## CASE REPORT

*A. W. Jones,*[1] *Ph.D., D.Sc. and L. Andersson,*[2] *B.Sc.*

# Biotransformation of Acetone to Isopropanol Observed in a Motorist Involved in a Sobriety Check

**REFERENCE:** Jones, A. W. and Andersson, L., "**Biotransformation of Acetone to Isopropanol Observed in a Motorist Involved in a Sobriety Check,**" *Journal of Forensic Sciences,* JFSCA, Vol. 40, No. 4, July 1995, pp. 686–687.

**ABSTRACT:** We report the identification of acetone (0.45 mg/mL) and isopropanol (0.17 mg/mL) but without the presence of ethanol in a blood sample from a man suspected of driving under the influence of alcohol. A preliminary breath screening test with an electrochemical instrument (Alcolmeter S-L2) was positive and an evidential breath-test with a dual wavelength infrared analyzer (Intoxilyzer 5000), recognized the presence of an interferant in the subject's breath. The man admitted drinking moderate amounts of alcohol (vodka) the previous evening and was being treated by his doctor for hyperglycemia by special dietary control. This case scenario provides a good example of severe metabolic ketoacidosis in an ostensibly healthy man driving on the highway. Biotransformation of the abnormally high concentration of blood-acetone to isopropanol occurs through the alcohol dehydrogenase pathway.

**KEYWORDS:** toxicology, acetone, breath analysis, DWI, isopropanol, ketoacidosis

The low molecular weight alcohols methanol, ethanol, n-propanol, and isopropanol are highly soluble in water and easily absorbed from the gastrointestinal canal after ingestion [*1*]. On reaching the portal vein, the blood carries these alcohols to the liver where metabolic breakdown and detoxification can begin. The liver cells (hepatocytes) contain the enzyme alcohol dehydrogenase (ADH) which specializes in the oxidation of short-chain alcohols [*2*]. Accordingly, the primary alcohols methanol, ethanol, and n-propanol are converted into the corresponding aldehydes and these are oxidized further by the enzyme aldehyde dehydrogenase (ALDH) into carboxylic acids [*2*]. The same hepatic ADH enzyme converts the secondary alcohol isopropanol into acetone but this metabolite is fairly resistant to further oxidation [*3*]. This means that the concentration of acetone in the bloodstream can increase to reach a very high level if a person drinks isopropanol [*4*].

The biotransformation of alcohols in the liver is a reversible enzymatic reaction and under some circumstances aldehydes can be reduced to primary alcohols and ketones are therefore reduced to secondary alcohols. This means that acetone can be converted into isopropanol according to the scheme shown in Fig. 1. Acetone is a well known endogenous substance arising from nonenzymatic decarboxylation of acetoacetate derived from fatty acid precursors. Some of the acetone present in the blood is excreted unchanged in breath and urine [*5*]. The mean concentration of acetone in blood samples from healthy non-fasting individuals is normally about 0.0013 mg/mL [*6*]. The highest concentration of preformed acetone in 500 blood samples from drinking drivers was 0.062 mg/mL and the median was 0.002 mg/mL. By contrast a blood-acetone concentration of 2.2 mg/mL was recently reported in a person who had ingested pure isopropanol [*4*]. Furthermore, after drinking denatured alcohol containing acetone and 2-butanone, both these ketones and their metabolites, isopropanol and 2-butanol respectively, were determined in blood samples [*7*].

When a person is deprived of food, eats low carbohydrate diets, or engages in a prolonged fast, the concentration of acetone in blood and breath increases appreciably [*5*]. Furthermore if the utilization of dietary carbohydrate is impaired as occurs in untreated diabetes mellitus, the ketone bodies, acetoacetate, β-hydroxybutyrate, and acetone reach abnormally high concentrations [*8*]. During diabetic ketoacidosis the brain, kidney, and other tissue derive energy from fatty acids instead of from the ubiquitous nutrient glucose. The further oxidation of acetone is a relatively slow metabolic process, so whenever abnormally high concentrations of this ketone circulate in the blood the reductive pathway leading to the secondary alcohol isopropanol becomes a possibility. Indeed, this reductive pathway is facilitated if an abundance of the reduced coenzyme NADH exists in the hepatocytes (Fig. 1).

Much less information is available in the literature about the possibility of isopropanol being generated from endogenous acetone owing to disturbances in carbohydrate metabolism in ostensibly healthy individuals. However, Bailey [*9*] published several well documented reports of acetone being reduced to isopropanol in hospitalized type-I diabetics. Serum concentrations reached 0.29 mg/mL for isopropanol and 0.32 mg/mL for acetone. We extend this finding by documenting the metabolic transformation of acetone to isopropanol in a person driving on the highway. The circumstances of this incident and the relevant analytical data are presented here. Venous blood samples were analyzed by headspace gas chromatography [*10*] and breath samples were analyzed with an Alcolmeter S-L2 device with an electrochemical detector, and also with an Intoxilyzer 5000 instrument with a dual wavelength infrared detector.

Received for publication 16 Sept. 1994; revised manuscript received 1 Nov. 1994; accepted for publication 28 Nov. 1994.

[1]Department of Alcohol Toxicology, National Laboratory of Forensic Chemistry, University Hospital, Linköping, Sweden.

[2]National Laboratory of Forensic Science, Linköping, Sweden.

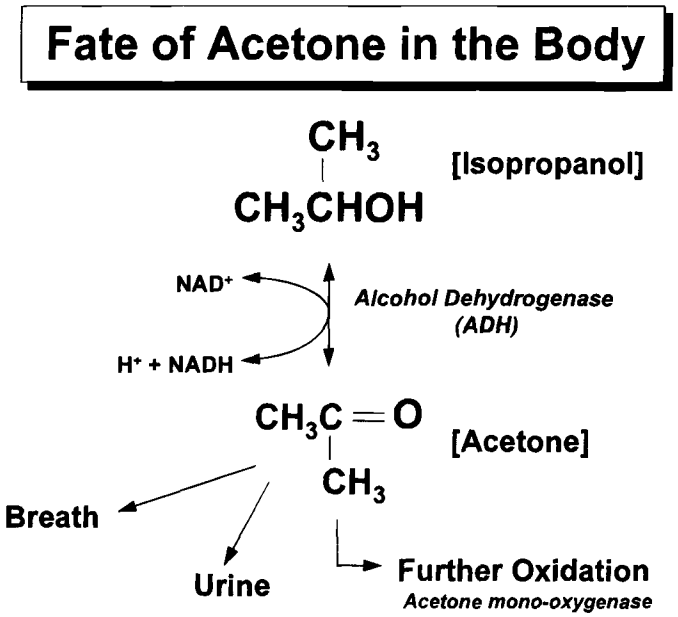


FIG. 1—*Metabolic conversion of acetone to isopropanol through the alcohol dehydrogenase (ADH) pathway. $NAD^+$ = coenzyme nicotinamide adenine dinucleotide, NADH = reduced form of the coenzyme.*

## Case History

A 54-year-old man was stopped by the police in connection with a routine sobriety check of traffic at 3:00 pm in the afternoon. The man showed no signs of being impaired by alcohol or drugs and apparently there was no smell of alcohol on the breath. However, following normal procedures in Sweden, the man was given a breath-alcohol screening test with an approved instrument, an Alcolmeter S-L2 which incorporates an electrochemical (fuel-cell) detector. The result of the breath test was positive indicating that the man's blood-alcohol concentration exceeded 0.20 mg/g (0.021 g%), the legal limit for driving in Sweden. The apprehended driver was taken to a police station where an evidential breath test was conducted at 3:18 pm with a quantitative infrared analyzer, Intoxilyzer 5000. However, the evidential test could not be completed satisfactorily because the instrument detected an interfering substance in the breath sample. Accordingly, a blood sample was taken from a cubital vein at 3:36 pm and sent to the National Laboratory of Forensic Chemistry for analysis. Note that the vein used to sample blood was not prepared with an isopropanol or alcohol-containing swab. The concentration of ethanol in the sample was below the limit of detection of the method. However, two other substances were identified on the gas chromatogram and these blood volatiles were acetone (0.45 mg/mL) and isopropanol (0.17 mg/mL).

The positive breath screening test can be explained by the presence of isopropanol which is oxidized by the electrochemical detector of the Alcolmeter S-L2 instrument [*11*]. The evidential breath analyzer, Intoxilyzer 5000, flagged for an interfering substance in the subject's breath sample and the test was rejected. However, stored in the instrument memory was a response of 0.06 mg/L "apparent ethanol" which corresponds to the vapor from a wetbath simulator charge containing 0.24 mg isopropanol per mL at 34°C. The apprehended driver was questioned about his general state of health and he mentioned seeing his doctor for high blood sugar (hyperglycemia). Indeed, the man had been diagnosed with latent diabetes and was receiving treatment that involved control of his diet. When questioned about his drinking habits, the man admitted drinking vodka with friends until late the previous evening and had apparently not eaten any lunch the day he was apprehended. During the metabolism of ethanol the ratio NADH/$NAD^+$ rises and this altered redox state of the liver facilitates the reduction of acetone to isopropanol (see Fig. 1). The man had no prior convictions for driving under the influence of alcohol and no history of alcohol abuse. He held a responsible job as a train driver.

This case scenario gives a well documented example of the metabolic conversion of acetone to isopropanol in an ostensibly healthy individual driving on the highway. This report also provides information about the selectivity of some currently available breath-alcohol analyzers when two different interferants are present in a person's breath. In conclusion, it seems that the abnormally high concentration of acetone in blood was the result of metabolic ketoacidosis associated with hyperglycemia. This interpretation is supported by information from the man himself and the fact he was consulting a doctor for hyperglycemia. The man's metabolic acidosis was probably exaggerated by the negligible intake of food on the day he was involved in the traffic control. An attempt was made to measure glucose in the forensic blood samples but they were completely hemolyzed making the results unreliable. This case report confirms the work of Bailey [*9*] showing that under certain circumstances acetone can be reduced to isopropanol through the alcohol dehydrogenase pathway.

## References

[*1*] Ellenhorn, M. J. and Barceloux, D. G. *Medical Toxicology,* Amsterdam, Elsevier, 1988.

[*2*] Jones, A. W., "Forensic Science Aspects of Ethanol Metabolism," In *Forensic Science Progress,* Vol. 3, A. Maehly and R. L. Williams, Eds., Springer Verlag, Berlin, 1991, pp. 31–89.

[*3*] Natowicz, M., Donahue, J., Gorman, L., Kane, M., McKissick, J., and Shaw, L., "Pharmacokinetic Analysis of a Case of Isopropanol Intoxication," *Clinical Chemistry,* Vol. 31, 1985, pp. 326–328.

[*4*] Jones, A. W., "Driving Under the Influence of Isopropanol," *Clinical Toxicology,* Vol. 30, 1992, pp. 153–155.

[*5*] Jones, A. W., "Breath Acetone Concentrations in Fasting Healthy Men: Response of Infrared Breath-Alcohol Analyzers," *Journal of Analytical Toxicology,* Vol. 11, 1987, pp. 67–69.

[*6*] Jones, A. W., Sagarduy, A., Ericsson, E., and Arnqvist, H. J., "Concentrations of Acetone in Venous Blood Samples from Drinking Drivers, Type-1 Diabetic Outpatients and Healthy Blood Donors," *Journal of Analytical Toxicology,* Vol. 17, 1993, pp. 182–185.

[*7*] Jones, A. W., Lund, M., and Andersson, E., "Drinking Drivers in Sweden Who Consume Denatured Alcohol Preparations: An Analytical-Toxicological Study," *Journal of Analytical Toxicology,* Vol. 13, 1989, pp. 199–203.

[*8*] Foster, D. W. and McGarry, J. D., "The Metabolic Derangements and Treatment of Diabetic Ketoacidosis," *New England Journal of Medicine,* Vol. 309, 1983, pp. 159–169.

[*9*] Bailey, D. N., "Detection of Isopropanol in Acetonemic Patients Not Exposed to Isopropanol," *Clinical Toxicology,* Vol. 28, 1990, pp. 459–466.

[*10*] Jones, A. W. and Schuberth, J., "Computer-Aided Headspace Gas Chromatography Applied to Blood-Alcohol Analysis: Importance of Online Process Control," *Journal of Forensic Sciences,* Vol. 34, 1989, pp. 1116–1127.

[*11*] Jones, A. W. and Goldberg, L., "Evaluation of Breath Alcohol Instruments. I. In-vitro Experiments with Alcolmeter Pocket Model," *Forensic Science International,* Vol. 12, 1978, pp. 1–9.

Address requests for reprints or additional information to
Dr. A. W. Jones
Dept. of Forensic Toxicology
University Hospital
58185 Linköping
Sweden