The Role of Alcohol Biomarkers in Detecting a Physician's COVID-19-Related Acute Stress Response: A Case Report

Alexis G. Polles, MD, William S. Jacobs, MD, Chad Brazle, MA, and Lisa J. Merlo, PhD, MPE

Objectives: Alcohol biomarkers are used to detect alcohol exposure in clinical and forensic settings. This includes professional health program (PHP) monitoring of healthcare workers in recovery from substance use disorders. Here we present the case of a physician whose positive alcohol biomarker test result was complicated by a traumatic stress response to frontline work during COVID-19.

Methods: An anesthesiologist under PHP monitoring for substance use disorder and depression was interviewed extensively, urine and blood biomarkers were obtained, and longitudinal structured and semi-structured interviews related to anxiety, depression, posttraumatic stress, and cravings were used to monitor responses to the unanticipated death of a patient who succumbed to COVID-19.

Results: After an initial positive ethylglucuronide (EtG) and ethyl-sulfate (EtS) toxicology test result, all subsequent testing was negative. The physician described compulsive sanitizing hands/arms and mask with highly concentrated ethanol-based products. Standardized assessments and clinical interviews provided documentation of a COVID-19-related post-traumatic stress response. He was connected to additional therapeutic support services and monitoring continued. Conclusions: Inhalation of ethanol vapors was initially accepted as a possible explanation for the positive EtG/EtS results, though the physician later acknowledged that limited alcohol beverage consumption occurred 6 days prior to the positive test, further complicating its interpretation. Detection of aberrant behavior through ongoing monitoring helps to protect both healthcare workers and the patients they serve.

Key Words: ethylglucuronide, ethylsulfate, phosphatidyl ethanol, physician health program, random urine testing

(J Addict Med 2022;16: e62-e65)

The COVID-19 pandemic has contributed to documented increases in psychological distress and substance use in healthcare workers due to stressors including social isolation,

From the Professionals Resource Network, Inc., Fernandina Beach, FL (AGP, WSJ, CB); Department of Psychiatry, University of Florida College of Medicine, Gainesville, FL (LJM).

Received for publication October 14, 2020; accepted April 14, 2021.

Supported by Professionals Resource Network, Inc., an integral arm of the Florida Medical Association.

The authors report no conflicts of interest.

Send correspondence to Lisa J. Merlo, PhD, MPE, Department of Psychiatry, University of Florida College of Medicine, PO Box 100256, Gainesville, FL 32610-0256. E-mail: lmerlo@ufl.edu.

Copyright © 2021 American Society of Addiction Medicine

ISSN: 1932-0620/21/1601-0e62

DOI: 10.1097/ADM.0000000000000865

anxiety about contracting the virus, decreased opportunity to engage in healthy coping strategies such as treatment and/or mutual support groups, difficulties with balancing work and childcare, and exposure to COVID-19-related morbidity and mortality. These challenges have impacted physicians who are on the "front lines" in the global response to the COVID-19 pandemic, with certain physician subspecialties more severely impacted (eg, intensive care, anesthesiology, emergency medicine) due to increased risk for acquiring COVID-19 themselves and unprecedented exposure to dying patients. ^{1–3}

Before the COVID-19 crisis, physicians in general, and anesthesiologists in particular, were identified as exhibiting greater risk for developing substance use disorders (SUDs), possibly due to their increased exposure and access to potent drugs with high addictive potential. 4-6 In a recent review of SUDs in anesthesiologists, the most common primary substance class was opioids (55%), followed by alcohol (28%) and stimulants (8%). Stressors of work, exacerbated by the pandemic, also increase healthcare workers' vulnerability to stress-related use or return to use. ^{8–10} We present the unusual case of an anesthesiologist monitored by his state's professional health program (PHP) due to history of SUD and depression, whose positive toxicology test for alcohol biomarkers led to the uncovering of a significant workplacerelated traumatic stress response during the COVID-19 pandemic. The physician provided written consent for the publication of this report.

CASE

Near the onset of the COVID-19 pandemic, Dr. X, an experienced anesthesiologist at a 300-bed urban hospital, received a phone call from hospital administration and risk management informing him that a patient he had treated 4 days prior had died of the virus. The patient had presented with acute abdominal symptoms and screened negative regarding risk for COVID-19. Dr. X had interacted with this patient more than most, as they shared the same native language, and Dr. X had intubated the patient for a medical procedure. Upon hearing of the patient's COVID-19-related death, Dr. X inquired whether he could be tested for COVID-19, but was denied due to a shortage of tests. This resulted in feeling unsupported by administration, and also increased his concern regarding their judgment in responding to the pandemic

Before receiving notification of the patient's death, Dr. X had been using an ethyl alcohol-based hand sanitizer, rather than soap, for most hand hygiene. The sanitizer was

/ Addict Med • Volume 16, Number 1, January/February 2022

readily available in automatic dispensers, and offered a quick, easy option that was accessible throughout the hospital corridors and dried quickly between cases. Dr. X described applying the sanitizer on his hands and arms (up to his elbows) and wiping his stethoscope with it about 20 times per day. After receiving the call, he noted increasing use to approximately 100 times per day. In addition, Dr. X reported that he began working under the assumption that every patient was positive for COVID-19, and followed extensive sanitizing procedures with every patient and at every opportunity. For example, Dr. X reported cleaning his plastic-lined N-95 mask, which had to be re-used for 3 days, with a 90% ethyl alcohol spray approximately 10 to 20 times a day. This reflected a significant increase from his use before the patient's death, since the hospital had previously limited the use of scarce N-95 masks to those working with confirmed-positive COVID-19 cases.

Dr. X had a history of depression and SUD [with diagnoses of Ketamine Use Disorder-Severe, Opioid Use Disorder—Severe, Amphetamine-type (MDMA) Use Disorder-Severe, and Sedative Use Disorder-Severe]. His involvement with the PHP was instigated by an incident involving loss of consciousness in the workplace following injection of fentanyl, midazolam, and propofol (though his preferred substance was ketamine). About a month after his patient's COVID-19-related death, Dr. X's random urine toxicology test was positive for the alcohol biomarkers ethyl glucuronide (EtG) and ethyl sulfate (EtS), at levels of 1561 ng/mL (cutoff = 500 ng/mL) and 377 ng/mL (cutoff = 75 ng/mL), with a creatinine of 23.9 mg/dL. However, his blood-based phosphatidyl ethanol (PEth) test was negative. Dr. X was not scheduled to work the week following the positive test result. Due to our ability to rapidly obtain an independent clinical evaluation, observer reports, and results of additional toxicology testing, Dr. X was not formally removed from practice while the situation was further assessed.

At the time of the incident, Dr. X had demonstrated 2 years of documented adherence to all components of his monitoring agreement. This included excellent recent performance reports at work, lack of concerns from his professionally-led support group facilitator, documented abstinence from all mood-altering substances, absence of defensiveness, and openness to examination of the toxicology results by an independent evaluator. These indicators, combined with lack of prior alcohol use disorder and lack of symptoms indicating return to any substance use, suggested that Dr. X's abstinence remained intact. His initiation of excessive cleaning with ethanol-based sanitizing products following an unexpected, potentially life-threatening situation [ie, sustained exposure to a confirmed-positive COVID-19 patient without the appropriate level of personal protective equipment (PPE)], led the PHP team to explore the possibility that his behavior reflected a compulsive (ie, hypervigilant) behavioral response to a COVID-19-related traumatic experience.

We conducted further assessment, and results of his longitudinal assessments are listed in Table 1. Dr. X reported mild depressive symptoms with passive suicidal ideation (on both the Patient Health Questionnaire-9 and the Columbia Suicide Severity Rating Scale), moderate anxiety symptoms

on the Generalized Anxiety Disorder-7, and significant traumatic stress symptoms on the PTSD Checklist for DSM-5. Notably, he acknowledged having thoughts that he would be better off dead, de-realization, and being "extremely" bothered by "being super-alert, watchful, or on guard." Dr. X described his passive thoughts of suicide as being similar to what he had experienced previously, albeit more severely, on the day he had self-administered a potentially fatal combination of drugs over 2 years prior. He also identified prior workrelated and other adverse life experiences as having met Criterion A¹¹ for post-traumatic stress disorder, which neither he nor others had previously identified. As seen in Table 1, follow-up assessment (after a month during which Dr. X received ongoing support, intensified therapy, and muchimproved PPE) demonstrated that his symptoms had all subsided. Importantly, when completing the Post-traumatic Growth Inventory, Dr. X identified several areas of personal growth related to this experience.

Monitoring continued, with subsequent blood, hair, and urine toxicology results remaining negative for all substances. However, 11 months later, following a distressing break-up and related family conflict, Dr. X again self-administered a potentially lethal combination of substances. He was refrained from practice and returned to residential treatment. While in treatment, Dr. X acknowledged limited beverage alcohol consumption the prior year, maintaining that he consumed one glass of wine 6 days prior to the initial positive EtG/EtS result (i.e., in the evening after submitting a urine sample earlier in the day). This could not be independently verified for accuracy, further complicating interpretation of his positive EtG/EtS results. However, it highlights the importance of ongoing evaluation and monitoring for healthcare workers recovering from SUD, particularly given the additional stress they face while practicing in the context of a global pandemic.

DISCUSSION

Random urine drug testing is a vital tool for monitoring healthcare professionals in recovery. Positive test results may identify a lapse involving substance use and, through immediate intervention, can help to prevent a full relapse. In the current case, comprehensive assessment following a positive EtG/EtS test initially suggested incidental inhalation of alcohol vapors, rather than the purposeful ingestion of alcohol, was responsible.

Ethanol-based hand sanitizer use has been shown to cause positive findings in both urine EtG toxicology¹³ and breath testing,¹⁴ with studies suggesting that inhalation of ethanol vapors, rather than transdermal absorption, is most responsible for the positive results. In addition, though less sensitive to alcohol exposure than EtG/EtS and breath testing, PEth testing appears to be the most specific test to determine whether recent ethanol consumption has occurred.^{13,15} Review of the literature fails to identify any example involving a positive PEth result without consumption of ethanol. Though some literature suggests that direct biomarkers of ethanol in the keratin matrix are capable of distinguishing between ethanol consumption and incidental exposure,¹⁶ a review of the literature on EtG hair testing indicates that there are significant limitations in result reproducibility and

TABLE 1.	Results of	FABLE 1. Results of Assessments Conducted With	Conducted	d With Dr. X	×						
Assessment	18 d postevent	18d 24d 29d 35d 43d Assessment postevent postevent postevent	29 d postevent	35 d postevent	43 d postevent	44, 56, and 64 d 72 d postevent poste	72 d postevent	81 and 87 d 98 d postevent postev	98 d postevent	105,115, 119, 121, 133, 135, 161 d and 141 d postevent postevent	161 d postevent
EtG*	neg	1561 ng/mL	I	neg	neg	neg	1	neg	neg	neg	neg
EtS^{\dagger}		377 ng/mL		neg	neg	neg	I	neg	neg	neg	neg
PEth^{\ddagger}	I	1	neg	I	I	I	I		neg		neg
PHQ-9§		I	'		8 (mild depressive	I	1 (no concern)		'	I	'
GAD-7¶	I	I	I	I	symptoms) 8 (moderate anxiety	I	4 (mild anxiety	I	I	I	I
∥5- IJd	l		١		symptoms)	1	symptoms) 14 (unlikely PTSD)	l		l	
C-SSRS**					Low risk		(demonstry 1 (22)				
BSCS ^{††}	I	l		I	Minimal craving	I	I			I	
					reported for ketamine and alcohol						
$ ext{PTG}^{\ddagger \ddagger}$		l	I		I	I	80 (significant		I	I	I
							post-traumatic growth)				

C-SSRS, Columbia Suicide Severity Rating Scale; GAD-7, Generalized Anxiety Disorder-7; PCL-5, PTSD Checklist for DSM-5; PHQ-9, Patient Health Questionnaire-9; neg, negative test result; —, assessment not administered. *Ethyl glucuronide urine test (cut-off = 75 ng/mL). †Ethyl sulfate urine test (cut-off = 75 ng/mL). †Phosphatidyl ethanol blood test (cut-off = 20 ng/mL).

[§]Patient Health Questionnaire-9 item depressive symptom screener (range = 0–27). ¶Generalized Anxiety Disorder-7 item anxiety symptom screener (range = 0–21).

Post-traumatic Checklist for DSM-5 (range = 0-80).

^{&#}x27;Columbia Suicide Severity Rating Scale (Screening Version).

[†]Brief Substance Craving Scale.

[?]Post-traumatic Growth Inventory (range = 0-105).

interpretation of findings.¹⁷ As a result, hair testing was not utilized in this case. In addition, though many ethanol-based hand sanitizers also contain approximately 10% 2-propanol [whose metabolite 2- propylglucoronide (2-PpG) can be detected in urine samples], that was not the case for the sanitizer being used by Dr. X. As a result, we were unable to assess for the presence of 2-PpG as an additional indicator of incidental exposure to help explain the positive EtG results.¹⁸

Although the initial formulation, subsequently disproved, was that Dr. X did not purposely ingest any alcohol, his random drug testing nonetheless prompted identification of previously unrecognized and untreated post-traumatic stress in a frontline healthcare worker during the early days of the COVID-19 pandemic. Subsequent clinical intervention to address this condition along with continued monitoring resulted in improved clinical care. Specifically, absent the monitoring process, Dr. X likely would not have received the treatment that led to remission of his acute stress disorder symptoms, which likely prevented an escalation of his substance use. As demonstrated by this case, occupational exposure for anesthesiologists to both highly addictive substances and COVID-19-related work stress is significant, and the combination of the frequently co-occuring symptoms of traumatic stress and substance use disorders is important to fully explore. As a result, it is imperative that rapid response and facilitation of thorough assessment and intervention are undertaken when questions about SUDs arise among individuals in high-stress environments, particularly those in safetysensitive professions such as healthcare workers.

REFERENCES

- Morcuende M, Guglielminotti J, Landau R. Anesthesiologists' and intensive care providers' exposure to COVID-19 infection in a new york city academic center: a prospective cohort study assessing symptoms and COVID-19 antibody testing. *Anesth Analg.* 2020;131(3):669–676.
- Garcia-Mendez N, Lagarda Cuevas J, Otzen T, Manterola C. Anesthesiologists and the high risk of exposure to COVID-19. *Anesth Analg*. 2020;131(2):e92–e93.
- Que J, Shi L, Deng J, et al. Psychological impact of the COVID-19 pandemic on healthcare workers: a cross-sectional study in China. *Gen Psychiatr*. 2020;33(3):e100259.

- Kintz P, Villain M, Dumestre V, Cirimele V. Evidence of addiction by anesthesiologists as documented by hair analysis. *Forensic Sci Int.* 2005;153(1):81–84.
- McAuliffe PF, Gold MS, Bajpai L, et al. Second-hand exposure to aerosolized intravenous anesthetics propofol and fentanyl may cause sensitization and subsequent opiate addiction among anesthesiologists and surgeons. *Med Hypotheses*. 2006;66(5):874–882.
- Cummings SM, Merlo L, Cottler L. Mechanisms of prescription drug diversion among impaired physicians. *J Addict Dis*. 2011;30(3): 195–202.
- Lefebvre LG, Kaufmann IM. The identification and management of substance use disorders in anesthesiologists. Can J Anaesth. 2017;64(2): 211–218.
- 8. Sinha R. How does stress increase risk of drug abuse and relapse? *Psychopharmacology (Berl)*. 2001;158(4):343–359.
- Lazarus A. Traumatized by practice: PTSD in physicians. J Med Pract Manage. 2014;30(2):131–134.
- Columb D, Hussain R, O'Gara C. Addiction psychiatry and COVID-19: impact on patients and service provision. *Ir J Psychol Med.* 2020;37(3): 164–168.
- Association AP. Diagnostic and Statistical Manual of Mental Disorders (DSM-5). 5th Ed. Washington DC: American Psychiatric Publishing; 2013
- 12. DuPont RL, McLellan AT, Carr G, Gendel M, Skipper GE. How are addicted physicians treated? A national survey of Physician Health Programs. *J Subst Abuse Treat*. 2009;37(1):1–7.
- Arndt T, Schrofel S, Gussregen B, Stemmerich K. Inhalation but not transdermal resorption of hand sanitizer ethanol causes positive ethyl glucuronide findings in urine. *Forensic Sci Int.* 2014;237:126–130.
- Brewer C, Streel E. Is alcohol in hand sanitizers absorbed through the skin or lungs? Implications for disulfiram treatment. *Alcohol Alcohol*. 2020;55(4):354–356.
- 15. Reisfield GM, Teitelbaum SA, Opie SO, Jones J, Morrison DG, Lewis B. The roles of phosphatidylethanol, ethyl glucuronide, and ethyl sulfate in identifying alcohol consumption among participants in professionals health programs. *Drug Test Anal.* 2020;12(8):1102–1108.
- Salomone A, Bozzo A, Di Corcia D, Gerace E, Vincenti M. Occupational exposure to alcohol-based hand sanitizers: The diagnostic role of alcohol biomarkers in hair. *J Anal Toxicol*. 2018;42(3):157–162.
- 17. Biondi A, Freni F, Carelli C, Moretti M, Morini L. Ethyl glucuronide hair testing: A review. *Forensic Sci Int.* 2019;300:106–119.
- 18. Andresen-Streichert H, Beres Y, Weinmann W, et al. Improved detection of alcohol consumption using the novel marker phosphatidylethanol in the transplant setting: results of a prospective study. *Transpl Int*. 2017;30(6):611–620.