JOURNAL OF FORENSIC SCIENCES

*J Forensic Sci,* January 2011, Vol. 56, No. S1
doi: 10.1111/j.1556-4029.2010.01625.x
Available online at: onlinelibrary.wiley.com

**TECHNICAL NOTE**

**PATHOLOGY/BIOLOGY; TOXICOLOGY**

*Lan Zhou,*[1,2] *M.D.; Liang Liu,*[1,2] *M.D.; Lin Chang,*[1] *M.D.; and Ling Li,*[1–3] *M.D.*

# Poisoning Deaths in Central China (Hubei): A 10-year Retrospective Study of Forensic Autopsy Cases

**ABSTRACT:** A retrospective study of autopsy cases was conducted at the Department of Forensic Medicine, Tongji Medical College (DFM-TMC), in Hubei, China to describe the characteristics of poisoning deaths from 1999 to 2008. A total of 212 poisoning deaths were investigated by DFM-TMC during the 10-year period. The poisoning deaths ranged from 17 cases in 1999 to 27 cases in 2008. Of the 212 cases, 82 deaths (38.7%) were from pesticides, 36 deaths (17.0%) from carbon monoxide, 34 deaths (16.0%) from drugs, 22 deaths (10.4%) from alcohol, 17 deaths (8.0%) from other chemicals, 15 deaths (7.1%) from poisonous plants and animals, and six deaths (2.8%) from heavy metals. Of the 82 pesticide poisoning deaths, 43 (52.4%) cases were caused by rodenticides, mainly tetramine ($N = 39$). The majority of poisoning deaths were accidents (63.7%), followed by suicides (25.9%) and homicides (3.8%). The manner of death could not be determined in 14 cases (6.6%).

**KEYWORDS:** forensic science, forensic toxicology, forensic pathology, poisoning death, pesticides, tetramine, illicit drug abuse, autopsy

Poisonings cause considerable morbidity and mortality through the world (1–4), with an estimated 315,000 deaths caused by unintentional poisoning and 250,000 deaths resulting from intentional ingestion of chemicals worldwide in 2000, according to the World Health Organization (WHO) data (1,4). In China, unintentional poisoning was the ninth most common cause of death in young adults from 15 to 29 years of age (4). The most common agents responsible for poisoning deaths in China as well as in other developing countries are pesticides (5–7). Pesticide poisoning remains the major cause of public health problem in the developing countries.

There has been relatively little detailed analytical data from autopsy studies on the poisoning deaths in the China. The objective of this study is to assess the trends and characteristics of poisoning deaths in the region of central China, Hubei province, as they were recorded among the autopsy cases examined by the Department of Forensic Medicine, Tongji Medical College (DFM-TMC).

## Materials and Methods

Hubei province is located in the central part of China, with a population of 56,990,000 (2007). DFM-TMC is one of the three major forensic institutes with responsibility to oversee and to provide forensic pathology and related services in central China, mainly Hubei province. The DFM-TMC handles the cases sent to them by the police, courts, and prosecutors' offices, sometimes requested by the decedents' families. The cases selected for autopsy are deaths with suspicion, sudden unexpected deaths, possible poisoning deaths, and deaths related to medical misadventures. If the cause of death is apparent by scene investigation and review of clinical history, external examination (inspection) is a general rule. In addition, almost all the autopsy cases at the DFM-TMC have to have permission from the family members. Therefore, the autopsy rate is relatively lower when compared with other developed countries.

All autopsy cases were subjected to comprehensive toxicology testing for pesticides, drugs, alcohol, and heavy metals. Certain chemicals, carbon monoxide, Chinese herbs, and poisonous plants/animals are tested if they are suspected. Specimens including blood, urine, bile, stomach contents, and liver were collected from each victim at autopsy. Gas chromatography/mass spectrometry (GC/MS) and liquid chromatography/mass spectrometry (LC/MS) were used to detect pesticides, alcohol, drugs, and toxic components of Chinese herbs. Quantitative analysis of tetramine was performed with GC/MS operated in selected ion monitoring mode method for ions m/z 212, 240, and 360 (data rate at 20 Hz). Cyanide, nitrite, and carboxyhemoglobin were detected by the spectrophotometric method. Heavy metals were detected by atomic fluorescence spectrometric method and atomic absorption spectrometric method.

All autopsy cases investigated by the DFM-TMC were reviewed, and cases included in the study were selected based on autopsy and toxicology reports in which deaths were classified as poisoning from January 1, 1999 to December 31, 2008. This study was a retrospective review of all poisoning deaths examined by the DFM-TMC in the past 10 years. Age, gender, investigation reports, autopsy findings, including the types of drugs detected by toxicology test, and the cause and manner of death were analyzed.

For the purpose of this study, a poison is any substance that is harmful to the human body when ingested, inhaled, injected, or

[1]Key Laboratory of Evidence Science, China University of Political Science and Law, 25 West Tucheng Road, Haidian District, Beijing 100088, China.

[2]Department of Forensic Medicine, Tongji Medical College at Haozhong University of Science and Technology, 13 Hong Kong Road, Wuhan 430030, China.

[3]Department of Pathology, University of Maryland School of Medicine, 22 South Greene Street, Baltimore, MD 21201.

Received 23 Oct. 2009; and in revised form 18 Dec. 2009; accepted 24 Dec. 2009.

absorbed through the skin. A poisoning death is any death in which a toxic level of poison is found with no other cause of death present. The definition of drugs of abuse is the misuse or nonmedical use of controlled substances, prescribed drugs, and over-the-counter drugs. The definition of drugs of therapy is the medical use of prescribed drugs and over-the-counter drugs.

## Results

Between 1999 and 2008, a total of 2416 deaths were investigated by DFM-TMC. Based on the scene investigation, autopsy examination, and toxicology study, 212 of the 2416 (8.8%) deaths were determined to be caused by poisonings. The ages of the victims ranged from 45 days to 79 years, with more than 50% of the victims being in their 30s and 40s.

The leading cause of poisoning deaths was pesticides, followed by carbon monoxide, drugs, alcohol, other chemicals, poisonous plants/animals, and heavy metals (Table 1). Among the pesticides, rodenticides accounted for 52.4% of the cases and insecticides and herbicides accounted for 47.6% of the cases. Tetramine was the major rodenticide responsible for 39 of 82 deaths from the pesticides (Table 2).

Of the 34 drug deaths, 15 (44.1%) cases were caused by drugs of abuse, mainly heroin/morphine and ketamine, seven (20.6%) cases involved accidental overdose of prescribed medications, and 12 (35.3%) cases were the result of the therapeutic misadventure when patients were inadvertently given lethal dosage of medications intravenously in hospital settings.

Overall, the number of poisoning deaths stayed relatively constant except for the years of 2000, 2005, and 2008 with comparably more deaths than those in the other years (Fig. 1). The deaths ranged from 17 to 29 cases with an average of 21 cases per year.

However, poisoning deaths from pesticides declined continuously from 26 cases in 1999 and 2000 to only eight in 2007 and 2008, a 325% decrease (Fig. 2). Deaths from carbon monoxide intoxication, on the other hand, showed a significant increase during 2005 and 2006. There was an increased trend of deaths from drugs of abuse in the central China, Hubei area, mainly from heroin/morphine and ketamine.

The majority of poisoning deaths were accidents (63.7%), followed by suicides (25.9%) and homicides (3.8%). The manner of death could not be determined in 14 cases (6.6%). The manner of death by agents can be seen in Table 3. Pesticides were implicated in the majority of the poisoning suicide deaths. Of the 82 deaths caused by pesticide poisoning in Hubei, 51 were suicides.

During the past 10 years, a total of 39 (18.4%) poisoning deaths were caused by the ingestion of tetramine. Of the 39 cases, 20

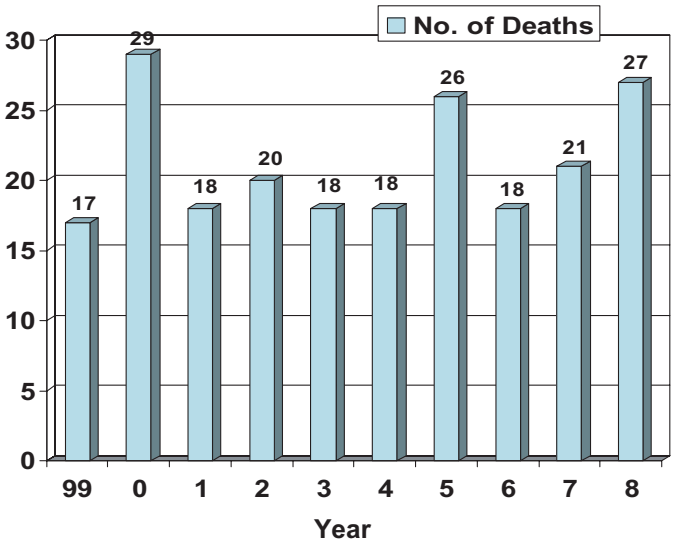


FIG. 1—*Poisoning deaths during 1999–2008.*

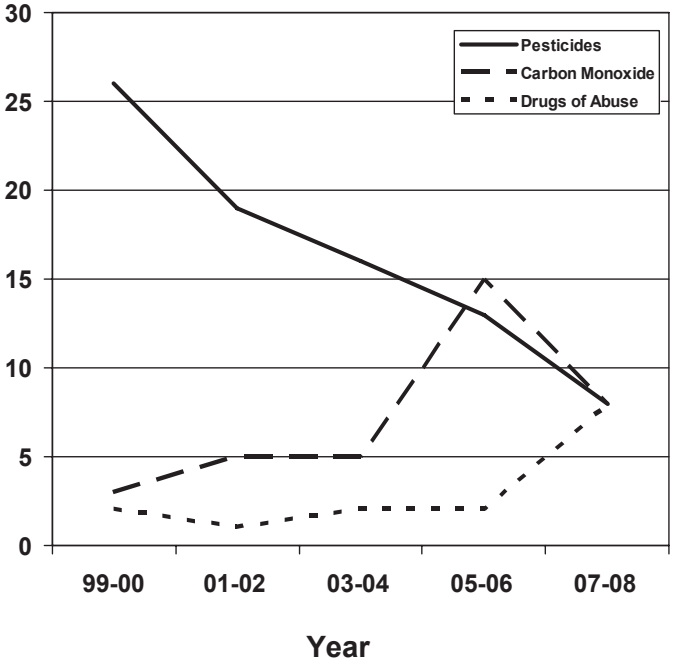


FIG. 2—*The trend of poisoning deaths by major poisons during 1999–2008.*

TABLE 1—*Distribution of poisoning deaths by agents.*

| Poisoning Agents | No. of Deaths | % |
|---|---|---|
| Pesticides | 82 | 38.7 |
| Carbon monoxide | 36 | 17.0 |
| Drugs | 34 | 16.0 |
| Alcohol | 22 | 10.4 |
| Other chemicals* | 17 | 8.0 |
| Poisonous plants/animals | 15 | 7.1 |
| Heavy metals | 6 | 2.8 |
| Total | 212 | |

*Sulfuric acid, potassium cyanide, chlorosufonic acid, benzene, cyanide, methyl fluoroacetate, nitrite, mixed organic solvent, methanol, hydrogen sulfide, and dichloromethane.

TABLE 2—*Poisoning deaths by pesticides.*

| Pesticides | No. of Deaths | % |
|---|---|---|
| Rodenticides | 43 | 52.4 |
| Tetramine | 39 | 90.7 |
| Fluoroacetamide | 3 | 7.0 |
| Bromadiolone | 1 | 2.3 |
| Insecticides/herbicides | 39 | 47.6 |
| Organophosphate pesticides | 21 | 53.8 |
| Dimehypo | 6 | 15.4 |
| Carbamates | 4 | 10.3 |
| Others | 8 | 20.5 |
| Total | 82 | |

TABLE 3—*Manner of poisoning deaths by agents.*

| Agents | Accident | Suicide | Homicide | Undetermined | Total |
|---|---|---|---|---|---|
| Pesticides | 16 (11.9) | 51 (92.7) | 5 (62.5) | 10 (71.4) | 82 |
| Carbon monoxide | 35 (25.9) | 0 (0.0) | 0 (0.0) | 1 (7.2) | 36 |
| Drugs | 32 (23.7) | 1 (1.8) | 0 (0.0) | 1 (7.2) | 34 |
| Alcohol | 22 (16.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 22 |
| Poisonous plant/animals | 15 (11.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 15 |
| Other chemicals | 12 (8.9) | 2 (3.7) | 1 (12.5) | 2 (14.2) | 17 |
| Heavy metals | 3 (2.2) | 1 (1.8) | 2 (25.0) | 0 (0.0) | 6 |
| Total | 135 | 55 | 8 | 14 | 212 |

TABLE 4—*Scene investigation findings of carbon monoxide poisoning.*

| Scene Location | No. of Deaths | % |
|---|---|---|
| Residence/home | 18 | 51.4 |
| Hotel | 12 | 34.3 |
| Rented apartment | 5 | 14.3 |
| Source of gas | | |
| Water-heater leakage | 18 | 51.4 |
| Gas-oven leakage | 1 | 2.9 |
| Gas pipe leakage | 1 | 2.9 |
| Burning coal for heating | 1 | 2.9 |
| House fire | 2 | 5.7 |
| Unknown | 12 | 34.2 |
| Total | 35 | |

deaths (51.3%) were caused by self-inflicted poisoning, nine deaths (23.1%) were caused by accidental poisoning, and three deaths (7.7%) involved intentional poisoning by homicide. The manner of death could not be determined in seven deaths caused by tetramine. The common clinical symptoms of tetramine poisoning ranged from nausea, vomiting, and abdominal pain, to seizures, reduced level of consciousness, coma, and death from respiratory failure and multiple organ failures. Autopsy examination revealed nonspecific pathologic changes, such as pulmonary congestion and edema, and complications from multi-organ failure. Postmortem diagnosis was based on scene investigation, review of the clinical history, and specific postmortem toxicology testing for tetramine.

Carbon monoxide intoxication was the number one cause of accidental poisoning deaths in our study group. Thirty-five of 36 (97.2%) carbon monoxide poisoning deaths were accidental; the manner of death could not be determined in one carbon monoxide poisoning case (Table 3). Of the 35 accidental deaths from carbon monoxide poisoning, 32 were exclusively caused by gas inhalation, two deaths were the result of house fire, and one death was caused by burning coal indoors for heating without a good ventilation system. The majority (18/35) of the accidents were caused by gas leakage from water-heaters (Table 4). The highest frequency of carbon monoxide deaths was during the winter months (December, January, and February) in 68.6% of the cases.

In our study, more men (63.2%) died of poisonings than women. The majority of accidental poisoning deaths were male victims (71.1%). However, deaths caused by suicidal poisoning were slightly higher in female victims ($N = 30$) than in male victims ($N = 25$).

## Discussion

There are significant differences in the nature of the agents involved in the poisoning deaths between developing countries and developed countries (2,6–9). Pesticides are the most common agents responsible for poisoning deaths in many developing countries (6–8), whereas pharmaceuticals are the most common means of fatal poisoning in the developed countries (2,9–11).

Pesticide poisoning remains the major public health problem in China. Recent global estimates of deaths from poisoning suggest that more than 150,000 deaths occur each year in all of China from pesticides poisoning alone (11). Our data showed that poisoning from pesticides was the leading cause of death among all the poisoning deaths, and pesticide ingestion was the most common means of fatal self-inflicted poisoning in our study population, accounting for 92.7% of the total suicides. Of the pesticides poisoning cases, rodenticide tetramine alone accounted for more than one-third of the deaths. Tetramine (tetramethylene disulfotetramine) is an odorless, tasteless, white, crystalline powder that easily dissolves in water, with its molecular formula $C_4H_8N_4O_4S_2$. Tetramine is a neural toxin and acts by blocking the chloride channel of the inhibitory neurotransmitter receptor of the gamma-aminobutyric acid (12). It is extremely hazardous, being 100 times more toxic than cyanide (13). Very small amounts of tetramine, estimated as low as 0.1 mg/kg weight (oral $LD_{50}$) in mammals, can lead to convulsions and death, with a dose of 5–12 mg considered lethal in humans (14). The symptoms of tetramine poisoning ranged from nausea, vomiting, and abdominal pain, to epileptic seizures, coma, and death from respiratory failure and multiple organ failures (15). The unique features of tetramine poisoning are the rapid onset of convulsions that are difficult to control, multi-organ failure, and high mortality (13). Despite its unique features, diagnosis of tetramine poisoning can be very difficult. First, it is an illicit rodenticide and may not be listed on the product label. Second, the victims often become unconsciousness soon after ingestion and cannot provide any useful history. Third, presentation may mimic many medical conditions and poisoning caused by other substances (13). Finally, postmortem pathology findings are usually nonspecific. Although tetramine has been band worldwide because of its lethal toxicity, repeated outbreaks of poisoning continue to occur in Mainland China (16). In 2002, the first known case of human illness caused by tetramine intoxication was reported in the U.S. (17). It has been suggested that tetramine may be considered as a potential agent of terror because of the extreme toxicity of the compound, the absence of specific antidote, and the history of tetramine's use in intentional mass poisonings (18). To reach a correct diagnosis, a thorough scene investigation of the circumstance of the death with high alert on suspicion and a complete autopsy examination with toxicological detection of the tetramine are necessary.

Drug addiction in China began with the import of Indian opium by the British in the 16th century and brought severe social and health problems (19). While drug abuse abated following the establishment of the People's Republic of China, the implementation of open-door policies in the 1980s led to a re-emergence of illicit drug trade in China. Drug imports from the Golden Triangle region have made illegal substances widely available, causing severe drug abuse problems (20,21). Illicit drug abuse, particularly heroin abuse, has risen to epidemic levels over the last 10 years, and the use of amphetamine-type stimulants, including amphetamine, methamphetamine, and 3,4-methylenedioxymethamphetamine, has recently gained popularity in China (22,23). Our study showed an increased trend of illicit drug abuse deaths, mainly caused by heroin/morphine and ketamine, during the past 10 years in the central China. The new trends of drug addiction in China pose great public health challenges and require government interventions, focusing both on public education and treatments through drug addiction programs.

## Conclusion

Poisoning is a global public health problem. There has been an increased trend of deaths from illicit drug abuse in the central part of China over the past 10 years. But pesticide poisoning remains the leading cause of poisoning deaths in China as well as in many developing countries. Tetramine (tetramethylene disulfotetramine) ingestion is a common method of intentional and unintentional poisoning in China. The unique features of tetramine poisoning are the rapid onset of convulsions that are difficult to control, multi-organ failure, and high mortality. Diagnosis of tetramine poisoning can be very difficult. It is necessary to have a thorough scene investigation of the circumstance of the death with high alert on suspicion and a complete autopsy examination with specific toxicological detection of the tetramine.

**Conflict of interest:** The authors have no relevant conflicts of interest to declare.

*Acknowledgments*

Authors thank Professor Guang-zhao Hunag for his significant contributions in the medico-legal investigation and research on poisoning deaths in China throughout the years and his thoughtful participation in the collection of the data on poisoning cases during his tenure as chairperson at the Department of Forensic Medicine, Tongji Medical College.

## References

1. The World Health Organization. Deaths by cause, sex, and mortality stratum in WHO regions, estimates for 2000. The World Health Report 2001 Statistic Annex. The World Health Organization, 2001;148, http://www.who.int/whr/2001/en/annex2_en.pdf (accessed October 10, 2010).
2. National Center for Injury Prevention and Control, Division of Unintentional Injury Prevention. Poisoning deaths in the United States, Fact Sheet. Atlanta, GA: Centers for Disease Control and Prevention, 2008.
3. Kivistö JE, Mattila VM, Parkkari J, Kannus P. Incidence of poisoning deaths in Finland in 1971–2005. Hum Exp Toxicol 2008;27(7):567–73.
4. The International Programme on Chemical Safety. Poisoning prevention and management. http://www.who.int/ipcs/poisons/en/ (accessed October 10, 2010).
5. Gunnell D, Eddleston M. Suicide by intentional ingestion of pesticides: a continuing tragedy in developing countries. Int J Epidemiol 2003;32:902–9.
6. Mohan D, Varghese M. Injuries in South-East Asia region. New Delhi/India: Disability/injury prevention and rehabilitation, WHO Regional Office for South-East Asia, 2002:18.
7. Phillips MR, Yang G, Zhang Y, Wang L, Ji H, Zhou M. Risk factors for suicide in China: a national case-control psychological autopsy study. Lancet 2002;360:1728–36.
8. Roberts DM, Karunarathna A, Buckley NA, Manuweera G, Sheriff MH, Eddleston M. Influence of pesticide regulation on acute poisoning deaths in Sri Lanka. Bull World Health Organ 2003;81(11):789–98.
9. Singh D, Tyagi S. Changing trends in acute poisoning in Chandrigah zone. A 25-year autopsy experience from a tertiary care hospital in northern India. Am J Forensic Med Pathol 1999;20:203–13.
10. Flanagan RJ, Rooney C. Recording acute poisoning deaths. Forensic Sci Int 2002;128:3–19.
11. Li Y, Sun C, Qiu Z, Ma S, Yu X, Wang Z, et al. Clinical toxicology in China: current situation and future development. Clin Toxicol (Phila) 2009;47(4):263–9.
12. Esser T, Kaur AE, Toia RF, Casida JE. Recognition of tetramethylenedisulfotetramine and related sulfamides by the brain GABA-gated chloride channel and a cyclodiene-sensitive monoclonal antibody. Chem Res Toxicol 1991;4:162–7.
13. Poon WT, Chan K, Lo MH, Lee AYW. A case of tetramine poisoning, a lethal rodenticide. Hong Kong Med J 2005;11:507–9.
14. Zhang SL, Ding MB. Diagnosis and treatment of tetraime poisoning. Chin J Internal Med 2001;14:163–5.
15. Huang SQ, Zhao DL, Guan FY. Acute tetramine poisoning: 161 cases reports. Chin J Emerg Med 1997;6:202–4.
16. Croddy E. Rat poisoning and food security in the People's Republic of China: focus on tetramethylene disulfotetramine (tetramine). Arch Toxicol 2004;78:1–6.
17. Barrueto F, Nelson LS, Hoffman RS. Poisoning by an illegally imported Chinese rodenticide containing tetramethylenedisulfotetramine–New York City, 2002. MMWR Morb Mortal Wkly Rep 2003;10:199–201.
18. Whitlow KS, Belson M, Barrueto F, Nelson L, Henderson AK. Tetramethylenedisulfotetramine: old agent and new terror. Ann Emerg Med 2005;45(6):609–13.
19. Lu L, Fang Y, Wang X. Drug abuse in China: past, present and future. Cell Mol Neurobiol 2008;28:479–90.
20. Hao W. Longitudinal surveys of prevalence rates and use patterns of illicit drugs at selected high-prevalence areas in China from 1993 to 2000. Addiction 2004;99:1176–80.
21. Lu L, Wang X. Drug addiction in China. Ann NY Acad Sci 2008;1141:304–17.
22. Xue L. Retrospective investigation of the epidemiology and characteristics of drug abuse in Shanghai. Chin J Drug Depend 2002;11:47–50.
23. Fang YX, Wang YB, Shi J, Lui ZM, Lu L. Recent trends in drug abuse in China. Acta Pharmacol Sin 2006;27:140–4.

Additional information and reprint requests:
Ling Li, M.D.
Key Laboratory of Evidence Science
China University of Political Science and Law
25 West Tucheng Road, Haidian District
Beijing 100088, China
E-mail: Ling001@aol.com