Thirdhand Exposure to Methamphetamine Syndrome: Symptoms Resulting From Environmental Exposure to Methamphetamine Contamination Arising From Manufacture or Use

Abstract Thirdhand exposure to methamphetamine occurs through contact with environments that have become contaminated during the manufacture or use of the substance. This exposure is a serious emerging public health concern. Exposure can cause adverse health effects in unwitting residents, particularly children. As an increasing number of reports appear in the scientific literature, we propose “thirdhand exposure to methamphetamine syndrome” as a collective term to describe the various nonspecific symptoms that are related to methamphetamine exposure. This proposed term could provide a searchable keyword to facilitate the coordination of research to better understand the health-related consequences of exposure to methamphetamine that result from its manufacture and use.

Introduction Methamphetamine usage has been described as a global epidemic (Chomchai & Chomchai, 2015; European Monitoring Centre for Drugs and Drug Addiction & Europol, 2022; Hansell, 2006; Jones & Comparin, 2020; Pisarski, 2021). Worldwide, methamphetamine is the second most used illicit drug and the most commonly manufactured amphetamine-type stimulant (Bjilsma et al., 2021; European Monitoring Centre for Drugs and Drug Addiction & Europol, 2022; Jones & Comparin, 2020; Perez et al., 2022; Stoneberg et al., 2018). Recent reports indicate an increase in both use and the incidence of methamphetamine overdose (Han et al., 2021; Young et al., 2019).

Many countries conduct on an annual basis national drug surveys that consider a range of factors, including sociological demographics, substance abuse, and stage of addiction (European Monitoring Centre for Drugs and Drug Addiction & Europol, 2022; Substance Abuse and Mental Health Services Administration, 2020; Sutherland et al., 2022). As a result, the dose response and impact of methamphetamine on first-hand drug users have been extensively researched. There are also newspaper articles that highlight drug-related violence, drug trafficking, and drug busts by police (Rawstorne et al., 2020). Secondhand exposure is also reasonably well defined as it relates to the cohort of people, especially children, who are present during the manufacture or use of drugs (Holitzki et al., 2017; Meays et al., 2019). This exposure often includes family members and children who reside at the same property.

Both the manufacture and the personal use (e.g., smoking) of amphetamine-type stimulants (e.g., amphetamine, methamphetamine, 3, 4-methylenedioxymethamphetamine [MDMA]) can result in environmental contamination. Even though amphetamine is structurally similar, methamphetamine has a greater effect on dopamine levels and the corresponding transporter proteins (Chiu & Schenk, 2012). Methamphetamine is the amphetamine-type stimulant most commonly smoked; MDMA is usually taken in tablet form or snorted intranasally. Thus, methamphetamine is the main amphetamine-type stimulant of concern for third-hand exposure (Meyer, 2013).

Methamphetamine use can take place in a range of locations, including household properties, hotels, public bathrooms, and vehicles (Cherney et al., 2006; Green & Moore, 2013; Hannan, 2005). This use in a range of locations leads to porous materials, such as carpets and soft furnishings (including bedding), absorbing methamphetamine residues (Morrison et al., 2015; Wright et al., 2019). Furniture, benchtops, interior walls, and other impermeable surfaces can also have residual deposits that can be mobilized through air movement or foot traffic (Bitter, 2017; Martyny et al., 2007; Wright et al., 2019). Furthermore,
consider that there needs to be a collective exposure to methamphetamine. We propose term to describe the symptoms of thirdhand understanding these adverse health effects. inform best practices in regulation and in that are related to methamphetamine expo-
describe the various nonspecific symptoms “thirdhand exposure to methamphetamine (THEM) syndrome” as a collective term to describe the symptoms of thirdhand exposure to methamphetamine. We propose “thirdhand exposure to methamphetamine (THEM) syndrome” as a collective term to describe the various nonspecific symptoms that are related to methamphetamine exposure. This term will enable better tracking and collation of future research, which will inform best practices in regulation and in understanding these adverse health effects.

### Thirdhand Exposure Symptoms

Wright et al. (2020) analyzed 63 individuals who had previously resided in a methamphet-
amine-contaminated property. The symptoms and housing situations were documented and characterized for the 25 case studies. The individuals consented to hair analysis and permitted the property to be tested for methamphetamine. None of the participants were using or manufacturing methamphetamine themselves. The adverse health effects varied from short-term to chronic symptoms, and the time spent and/or lived at the property ranged from a few days to 10 years (Wright et al., 2020). Participants self-reported symptoms that were verified by health professionals, such as the family general practitioner or school nurse (Wright et al., 2020). For individuals <21 years and for adults, behavioral and cognitive issues (79% and 65%, respectively) and sleeping difficulties (72% and 68%, respectively) were the most prevalent adverse health effects recorded (Table 1).

Thrasher et al. (2009) published the adverse health effects experienced by people exposed to methamphetamine laboratories (i.e., where the cooking process of making methamphetamine had taken place), which included residents living in former clandestine laboratories. The six most reported symptoms from adult residents in this study were headaches, respiratory issues, nausea, cough, eye problems, and dizziness.

### Dose-Response Relationship

The term dose-response refers to a concentration or dose of a toxin that will cause an effect of a particular measurable response (endpoint) in the subject of a particular measurable response (endpoint). Dose-response curves generally assume a sigmoidal shape with increasing doses resulting in increasing effects (Vallero, 2010). There are difficulties in applying this model to methamphetamines. The first issue is the lack of data about exposure and effect (or symptoms), and the second issue is the nonspecific nature of the symptoms. Both of these impediments will be addressed to a degree by naming the syndrome and facilitating information collation.

When establishing guidelines to protect public health, observational research studies are used to identify the no-observed-adverse-effect level (NOAEL) and/or the lowest-observed-adverse-effect limit (LOAEL). While it is important to include both quantitative and qualitative results, it can be challenging to determine an exact threshold due to variation among individuals (Eaton & Gilbert, 2008; Ochoa, 2018). The vulnerability of the population that might be exposed is considered in the use of uncertainty factors, which are applied to the threshold (NOAEL or LOAEL). Establishing an LOAEL from observational studies has been identified by a number of researchers; however, the published research available is limited (Fahmi et al., 2010; Mayer & Miskelly, 2022; Thrasher et al., 2009; Wright et al., 2020).

Hair samples have long been used as evidence in courts of law for cases involving illicit substances; this technique provides valuable information about the time frame and levels of methamphetamine a person has been exposed to (Kintz, 2017). Recent research has shown that environmental contamination from illicit drugs can be established through hair analysis (Kintz et al., 2020, 2021). In general, increasing concentrations have been found in hair...
with increasing levels of exposure in individuals (Han et al., 2010, 2011; Polettini et al., 2012; Wright et al., 2020). Higher concentrations of methamphetamine were found in segmented hair sections compared with concentrations found using an external hair wash solution, indicating the difference between drugs settled on the outside of hair and drugs incorporated into the hair matrix by means of ingestion (Kintz, 2017; Kintz et al., 2020). In addition, variation in concentrations from the root to the tip of the hairs demonstrated that the hair matrix captured the drug as the hair matrix grew, and that the contamination varied over a period of time (Kintz et al., 2021).

**Syndromes and Acronyms**

Establishment of a defined term to describe the health consequences of thirdhand exposure to methamphetamine is needed to raise awareness, facilitate data collection, improve diagnoses, and encourage future research into potential long-term health consequences. Calvo et al. (2003) defined a syndrome as a group of known symptoms that can be attributed to a specific illness, even when the complete associations for that ailment might not be fully established. Other syndromes have been defined and given an acronym for future identification in research. For example, chronic fatigue syndrome (CFS; Brurberg et al., 2014), irritable bowel syndrome (IBS; Chey et al., 2015), and sick building syndrome (SBS; Redlich et al., 1997) are a few syndrome classifications with a number of nonspecific symptoms.

SBS has a number of similarities to third-hand exposure to methamphetamine, and thus we described it in some detail. In the 1980s, the World Health Organization characterized SBS as a combination of symptoms that are expressed through multiple organ systems when people are exposed to an enclosed built structure, such as an office building, hospital, or school (Redlich et al., 1997; Runeson-Broberg, 2020). Similar to exposure to methamphetamine, the symptoms are nonspecific. Individuals reported headaches, lethargy, itchy and watery eyes, nasal congestion, and skin irritation—symptoms that are commonly associated with other illnesses (Burge, 2004). Several factors have been documented that increase the prevalence of SBS within a cohort including allergies, sex, temperature, ventilation, outdoor air pollution, and volatile organic compounds (Mentese et al., 2020; Runeson-Broberg, 2020; Sajjo, 2020). Overall, SBS highlights the range of indoor air quality conditions and how symptoms can vary in individuals.

As such, like SBS, it is reasonable to presume there are some members of the public who have not reported adverse health issues or who have reported them but have attributed them to another illness (Runeson-Broberg, 2020). Exposure levels are dependent on the individual’s risk factors, activities, and exposure times (Kintz et al., 1995; Tsanaclis & Wicks, 2008; Wright et al., 2020). In conjunction with self-reported symptoms, however, exposure to amphetamine-type stimulant contamination can be verified by quantitative sampling of blood, urine, hair, and the person’s environment (Kintz et al., 1995; Tsanaclis & Wicks, 2008). We propose THEM syndrome as a name for the range of adverse health effects experienced by individuals due to contamination from amphetamine-type stimulants, specifically methamphetamine.

### Current Situation

Research has established that there has been an increase in autopsies of infants and children with methamphetamine present in their systems (Kenneally & Byard, 2020; Tse et al., 2020). There were seven case studies identified by forensic scientists in South Australia and eight from New Zealand (Kenneally & Byard, 2020; Tse et al., 2020). Of these 15 cases, 6 out of 7 (86%) from South Australia and 8 out of 8 (100%) from New Zealand were for infants under the age of 12 months. Using blood analysis, both studies determined that there was no deliberate ingestion and there was a known cause of death for all except two of the cases from South Australia.

Thus, these infants were exposed passively either in utero, from breastmilk or formula, or via environmental exposure (Kenneally & Byard, 2020; Tse et al., 2020). There have been several other studies that investigated methamphetamine exposure in children (Castaneto et al., 2013; Flannery et al., 2006; Kintz et al., 1995; Tsanaclis & Wicks, 2008; Wright et al., 2020); however, future research is needed to determine the health burden of thirdhand exposure.

This situation regarding thirdhand exposure is exacerbated by a housing shortage in many countries worldwide (Brill & Raco, 2021; Lima, 2021; Massimo, 2021; Richardson, 2022). As a result, sometimes housing is rented or sold without sufficient inspection (Ullah & Sepasgozar, 2020). Additionally, due to privacy laws, a detailed account about a property’s illicit drug history is not available even after law enforcement was involved. In Australia, it is estimated that only 1 in 10 clandestine laboratories are discovered, meaning many go undetected (Degenhardt et al., 2017) and rarely, if ever, is a house investigated due to methamphetamine use alone. In summary, the turbulent housing market might potentially result in an increase in THEM syndrome.

Furthermore, with the increase in roadside random drug testing and workplace testing for illicit drugs (Bade et al., 2018; Love et al., 2022; Mills et al., 2021; Smith et al., 2021), there are other unintended consequences of THEM syndrome. Residents who are exposed to methamphetamine contamination potentially could run the risk of testing positive in a workplace drug test (Buzby et al., 2021; Kapur & Aleksa, 2020; Tremonti & Haber, 2021), which would have numerous social and physiological consequences. This issue is further complicated by the potential for THEM syndrome to occur because of where an individual works; examples include police officers or social workers who unknowingly enter contaminated properties (Hannan, 2005; Norman et al., 2021; Witter et al., 2007).

### Recommendations for the Environmental Health Profession

The environmental health profession is profoundly local (Rodrigues et al., 2021). Environmental health professionals work on the front line to protect public health and can be the first point of contact for individuals who are concerned about methamphetamine-contaminated properties (Hannan, 2005; Norman et al., 2021; Witter et al., 2007). The environmental health profession is best positioned to take on the challenge of regulating this public health threat. Currently, however, there are many businesses working in this space. In Australia, it has been found that there is a concerning lack of industry regulation and additionally, some businesses have been found to have conflicts of interest (Kuhn, Walker, Wright, et al., 2021). For example, some companies have been conducting the initial testing for a property, the decontamination process, and then also the validation testing to confirm...
that their decontamination process worked (Kuhn, Walker, Whiley, et al., 2021). The environmental health profession should advocate for these processes to be conducted by independent businesses to ensure no conflict of interest and resulting bias.

The methods being used for testing by industry members are also problematic. Often there are no standardized methodologies and the presumptive test kits or lateral flow assays commonly used have lower limits of detection than reported by manufacturers (Kuhn et al., 2023). This lack of standardization can unnecessarily increase stress and anxiety for homeowners or residents. Presumptive test kits should be used as a screening tool, not as the basis of a remediation plan or decontamination validation. Environmental health professionals should be aware of this limitation and advise that quantitative testing should be conducted for any positive results from presumptive testing.

There are also several uncertainties that must be considered when assessing the public health risks associated with managing methamphetamine contamination. Future research is needed to inform best practices. For example, exposure time is one of the essential factors that can affect the health outcome of the individual; thus, contamination within residential properties is a main concern. People, especially young children, spend a significant portion of their time every day in the home (Wright et al., 2020). Residences in public places, such as shops or public restrooms, are less of a concern due to the relatively short exposure time in that space. A syndrome name will both facilitate the collation of information and raise awareness of thirdhand methamphetamine exposure, which will support the efforts of the environmental health profession to regulate this public health threat and protect public health.

**Conclusion**

There are many gaps in knowledge currently regarding environmental contamination with methamphetamine from use and manufacture, as well as unknowns of adverse health effects associated with methamphetamines. Future research is needed to further characterize the symptoms and potential long-term consequences of thirdhand methamphetamine exposure to human health. Our proposed syndrome definition and acronym of THEM syndrome will focus future research; provide a searchable keyword; and enable relevant studies to be more easily identified and tracked by medical professionals, researchers, and government officials.

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