 1, Jan. 1991) by Drs. Buja and Willerson, with great interest. It is appropriate to reiterate that death due to acute coronary artery insufficiency usually does not show a recent coronary artery thrombus, which I did not realize as a fledgling pathology resident. I would not disagree that the majority of the cases of sudden cardiac death show narrowing of at least 75% of the luminal area of at least one coronary artery; however, the criteria that I find useful are (1) at least 50% luminal (area) restriction of the proximal left anterior descending branch or (2) a combination of at least 50% restriction of the proximal circumflex branch *and* at least 50% restriction of the right coronary artery. Any luminal restriction less than that indicated above is not compatible with a sudden cardiac death due to coronary insufficiency if the total evidence/findings in the case are compatible. Certainly, restriction of the coronary arteries should not be used as the only criterion in the cause of death, since we have all seen numerous cases with very severe coronary artery atherosclerosis in which the death was caused by a noncardiac pathologic process.

I might also suggest another factor under "(2) myocardial ischemia, without infarction," which was listed in the Abstract. I would propose in item "(c) decreased oxygen availability" that carbon monoxide intoxication, low ambient partial pressure of oxygen,

airway obstruction, and other factors be included. In my forensic pathology work in a relatively high-altitude area, I have noted a number of cases in which there was severe coronary artery atherosclerosis with adequate myocardial oxygenation at sea level but myocardial hypoxia and cardiac decompensation at 6200-ft (1900-m) elevation, especially if the individuals smoked or were exposed to ambient cigarette smoke. Finally, I have noted a few cases in which there was an acute, purulent tracheobronchitis (clinically a "chest cold") with thick, tenacious, purulent mucus causing obstruction of the bronchi. In such of these cases which have a concomitant severe coronary artery atherosclerosis, I believe the bronchial obstruction causes hypoxia and contributes to sudden cardiac death.

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Authors' Response

Dear Sir:

We appreciate the thoughtful comments by Dr. Sander regarding the problem of sudden cardiac death. We agree that the majority of cases of sudden cardiac death do not show evidence of an occlusive coronary thrombosis (see Table 1 of our article) [1]. However, the work of Davies and Thomas suggests that plaque fissuring, with associated microthrombosis, occurs more frequently in cases of sudden cardiac death than was previously recognized [2].

Dr. Sander raises the question of the severity of coronary atherosclerosis that can be expected to be associated with myocardial ischemia. Experimental studies have shown that a 75% reduction in luminal cross-section area (equivalent to a 50% reduction in luminal diameter) is required before impairment in stress-induced hyperemic coronary blood flow occurs [3]. Even further reduction in luminal area is required to produce impairment in resting coronary blood flow [3]. Therefore, a 75% reduction in the cross-sectional luminal area of at least one coronary artery has generally been considered the threshold for critical coronary stenosis. As pointed out in our article, over 90% of cases of sudden cardiac death are associated with at least 75% stenosis of one or more major coronary arteries [1]. In a study by Davies and Pople, cases of sudden cardiac death were associated with at least 85% stenosis of at least one major coronary artery, whereas age-matched controls showed coronary stenosis of 75% or less [4]. It is clear that a number of factors, including cardiac hypertrophy and hypertension, can adversely impact the effect of a given degree of coronary stenosis. One can never exclude the possibility that a lesser degree of coronary stenosis may be of clinical significance. As suggested by Dr. Sander, 50% stenosis of the proximal left anterior descending coronary artery or a combination of 50% stenosis of the proximal left circumflex and right coronary arteries may well be associated with myocardial ischemia in some cases. However, the use of these less restrictive criteria will run the risk of considerable overlap of cases with and without sudden cardiac death. As also indicated by Dr. Sander, we agree that complete evaluation of individual cases is imperative, since the circumstances of death are as important as the anatomic findings in reaching a reasonable conclusion regarding the cause of death.

In order to emphasize the complex pathophysiology of sudden cardiac death, we have presented a general scheme of potential mechanisms [1]. These are acute myocardial infarction, myocardial ischemia without infarction, and a primary cardiac arrhythmia. We presented two potential causes of myocardial ischemia, that is, an exertion-induced increase in myocardial oxygen demand and an acute coronary event, often involving

plaque degeneration and platelet aggregation. However, we were remiss in not including the general category of decreased oxygen availability, which can have a number of causes, including carbon monoxide intoxication, low ambient partial pressure of oxygen, airway obstruction, and other causes, as was pointed out by Dr. Sander. Such conditions should be given consideration in the differential diagnosis, particularly in the forensic setting. We thank Dr. Sander for pointing out this important category.

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