Section II
Scientific Section and Presentations

Contributions to Knowledge About Human Pharmacokinetics of Ethanol

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Introduction

In a recent IACT newsletter (volume 26 (3) 2015), I presented a bibliography of published articles on the subject of absorption (A), distribution (D), metabolism (M) and excretion (E) of ethanol in humans (ADME). The information contained in these articles was considered relevant to consider when IACT members testify in court or write expert opinions about some aspect of ethanol pharmacokinetics. Based on a review of the literature and my own reprint collection I included references to about 350 papers published in peer-reviewed journals, although astute readers might have noticed that none of my own contributions were included. This was intentional because I wanted to make a more detailed appraisal of my own research work and include more information about what the results might have contributed to knowledge about ADME of ethanol.

The experimental work undertaken by me and my collaborators involved controlled drinking studies with healthy volunteers (mainly men), hospital patients and alcoholics during detoxification. For safety and ethical reasons the doses of ethanol given to the healthy volunteers were < 1.0 g/kg body weight and the drinks were mostly consumed on an empty stomach. Blood samples for determination of ethanol were either taken from a fingertip (capillary blood), a cubital vein or a radial artery via indwelling catheters. The sampling of arterial blood was possible thanks to a good collaboration with physicians at the University Hospital in Linköping, where my laboratory was located.

Studies of the ADME of ethanol or other drugs requires accurate, precise and specific methods of analysis. Furthermore, a sufficient number of blood samples must be taken to define the concentration-time profile unequivocally. Quantitative analysis of ethanol in blood was either done using an automated enzymatic (ADH) method or by computer-aided head-space gas chromatography. The latter method has become the accepted "gold standard" procedure in forensic science and toxicology laboratories worldwide.

Erik MP Widmark

My long-standing interest in the subject of ethanol pharmacokinetics was sparked, at least in part, by the contributions made by a veritable Swedish pioneer in alcohol and traffic safety research, namely Erik MP Widmark (1889-1945). Widmark was appointed full Professor of Physiological Chemistry at the University of Lund in Southern Sweden (founded in 1666) at the unusually young age of 31.

To commemorate the 100th anniversary of Widmark's birth a scientific symposium was organized at the University of Lund with invited guest speakers from various countries. The main organizer of the symposium was the late Dr. Rune Andreasson (1920-2013), who had written a book about the life and work of Widmark. I was happy to participate in this symposium and I presented data about the analysis of ethanol in alternative specimens (e.g., breath, saliva, sweat, and urine) including physiological principles and possible applications in clinical and forensic medicine.

During my trip to Lund, I took the opportunity to visit the house where Widmark had lived, which was now occupied by his son Dr. Per-Erik Widmark, who was a medical practitioner. I received a pile of Widmark's original reprints and I also took the opportunity to sit behind the great man's desk. For those members of IACT who might want to read more about the life and work of Widmark, I can recommend the following three articles.

- Erik MP Widmark; Swedish Pioneer in Forensic Alcohol Research. *Forensic Sci Int* 72; 1-14, 1995.
- The Life and Work of Erik MP Widmark. *Am J Forensic Med Pathol* 17; 177-190, 1996.
- Erik MP Widmark bridged the gap between forensic toxicology and alcohol and traffic safety research. *Blutalkohol* 45;15-23, 2009.

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The present article in the IACT newsletter contains about 50 citations to my own publications dealing with forensic pharmacokinetics of ethanol and these are grouped and discussed under various topics, domains or areas of forensic interest.

Review articles

1. Jones AW. Aspects of in-vivo pharmacokinetics of ethanol. *Alcohol Clin Exp Res* 24;400-402, 2000.
2. Jones AW. Forensic science aspects of ethanol metabolism. In: Forensic science progress, edited by A. Mahley and RL Williams, Springer Verlag, Berlin, 1991, pp 31-89.
3. Norberg Å, Jones AW, Hahn R, Gabrielsson J. Role of variability in explaining ethanol pharmacokinetics. Research and forensic applications. *Clin Pharmacokinet* 42;1-31, 2003.
4. Jones AW. Evidence based survey of the elimination rates of ethanol from blood with applications in forensic casework. *Forensic Sci Int* 200;1-20, 2010.
5. Jones AW. Pharmacokinetics of ethanol — Issues of forensic importance. *Forensic Sci Rev* 23;91-136, 2011.
6. Jones AW. Pharmacokinetic and pharmacodynamics interactions between ethanol and other drugs. Chapter 13 in Handbook of Drug Interactions — a clinical and forensic guide, 2nd edition, Humana Press, Totowa, 2011, pp 499-586.

Writing review articles is hard work, but it is also an important part of scholarship and allows the writer to integrate, summarize and appraise the scientific literature. In my opinion, a good review should always be accompanied by a long list of current and historical references to previous work on the same topic. Some examples of classic review journals include *"Annual Reviews of Pharmacology and Toxicology"* and *"Pharmacological Reviews."* More recently the Nature Publishing Group (NPG) has created a range of very successful review journals, and the one I most often consult is entitled *"Nature Reviews Drug Discovery."*

Forensic aspects of ethanol are covered in great depth in the review articles cited above and this includes historical developments, pharmacokinetic theory and applications in forensic science and toxicology. Besides the articles listed above, I have written chapters that have appeared in textbooks and encyclopedias devoted to forensic science and legal medicine.

Inter- and Intra-individual Variations in PK of Ethanol

7. Jones, AW. Inter-individual variations in disposition and metabolism of ethanol in healthy men. *Alcohol* 1; 385-391, 1984.
8. Jones, AW, Jönsson, KÅ, Neri, A. Peak blood-ethanol concentration and the time of its occurrence after rapid drinking on an empty stomach. *J Forensic Sci* 36; 376-385, 1991.
9. Jones, AW. The disappearance rate of ethanol from the blood of human subjects; Implications in forensic toxicology. *J Forensic Sci* 38;104-118, 1993.
10. Norberg Å, Gabrielsson J, Jones AW, Hahn RG. Within- and between-subject variations in pharmacokinetic parameters of ethanol analysed in breath, venous blood, and urine. *Br J Clin Pharmacol* 49;399-408, 2000.
11. Jones, AW, Jönsson, KÅ. Between-subject and within-subject variations in the pharmacokinetics of ethanol. *Br J Clin Pharmacol* 37; 427-431, 1994.

The biological variation inherent in blood-alcohol curves and blood-alcohol parameters is obviously important to document. This was done by conducting a large number of controlled drinking experiments with hundreds of volunteer subjects. The above five articles report the magnitude of variation between- and within-subjects for key pharmacokinetic parameters of ethanol, especially the Widmark β and rho factors, which refer to elimination rate of ethanol from blood and volume of distribution, respectively.

The results of these studies found that the β factor might vary by a factor of three (0.01-0.03 g% per h), whereas the rho factor varied by a factor of two (0.40-0.80 L/kg). Within a given population of moderate drinkers, the inter-subject variation is about ±25% (2 coefficients of variation). This needs to be taken into account when back extrapolation or forward prediction of BAC are required in criminal cases. Other PK parameters considered in these articles were variations in C_{max} and t_{max} as well as time required to eliminate ethanol from the whole body.

Effect of Food and Dietary Factors on BAC Profiles

12. Goldberg, L, Jones, AW, Neri, A. Effects of a sugar mixture on blood-ethanol profiles and on ethanol metabolism in man. *Blutalkohol* 16;421-438, 1979.
13. Jones, AW, Neri, A. Evaluation of blood-ethanol profiles after consumption of alcohol together with a large meal. *Can Soc Forensic Sci* J 24;165-173, 1991.
14. Jones AW, Jönsson, KÅ, Kechagias S. Effect of high-fat, high-protein, and high-carbohydrate meals on the pharmacokinetics of a small dose of ethanol. *Br J Clin Pharmacol* 44;521-26, 1997.

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15. Jones AW, Wigmore JG, House CJ. The course of the blood-alcohol curve after consumption of large amounts of alcohol under realistic conditions. *Can Soc Forensic Sci J* 39;125-140, 2006.

16. Jones AW, Jönsson KÅ. Food-induced lowering of blood-ethanol profiles and increased rate of elimination immediately after a meal. *J Forensic Sci* 39;1084-1093, 1994.

17. Hahn, RG, Norberg Å, Gabrielsson J, Danielsson A, Jones AW. Eating a meal accelerates the metabolism of ethanol given by intravenous infusion. *Alc & Alcohol* 29;673-677, 1994.

18. Lisander B, Lundvall O, Tommer J, Jones AW. Enhanced rate of ethanol elimination from blood after intravenous administration of amino acids compared with equicaloric glucose. *Alc & Alcohol* 41;39-43, 2006.

The above seven articles focus on the effects of eating a meal on ADME of ethanol. Food in the stomach before drinking delays gastric emptying and this leads to a lower and later occurring C_{max} and also a smaller area under the BAC time curve. Moreover, the time required to metabolize the dose of ethanol was shortened by about one hour when people consumed 0.8 g/kg ethanol after eating a standardized meal. This suggests that the combustion rate of ethanol is faster in the post-prandial state compared with drinking on an empty stomach. The mechanisms probably involves a more effective first-pass metabolism and/or a food-induced increase in liver blood flow after eating a meal.

The role played by macronutrients, that is, the relative amounts of protein, carbohydrate and fat content of the meal was investigated in one of the studies. We could verify that protein-rich meals were more effective in boosting the rate of ethanol metabolism. This was verified when ethanol and nutrients were given intravenously in fed and fasting states. It appears that in well-nourished individuals the hepatic ethanol metabolizing enzymes are more active.

The results reported in references 13 and 15 are particularly interesting, because the experimental design is similar to "real-world" drinking situations. Reference 13 reported BAC curves obtained during a dinner party when alcohol (1.43 g/kg) was consumed over 90 min at the same time as people consumed a three course meal. Despite the presence of food in the stomach, most of the ingested alcohol was absorbed fairly rapidly and 83 percent of the final peak BAC was reached 5 minutes after the end of drinking. However, the remainder of the ingested dose of ethanol was absorbed more slowly and in some subjects a BAC plateau developed. Under these circumstances, there was no change in BAC for about 1–2 hour before the post-absorptive declining phase of the curve began.

Reference 15 reported results of a drinking study done in Germany in which male subjects drank massive amounts of alcohol under social conditions with drinking times of 6–10 h. The subjects in the study reached very high BACs (0.25–0.4 g%), as might be observed in arrested drivers. The results showed that under these drinking conditions substantial quantities of ethanol failed to reach the systemic circulation, and was probably removed by first-pass metabolism or some other mechanism that reduces bioavailability of the dose of ethanol consumed. The exact mechanisms for this "loss of alcohol" is not known but pre-systemic oxidation by enzymes in the gastric mucosa and/or the liver seems a probable explanation.

Role of Physiological and Medical Conditions

19. Jones, AW, Neri, A. Age-related differences in blood-ethanol parameters and subjective feelings of intoxication in healthy men. *Alc & Alcohol* 20;45-52, 1985.

20. Hahn, RG, Jones, AW, Norberg, Å. Abnormal blood-ethanol profile associated with stress. *Clin Chem* 38;1193-1194, 1992.

21. Jones, AW, Andersson L. Influence of age, gender, and blood-alcohol concentration on the disappearance rate of alcohol from blood in drinking drivers. *J Forensic Sci* 41;922-926, 1996.

22. Jones AW. Body mass index and blood-alcohol calculations. *J Anal Toxicol* 31;177-178, 2007.

23. Jones AW, Zdolsek HJ, Sjöberg F, Lisander B. Accelerated metabolism of ethanol in patients with burn-injury. *Alc & Alcohol* 32;628-30, 1997.

24. Jones AW, Hahn, RG. Pharmacokinetics of ethanol in patients with renal failure before and after hemodialysis. *Forensic Sci Int* 90;175-83, 1997.

25. Klockhoff, H, Näslund I, Jones AW. Faster absorption of ethanol and higher peak concentration in women after gastric-bypass surgery. *Br J Clin Pharmacol* 54;587-591, 2002.

People arrested for driving under the influence of alcohol differ widely in relation to their age, gender, ethnicity, state of health, body composition (BMI), and other socio-demographic factors. Not all people who drink and drive are young healthy individuals and many might suffer from poor health and other medical conditions. Indeed, a high proportion of apprehended drivers, especially those with

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high BAC or BrAC, suffer from an alcohol use disorder and clinically they might be diagnosed as being alcohol dependent. Treatment instead of punishment for a DUI offence is being increasingly used as an option for repeat offenders.

Reference 25 has been highly cited, because it was one of the first controlled drinking experiments in people who had undergone gastric bypass surgery for obesity. The experiment was done 1–2 years after women had undergone gastric bypass surgery and when their body weight had decreased appreciably. The study results showed that absorption of ethanol was faster in bypass patients and that they reached a higher peak BAC for the same dose of ethanol. However, this effect was transient, because by about 90 min post-drinking the BAC was not significantly different from a control group of women matched for age and BMI with the operated group.

Drug-Ethanol Interactions

26. Jönsson, KÅ, Jones, AW, Boström, H, Andersson, T. Lack of effect of omeprazole, cimetidine and ranitidine on the pharmacokinetics of ethanol in fasting male volunteers. *Eur J Clin Pharmacol* 42;209-212, 1992.

27. Jones, AW, Neiman, J, Hillbom, M. Concentration time profiles of ethanol and acetaldehyde in human volunteers treated with alcohol sensitizing drug, calcium carbimide. *Br J Clin Pharmacol* 25;213-221,1988.

28. Kechagias, S, Jönsson, KÅ, Norlander B, Carlsson, B, Jones, AW. Low-dose aspirin decreases blood-alcohol concentration by delaying gastric emptying. *Eur J Clin Pharmacol* 53;241-46 1997.

29. Kechagias S, Jönsson KÅ, Jones AW. Impact of gastric emptying on the pharmaco-kinetics of ethanol as influenced by cisapride. *Br J Clin Pharmacol* 48;728-32, 1999.

In today's society people often take multiple drugs, which is commonly referred to as poly-pharmacy, and this practice is especially common in the elderly. An over-the-counter medicine might be combined with a prescription drug and/or a dietary supplement and some people co-ingest recreational illicit drug with alcohol. This raises the question of a possible adverse drug-drug or drug-alcohol interaction. Such interactions are usually classified as pharmacodynamic (PD) or pharmacokinetic (PK) as reviewed in reference 6. The articles numbered 26-29 above deal with the influence of commonly used drugs, both over-the-counter (OTC) and those available on prescription, on ADME of ethanol. In this connection ethical approval to allow people to take an illicit drug (e.g., cannabis or marijuana) together with ethanol was not granted by the hospital review board.

Distribution of Ethanol in Body Water Compartments

30. Jones, AW, Hahn, RG, Stalberg, HP. Update on the determination of total body water by ethanol dilution: the importance of the concentration units used. *Clin Sci* 81;701-702, 1991.

31. Jones, AW, Hahn, R, Stalberg, HP. Pharmacokinetics of ethanol in plasma and whole blood; Estimation of total body water by the dilution principle. *Eur J Clin Pharmacol* 42;445-448, 1992.

32. Hahn R, Norberg Å, Jones AW. Rate of distribution of ethanol into the total body water. *Am J Therap* 2;50-56, 1995.

33. Hahn, RG, Norberg, Å, Jones, AW. "Over-shoot" of ethanol in the blood after drinking on an empty stomach. *Alc & Alcohol* 32;501-6, 1997.

34. Norberg Å, Sandhagen B, Bratteby L-E, Gabrielsson J, Jones AW, Fan H, Hahn RG. Do ethanol and deuterium oxide distribute into the same water space in healthy volunteers. *Alcohol Clin Exp Res* 25;1423-30, 2001.

35. Jones, AW. Pharmacokinetics of ethanol in saliva; Comparison with blood and breath alcohol profiles, subjective feelings of intoxication and diminished performance. *Clin Chem* 39;1837-1844, 1993.

After drinking ethanol distributes into the total body water compartment. Total body water (TBW) in humans represents approximately 50–60% of body weight (35-42 L), being lower in females compared with males and also decreasing in the elderly, especially in men. Most of the body water is located within the cells (intracellular ~23 L (33 percent of body weight) and extracellular water is ~19 L or 27 percent of body weight. The latter comprises the blood plasma of ~3 L and interstitial water, which accounts for ~11 L. Blood (78-82% w/w water) and/or plasma (89-91% w/w water) are the two most important bodily fluids for analysis of ethanol and other drugs, because the analytical results provide information about concentrations of drugs reaching the brain.

Total body water is usually measured by isotope dilution after administration of deuterium labelled or tritium labelled water as tracer molecules. However, TBW can also be determined by ethanol dilution, although one needs to assume that there is 100% bioavailability of the dose or alternatively ethanol can be given by intravenous infusion. Five of the above articles were included in a PhD thesis presented by a student of

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mine Åke Norberg entitled *"Clinical pharmacokinetics of intravenous ethanol: Relationship between the ethanol space and the total body water"* (Karolinska Institutet, 2001, pp 1-74).

Elimination Rates of Ethanol in Alcoholics and Drunken Drivers

36. Jones, AW, Sternebring, B. Kinetics of ethanol and methanol in alcoholics during detoxification. *Alc & Alcohol* 27;641-647, 1992.

37. Jones AW. Ultra-rapid rate of ethanol elimination from blood in drunken drivers with extremely high blood-alcohol concentration. *Int J Legal Med* 122;129-134, 2008.

38. Neuteboom, W, Jones, AW. Disappearance rate of alcohol from the blood of drunk drivers calculated from two consecutive samples; What do the results really mean? *Forensic Sci Int* 45;107-115 1990.

39. Jones AW, Andersson L. Influence of age, gender and blood-alcohol concentration on the disappearance rate of alcohol from blood in drinking drives. *J Forensic Sci* 41;922-926, 1996.

There is abundant evidence that people arrested for DUI suffer from a personality disorder and/or an alcohol abuse problem when one considers that the average BAC in traffic offenders is 0.15–0.17 g% in most nations. Such high BACs can only be reached by binge drinking. For ethical reasons it is not possible in Sweden to administer alcohol to people diagnosed with an alcohol problem or who might be undergoing treatment for alcoholism. Other ways are needed to investigate ethanol PK in alcoholics and alcohol abusers.

Much of my research was done in close collaboration with physicians engaged in treatment of alcoholics admitted for detoxification to a university hospital clinic (Reference 36). We took the opportunity to sample blood from these patients during the first 24 h of detoxification and found that rate of ethanol elimination from blood ranged from 0.013 to 0.035 g% per h with an average of 0.022 g% per h. Some of the patients suffered from liver dysfunction (hepatitis and/or cirrhosis), but this did not seem to impact on ethanol elimination rate. Another way to obtain information about elimination rates of ethanol in heavy drinkers is to take two blood samples about one hour apart and this was done in over 1000 people arrested by the police for DUI. Approximately 1 h elapsed after the driver was arrested until the first blood sample was taken. The second sample of blood was drawn about 60 min after the first sample, while the suspect was still in custody and under observation by the police.

With double blood samples the elimination rate of ethanol from blood is calculated as ($BAC_1 - BAC_2$) divided by time elapsed between taking samples. However, it becomes necessary to assume that all drivers were in the post-absorptive phase of the BAC curve when the first sample was taken and that zero-order kinetics operate. Unfortunately, these assumption are not valid for all traffic offender, which probably explains the abnormally high and low results for some individuals, although a good average for this population of drinkers was 0.019 g% per h.

Ethanol Distribution in the Vascular System

40. Jones, AW, Jönsson, K-Å, Jorfeldt, L. Differences between capillary and venous blood-alcohol concentration as a function of time after drinking with emphasis on sampling variations in left vs right arm. *Clin Chem* 35;400-404, 1989.

41. Norberg Å, Jones AW, Hahn RG. Pharmacokinetics of ethanol in arterial and venous blood and in end-expired breath during vasoconstriction and vasodilatation. *Am J Therap* 2;954-961, 1995

42. Jones AW, Norberg Å, Hahn RG, Concentration-time profiles of ethanol in arterial and venous blood and end-expired breath during and after intravenous infusion. *J Forensic Sci* 42;1086-1092, 1997.

43. Jones AW, Lindberg L, Olsson S-G. Magnitude and time-course of arterial-venous differences in blood-ethanol concentrations in healthy men. *Clin Pharmacokinet* 43;1157-1166, 2004.

44. Lindberg L, Brauer S, Wollmer P, Goldberg L, Jones AW, Olsson S-G. Breath alcohol concentration determined with a new analyzer using free exhalation predicts almost precisely the arterial blood alcohol concentration. *Forensic Sci Int* 168;200-207, 2007.

45. Jones AW, Andersson L. Comparison of ethanol concentrations in venous blood and end-expired breath during a controlled drinking experiment. *Forensic Sci Int* 132;18-25, 2003.

Ethanol is not distributed evenly in the vascular system. During the absorption phase of the BAC curve, the concentration in arterial blood (e.g., radial artery) is higher than in venous blood (e.g., cubital vein). The A-V difference was greatest early after the end of drinking and gradually decreased as time after drinking increased. By about 60–90 min post-dosing, the concentrations in arterial and venous blood were the same. Thereafter, and providing that no further alcohol was consumed, the concentra-

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tions in venous blood were slightly higher than in arterial blood.

The magnitude of the A-V difference during absorption was greater than the V-A difference during the post-absorptive phase of the BAC curve. The results of the A-V difference experiments have implications when breath-alcohol analyzers are used, because BrAC runs closer to the ABAC rather than VBAC (see reference 44).

The work reported in reference 45 attempted to compare elimination kinetics of ethanol in blood and end-expired breath using Intoxilyzer 5000 as an evidential breath-alcohol analyzer. A compilation of papers making use of evidential breath analyzers to investigate PK of ethanol would be a worthwhile project to prepare an evidence-based review. In this connection, it is worth mentioning that a measured BrAC should not be converted into a presumed BAC when a back-extrapolation or other alcohol calculation is required because the venous blood-breath ratio is a moving target.

Other Questions of Forensic Interest

46. Jones, AW. Concentration-time profiles of ethanol in capillary blood after drinking beer. *J Forensic Sci Soc* 31;429-439, 1991.

47. Jones, AW. Back-estimation of blood alcohol concentration. *Br J Clin Pharm* 35;669-670, 1993.

48. Gullberg RG, Jones AW. Guidelines for estimating the amount of alcohol consumed from a single measurement of blood-alcohol concentration: Re-evaluation of Widmark's equation. *Forensic Sci Int* 69;119-130, 1994.

49. Jones, AW, Neri, A. Reinvestigation of Widmark's method for quantitative evaluation of blood-ethanol profiles: Influence of alcohol dose and mode of drinking. *Clin Chem* 33;1469, 1987.

The above four articles were concerned with other forensic aspects of ethanol such as the shapes of BAC curves after drinking low alcoholic beers, the pros and cons of making back-calculations, errors inherent in predicting BAC etc.

Additional Research

Research on the disposition and fate of ethanol in the body during the past 15 years has mainly concerned two minor non-oxidative metabolites, namely ethyl glucuronide (EtG) and ethyl sulfate (EtS). Sensitive and specific methods are available for the analysis of EtG in biofluids by GC-MS or LC-MS. The hydroxyl group (-OH) in ethanol molecules undergoes a phase II conjugation reaction in the liver to produce EtG and EtS. These metabolic pathways account for only about 0.1 percent of the dose of ethanol administered. EtG is measurable in body fluids for 6-12 h longer than ethanol and can disclose recent drinking even after ethanol is no longer measurable in blood or urine.

After subjects drank a moderate dose of ethanol (0.5 g/kg), the peak EtG concentration in blood was about 1000 times lower than the concentration of ethanol. Moreover, the BAC and EtG curves were shifted in time with peak EtG occurring 1–2 hours later than peak blood-ethanol. Analysis of EtG is advocated as a biomarker of recent drinking.

Analysis of EtG in blood, urine and vitreous humor provides useful information in post-mortem toxicology, especially if the body has undergone decomposition. Under these circumstances ethanol might be generated after death by fermentation processes (e.g., from blood glucose). If body fluids contain EtG this indicates that ethanol has undergone metabolism, a process that only occurs during life. I have only made two contributions to knowledge about EtG and its applications in forensic toxicology.

- Bergström J, Helander A, Jones AW. Ethyl glucuronide concentrations in two successive voids from drinking drivers: relationship to creatinine content and blood and urine ethanol concentrations. *Forensic Sci Int* 133;86-94, 2003.
- Sundström M, Jones AW, Ojanperä I. Utility of urinary ethyl glucuronide analysis in post-mortem toxicology when investigating alcohol-related deaths. *Forensic Sci Int* 241;178-182, 2014.

The presence of EtG in hair strands has received a lot of attention as proof of drinking alcohol, but a positive EtG in hair cannot be used to prove abstinence or to predict the amounts of alcohol consumed. Hair EtG analysis is being increasingly used in child custody cases or when a person is expected to refrain from drinking as a condition of employment. Correct interpretation of hair EtG results is not easy and there are many artifacts to consider, including use of ethanol-containing cosmetics, shampoos, coloring agents etc.

The analysis of EtG in double blood samples has been suggested as a way to evaluate claims of drinking alcohol after driving, the so-called hip-flask defense. However, this approach has some limitations, because after repetitive drinking the amount of EtG in the body accumulates, owing to its slower elimination from the blood compared with the rate of ethanol elimination.

Concluding Remarks

This review of my own publications on ADME of ethanol covers many questions that might arise or have arisen in forensic casework and DUI litigation. The results of my

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research confirm and extend the pioneering work of Widmark and others. I found that the volume of distribution of ethanol (V_d), denoted "rho factor" by Widmark, varied by a factor of two. In any individual subject the V_d depends on a person's age, gender and degree of adiposity. Values might range from 0.40 L/kg (obese female) to 0.85 L/kg (muscular male).

The zero-order elimination rate constant, denoted "β factor" by Widmark, corresponds to the negative slope of the post-absorptive descending phase of the BAC curve (burn-off rate). This parameter was found to vary by a factor of three, from 0.01 g% per hour to 0.03 g% per h. These rates of elimination should apply to the vast majority of people, including moderate and heavy drinkers. Low rates of elimination are expected in malnourished individuals or those who might eat low-protein diets. High rates of elimination of ethanol from blood are expected in hyper-metabolic states (e.g., burn trauma) or when hepatic CYP2E1 enzymes are boosted as a result of chronic heavy drinking.

Biological variations in ADME of ethanol need to be considered when forensic experts write statements or testify in court about the disposition and fate of ethanol in the body. One suggestion is to work with a range of values, such as burn-off rates between 0.01 g% and 0.025 g% per h, although in my opinion 0.015 g% per h is still a good average rate for healthy individuals with moderate drinking habits. Expert witnesses need to explain any assumptions they make in BAC calculations and divulge the source of their information, hopefully citing articles published in peer-reviewed journals. Any inherent limitations and uncertainty in the final results should also be clarified and explained to the court in a pedagogic way.

Case Law Summary

***State v. Senn*, 882 NW 2d 1 (Iowa 2016)**

Defendant was arrested for DUI and transported to the jail for a breath test. While at the jail, Defendant was allowed a phone call pursuant to Iowa's statutes. However, the statute only allows for phone calls in the presence of the custodial officer. Defendant asserted that because of the presence of the officer he was unable to consult with his counsel about whether to submit to the chemical test of his breath and this violated his right to counsel.

The Court examined a long line of U.S. Supreme Court cases, as well as various state cases examining the development of the right to counsel under the 6th Amendment. The Court concluded that Iowa's statute did not violate Defendant's right to counsel. Specifically, the Court reasoned that the right to counsel attaches when the prosecution proceeds against the Defendant. The Court contrasted the proceedings in the implied consent process, concluding they are merely investigative, and therefore a right to counsel does not attach until formal charges are filed. As such, the Court reasoned the Defendant was not entitled to a private consultation with an attorney to determine if he should take or refuse the breath test.

***State v. Darrow*, 374 P.3d 673, Sup. Ct. Kan (2016)**

Defendant was arrested for attempting to operate a vehicle while impaired. The arresting officer was called to the scene of an accident where the Defendant was passed out behind the wheel of a running vehicle. The car was not in gear. When the arresting officer awoke the Defendant, she "fumbled with the gear shift" but never put the car in gear.

The Court found to "operate" means to "drive"; "driving" requires movement of the vehicle; therefore, "operating" requires movement of the vehicle, and an "attempt to operate" means to attempt to move the vehicle. Taking actual physical control of the vehicle is insufficient to attempt to operate that vehicle without an attempt to make it move. As such, the Court overruled the ruling of the lower court that found "actual physical control" to be sufficient to support a conviction for attempting to operate a vehicle while under the influence.

However, the Court went on to rule that it must view all of the facts and inferences from those facts in favor of the prosecution. As such, the fact that Defendant placed herself in the driver's seat, with the engine running, and attempted to engage the transmission fit the definition of attempting to drive the vehicle, and was not merely "actual physical control." As such, Defendant's conviction was upheld.

***State v. Jones*, 375 P.3d 279, Sup. Ct. Id. (2016)**

Defendant was arrested for DUI after driving the wrong way on a one-way street. After his arrest he was transported to the hospital and blood was collected for testing. Defendant's blood test revealed a BAC of 0.207, with a measurement uncertainty of +/- 0.0103. The trial court excluded evidence of the measurement uncertainty because it was irrelevant. Defendant appealed.

The Court ruled that under Idaho's DUI statutes the test result, not the actual BAC, is the relevant factor in determining guilt or innocence for a DUI. Therefore, the Court ruled the trial court properly excluded the evidence of uncertainty.

***State v. Rask*, 883 NW 2d 688, Sup. Ct. Neb. (2016)**

Defendant was charged with DUI and the separate criminal offense of refusing a breath test. The charge for refusing a breath test was

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