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Peak Blood-Ethanol Concentration and the Time of Its Occurrence After Rapid Drinking on an Empty Stomach

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ABSTRACT: Healthy men, 20 to 60 years old, drank a moderate dose of ethanol in the morning after an overnight fast. They consumed either neat whisky in amounts corresponding to 0.34, 0.51, 0.68, 0.85, or 1.02 g of ethanol per kilogram of body weight or 0.80 g/kg ethanol solvent diluted with orange juice. The peak blood-ethanol concentration (BEC) increased with the dose administered, but the time required to reach the peak was not markedly influenced over the range of doses studied. At a dose of 0.68 g/kg, the peak BEC ranged from 52 to 136 mg/dL (N = 83), and slow absorption (a late-occurring peak) produced a lower peak BEC. The peak BEC was reached between 0 and 45 min for 77% of the subjects (N = 152) and between 0 and 75 min for 97% of them. The time of peaking in venous blood occurred, on average, 10 min later than in capillary (fingertip) blood although the peak BEC was not appreciably different; the mean venous BEC was 97.0 mg/dL (range, 76 to 112 mg/dL), and the mean capillary BEC was 99.6 mg/dL (range, 75 to 123 mg/dL). When subjects drank 0.80 g/kg ethanol diluted with orange juice over 30 min, the average BEC increment between the end of drinking and the peak was 33 mg/dL (range, 0 to 58 mg/dL). The rate of absorption of ethanol was 1.78 mg/dL/min (range, 0.52 to 4.8 mg/dL/min), and the peak BEC occurred within 60 min after the end of drinking in 92% of the trials. The largest BEC increment (mean, 21 mg/dL; range, 0 to 44 mg/dL) was seen during the first 15 min after the drinking period.

KEYWORDS: toxicology, blood alcohol, ethanol, absorption rate, blood ethanol, drinking behavior, peak level, time to peak, increment after drinking, driving under the influence, defense challenges

Apprehended drunk drivers sometimes plead a rising blood-ethanol concentration (BEC) as their defense [*1,2*]. This defense tactic rests on the assumption that the BEC was below the statutory limit at the time of the offense but above the limit when specimens of blood or breath were obtained for quantitative determination of ethanol. The status of ethanol absorption in drunk drivers is an important consideration when attempts are made to estimate the BEC at the time of the offense from the BEC determined at the

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time of sampling, which is often a few hours later [3,4]. This technique is called back-tracking BEC, or retrograde extrapolation, and is a dubious practice [5]. Expert testimony on both these issues requires careful consideration of the absorption kinetics of ethanol and the factors influencing this process [6,7].

We report absorption profiles of ethanol determined in experiments conducted by our research group over the past 15 years. The result will be useful in driving-under-the-influence (DUI) litigation when the question of rising BEC is raised or when back extrapolations are contemplated.

Methods

Subjects and Conditions

Healthy men with moderate drinking habits volunteered for these experiments. Their ages ranged from 20 to 60 and their body weights ranged from 60 to 109 kg. The subjects arrived at the laboratory at about 7:30 a.m. without eating breakfast. They started to drink ethanol at about 9:00 a.m., and the duration of intake was 15, 20, 25, or 30 min, depending on the dose. In the largest test series, 152 men consumed neat whisky in doses ranging from 0.34 to 1.02 g of ethanol per kilogram of body weight. In other experiments, ethanol solvent 95% volume per volume (v/v) was diluted with orange juice to make a 20 to 30% v/v cocktail. This drink was finished in 30 min.

Blood Sampling and Determination of Ethanol

Specimens of capillary (fingertip) and venous blood (cubital vein) were obtained for analysis of ethanol at regular intervals after the start of drinking, usually at 15 to 30-min intervals for 2 h and then at 60-min intervals for 7 to 8 h. Triplicate 10-μL aliquots were taken directly from a fingertip into glass microcaps and diluted with 1 mL of sodium fluoride (NaF) (0.05% v/v) in Autoanalyzer cups. Ethanol was determined by an automated enzymatic method with alcohol dehydrogenase, described in detail elsewhere [8].

In one experiment, nearly simultaneous specimens of capillary and venous blood were obtained as described previously [9]. Capillary blood was taken from fingers on both hands and venous blood from cubital veins on both arms. The average results (left and right arms) were used to plot the BEC time profile for each subject. In another study, twelve healthy men drank a dose within 30 min of 0.8 g/kg ethanol diluted with orange juice in the morning after an overnight fast. Venous blood specimens were taken from an indwelling needle at 10, 20, 30, 45, 60, 90, 120, 150, 180, 240, and 300 min, timed from the start of drinking. The 5-mL Vacutainer tubes of blood contained 25 mg of NaF and 20 units of sodium heparin and were stored in a refrigerator for a few days pending analysis by headspace gas chromatography [10]. With this experimental design, the absorption profile of ethanol was studied in detail.

Evaluation of Results

BEC profiles were plotted for each subject, and the peak BEC and the time required to reach the peak BEC were read from the curves. The rate of absorption of ethanol (in milligrams per decilitre per minute) was calculated by dividing the peak BEC by the time taken to reach the peak. The half-life of ethanol absorption from the gut ($t_{1/2}$) and the absorption rate constant (k_{abs}) were calculated according to the method of residuals [11]. Mean, mode, median, and range of values were calculated depending on the underlying distributions. When blood was drawn exactly at the end of drinking, the BEC increments before reaching the peak were noted. If the peak BEC was the same at two sampling points, the first recorded time was used in the summary statistics.

Results

Blood-Ethanol Profiles After Neat Whisky

Figure 1 shows capillary blood profiles of ethanol for three subjects selected to show the existence of an overshoot peak followed by a diffusion plunge immediately afterwards. In these examples, the maximum BEC exceeds the theoretical value expected if absorption and distribution of the entire dose occurred instantaneously. The apparent rate of elimination of ethanol from blood (β) is erroneously high if calculated during a diffusion plunge. We found values of 34 mg/dL/h (range, 22 to 54 mg/dL/h), 40 mg/dL/h (range, 22 to 92), and 39 mg/dL/h (range, 22 to 66) after ethanol doses of 0.51, 0.68, and 0.85 g/kg, respectively. Figure 2 shows good agreement between the BEC profiles obtained when the same dose of ethanol was consumed by the same subject on two occasions 14 days apart.

Peak BEC and the Time of Its Occurrence After Drinking Neat Whisky

Table 1 shows that higher doses of ethanol result in higher peak BECs, although the time required to reach the peak was not markedly influenced by the dose within the range studied. A peak BEC occurring earlier (more rapid absorption) resulted in a higher peak BEC. After ethanol doses of 0.68 and 0.85 g/kg, the peak BEC and the time required to reach the peak were negatively correlated: $r = -0.70$ ($p < 0.01$) and $r = -0.46$ ($p < 0.05$), respectively. The times needed to reach the peak after drinking were not normally distributed; the mode was 30 min after the start of drinking, corresponding to between 5 and 15 min after the end of drinking. A total of 77% of the subjects reached

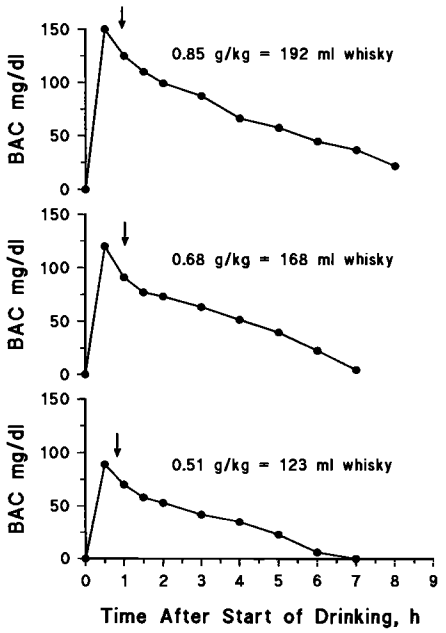

FIG. 1—*Ethanol concentration-time profiles in capillary (fingertip) blood of three male subjects after they drank 0.51, 0.68, and 0.85 g of ethanol per kilogram of body weight as neat whisky on an empty stomach. The drinking times were 15 min (0.51 g/kg), 20 min (0.68 g/kg), and 25 min (0.85 g/kg). The arrows mark the diffusion plunge immediately following the BEC overshoot effect.*

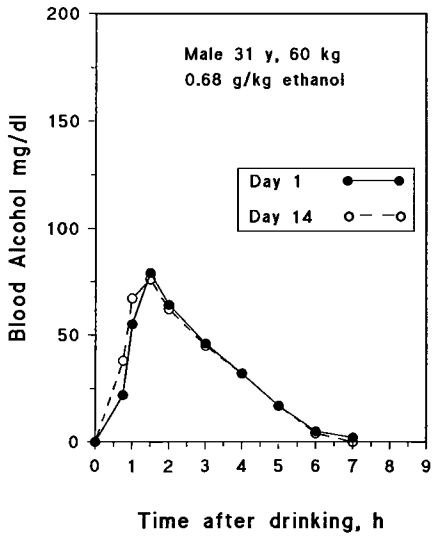

FIG. 2—*Ethanol concentration-time profiles in capillary (fingertip) blood in the same subject after consuming 0.68 g of ethanol per kilogram of body weight as neat whisky on an empty stomach on two occasions 14 days apart.*

TABLE 1—*Peak concentrations of ethanol in capillary blood and the time required to reach the peak after healthy men drank neat whisky within 15 to 25 min after an overnight fast.*[a]

Ethanol, g/kg	N	Peak BEC, mg/dL		Number of Subjects Reaching Peak Within Time, min			
		Mean	Range	5–15	35–45	65–75	95–105
0.34	6	56	43–67	5	1	0	0
0.51	16	74	54–91	11	3	1	1
0.68	83	92	52–136	33	26	21	3
0.85	44	120	83–178	13	24	7	0
1.02	3[b]	134	116–149	0	1	1	1
Totals	152	94[c]	43–149	62	55	30	5

[a]*N* is the number of subjects at each dose of ethanol. The times required to reach the peak are measured from the end of drinking; those times are 15 min (0.34 and 0.51 g/kg), 20 min (0.68 g/kg), and 25 min (0.85 and 1.03 g/kg).
[b]One subject vomited when the BEC passed 150 mg/dL within 35 min after the end of drinking.
[c]Weighted mean.

their peak BEC between 0 and 45 min after the end of drinking and 92% between 0 and 75 min after drinking. Five subjects (3.2%) reached peak BEC between 95 and 105 min after drinking.

Blood-Ethanol Profiles After Drinking Ethanol Solvent Mixed with Orange Juice

Figure 3 illustrates the wide interindividual variation in blood-ethanol profiles during the absorption period after the same dose per kilogram of body weight. In the postpeak phase, however, the BEC in both subjects agreed within the 95% confidence interval calculated according to Widmark's equation [6]. In the slow absorber, the absorption

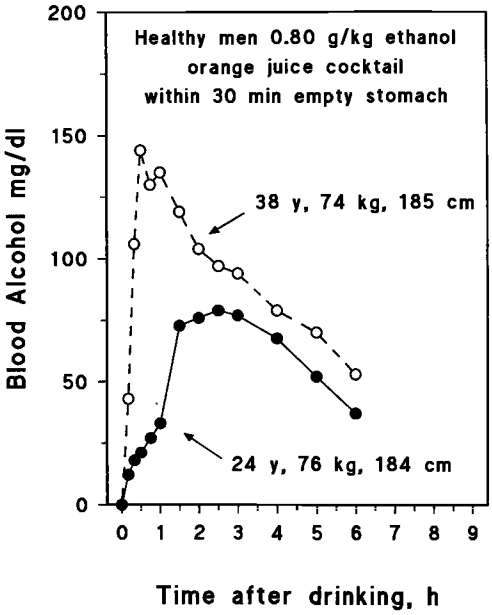

FIG. 3—*Ethanol concentration-time profiles in venous (cubital vein) blood for two different subjects after they drank 0.80 g of ethanol per kilogram of body weight as ethanol solvent diluted with orange juice in 30 min on an empty stomach. The point where an abrupt change in the rate of absorption occurs for the slow absorber 30 min after the end of drinking is indicated by an arrow.*

profile is clearly biphasic. After 60 min (marked by the arrow), the stomach contents presumably begin to enter the small intestine, and this is reflected in a faster absorption. The absorption half-life during the first phase was 103 min and 40 min thereafter. In the rapid absorber, the half-life was 5 min.

Peak BEC and the Time of Occurrence After Drinking Ethanol Solvent Mixed with Orange Juice

Table 2 compares the peak BEC, the time required to reach the peak, and the rise in BEC after drinking for both capillary (fingertip) and venous (cubital vein) blood specimens. The time required to reach the peak venous BEC was, on average, 10 min later than that for the capillary BEC, although the maximum level was only 3 mg/dL lower in specimens of venous blood. The median increase in BEC after drinking ended was 17

TABLE 2—*Peak venous and capillary BEC and the time required to reach the peak after the start of drinking and the BEC increment from the end of drinking to the peak for twelve healthy men who drank 0.80 g/kg ethanol as a 20 to 30% v/v cocktail diluted with orange juice in exactly 30 min.*

Type of Blood	Peak BEC, mg/dL		Time for Subjects to Reach Peak, min				BEC Rise, mg/dL		
	Mean	Range	30	60	90	120	Mean	Median	Range
Capillary	100	75–123	2	7	3	0	18	17	0–43
Venous	97	76–112	0	8	3	1	31	27	5–45

mg/dL (range, 0 to 43 mg/dL) for capillary blood and 27 mg/dL (5 to 45 mg/dL) for venous blood.

Table 3 gives the successive increments in BEC for twelve subjects during and after drinking 0.8 g/kg ethanol mixed with orange juice in 30 min. The maximum BEC increment occurred during the first 15 min after drinking ended, with a mean of 21 mg/dL (range, 0 to 44 mg/dL). The mean rate of absorption was 1.78 mg/dL/min (range, 0.52 to 4.8 mg/dL/min); the half-lives ranged from 5 to 103 min, with a mean of 22 min. In two of the subjects, the absorption kinetics seemed to be a linear function of time and $t_{1/2}$ was not computed.

Relationship Between the Dose of Ethanol and the Peak BEC

The functional relationship between the peak BEC (y-variate) and the dose of ethanol (x-variate) is shown in Fig. 4 for the experiments in which the subjects drank neat whisky. The regression relationship was $y = 7 + 129x$, and the standard error estimate was 18 mg/dL. The value of the regression coefficient 129 (± 10.3 standard error) implies that after a dose of 1.0 g/kg as neat whisky, the peak BEC might range between 107 and 151 mg/dL in 95 of 100 trials for a similar population of subjects. If the dose of ethanol administered is 0.70 g/kg (mean x-variate), the mean expected peak BEC will be 97 mg/dL, and the 95% confidence interval will be 61 to 133 mg/dL. This agrees fairly well with the empirical range of peak BEC after 0.68 g/kg ethanol, which was 52 to 136 mg/dL ($N = 83$), according to Table 1.

Discussion

The absorption profile of ethanol differs widely among individuals, and the peak BEC and the time of its occurrence depend on numerous factors. Among other factors, the drinking pattern, the type of beverage consumed, the fed or fasted state, the nature (liquid or solid) and composition (fat, protein, or carbohydrate) of foodstuff in the stomach, the anatomy of the gastrointestinal canal, and the mental state of the subject are considered to play a role [*12–14*]. Subjects with a gastrectomy seem to absorb ethanol faster than control drinkers with an intact gut [*15*]. Only general guidelines can be given about the speed of absorption and the time of occurrence of the peak BEC in a random subject from the population. To provide an expert opinion about the status of ethanol absorption in a drunk driver, that is, whether the BEC is rising on a plateau or falling at the time of testing, forensic scientists must have accurate information about the preceding drinking spree, such as the volume and kinds of beverages consumed, single or divided doses, and the intake of food before, after, or during the consumption of ethanol. Whether the individual vomited at any time during or after the drinking episode is also useful information. As a last resort to resolve the question, one might consider a controlled experiment using the same individual and the same drinking pattern, time of day, and intake of food. We have demonstrated that the absorption profile of ethanol on a fasting stomach is reproducible in the same individual at least over a period of several weeks or months (to be published).

After rapid consumption of a moderate dose of ethanol on an empty stomach, the peak BEC may show an overshoot effect [*16,17*]. This is reflected in an early peak, higher than would be expected for the dose administered and the body weight of the drinker according to Widmark calculations. This is more likely to occur when the concentrations of ethanol are measured in arterial or capillary blood than in venous blood [*18*]. The overshoot is a transient effect and almost always occurs immediately after drinking. If the apparent rate of elimination of ethanol is calculated from the change in BEC between two time points immediately after an overshoot, that is, on a diffusion plunge, the results

TABLE 3—*Successive increments in venous BEC during and after the consumption of 0.8 g/kg ethanol in 30 min on an empty stomach [rate of absorption (mg/dL/min) = peak BEC/time to peak; absorption rate constant* k_{abs} *(min*$^{-1}$*) =* $0.7/t_{1/2}$*].*

Venous BEC, mg/dL, During Absorption								Rate of Ethanol Absorption		
10	20	30	45	60	90	120	150	mg/dL/min	$t_{1/2}$, min	k_{abs}, min^{-1}
11	49	60	84	87	98	. . .	. . .	1.08	18	0.038
12	18	21	27	33	73	76	79	0.52	103[a]	0.007
9	18	44	79	91	. . .	. . .	. . .	1.51	10	0.070
43	106	144	. . .	. . .	. . .	. . .	. . .	4.8	5	0.146
46	56	63	72	76	84	. . .	. . .	0.93	32	0.022
13	20	63	94	. . .	. . .	. . .	. . .	2.09	6	0.117
14	43	65	109	. . .	. . .	. . .	. . .	2.42	20	0.035
10	53	106	120	. . .	. . .	. . .	. . .	2.66	6	0.117
35	62	89	92	83	109	. . .	. . .	1.21	18	0.039
13	32	85	114	130	. . .	. . .	. . .	2.16	[b]	[b]
6	28	80	117	. . .	. . .	. . .	. . .	2.60	[b]	[b]
3	27	43	66	76	85	. . .	. . .	0.94	24	0.029

[a]Initial absorption phase.
[b]Apparent zero-order absorption profile.

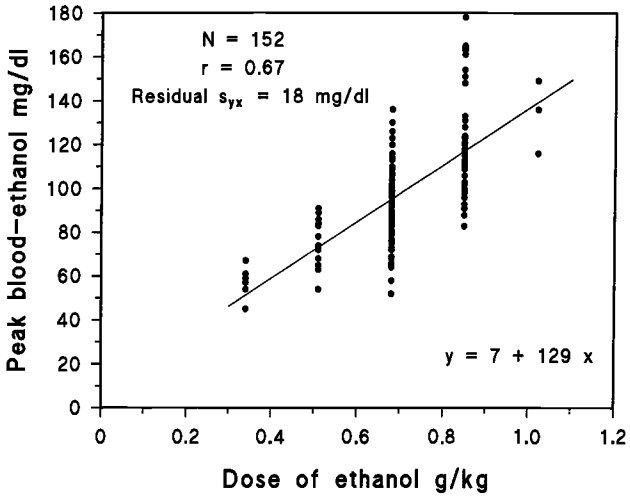

FIG. 4—*Relationship between the dose of ethanol (in grams per kilogram) consumed as neat whisky and the resulting peak blood-ethanol concentration for 152 subjects:* r = *correlation coefficient:* $s_{y.x}$ = *the mean residual variation from the regression line; regression line* y = 7 + 129x.

are abnormally high. It is important not to confuse this nonequilibrium distribution of ethanol between the blood and body water with the rate of metabolism of ethanol in the liver. The change in BEC between two sampling points, however timed, is an unreliable index of the rate of metabolism for that individual. The oxidation of ethanol occurs in the liver and not in the peripheral blood.

Two subjects needed 100 min and a third 105 min to reach peak BEC after the end of drinking neat whisky. This probably reflects a delayed emptying of the stomach caused by a pyloric spasm, but we have no direct evidence for this. The absorption surface area is much greater in the duodenum and small bowel, and absorption of ethanol in this region of the gut is faster than in the stomach. The intake of neat spirits on an empty stomach might irritate the gastric surfaces and trigger a pylorospasm [*19*].

The experiments by Shajani and Dinn [*20*] indicate a mean of 35 min as the time required to reach the peak after the end of drinking (range, 17 to 68 min) when ethanol was consumed as mixed drinks for longer periods. Gullberg [*21*] made tests with 39 subjects who were allowed to drink various doses of ethanol with and without food. He found a mean time before the peak BEC was reached of 19 min (range, 0 to 80 min), and 81% of his subjects peaked within 30 min. Zink and Reinhardt [*22*] allowed subjects to drink large quantities of ethanol ranging from 3.0 to 5.7 g/kg over a period of 4 to 10 h. This consumption pattern might resemble that of a potential drunk driver on a drinking spree. Venous BEC was determined at 15-min intervals during and after the drinking ended. The peak BEC ranged from 192 to 380 mg/dL. Interestingly, for 8 of 14 subjects (57%) this occurred either before or at the same time as the last drink was finished (mean, 14 min; range, 0 to 56 min); the last drink after this high initial ethanol consumption failed to increase the venous BEC. In the remaining six subjects, the peak BEC occurred, on average, 22 min after the drinking ended (range, 10 to 50 min). These results support the notion that after heavy social drinking, the BEC time profile has probably passed the peak and is decreasing by the time specimens of blood are obtained for legal purposes [*23,24*].

The most pronounced rise in BEC occurs when a bolus dose is taken on an empty stomach, as is demonstrated in this paper. The arteriovenous differences in the concen-

tration of ethanol are also more extreme under these conditions because the blood and body water initially contain no ethanol. The consumption of ethanol, together with or after a meal, results in a much lower maximum BEC and a flat-topped curve with a plateau is often seen instead of a sharp peak. McCallum et al. [*25,26*] found that the time required to reach the maximum BEC was shorter when ethanol was consumed after a substantial meal as opposed to an empty stomach. The mean time before the peak BEC after subjects drank beer was 55 min (range, 20 to 114 min) and the peak BEC was 132 mg/dL (range, 40 to 260 mg/dL). More research is needed to establish ethanol absorption profiles and the range of times required to reach the peak when ethanol is taken with different kinds of food in small, medium, and large quantities.

A large body of evidence can be mustered to support the notion that most drunk drivers have passed the peak BEC and are most probably in the postabsorptive phase of ethanol metabolism when biological specimens are obtained for analysis of ethanol in traffic-law enforcement. This conclusion comes from evaluating a large number of double blood specimens (30 to 60 min apart) from apprehended drunk drivers [*27–29*]. The change in BEC per unit of time almost always showed a decreasing trend. The median rate of ethanol disappearance from the blood calculated in this way ranged from 17 to 22 mg/dL/h, making it highly likely that the peak BEC was indeed passed at the time specimens were obtained. The status of ethanol absorption in drunk drivers at the time of the offense is a more difficult question to tackle. In practice, this will depend on such circumstances as the previous drinking spree—the duration and quantities consumed—and the time lapse from the end of drinking to the time of arrest or the time an accident occurred. Speculation about the status of alcohol absorption in drunk drivers can be avoided by statutory definition of the analytical result at the time of the test as the relevant figure for prosecution. This approach is highly recommended when per se statutory limits of alcohol concentration are enforced.

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