### **Outbreak Reports**

## An Occupational Dimethylacetamide Poisoning Incident Responded Efficiently in Health Emergency Response Network — Zhuhai City, Guangdong Province, China, August 2023

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### **Summary**

### What is already known about this topic?

Dimethylacetamide (DMA), a colorless liquid with low toxicity, is commonly used as a solvent in the production synthetic of materials, petroleum pharmaceutical manufacture. In processing, and substances of higher toxicity, comparison to occupational exposure to DMA presents a deceptive risk due to its insidious, subacute progression, increasing the likelihood of escalating into major incidents.

#### What is added by this report?

In August 2023, an incident of occupational DMA poisoning involving six cases was reported at a spandex manufacturing factory in Zhuhai City, Guangdong Province, China, following post-fire management activities. All affected individuals were employees of an equipment maintenance company tasked with cleaning polymerizers. With the coordinated efforts of the health institutions in Guangdong *Health Emergency Response Network for Poisoning Emergencies (HERNPE)*, the situation was promptly identified and addressed.

# What are the implications for public health practice?

HERNPE serves as an effective framework for enhancing the integration of health institutions across various levels, facilitating a coordinated response that combines clinical services with public health initiatives. By leveraging the leadership of national centers, HERNPE plays a crucial role in the early detection, prevention, and management of large-scale health events.

The Health Emergency Response Network for Poisoning Emergencies (HERNPE) in Guangdong Province represents a collaborative model established in recent years for sharing information and resources

among health institutions. This network designates the Guangdong Province Hospital for Occupational Disease Prevention and Treatment (GDHOD), a recognized national facility, as its technical hub. Furthermore, municipal hospitals that collaborate with chemical laboratories serve as branch nodes, while additional health institutions function as auxiliary components. This structure supports a robust framework for managing health emergencies in the region.

On August 20, 2023, the GDHOD was consulted by a hospital in Guangzhou city concerning two inpatients from Zhuhai City diagnosed with toxic hepatopathy due to occupational exposure to dimethylacetamide (DMA). Additionally, two other workers were reported to exhibit similar symptoms. The following day, GDHOD received a report from the Zhuhai Hospital for Occupational Disease Prevention and Treatment (ZHHOD). According to this report, a group of workers, who withheld their company's information, sought occupational health screenings specifically for liver function in Zhuhai. Several of these individuals presented with elevated results in liver function tests, notably in the Alanine transaminase (ALT) indices.

Given the possibility that these cases originated from the same incident, the GDHOD and ZHHOD collaboratively responded and identified the cases as occupational acute DMA poisoning. In total, 169 workers were affected by the incident. Of those, 32 individuals, who presented with elevated ALT levels, were either hospitalized or placed under ambulatory surveillance. Eventually, 6 workers were definitively diagnosed with occupational acute DMA poisoning, categorized as 1 severe, 1 moderate, and 4 mild cases.

### **INVESTIGATION AND FINDINGS**

All 6 male cases were employees of the same equipment maintenance company tasked with cleaning polymerizers as part of post-fire management at a spandex manufacturing factory in Zhuhai City. Between 5 and 13 days after exposure to DMA, these individuals developed hepatopathy, which manifested as fatigue and vomiting. Additionally, all cases experienced varying degrees of skin irritation, followed by erythema and desquamation primarily affecting the limbs that had been exposed to moisture during their work activities.

A joint team from GDHOD and ZHHOD established the case definition and identified a total of 6 cases, five of whom were hospitalized (two in Guangzhou and three in Zhuhai). Subsequent investigations led to all six cases being transferred to specialized hospitals in Guangzhou via the "green lane" in the *HERNPE*. The outcomes of field investigations and laboratory analyses informed the treatment protocols. Five of the cases were successfully cured and discharged after receiving symptomatic and supportive therapy for between 12 to 35 days. The remaining case showed improvement but was discharged against medical advice after 15 days. The basic information and diagnoses are summarized in the Table 1.

A joint team embarked on a field investigation at the factory on August 21–22 and identified the primary hazard point as the cleaning of a polymerizer in a confined space during post-fire management (notably, a similar incident in 2011 involved two workers who, while performing routine cleaning in this space with inadequate protection, suffered from DMA poisoning). Following a fire that occurred four days prior, on July

20, the factory engaged four equipment maintenance companies to manage the post-fire situation. Several tonnes of manufacturing materials — predominantly spandex blended with DMA, ethylenediamine, diethylamine, and other auxiliary materials — had progressively solidified inside the polymerizer located on the third floor of the Polymerization Workshop.

According to the survey and records, only 10 workers from a single company registered to clean the polymerizer; this group included 6 cases, half of whom were newly-recruited part-time employees. An additional 159 workers were involved in cleaning, loading, unloading, and handling operations within the same workshop and might have been exposed to the same toxicants. In total, 169 workers were involved in these activities.

The process for cleaning the polymerizer in post-fire management, compared to conventional methods, was outlined as follows: 1) Detection of air quality within the polymerizer, noting poor ventilation. 2) Draining of contents from the polymerizer, including solid and liquid residues. 3) Flushing of the polymerizer with tap water, following a non-standardized standard operating procedure. 4) Manual entry into the polymerizer to scrape off residues, noting an increased residue presence and inadequate protective measures. 5) Exiting the polymerizer and removal of residues, characterized by extended duration and absence of specialized protective equipment.

Each shift lasted 8 hours per day, with workers organized into pairs within a group. Each pair alternated tasks every hour; while one pair entered the polymerizer to perform cleaning duties, the other

TABLE 1. The basic information and diagnosis of 6 cases in Zhuhai City, Guangdong Province, China, August 2023.

Patient No.	Age (years)	Duration of exposure to DMA (day)	N- methylacetamide in urine (mg/g Cr) <sup>1</sup> , (day) <sup>2</sup>	manifest period	Serum total bilirubin at manifest period (µmol/L), (day) <sup>2</sup>	Main clinical manifestations <sup>3</sup>	Severity scale	Hospital day
Case A	46	13	1,639.78 (5d)	474 (6d)	269.7 (6d)	acute liver failure, fatigue, poor appetite, vomiting	severe	17 (clinical cured)
Case B	48	5	239.79 (5d)	3,499 (4d)	43.6 (4d)	nausea, vomiting, fatigue, poor appetite	mild	12 (clinical cured)
Case C	57	8	36.90 (7d)	1,448 (5d)	53.90 (5d)	nausea, fatigue, jaundice	moderate	28
Case D	56	8	9.79 (5d)	349 (7d)	9.65 (7d)	fatigue, poor appetite	mild	24
Case E	50	8	52.81 (6d)	915 (4d)	34.7 (4d)	poor appetite, fatique, vomiting	mild	35
Case F	44	6	12.86 (8d)	252 (7d)	10.75 (7d)	fatigue, poor appetite	mild	15 (against advice)

Note: Occupational exposure limit of N-methylacetamide in urine emendating with Cr is 20.0 mg/g Cr (off the working week); (day) refer to the time of removal from DMA; Viral or biological hepatitis had been excluded for all cases.

Abbreviation: Cr=creatinine; DMA=dimethylacetamide.

remained outside to assist and rest. In total, 10 workers were equipped with long tube breathing apparatus featuring a full face mask and circulating air (sourced from a remote air supply room). Additionally, they wore rubber gloves, labor shoes, and cotton long-sleeved clothing inside the polymerizer. When outside of the polymerizer, the workers only had disposable masks and cotton gloves for protection — this was the same for the 159 other workers in the workshop. The ventilation within the factory was poor due to a malfunctioning exhaust fan, and only some windows were left open to facilitate airflow. Moreover, the factory and four other companies lacked the awareness and capability to monitor DMA exposure effectively.

The site of the incident could no longer be replicated following the conclusion of post-fire management activities. A joint team conducted on-site detection in the workshop on August 22. Laboratory results indicated that the C-STEL of DMA for two samples "near the polymerizer door" was 33.60 mg/m<sup>3</sup> 36.06  $mg/m^3$ , respectively. Meanwhile, measurements from four samples "in the workshop passageway" showed concentrations of 27.53 mg/m<sup>3</sup>, 22.49 mg/m<sup>3</sup>, 16.88 mg/m<sup>3</sup>, and 12.34 mg/m<sup>3</sup>. Based on these findings, it was inferred that DMA concentrations during the incident likely exceeded the PC-TWA of 20 mg/m $^3$ .

Moreover, two distinct batches of manufacturing materials were sent to the GDHOD for qualitative analysis using gas chromatography-mass spectrometry (GC-MS). In the sample provided by Case A on August 19, DMA (30.09%) and dimethylformamide (DMF) (0.10%) were detected. In contrast, DMA (13.74%) and diethylamine (0.10%) were identified in the sample submitted by the joint team on August 21. Consequently, the primary cause of concern was determined to be exposure to DMA, after ruling out spandex and other auxiliary materials due to differing toxic effects or insufficient dosages.

Within two days, a joint team compiled a comprehensive list of 163 workers (excluding the 6 cases) and conducted emergency health screenings from August 23–26. Although no clinical symptoms were present, 26 workers exhibited elevated levels of ALT, with median ( $P_0$ – $P_{100}$ ) levels of 78.5 U/L (range 52.0–616.0 U/L). Additionally, 9 of these 26 workers showed high levels of urinary N-methylacetamide, with median ( $P_0$ – $P_{100}$ ) levels of 25.20 mg/g Cr (range 20.79–109.98 mg/g Cr). In response to these findings, the team established a categorical management guideline and set up ambulatory surveillance for liver

pathology, which varied in frequency and duration across different individuals. The elevated ALT levels observed in some workers could potentially be diagnosed as physiological responses to DMA exposure, with prospects of recovery facilitated by early detection. However, for the majority, these biochemical anomalies were attributed to factors such as sleep deprivation, alcohol consumption, and high-fat diets.

Furthermore, the collaborative team implemented supervision and provided industry guidelines to reduce the risk of occupational poisoning from DMA. This included the identification of hazards among 143 DMA users through the Guangdong Province Occupational Health Quality Control Platform, which reported no instances of limit exceedance in the past three years. Additionally, 14 technical guidelines, including methods for determining DMA, were issued to public health service institutions. The team also mandated that a certified chemical-waste disposal company securely store any residual waste. Following these interventions, no new cases were reported over the course of a month.

### **PUBLIC HEALTH RESPONSE**

The emergency response timeline proceeded as follows: 1) August 20–21: The GDHOD and ZHHOD engaged in information gathering and coordinated response efforts. 2) August 21–22: conducted a survey of 5 cases and a field investigation, which identified the sixth case. 3) August 22: performed on-site detection, compiled a list of workers, and provided supervision and industry-specific guidance. 4) August 23: six cases were referred to specialized hospitals. 5) August 23–26: screened a total of 163 workers. 6) August 24–September 26: organized intensive treatment and ongoing ambulatory surveillance.

Targeted interventions within the *HERNPE* were crucial, including the exchange of information about outbreaks to facilitate early detection, especially in instances where employers might conceal information or provide false evidence. These interventions were supported by expert guidance from national authorities, the prioritization of patient admissions and referrals through designated "green lanes", the implementation of coordinated investigation and detection efforts, and comprehensive screening and surveillance measures in large groups.

### **DISCUSSION**

DMA has increasingly been used as a substitute for DMF due to its high thermal stability, low corrosiveness, and reduced toxicity, among other advantages. Despite these benefits, incidents of DMA poisoning have been reported periodically. According to partial data, there have been over six incidents involving more than 30 cases in China, all within the chemical fiber manufacturing industry (1,2).

DMA may target the liver, resulting in acute poisoning, and may also irritate the skin, typically displaying a subacute insidious progression or, less commonly, recurrence (3). Chronic exposure to DMA can lead to neurasthenia, respiratory irritation, and varying levels of hepatic damage (4). The presence of N-methylacetamide in urine, which positively correlates with the concentration of DMA in the air, serves as a useful biomonitoring indicator (5).

Several factors contributed to the severity of this mass exposure event: cases were subjected to high concentrations of DMA; the incident occurred in a confined space within the polymerizer, where toxicant levels were significantly elevated; workers engaged in post-fire management operations for extended periods without adhering to standard procedures; and lastly, both the company and its employees demonstrated inadequate awareness and implementation of protective measures. Proper emergency response protocols are crucial.

Thanks to the collaborative efforts of various health institutions, the integrated clinical and public health response system, and technical guidance from the national headquarters at *HERNPE*, this incident was efficiently identified and managed in a short timeframe, despite involving a large number of workers. This prompted an extensive demand for streamlined admission and referral processes, timely on-site detection, field investigations, diagnostic and treatment guidance, category management guidelines, and other measures.

To prevent such incidents, it is recommended that employers prioritize the hiring of personnel who possess qualifications relevant to handling hazardous chemicals and develop robust disaster management strategies. Additionally, limiting working hours and enhancing health education and personal protection initiatives are crucial. Medical institutions should enhance the sensitivity of their surveillance systems and be vigilant about patients' occupational histories or potential exposures, particularly when clusters of similar medical findings emerge within a short timeframe. Additionally, timely sharing of information through *HERNPE* is critical in the event of a mass exposure.

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### REFERENCES

- 1. Li JP, Li JM, Chen XB. Investigation on a dimethylacetamide poisoning accident. Occup Health Emerg Rescue 2022;40(6):741 3. https://doi.org/10.16369/j.oher.issn.1007-1326.2022.06.024.
- Zhou P, Lu CH, Gao HP, Yin SW, Zhou ZW. Investigation of a mass dimethylacetamide poisoning incidents. Ind Health Occup Dis 2022;48 (2):167-8. http://dx.doi.org/10.13692/j.cnki.gywsyzyb.2022.02.024. (In Chinese).
- Gong W, Liu X, Zhu BL. Dimethylacetamide-induced occupational toxic hepatitis with a short term recurrence: a rare case report. J Thorac Dis 2016;8(6):E408 – 11. https://doi.org/10.21037/jtd.2016.04.44.
- Jiang QT, Gong W, Zhu BL, Liu X. Occupational health hazards of dimethylacetamide in Jiangsu Province, 2015. Pract Prev Med 2018;25 (2):168 – 70. https://doi.org/10.3969/j.issn.1006-3110.2018.02.012.
- Yang F, Guo WW, Li CQ, Shen CY, Xie QM, Hu XJ, et al. Establishing occupational biological exposure limits of dimethylacetamide. J Environ Occup Med 2017;34(11):947 – 52. https://doi.org/10.13213/j.cnki. jeom.2017.17338.

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