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# The Role of Ethanol Abuse in the Etiology of Heroin-Related Death

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**ABSTRACT:** Toxicology analyses and other forensic science data were used to examine the mechanisms through which ethanol increased the risk for death caused by injected street preparations of heroin. The authors studied 505 victims of fatal heroin overdose and compared subjects who had concentrations of blood ethanol greater than 1000 mg/L ($n$ = 306) with those who had concentrations less than, or equal to 1000 mg/L ($n$ = 199). We found significant negative correlations between concentrations of ethanol and morphine (a heroin metabolite) in blood ($R^2$ = 0.11, $P$ = 0.0001 for $\log_{10}$-transformed variables) as well as between concentrations of blood ethanol and bile morphine ($R^2$ = 0.16, $P$ = 0.0001 for $\log_{10}$ bile morphine versus blood morphine). Toxicologic evidence of infrequent heroin use was more common in decedents with blood ethanol concentrations greater than 1000 mg/L than in those with lower concentrations. Our data suggest that ethanol enhances the acute toxicity of heroin, and that ethanol use indirectly influences fatal overdose through its association with infrequent (nonaddictive) heroin use and thus with reduced tolerance to the acute toxic effects of heroin.

**KEYWORDS:** toxicology, heroin, ethanol

A recent epidemiologic study of heroin-related deaths (HRDs) in the District of Columbia identified ethanol use as a significant risk factor [*1*]. This study found that blood ethanol concentrations in excess of 1000 mg/L raised by a factor of 22 the odds of a heroin user experiencing a fatal overdose. The high-risk practice of using both heroin and ethanol has become more popular in the District of Columbia in recent years, as is reflected in the increase in HRDs with ethanol detected in the blood, which rose from 13 (44% of all HRDs) in 1976 to 70 (66% of all HRDs) in 1986 (Fig. 1).

Although the concomitant use of heroin and ethanol is well recognized and considered dangerous, no study has explained why this combination is lethal. In this article, we used forensic science data for HRDs to explore possible mechanisms for this lethal combination. We examined relationships between concentrations of heroin and ethanol in the blood, urine, and bile of HRDs. We also analyzed differences between HRDs with blood ethanol concentrations greater than 1000 mg/L [high ethanol (HE) decedents] and those with concentrations less than, or equal to 1000 mg/L [low ethanol (LE) decedents].

The phenomenon of combining ethanol and opiate use and the resultant toxic effects

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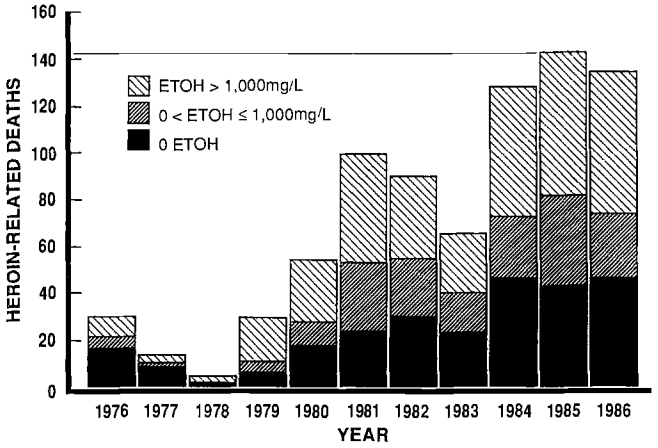


FIG. 1—*Heroin-related deaths in the District of Columbia by concentration of ethanol in blood, 1976–1986.*

were noted as early as 1881 [*2*], and ethanol consumption by narcotic abusers in the United States has been commonly reported in epidemiologic studies since the late 1960s [*3–12*]. Studies of heroin addicts in drug treatment programs have also highlighted the use of these drugs in combination [*6,13–18*] and have shown that heroin addicts in the 1970s abused ethanol more frequently than persons not addicted to heroin [*19*]. However, according to anecdotes from drug treatment counselors and heroin users, ethanol was shunned by heroin users prior to the 1960s [*20,21*], as is revealed in William Burroughs' graphic description [*22*]:

> As I began using stuff every day, or often several times a day, I stopped drinking and going out at night. When you use junk you don't drink. Seemingly, the body that has a quantity of junk in its cells will not absorb alcohol. The liquor stays in the stomach, slowly building up nausea, discomfort, and dizziness, and there is no kick. Using junk would be a sure cure for alcoholics.

Interviews with heroin users and drug abuse treatment personnel have identified the practice of substituting ethanol for heroin when the latter drug is either unavailable or unaffordable [*6,20*]. O'Donnell [*21*] reported that narcotics users clearly preferred heroin to ethanol, but that they often substituted ethanol for heroin when heroin was unavailable, or in response to social pressure. It is not clear when or why the combined use of heroin and ethanol became popular in the United States. This practice is now common, however, and evidently associated with epidemics of HRDs.

In our study, we examined three hypotheses for the pharmacologic basis of this lethal combination: (1) ethanol and heroin act additively or synergistically on the central nervous and respiratory systems to produce a cardiopulmonary arrest that is more frequently fatal than that produced by heroin alone; (2) ethanol interferes with the metabolism of heroin and prolongs the toxic effects of this narcotic; and (3) ethanol consumption is commonly associated with infrequent (nonaddictive) use of heroin [*7*], which results in reduced tolerance to the acute toxicity of heroin [*23*].

## Report of Cases

### *Case 1*

A 28-year-old black female, employed as a clerk-typist, had abused alcohol and heroin in the past. Eight months before death she received inpatient treatment for ethanol

dependency. Though she never quit drinking, she had reduced her ethanol consumption markedly after treatment. The victim had no other known medical problems. Friends stated that she used narcotics occasionally but did not have a regular habit.

After drinking an unspecified quantity of beer, the victim injected a street preparation of heroin. About 30 min later she reportedly had a seizure and lost consciousness. A friend drove her to a nearby hospital, where cardiopulmonary resuscitation was administered unsuccessfully.

At autopsy the lungs weighed 1500 g, and the 2500-g liver showed grow evidence of fatty metamorphosis (FM). The blood ethanol concentration was 2500 mg/dL, and concentrations of total morphine (the sum of the bound and free morphine) in the blood, urine, and bile were, respectively, 0.2, 0.5, and 0.5 mg/L. Multiple recent injection sites were noted on both arms, but no needle tracks were evident.

*Case 2*

The decedent was a 35-year-old healthy black male who was apparently a narcotics dealer. He was found dead in his bedroom with the needle of a hypodermic syringe still inserted in a vein of his leg. Empty plastic envelopes with apparent heroin residue were in the room.

The decedent's sister reported that her brother had been using heroin for the past ten years and that he alternated between periods of addiction and abstinence. She also noted that he was a heavy beer drinker and that he had overdosed using heroin at least three times in the past, most recently two months before his death. The victim had told his sister that the overdoses resulted from drinking and using heroin after periods when he used heroin infrequently.

Significant autopsy findings include a combined lung weight of 1310 g, and a grossly normal liver that weighed 1650 g. There were needle tracks on both arms and recent and old injection sites on the left arm and leg. The blood ethanol concentration was 2100 mg/L, and the total blood morphine concentration was 0.4 mg/L. Morphine was detected but not quantified in the urine, and the bile was not analyzed.

## Analysis of Autopsy Toxicology Data for a Series of HRDs

*Methods*

Data for the 505 HRDs that occurred in the District of Columbia between 1 Jan. 1980 and 31 March 1985 were abstracted from the records of the Office of the Chief Medical Examiner. For this study, the definition of HRD excluded decedents who had toxicologic evidence of heroin in combination with other drugs that may have contributed to death, including cocaine, methadone, and barbiturates. The autopsies, crime scene investigations, and toxicologic analyses were performed in a uniform manner during this period. The toxicologic methods, described in detail elsewhere [*1,24*], included gas chromatography for measurement of the blood ethanol concentrations and radioimmunoassay for the total morphine quantification.

Beginning in 1984, in an effort to reduce operating costs, the Medical Examiner's Office performed quantitative analyses for morphine in bile and urine less frequently than in previous years. We found no relationship between the HRDs without these measurements and concentrations of ethanol in the blood and conclude that this change in practice has not biased our results. Measurements of ethanol and morphine concentrations were excluded from analyses for 54 subjects who were admitted to a hospital, who survived longer than 12 h after injection, or for whom the medical treatment after overdose was not specified. This was done to minimize the distortion of toxicologic results by antemortem metabolism of these compounds.

For linear regression models, the $\log_{10}$ transformation of a variable was reported if the analysis of standardized residuals supported this transformation and if it improved the model correlation coefficient [*25*]. The sample sizes for the toxicologic variables differed between regression analyses because only those subjects having measurements for both model variables could be included, and measurements of urine and bile morphine were not made for all subjects.

The ratios of blood morphine to urine morphine and of blood morphine to bile morphine were computed for each subject to adjust for the quantity of heroin used prior to overdose and for individual differences in the metabolism of morphine. The morphine ratios also reflect heroin use in the days before death, as morphine has been detected in urine up to 96 h after injection of heroin or morphine [*26–30*] and in bile for a similar period [*26,29,31,32*]. The effects of ethanol on the distribution of heroin metabolites were assessed by comparing the ratios for LE decedents with those of HE decedents.

When the ratios for toxicologic variables were compared between HE and LE groups, fewer than ten subjects were excluded from each comparison because of ratios with denominators of zero. The actual number of subjects excluded from each analysis can be determined by subtracting the number of subjects specified for each analysis from the number of subjects for which the age (a variable determined for all subjects) was reported.

## *Results*

Figure 2 is a scatter plot of concentrations of morphine and ethanol in the blood for the 445 HRDs for which both measurements were made. There was a significant inverse

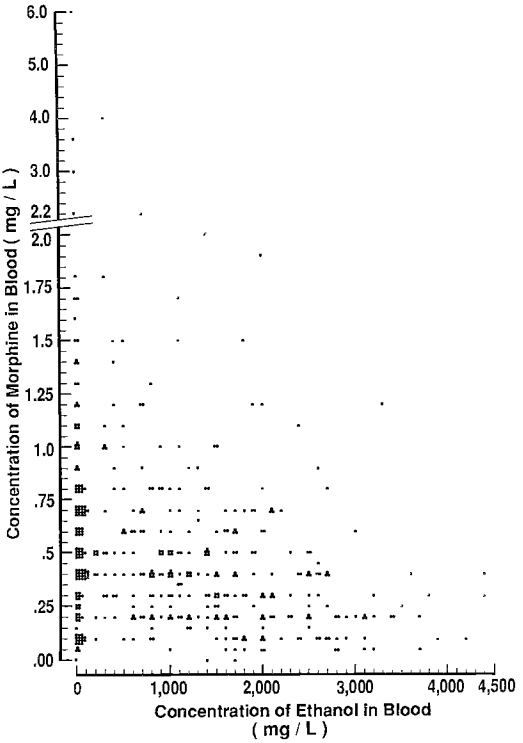


FIG. 2—*Blood morphine versus blood ethanol concentrations for heroin-related deaths in the District of Columbia, January 1980–March 1985.*

correlation between these two variables (Table 1). We also found an inverse correlation between the bile morphine and blood ethanol. This correlation was statistically as strong as the one between blood morphine and blood ethanol, and the standardized regression coefficient for the model with bile morphine was much larger than the coefficient for the model with blood morphine. Though HE decedents were significantly older than LE decedents (Table 2), we found no association between age and blood ethanol concentration (linear regression coefficient = 0.001, $R^2 < 0.01$, $P = 0.1072$).

Compared with the HE decedents, the LE decedents had significantly higher concentrations of morphine in the blood, bile, and urine (Table 2). The mean liver weight was significantly higher in the HE than in the LE group. In addition, 57% of the HE decedents had gross evidence of FM, in comparison with 34% for the LE group [$X^2$ (1) = 22.8, $P < 0.001$].

The morphine ratios between the blood and urine and between the blood and bile were higher in the HE group than in the LE group. In linear regression analyses performed for the LE and HE groups separately and for all HRDs combined, the blood ethanol concentrations did not explain the variation in either ratio; the regression coefficients were statistically insignificant and the values for $R^2$ were less than 0.07. The difference between morphine ratios for the HE and LE groups in Table 2 appears to be due to the differences between the urine and bile morphine concentrations.

Table 3 presents toxicology data stratified by blood ethanol concentration and gross liver pathology. The concentrations of blood morphine for decedents with FM were similar to those for decedents with normal livers. However, the HE decedents with FM had the lowest bile and urine morphine concentrations, and the LE decedents had the highest. Both bile and urine morphine concentrations were lower in the decedents with FM than in those with normal livers, regardless of the blood ethanol concentration. The ratios of blood morphine to bile morphine and blood morphine to urine morphine were both higher in decedents with FM, regardless of blood ethanol concentration.

These differences are probably not due to the mistaken inclusion of decedents with true (microscopically confirmed) FM in the group with grossly normal livers. An error of this type would have resulted in reduced urine and bile morphine concentrations for the group with normal livers and would have reduced, rather than accentuated, the differences we identified.

Because the age at death and the presence of gross FM could have confounded the observed relationships between blood ethanol and morphine concentrations in the bile and urine, the effects of these two factors were evaluated separately with linear regression analysis (for models with age as an independent variable) and analysis of variance (for models with liver pathology as an independent variable). Neither the age nor the presence of FM was a significant predictor of the variation in the blood ethanol, urine morphine, or bile morphine concentrations ($R^2 < 0.08$). We did detect an extremely weak relationship between FM and age ($R^2 = 0.05$, $P = 0.0001$, with a least-squares mean age of 30.6 years for subjects with normal livers and 33.6 years for those with FM).

## Discussion

We determined that HE decedents had significantly lower blood morphine concentrations than LE decedents and identified a significant inverse correlation between concentrations of ethanol and morphine in the blood. These findings suggest that there is a dose-response relationship between the consumption of ethanol and the acute toxicity of heroin. However, blood ethanol concentrations explained only 11% of the variation in blood morphine concentrations, indicating that additional factors are probably involved in the etiology of fatal overdose by users of heroin and ethanol.

There is no evidence from our study that ethanol interferes with the metabolism of

TABLE 1—*Linear regression results*[a] *for selected autopsy variables.*

| Dependent Variable | Independent Variable | $N$ | $R^2$ | Regression Coefficient | Standard Error | $P$ |
|---|---|---|---|---|---|---|
| Blood morphine | blood ethanol | 443 | 0.07 | −0.14 | 0.02 | 0.0001 |
| Log blood morphine | log blood ethanol | 309 | 0.11 | −0.39 | 0.06 | 0.0001 |
| Urine morphine | blood ethanol | 282 | 0.03 | −3.66 | 1.24 | 0.0034 |
| Log urine morphine | blood ethanol | 275 | 0.05 | −2.12 | 0.55 | 0.0002 |
| Bile morphine | blood ethanol | 390 | 0.08 | −8.35 | 1.44 | 0.0001 |
| Log bile morphine | blood ethanol | 386 | 0.16 | −3.16 | 0.37 | 0.0001 |
| Blood morphine | urine morphine | 278 | 0.01 | 0.00 | 0.00 | 0.1123 |
| Bile morphine | urine morphine | 277 | 0.32 | 0.76 | 0.07 | 0.0001 |
| Log bile morphine | log urine morphine | 267 | 0.41 | 0.52 | 0.04 | 0.0001 |
| Blood morphine | bile morphine | 346 | 0.08 | 0.00 | 0.00 | 0.0001 |

[a]$\text{Log}_{10}$ transformations are reported when considered appropriate after examination of the diagnostic statistics and when the transformation improved the model regression coefficient or the correlation coefficient.

TABLE 2—*Measures of the central tendency[a] of blood ethanol concentration for selected autopsy variables in heroin-related deaths.*[b]

| Variable | Blood Ethanol Concentration ($n$ = 505) | | | | $P$ |
|---|---|---|---|---|---|
| | Low (≤1000 mg/L) ($n$ = 306) | | High (>1000 mg/L) ($n$ = 199) | | |
| Age | 30 | (306) | 32 | (199) | 0.0037 |
| Blood ethanol, mg/L | 0 | (252) | 1900 | (199) | |
| Blood morphine, mg/L | 0.5 | (247) | 0.3 | (196) | <0.0001 |
| Bile morphine, mg/L | 7.0 | (221) | 1.8 | (172) | <0.0001 |
| Urine morphine, mg/L | 2.0 | (151) | 0.5 | (131) | 0.0003 |
| Morphine ratios | | | | | |
| Blood/bile | 0.07 | (212) | 0.20 | (167) | 0.0001 |
| Blood/urine | 0.26 | (145) | 0.40 | (126) | 0.0884 |
| Bile/urine | 2.50 | (146) | 3.33 | (125) | 0.9578 |
| Liver weight, g | 1850[c] | (301) | 2000[c] | (196) | 0.0012 |
| Lung weight, g | 1250[c] | (254) | 1280[c] | (197) | 0.7772 |

[a]Unless otherwise specified, the variables do not have normal distribution; hence, the medians and $P$ values for the Wilcoxon rank-sum test are reported.

[b]The sample sizes are in parentheses.

[c]The means and $t$-test results are reported for variables that are normally distributed.

heroin. If ethanol increased the risk of HRD by blocking the deacetylation of heroin, then blood morphine concentrations would have been higher in the HE group than in the LE group. The absence of positive correlations between the blood ethanol and blood morphine, and between the blood ethanol and either of the blood morphine ratios also suggests that ethanol does not affect heroin metabolism.

Our data suggest that decedents who consumed large quantities of ethanol before death also had used heroin infrequently in the days before death. This conclusion is supported by the finding that, compared with LE decedents, HE decedents had significantly lower concentrations of morphine in the bile and urine and the finding that morphine metabolites are transported to bile faster and in higher concentrations in narcotic-tolerant animals than in nontolerant ones [*26,32*]. The significant but weak inverse correlation between concentrations of blood ethanol and bile morphine is also consistent with this conclusion.

## Conclusions

Data presented here and in other studies [*1,33*] indicate that fatal heroin overdose can be influenced by the toxic effects of other drugs and by other risk factors and is not merely the consequence of injecting unusually high doses of heroin. Our results suggest that simply discouraging the practice of drinking and injecting heroin may not be effective in preventing fatal overdose. Combining chronic ethanol abuse with infrequent (nonaddictive) heroin use should also be discouraged. Since fatal heroin overdoses are commonly associated with ethanol use, public health measures directed towards those who use both drugs may help reduce the incidence of these deaths.

TABLE 3—*Measures of the central tendency[a] of blood ethanol concentration and liver pathology for selected autopsy variables in heroin-related deaths.[b]*

| Variable | Low Blood Ethanol (≤1000 mg/L) ($n$ = 284) | | | High Blood Ethanol (>1000 mg/L) ($n$ = 182) | | |
|---|---|---|---|---|---|---|
| | Liver Pathology | | | Liver Pathology | | |
| | Normal ($n$ = 187) | FM[c] ($n$ = 97) | $P$ | Normal ($n$ = 79) | FM[c] ($n$ = 103) | $P$ |
| Age | 29 (187) | 32 (97) | 0.0002 | 31 (79) | 33 (103) | 0.0343 |
| Blood ethanol, mg/L | 0 (164) | 300 (76) | 0.0477 | 1700 (79) | 2000 (103) | 0.0540 |
| Blood morphine, mg/L | 0.5 (163) | 0.5 (76) | 0.3373 | 0.3 (78) | 0.3 (103) | 0.6834 |
| Bile morphine, mg/L | 7.5 (148) | 4.0 (61) | 0.0396 | 3.0 (67) | 1.5 (90) | 0.1370 |
| Urine morphine, mg/L | 2.0 (101) | 1.0 (44) | 0.1670 | 1.2 (52) | 0.4 (69) | 0.0048 |
| Morphine ratios | | | | | | |
| Blood/bile | 0.06 (145) | 0.13 (61) | 0.0162 | 0.13 (64) | 0.23 (90) | 0.1115 |
| Blood/urine | 0.24 (100) | 0.50 (43) | 0.1680 | 0.21 (52) | 0.55 (66) | 0.0285 |
| Bile/urine | 2.61 (100) | 1.90 (40) | 0.4408 | 2.00 (51) | 7.33 (66) | 0.0496 |

[a]The variables do not have normal distributions or medians, and $P$ for the Wilcoxon rank-sum test are reported.
[b]The sample sizes are in parentheses.
[c]Fatty metamorphosis by gross examination.

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