

## Rodenticide Poisoning

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### Features



Rodenticide poisoning is commonly encountered in clinical practice. The Hong Kong Poison Information Centre has received 8 consultations and reportings of rodenticide exposure in eight months for the period of July 2005 to February 2006.

The rodenticides registered for use in Hong Kong include anticoagulants (such as warfarin and superwarfarins), cholecalciferol (vitamin D, causing hypercalcaemia) and cellulose (causing intestinal obstruction).<sup>(1)</sup> Anticoagulants are the most commonly used and encountered rodenticides in poisoning.

Warfarin acts by inhibiting the activation of vitamin K-dependent clotting factors II, VII, IX and X. While superwarfarins (e.g. bromadiolone, brodifacoum and difethialone) act in a similar manner, they have a much higher potency (about 100 times that of warfarin) and prolonged elimination half-life (16 to 69 days) compared with warfarin (about 36 hours).<sup>(2,3)</sup> (Table 1)

In acute exposure, the anticoagulation effect may be delayed up to 36 hours until the pre-formed activated clotting factors are used up.<sup>(4)</sup> Checking International Normalised Ratio (INR) at 48 to 72 hours should identify all patients at risk of coagulopathy.

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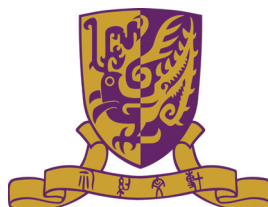
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Table 1 Examples of Anticoagulants

<i>First-generation anticoagulants</i>	<i>Second-generation anticoagulants (Superwarfarins)</i>
Warfarin Coumatetralyl Chlorophacinone Diphacinone	Bromadiolone Brodifacoum Difethialone



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If the patient has a normal INR at 48 to 72 hours after ingestion (which is the usual case in accidental ingestion), the patient is unlikely to have poisoning from the anticoagulant exposure and no antidote is needed. Physicians should refrain from giving a “prophylactic” dose of vitamin K1 in asymptomatic patient who presents early as this would mask the anticoagulation effects of the rodenticide and make the interpretation of clotting profile difficult.<sup>(5)</sup>

If the patient has coagulopathy (which is not common and in general requires more than one pack of mouse rice ingestion), treatment should start with oral vitamin K1 and monitoring of the INR until it is plateau. Oral vitamin K1 could be started at standard dose but in case of superwarfarin poisoning, prolonged course (up to months) and a large dose of vitamin K1 (up to 100 mg per day, titrated according to the INR) may be required.<sup>(6)</sup> If the patient has active severe bleeding, fresh frozen plasma should also be given. A rapid intravenous bolus dose of vitamin K1 injection has been associated with mortality<sup>(7)</sup> and administration by the oral route is preferred.



## References

- (1) Agriculture, Fisheries and Conservation Department. Booklet on Anti-rodent Measures.
- (2) Jiri Pavlu. Superwarfarin poisoning. *Lancet* 2005; 365(9459): 628
- (3) Weitzel JN et al. Surreptitious ingestion of a long-acting vitamin K antagonist/rodenticide, brodifacoum: clinical and metabolic studies of three cases. *Blood* 1990; 76(12): 2555-9
- (4) Michael E. Mullins et al. Unintentional Pediatric Superwarfarin exposures: Do we really need a prothrombin time? *Pediatrics* 2000; 105(2): 402-4
- (5) Kent R Olson. *Poisoning & Drug Overdose* 4<sup>th</sup> edition. McGrawHill, 2004, p. 380
- (6) Sanja Sarin, Hamid Mukhtar, Mohd A. Mirza. Prolonged coagulopathy related to superwarfarin overdose. *Annals of Internal Medicine* 2005; 142(2): 156
- (7) Louis D. Fiore. Anaphylactoid Reactions to Vitamin K. *Journal of Thrombosis and Thrombolysis* 2001; 11(2): 175-83



## Warfarin: Herb-Drug Interaction & Drug-Drug Interaction

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**Poison and Medicine  
Are Alike**

**“Poisons and medicines are oftentimes the same substance given with different intents” ~ Peter Mere Latham (1789-1875)**

The inherent risks of taking warfarin are ascribed to its three unfavourable pharmacokinetic characteristics (high protein binding, cytochrome P450 dependent metabolism and very narrow therapeutic range) and its interference with the blood clotting cascade.<sup>(1)</sup> Co-administration of warfarin with food, dietary supplement, and other drugs or herbs that may potentiate the anticoagulant effect of warfarin can turn this life-saving medicine into a potentially life-threatening “human” poison.

Published clinical data on drug-warfarin interactions are mainly derived from case reports as clinical trials seem unethical to conduct. The current scientific data on herb-warfarin interactions are even more limited and mostly in the form of experimental data; case reports are scarce. Therefore, the true prevalence of interaction with warfarin is unknown.<sup>(2)</sup> In view of the extensive use of herbal medicinal products and supplements in Hong Kong, checking on the use of alternative therapy by the patients is as important as checking for potential drug-warfarin interaction when monitoring the anticoagulant therapy of warfarin.

The possible interactions of some commonly used herbs/drugs with warfarin are shown in Table 1 below. The list presented is not meant to be exhaustive.

**Table 1. Herbs/Drugs Interaction with Warfarin -- “Possible Potentiation of Anticoagulant Effect of Warfarin”**

Herbs <sup>(2),(3),(6)</sup>	Mechanism of Interaction	Drugs <sup>(4),(5),(7)</sup>	Mechanism of Interaction
Danshen 丹參 ( <i>Salvia miltiorrhiza</i> )	- Additive effect on coagulation mechanisms	Acetaminophen, Cephalosporins (parenteral), Quinidine, Quinine, Thyroid, Vitamin E(≥ 400IU)	- Interference with clotting factor
Dongquai 當歸 ( <i>Angelica sinensis</i> )		Acetaminophen, Amiodarone, Azithromycin, Azole antifungal agents, Chloramphenicol, Cimetidine, Clarithromycin, Erythromycin, Fluvastatin, Gemfibrozil, Lovastatin, Metronidazole, Simvastatin, Sulfonamides	- ↓Metabolism
*Garlic 大蒜 ( <i>Allium sativum</i> )		Cephalosporins (parenteral), NSAIDs, Salicylates	- ↓Platelet aggregation
Ginkgo 銀杏 ( <i>Ginkgo biloba</i> )		Chloral Hydrate, Clofibrate, Gemfibrozil, Miconazole, Nalidixic Acid, #Phenytoin, Salicylates, Sulfonamides	- Protein binding displacement
Devil's Claw 魔鬼爪 ( <i>Harpagophytum procumbens</i> )	- Unknown	Ciprofloxacin, Danazol, Glucagon, Levofloxacin, Norfloxacin, Ofloxacin	- Unknown

\* *Ingestion of small amount of garlic in food may not pose a problem*<sup>(3)</sup>

# *Phenytoin may initially displace warfarin from protein binding sites followed by increasing warfarin metabolism*<sup>(7)</sup>

### References

- (1) Harder S and Thurmann P, Clinically Important Drug Interactions with Anticoagulants, An Update, *Clinical pharmacokinetics* 1996; 30(6):416-44.
- (2) Adriane FB, Herb-drug interactions, *The Lancet* 2000; 355(9198): 134-8.
- (3) Heck AM, DeWitt BA, Lukes AL, Potential Interactions between Alternative Therapies and Warfarin, *American Journal of Health-system Pharmacy(AJHP)* 2000;57(13):1221-7.
- (4) Lacy CF, Armstrong LL, Goldman MP, Lance LL, Warfarin monograph in LEXI-COMP'S Drug Information Handbook, USA: Lexi-comp Inc, 12<sup>th</sup> ed. 2005.
- (5) Thomson MICROMEDEX, Warfarin monograph, USA: The DRUGDEX System Drug Evaluations (online) <http://www.ekg.org.hk/html/gateway/index.htm> (accessed on 5th April 2006).
- (6) Angelo AI, Giulia DC, Francesca B, Edzaed E, Cardiovascular pharmacotherapy and herbal medicines: the risk of drug interaction, *International Journal of Cardiology* 2005;98:1-14.
- (7) Tatro DS, Drug Interaction Monographs, Drug Interaction Facts, USA: Facts and Comparison, 2006.

# Fatality due to Tetramine (毒鼠強) Poisoning

Case Report

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## Introduction

Rodenticide poisoning is common in HK. Registered rodenticides in HK consist mainly of anticoagulants such as warfarin and superwarfarins. However, it is important to be aware of exceptions.

## History

A 53-year-old man with good past health was found collapsed in a toilet of a public library. A suicidal note and a bag of food residues were found. The ambulance crew noticed tonic clonic convulsions on the way to the emergency department.

## Clinical findings

On admission, he was unconscious and went into cardiac arrest. He was resuscitated and intubated. The Glasgow Coma Scale score was 3/15. No focal neurological sign was detected. General examination otherwise was unremarkable.

## Summary of initial investigations and tentative diagnosis

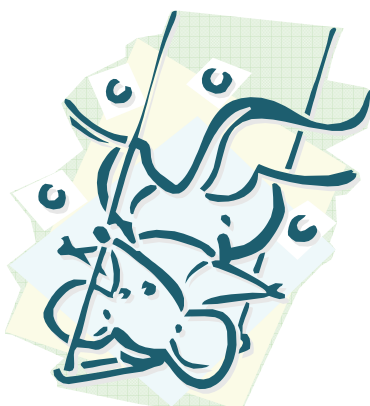
- ★ Arterial blood gases – severe metabolic acidosis (pH 6.338)
- ★ Baseline biochemistry, glucose, ECG and chest X-ray were normal
- ★ Poisoning suspected and emergency toxicology investigation requested

## Further investigation and diagnosis

Hospital Authority Toxicology Reference Laboratory was consulted. Tetramine poisoning was suspected from the clinical history and confirmed in the same day by the demonstration of large amount of tetramine in food residues and high concentration of tetramine in patient's blood and urine.

## Progress

He developed high fever soon after admission, followed by rapid progression of renal and hepatic derangement, disseminated intravascular coagulopathy, rhabdomyolysis, gastrointestinal bleeding and profound shock. He was put on continuous venovenous haemofiltration, but his condition did not improve and finally succumbed the next day.



## Background information on tetramine

Tetramine (tetramethylene disulphotetramine) is an odourless and tasteless rodenticide. Also commonly named as “毒鼠強”, “三步倒” etc, it is a potent neural toxin which acts by binding non-competitively and irreversibly to the gamma-amino butyric acid receptor on neuronal cell

membrane and blocks chloride channels. This leads to excitation of the central nervous system and induces convulsions. It is extremely hazardous, being 100 times more toxic than cyanide.

Tetramine has been banned worldwide because of its lethal toxicity, but repeated outbreaks of poisoning continue to occur in Mainland China. Sporadic cases have also been reported in the United States and recently in Hong Kong.

Symptoms of nausea, vomiting, abdominal pain, and reduced level of consciousness with convulsions 10 to 30 mins after ingestion are typical of tetramine poisoning. Severe poisoning results in coma and death from respiratory and multi-organ failure. The unique features of tetramine poisoning are the rapid onset of convulsions that are difficult to control, multi-organ failure and high mortality.

Laboratory confirmation requires detection of tetramine in the blood, vomitus or urine of suspected victims. Severity of poisoning is related to the blood tetramine level. Routine toxicology does not currently screen for tetramine which will go undetected unless specific assays are employed.

Treatment includes elimination of tetramine by gastric lavage and activated charcoal, seizure control with anticonvulsants, and various supportive measures. There is no established antidote but the use of sodium dimercaptopropane sulphonate (Na-DMPS) is advocated by experts. Haemoperfusion and haemofiltration may reduce mortality and morbidity if commenced within 12 hours of ingestion.

## Conclusion

Tetramine is a lethal rodenticide not registered in HK. It acts rapidly to produce prolonged convulsions leading to multi-organ failure. A few cases of tetramine poisoning have been reported locally. Early recognition and treatment are essential and health care workers should be alert for this toxin.

## Acknowledgements

A more detailed account of this case has been published in the Hong Kong Medical Journal. We have obtained the kind permission from the Hong Kong Medical Journal to use the material for this educational purpose.

## Further readings

- (1) Poon WT, Chan K, Lo MH, Yip KK, Lee T, Chan AY. A case of tetramine poisoning: a lethal rodenticide. Hong Kong Med J. 2005; 11: 507-9.
- (2) Food and Environmental Hygiene Department. Anti-rodent Measure. [http://www.fehd.gov.hk/safefood/library/rodent/images/anti\\_rodent\\_measure.pdf](http://www.fehd.gov.hk/safefood/library/rodent/images/anti_rodent_measure.pdf) (accessed on 15 Jan 2006)



# Toxicological Surveillance

There were 995 cases of poisoning (excluding infective food poisoning) recorded by the Accident & Emergency Departments of 6 acute regional hospitals during the period from 1 July to 31 December 2005. The male to female ratio is approximately 2:3. The age distribution of patients is shown in Figure 1.

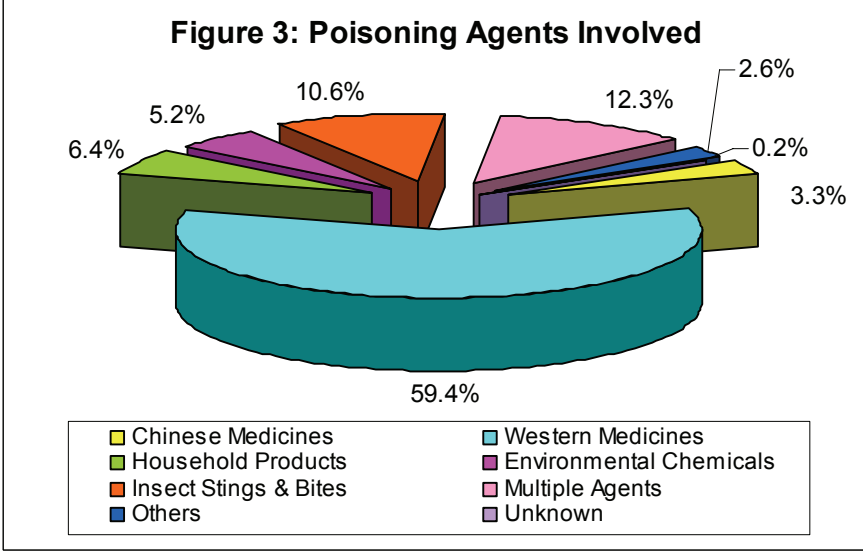
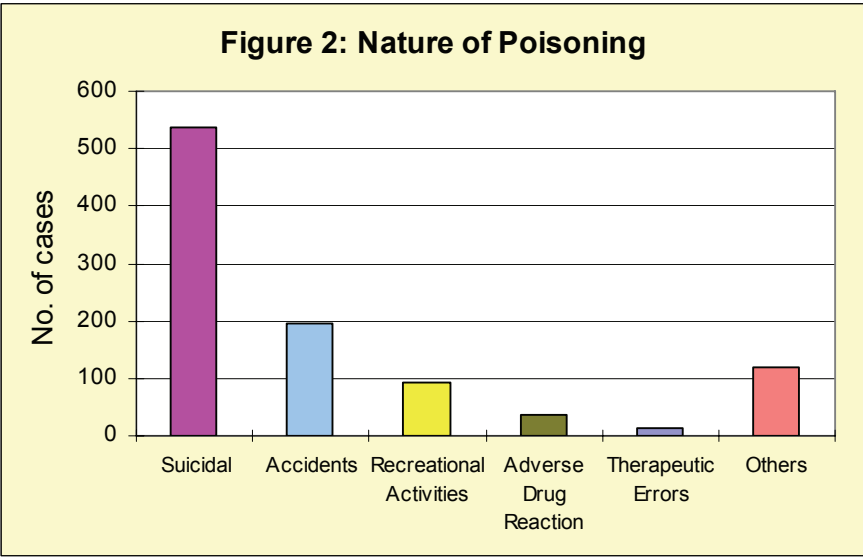
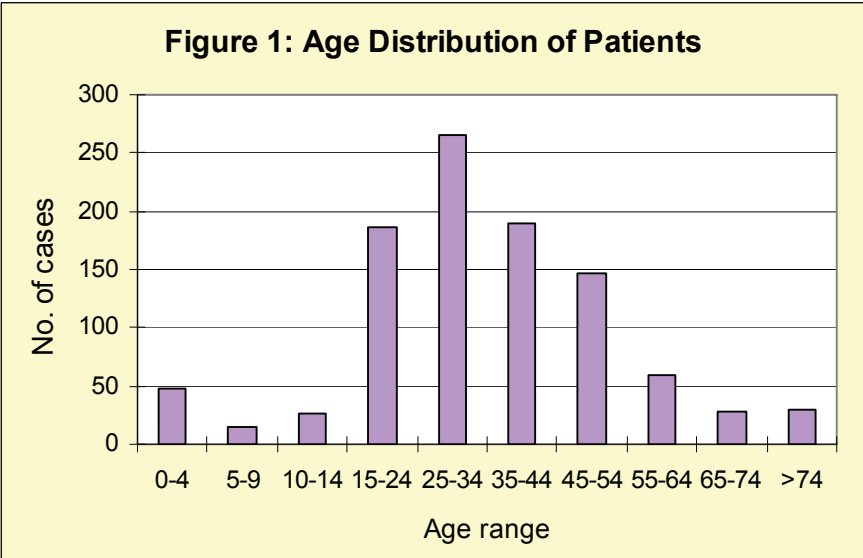
Over half of the poisonings (54%) occurred at home while 4% occurred at workplaces. The place of exposure for the rest of the cases was either unknown or others.

More than half of all cases (54%) were suicidal in nature while 20% and 9% of the cases were due to accidents and recreational activities respectively (Figure 2).

Western medicines, accounting for 59% of cases, remained the most common poisoning agent. 12% of poisoning cases involved the use of multiple agents, such as the use of Western medicines together with household products, while insect stings and bites, household products, and environmental chemicals accounted for 11%, 6% and 5% of the cases respectively (Figure 3). Examples of environmental chemicals were toxic gases like carbon monoxide and sulphur dioxide; alcohols like ethanol and isopropyl alcohol; and agricultural products like diazinon.

For cases due to Western medicines, the most common poisoning agents were benzodiazepines and related compounds (e.g. midazolam and zopiclone) (31%), followed by antidepressants (e.g. amitriptyline and paroxetine) (12%) and paracetamol (11%) as detailed in Table 1.

For cases due to the use of Chinese medicines, about 69% of the poisoning agents were proprietary Chinese medicines while 31% were Chinese herbal medicines.





Two cases of death were reported between September and December 2005. The first case involved a 50-year-old woman who committed suicide by ingesting antidiabetics. The other case involved a 15-year-old girl, who had taken ecstasy before being found unconscious. She succumbed shortly after admission to hospital.



**Table 1 Cases related to western medicines**

Pharmaceutical	Percentage (%)
Benzodiazepines and related compounds	31
Antidepressants	12
Paracetamol	11
Anticholinergics and Antihistamines	7
Central stimulants	5
Antipsychotics	5
Opioids	5
Cardiovascular drugs	4
Flu and cold medication	3
NSAIDs	3
Others*	14

\* included antimicrobials, anticonvulsants, anticoagulants, antidiabetics, gastrointestinal drugs, vitamins and minerals supplements.

### Hong Kong Poison Information Centre

The Hong Kong Poison Information Centre (HKPIC) provides health care professionals with information and advice on the diagnosis and management of acute and chronic poisoning by drugs, chemicals, household products, health products, herbal medicines or natural toxins. Urgent consultation service is provided by phone during the operating hours, while non-urgent consultations and enquiries can be made by facsimile or E-mail at any time.

The hours of operation and contact details of the HKPIC are as follows:

Operating hours	9 am to 9 pm daily
Telephone	2635 1111
Facsimile	3513 5649
E-mail	hkpic@ha.org.hk

Please feel free to contact Dr FL LAU, Director of the HKPIC at 3513 5089 for matters related to the HKPIC.

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