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Characterizing Exposures to Methanol-based Hand Sanitizers During the COVID-19 Pandemic: Use of the National Poison Data System (NPDS) to Conduct Enhanced Surveillance During Response

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Abstract

Objectives: The Centers for Disease Control and Prevention (CDC) released an official health advisory after receiving reports of patients in New Mexico and Arizona who experienced serious adverse health effects after swallowing methanol-based hand sanitizer (MBHS). CDC and America's Poison Centers conducted enhanced surveillance using the National Poison Data System (NPDS) for all calls to poison centers (PCs) that reported exposure to MBHS.

Methods: We queried NPDS for human exposure cases to MBHS between June 22, 2020 and September 14, 2020. We conducted descriptive statistics to analyze by daily case volume, age group, sex, caller site, management site, exposure route, medical outcome, reason for exposure, clinical effects, and treatment.

Results: Forty-nine states, Washington, DC, and the US Virgin Islands reported at least 1 exposure, with a total of 2164 cases. Adults aged 20-59 represented the largest proportion of cases (44.8%). Most calls (94.2%) were from a non-health care facility and were managed on site (82.4%). The exposure route was primarily dermal (88.8%) followed by ingestion (12.0%). **Conclusions:** Quick response and action for exposures to MBHS containing products is essential

to ensure public health safety. PCs remain a valuable resource for providing guidance and advice for toxic exposures.

Proper hand hygiene is an important prevention strategy against SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19). During the COVID-19 pandemic, keeping hands clean was especially important to prevent viral spread. The Centers for Disease Control and Prevention (CDC) recommends cleaning hands with an alcohol-based hand sanitizer containing at least 60%-95% alcohol (\geq 60% ethanol or \geq 70% isopropanol) when soap and water are unavailable. However, misuse of hand sanitizer can result in serious injury.

Most alcohol-based hand sanitizers or rubs contain either ethanol or isopropanol as active ingredients. However, in June 2020, New Mexico and Arizona reported oral ingestions to hand sanitizers containing methanol, a toxic alcohol inappropriately used as an active ingredient. In response, the US Food and Drug Administration (FDA) advised consumers against any hand sanitizers manufactured by "Eskbiochem SA de CV" in Mexico because of the potential presence of methanol. As of September 25, 2020, FDA identified over 196 additional hand sanitizer products containing methanol and other toxic alcohols and coordinated a voluntary recall of these products.

Methanol, or wood alcohol, is a clear liquid used in industrial processes, and can be absorbed via inhalation, ingestion, and even dermally. Toxic exposure can cause clinical effects like intoxication, nausea, vomiting, abdominal pain, metabolic acidosis, vision abnormalities (including blindness), and, rarely, renal failure. Methanol is metabolized into formaldehyde and then formic acid, with methanol primarily causing inebriation, while formic acid leads to the more severe clinical features, such as potential blindness and metabolic acidosis. The most severe effects are usually associated with intentional ingestion. The toxic byproducts of methanol metabolism pose a higher risk of serious adverse effects than other common alcohols in hand sanitizers, like ethanol and isopropanol.

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The 55 poison centers (PCs) in the US provide free, confidential, 24-hour professional advice and medical management information on exposures to a variety of substances including chemicals, drugs, and medications. Call data are uploaded in near real-time to the National Poison Data System (NPDS), owned and operated by the America's Poison Centers. During the height of the COVID-19 pandemic, PCs received thousands of calls daily related to COVID-19 and harmful, non-traditional actions taken to prevent, treat, or cure the virus (e.g., exposure to cleaning products, misuse of hand sanitizers, ingestion of hydroxychloroquine). Based on these data, CDC, in collaboration with America's Poison Centers and regional PCs, released a health alert network (HAN) advisory after receiving the reports of patients in New Mexico and Arizona experiencing serious adverse health effects, including blindness and death, after purportedly swallowing alcohol-based hand sanitizers or rubs. 4,8

CDC, in coordination with America's Poison Centers, conducted enhanced surveillance using NPDS to monitor reported exposure to methanol-based hand sanitizer (MBHS) and provided affected states with weekly summary reports of such calls between August 3 and September 14, 2020. This article aims to describe these MBHS exposure calls to PCs to better understand national exposure to this toxic substance and provide case vignettes highlighting adverse reactions.

Methods

We queried NPDS data for cases from the public and health care professionals reporting human exposures to MBHS for the 3-month timeframe between June 22 and September 14, 2020. The 2 MBHS product codes created by America's Poison Centers in June 2020 enabled CDC and America's Poison Centers to track these exposures in near-real time. We excluded cases coded as a "confirmed non-exposure" (i.e., calls verifying no exposure occurred). Age (in years) was categorized as preschool children (0-5), school-aged children and adolescents (6-19), adults (20-59), and older adults (60+) consistent with NPDS age breakdown. We conducted descriptive statistics using MS Excel to analyze daily case volume, age group, sex, caller site, management site (health care facility, on-site, or other/unknown), exposure route (dermal, ingestion, inhalation, ocular, or other/unknown), medical outcome, reason (intentional,

unintentional, or other/unknown), clinical effects, and treatment. Medical outcomes are classified per America's Poison Centers definitions and include minor, moderate, major outcomes, and death, with major outcomes and deaths combined to protect privacy. We present 3 illustrative case vignettes highlighting adverse effects of MBHS exposure calls managed by PCs.

Results

Forty-nine states, Washington, DC, and the US Virgin Islands reported at least 1 exposure to MBHS during the timeframe. Daily exposure calls peaked in July, followed by an overall decline (Figure 1). As part of the enhanced surveillance, CDC sent weekly notifications to affected states, averaging 23 emails per week, with most (62.9%-92.6%) reporting fewer than 5 calls per week.

Between June 22 and September 14, 2020, PCs reported 2164 exposure cases related to MBHS. Adults aged 20-59 represented the largest proportion (44.8%), while 20.1% of cases were 0-19 years. More females (57.5%) than males reported exposures. Most calls (94.2%) were from a non-health care facility (HCF) and managed on site (82.5%). The primary exposure route was dermal (88.8%) followed by ingestion (12.0%). For medical outcome, the majority reported no effect (32.6%) or were not followed (46.3%). Few cases reported medical outcomes: 5.3% were minor, 1.0% were moderate, and 0.9% were major/death. Reasons for exposure included 35.9% unintentional, 2.1% intentional, and 62.0% other/ unknown. Roughly a third of callers (n = 765; 35.4) reported at least 1 clinical effect, with the most common being headache (23.0%), nausea (16.6%), blurred vision (9.8%), and dizziness/vertigo (8.1%). A quarter (n = 542; 25.0%) of calls reported treatment, mainly dilute/irrigate/wash (82.5%), followed by food/snack (7.7%), fomepizole (6.6%), and fluids, IV (5.2%). Additionally, 2.8% needed hemodialysis and 0.92% required continuous renal replacement (Table 1). All major/death outcomes reported ingestions as a route of exposure (19 cases; data not shown).

While most calls reported minor or no effect, several experienced adverse outcomes. Below are 3 case vignettes illustrating the types of calls PCs received and their management.

 A 54-year-old female contacts the PC about methanol exposure after using a recalled hand sanitizer. She denies ingestion

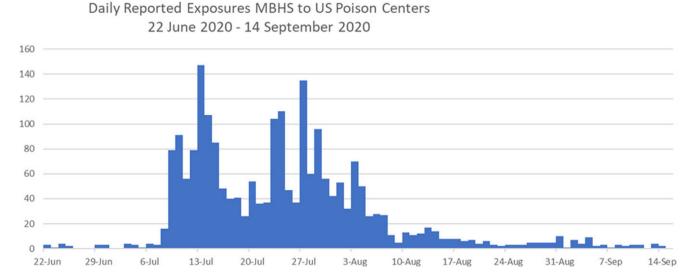


Figure 1. National epidemic curve of methanol-based hand sanitizer exposures reported to US Poison Centers.

Table 1. Characteristics of methanol-based hand sanitizer cases, June 22, 2020-September 14, 2020

Characteristic	Number (%)
Total calls	2164
Sex	
Male	866 (40.0)
Female	1245 (57.5)
Unknown	53 (2.4)
Age range, years	
0–5	226 (10.4)
6–19	210 (9.7)
20–59	969 (44.8)
60+	306 (14.1)
Unknown/blank	453 (20.9)
Caller site	
HCF*	118 (5.5)
Non-HCF	2039 (94.2)
Unknown	7 (0.3)
Management site	
HCF	353 (16.3)
On Site	1785 (82.5)
Other/Unknown	26 (1.2)
Exposure route**	
Dermal	1921 (88.8)
Ingestion	260 (12.0)
Inhalation	34 (1.6)
Ocular	12 (0.6)
Unknown	1 (0.0)
Medical outcome	
No effect	706 (32.6)
Minor	114 (5.3)
Moderate	21 (1.0)
Major/death	19 (0.9)
Unrelated	301 (13.9)
Not followed	1003 (46.3)
Reason	
Intentional	46 (2.1)
Unintentional	777 (35.9)
Other/unknown	1341 (62.0)
Top clinical Effects (<i>n</i> =765) [†]	
Headache	176 (23.0)
Nausea	127 (16.6)
Blurred Vision	75 (9.8)
Dizziness/Vertigo	62 (8.1)
Vomiting	47 (6.1)
0	(Continu

Table 1. (Continued)

Characteristic	Number (%)
CNS Depression	42 (5.5)
Abdominal Pain	37 (4.8)
Other	442 (57.8)
Treatment (n=542) [‡]	
Dilute/irrigate/wash	447 (82.5)
Food/snack	42 (7.7)
Fomepizole	36 (6.6)
Fluids, IV	28 (5.2)
Oxygen	18 (3.3)
Folate	17 (3.1)
Ventilator	17 (3.1)
Hemodialysis	15 (2.8)
Other [¶]	227 (41.9)

^{*}HCF = health care facility

- and has applied the product to her hands 3-5 times daily for 2 weeks. She denies any symptoms including nausea, vomiting, or blurred vision. The PC reassures her about negligible absorption of methanol through intact skin, but strongly recommended immediate discontinuation of the product.
- 2. A 52-year-old female contacts the PC with complaints of blurry vision and headache after using a recalled hand sanitizer every hour for several days. She denies any ingestion, but reports her symptoms of blurry vision and headache have persisted for several days. Because of the excessive dermal use and possible inhalation exposure, she was referred to a health care facility for evaluation. In the emergency department, her visual acuity and laboratory values were normal, with no anion gap metabolic acidosis. A methanol level was negative. She was counseled to stop using the recalled product and discharged to home.
- s. An adult with alcohol use disorder presented to a critical access hospital after ingesting Blumen hand sanitizer as an alcohol substitute (labeled 70% ethyl alcohol). The hospital was alerted to the possibility of methanol poisoning. The patient began to deteriorate and was transferred to a tertiary care hospital. Labs showed a profoundly low pH and bicarbonate, along with an increased anion and osmol gap. Fomepizole was administered, and dialysis started, but the patient became unstable and died despite aggressive resuscitation. A methanol level at admission to the tertiary care hospital was 406 mg/dl, which would be expected to cause severe metabolic acidosis and death if untreated.

Discussion

In mid-June 2020, reports of MBHS prompted several national alerts and an FDA-advised voluntary recall.⁵ Following discussions

^{**}Cases can report more than 1 exposure route.

 $^{^{\}dagger}$ N=765 (35.3%) cases who reported at least 1 clinical effect coded as "related" or "unknown if related;" cases can report more than 1 clinical effect.

 $^{^{\}ddagger}\text{N=}542~(25.0\%)$ cases that have at least 1 treatment reported; cases can report more than 1 treatment.

Other includes benzodiazepines, thiamine, continuous renal replacement, propofol, etc.

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with America's Poison Centers and regional PCs, CDC advised clinicians and public health officials to recommend the public stop using products on the "FDA's testing and manufacturer's recall's list," avoid ingesting any alcohol-based hand sanitizer, and seek immediate medical attention or call their PC if they have swallowed hand sanitizer or experienced any symptoms.⁴ This health alert led to enhanced surveillance of NPDS data to monitor the response and alert state health departments of potential exposures within their jurisdictions.

Exposures to MBHS peaked in July, coinciding with reports of increased products availability and media coverage. While thousands of exposure calls were reported to PCs, the majority were managed at home, likely conserving health care resources as PCs provide expert professional advice and medical management information 24 hours a day, 7 days a week. ^{7,9,10}

All cases reporting major or death medical outcomes involved ingestion as the exposure route, while most exposures with no effect, minor effect, unrelated, or not followed occurred from dermal exposures. Headache were frequently reported; however, headache is not commonly associated with methanol toxicity. This finding could be explained by individuals having other etiologies for their symptoms such as preexisting conditions, anxiety, the irritating smell of the products, or other exposures. Reported therapies included standard treatments for toxic alcohol poisoning, including fomepizole, folate, and extracorporeal elimination (hemodialysis and continuous renal replacement therapy). The most reported therapies were dilute/irrigate/wash and food/snack, and this likely indicates the low concern for significant toxicity after minimal exposures with the majority being dermal exposures. The reason behind food/snack as a therapy is unclear but may include decreased chance of gastric irritation, confirming if an individual can tolerate food by mouth, or prophylactically treating patients where there is concern for ethanol ingestion in patients at risk for potential hypoglycemia. Hemodialysis and continuous renal replacement were recommended treatments for 2.8% and 0.92% of cases with treatment information, respectively. These are often used to treat serious methanol toxicity and can indicate the severity of clinical effects seen in ingestion of methanol-based hand sanitizers.

This study has several limitations. NPDS data may underestimate the total incidence and severity of MBHS, being limited to those voluntarily calling PCs. 10 Other exposures during this period may not have been reported or managed in clinical settings, and did not involve PCs. Additionally, we did not exclude calls with unrelated clinical effects intentionally, as even if the PC deemed the clinical effect unrelated, the individual still used a recalled product. This may partially explain the high level of reports indicating no effect or minor medical outcomes. Another limitation is missing information; some calls had incomplete therapy information, despite reported adverse outcome. More detailed information could strengthen public health messaging to prevent or reduce further adverse outcomes. Finally, current NPDS data fields do not allow for recording of methanol blood concentrations, preventing us from commenting on dose-response relationships or making statements regarding exposures to toxic doses. Enhancing NPDS to record blood concentrations to exposures of interest could an important update.

Importantly, NPDS provides timely information which can lead to rapid public health action. The collaboration between CDC, America's Poison Centers, and regional PCs for the weekly summary reports provided an additional communication channel between impacted states and their PCs. This collaboration is essential to a coordinated public health response to potential poisonings,

such as MBHS, as PCs can provide state health departments with detailed information on incidents of potential public health significance and assist with follow-up and management.

Exposure to MBHS is an example of a preventable cause of poisoning and injury. Surveillance using PC data can provide public health officials with a timely warning of emerging public health threats, as well as allow for efficient interventions to mitigate ongoing exposures. As the FDA continued to push messaging regarding potentially contaminated products and worked for voluntary recalls in July, the number of related calls to PCs declined. Continued messaging on proper use and safe storage of hand sanitizers is vital to preventing injury, especially as the COVID-19 pandemic continues and sanitization remains a top public health prevention strategy.

Conclusion

Quick response and action related to methanol containing hand sanitizer products, such as recalls and HANs disseminated by FDA and CDC, is essential to ensure public health safety and continued trust. Most exposures to MBHS presented with mild or no symptoms and were successfully managed at home after calling the PC. America's Poison Centers remain a valuable resource for providing guidance and advice for toxic exposures, including hand sanitizers. The collaboration between CDC and America's Poison Centers enabled the success of this coordinated public health response.

Author contributions. Arianna Hanchey: Concept development; data collection, cleaning, and analysis; lead writing author.

Amy Schnall: Team lead; concept development; data cleaning and analysis; report write-up.

Art Chang: Senior author, concept development, toxicological expertise, report write-up.

 $Colin\ Therriault:\ Toxicological\ expertise,\ research,\ report\ write-up.$

Al Bronstein: Toxicological expertise, report write-up, methods.

Doug Borys: Toxicological expertise, report write-up, methods, case study inclusion and review.

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