# Deaths from PMMA-contaminated ecstasy: A coordinated multi-agency public health response

Ecstasy is a common party drug taken for its stimulant, euphoric, and empathogenic effects. In 2013, 4% of youth age 12 to 19 surveyed in the BC Adolescent Health Survey reported using ecstasy.[1] In a convenience sample of adults using illicit drugs recreationally or while attending parties, 63% reported using ecstasy between 2008 and 2014 in Victoria, and the same proportion in Vancouver between 2008 and 2012.[2] Annually, there are between 15 and 23 ecstasy-related deaths in BC, and emergency departments frequently treat patients with ecstasy overdose.[3]

In October and November 2011, the BC Drug and Poison Information Centre received calls from physicians caring for four patients who developed unusually profound hyperthermia after using ecstasy. Two of these patients died during this period. Personnel at the BC Drug and Poison Information Centre wondered if another substance was included in the ecstasy they consumed besides 3,4methylenedioxymethamphetamine (MDMA). While MDMA is the main ingredient in ecstasy, most tablets/capsules contain multiple substances.[4,5]

The concern was reported to the BC Drug Overdose and Alert Partnership (DOAP), a committee with representatives from harm reduction, public health, toxicology, law enforcement, health authorities, the Coroners Service, and people who use drugs. These established relationships developed through DOAP enabled timely information sharing and a rapid and coordinated public health response to these fatalities. Personnel at the BC Drug and Poison Information Centre worked together with regional health authorities to develop alerts for health care professionals. The BC provincial health officer was briefed and spoke publicly. Information was distributed to schools and the public through TV, radio, print materials, and social media.

A similar pattern of illness was noted in Alberta and, in response, clinical management guidelines were developed by the BC Drug and Poison Information Centre, Alberta Poison and Drug Information Service, and BC Ambulance Service. Drug samples from affected patients were obtained and tested by the BC Provincial Toxicology Laboratory. In January 2012 the BC Provincial Toxicology Laboratory identified an unknown substance along with MDMA in the samples, which the Alberta Provincial Toxicology Laboratory identified as paramethoxymethamphetamine (PMMA).

PMMA is a ring-substituted amphetamine similar in structure to MDMA or ecstasy, but more toxic. Nearly 50 deaths due to PMMA have been reported worldwide and PMMA has gained the street names "Death" and "Dr Death."

Between June 2011 and April 2012 there were 27 deaths caused by exposure to ecstasy containing PMMA in Alberta and BC.[6] Clinical features of the patients have been characterized. Many of these patients developed hyperthermia. The mean first recorded temperature was 39.4°C. Serotonin syndrome was present in 94% of patients and many patients developed multiple end-organ dysfunction. There was often a delay in seeking medical attention. The mean time from exposure to arrival at the emergency department was 6 hours. The mean time from ingestion to death was 17 hours.

The profound toxicity of PMMA is related to its toxicological properties. PMMA has a very narrow safety margin and lethal doses are only 2 to 4 times greater than therapeutic doses. Because the time of onset of symptoms is slower following PMMA than MDMA, users may not experience the expected effect and take additional doses of PMMA-laced ecstasy. PMMA causes release of serotonin and dopamine from presynaptic neurons, and it has monoamine oxidase inhibition activity, which prolongs activity of the amines. These effects can produce the serotonin syndrome. A spectrum of toxicity from mild to life threatening occurs in serotonin syndrome. Clonus and hyperreflexia are common and hyperthermia occurs in severe toxicity. PMMA appears to have a greater propensity for causing profound hyperthermia than MDMA. Algorithms for diagnosis have been proposed.[7,8]

Patients with serotonin syndrome should receive supportive care and precipitating drugs should be removed. Patients with a temperature above 41°C must be treated aggressively with immediate sedation, neuromuscular paralysis, orotracheal intubation, and rapid cooling. Succinylcholine should not be used because of the risk of hyperkalemia caused by rhabdomyolysis. Benzodiazepines may be effective; however, the efficacy of cyproheptadine, a 5-$HT_{2A}$ antagonist, has not been proved. Neither propranolol nor bromocriptine should be used.

In BC the ability to respond quickly to this event was enhanced by

*This article is the opinion of the Council on Health Promotion and has not been peer reviewed by the* BCMJ *Editorial Board.*

working with existing multi-agency BC DOAP members. In Alberta a working group was created in response to the crisis with representatives from public health, addictions and mental health, and the Poison and Drug Information Service. The coordinated public health response in both provinces played a role in the decline of deaths due to PMMA. As seen in this outbreak of PMMA fatalities, it is important to have ongoing close communication and collaborative efforts between representatives of various stakeholder agencies in order to identify and address new issues as they arise, which facilitate an effective and coordinated public health response.

**—Roy Purssell, MD**
**Emergency Medical Services Committee**
**Medical Lead, BC Drug and Poison Centre**

**PMMA is a ring-substituted amphetamine similar in structure to MDMA or ecstasy, but more toxic. Nearly 50 deaths due to PMMA have been reported worldwide and PMMA has gained the street names "Death" and "Dr Death."**

### References

1. McCreary Centre Society. From Hastings Street to Haida Gwaii: Provincial results of the 2013 BC Adolescent Health Survey. Accessed 14 August 2015. www.mcs.bc.ca/pdf/From_Hastings_Street_To_Haida_Gwaii.pdf.
2. Centre for Addictions Research of BC. Substance use in high-risk populations in BC. Accessed 14 August 2015. www.uvic.ca/research/centres/carbc/stats/high-risk-populations/index.php.
3. BC Coroners Service. MDMA (ecstasy) related deaths, 2006–2012. Accessed 14 August 2015. www.pssg.gov.bc.ca/coroners/reports/docs/stats-mdma-deaths-2006-2012.pdf.
4. Wood DM, Stribley V, Dargan PI, et al. Variability in the 3,4-methylenedioxymethamphetamine content of "ecstasy" tablets in the UK. Emerg Med J 2011;28:764-765.
5. Morefield KM, Keane M, Felgate P, et al. Pill content, dose and resulting plasma concentrations of 3,4-methylenedioxymethamphetamine (MDMA) in recreational "ecstasy" users. Addiction 2011;106:1293-1300.
6. Nicol JJE, Yarema MC, Jones GR, et al. Deaths from exposure to paramethoxymethamphetamine in Alberta and British Columbia, Canada: A case series. CMAJ Open 2015;3:E83-E90.
7. Boyer EW, Shannon M. The serotonin syndrome. N Engl J Med 2005;352:1112-1120.
8. Dunkley EJ, Isbister GK, Sibbritt D, et al. The Hunter Serotonin Toxicity Criteria: Simple and accurate diagnostic decision rules for serotonin toxicity. QJM 2003;96:635-642.