2023

International Symposium November 17th & 18th for Poison Control and Research Development

Taiwan Poison Control Center 臺北榮總毒藥物防治諮詢中心

Symposium Manual

指導單位：
衛生福利部、環境部化學物質管理署

INDEX

Agenda

Abstracts

About Taiwan Poison Control Center & Contact Us

FRIDAY 17th NOV 2023 MORNING

08:00 – 08:20 Registration & Opening Remarks

08:20 – 10:20 Section 1: Occupational Exposure and Clinical Toxicology

Moderator: Dr. Jou-Fang Deng, TVGH, *Taiwan* & Dr. Hsien-Yi Chen, CGMH, *Taiwan*

08:20 – 08:30 1-bromopropane (1-BP) poisoning
[10 min]
Dr. Te-Hao Wang, NYCUH, *Taiwan*

08:30 – 09:00 Neurotoxicity of 1-bromopropane
[30 min]
Prof. Gaku Ichihara, Tokyo University of Science, *Japan*

09:00 – 09:20 Death as a blue man: refractory methemoglobinemia after N,N-dimethyl-p-toluidine ingestion
[20 min]
Dr. Chih-Yang Mao, CGMH, *Taiwan*

09:20 – 09:45 E-commerce causing new poisoning from cyanide to gold cyanide
[25 min]
Prof. Winai Wananukul, Ramathibodi Poison Center, *Thailand*

09:45 – 10:20 Glyoxylate treatment restores redox balance and rescues mitochondrial toxicity
[35 min]
Prof. Randall T. Peterson, University of Utah, *U.S.A.*

10:40 – 12:10 Section 2: Occupational Exposure and Clinical Toxicology

Moderator: Professor Winai Wananukul, *Thailand* & Professor Yoshito Kamijo, *Japan*

10:40 – 10:50 Metformin acidosis
[10 min]
Dr. Chien-Lin Chang, TVGH, *Taiwan*

10:50 – 11:20 Lactic acidosis construct
[30 min]
Dr. Luke Yip, Centers for Disease Control and Prevention, *U.S.A.*

11:20 – 11:45 Use of a semi-quantitative urine drug testing method to aid in the diagnosis of suspected tramadol overdose
[25 min]
Dr. Chun-Man Chan Jones, Prince of Wales Hospital, *HK*

11:45 – 12:10 Over-the-counter (OTC) drug dependence and overdose among young generations in Japan
[25 min]
Prof. Yoshito Kamijo, Saitama Medical University Hospital, *Japan*

FRIDAY 17th NOV 2023 AFTERNOON

13:30 – 13:40 Opening Remarks

13:40 – 15:40 Section 3: Taiwan - Czech Republic Bilateral Clinical Toxicology Forum

Moderator: Professor Chen-Chang Yang, TVGH, *Taiwan* & Professor Daniela Pelclová, *Czech Republic*

13:40 – 14:10 Occupational intoxications in the Czech Republic in the past 50 years
[30 min]
Prof. Daniela Pelclová, Charles University, *Czech Republic*

14:10 – 14:40 Occupational intoxications in Taiwan
[30 min]
Dr. Jou-Fang Deng, TVGH, *Taiwan*

14:40 – 15:10 History and functions of the Toxicological Information Centre in the Czech Republic
[30 min]
Dr. Kateřina Kotíková, General University Hospital, *Czech Republic*

15:10 – 15:40 The function and role of Taiwan Poison Control Center
[30 min]
Professor Chen-Chang Yang, TVGH, *Taiwan*

16:00 – 17:40 Section 4: Taiwan - Czech Republic Bilateral Clinical Toxicology Forum

Moderator: Dr. Cheng-Chung Fang, NTUH, *Taiwan* & Dr. Kateřina Kotíková, *Czech Republic*

16:00 – 16:25 Trends in use of antidotes and antisera from Toxicologic Information Centre for the Czech Republic
[25 min]
Mgr. Milada Běhounková, General University Hospital, *Czech Republic*

16:25 – 16:50 The antidote preparedness and network supply in Taiwan
[25 min]
RPh. Hsiang-Ling Chen, TVGH, *Taiwan*

16:50 – 17:15 Selected addictive substances in the Czech Republic – trends recorded by Toxicological Information Centre
[25 min]
Mgr. Michal Čečrle, General University Hospital, *Czech Republic*

17:15 – 17:40 Recreational use of New Psychoactive Substances (NPS) in Taiwan
[25 min]
Dr. Cheng-Chung Fang, NTUH, *Taiwan*

17:40 – 18:00 Panel Discussion & Closing remarks

SATURDAY 18th NOV 2023 MORNING

08:00 – 08:20 Registration & Opening Remarks

08:20 – 10:15 Section 1: Molecular Biochemical Toxicology, Chemical Warfare and Heavy Metal

Moderator: Dr. Luke Yip, *U.S.A.* & Professor Shih-hung Tsai, TSGH, *Taiwan*

08:20 – 08:50 Identification of small molecules rescuing doxorubicin induced cardiomyopathy
[30 min]
Prof. Randall T. Peterson, University of Utah, *U.S.A.*

08:50 – 09:20 Thallium poisoning
[30 min]
Dr. Luke Yip, Centers for Disease Control and Prevention, *U.S.A.*

09:20 – 09:45 Sulfur mustard – case report
[25 min]
Colonel Prof. Kai Kehe, Bundeswehr, *Germany*

09:45 – 10:15 Sulfur mustard poisoning – picture linked to molecular toxicology
[30 min]
Colonel Prof. Kai Kehe, Bundesweh, *Germany*

10:30 – 12:00 Section 2: Heavy Metal and Natural Toxin

Moderator: Professor Ravikar Ralph, *India* (virtual) & Dr. Chun-Man Chan Jones, *HK*

10:30 – 10:55 Inorganic mercury exposure following Indian indigenous (Siddha) medicine intake - a rare cause of anti-VGKC antibodies-associated acquired neuromyotonia
[25 min]
Prof. Ravikar Ralph (virtual), Christian Medical College, *India*

10:55 – 11:15 Severe subacute inorganic arsenic poisoning caused by a folk medicine for treatment of psoriasis: A case series
[20 min]
Dr. Chun-Man Chan Jones, Prince of Wales Hospital, *HK.*

11:15 – 11:40 Role of poison information centers in management of complex snakebite envenoming cases in India through remote consultation: an illustrative case-series from a national-level poison center
[25 min]
Dr. Jambugulam Mohan (virtual), Christian Medical College, *India*

11:40 – 12:00 Role of Taiwan Poison Control Center in snakebite envenomation
[20 min]
Dr. Kai-Wen Cheng, TVGH, *Taiwan*

SATURDAY 18th NOV 2023 AFTERNOON

13:20 – 13:30 Opening Remarks

13:30 – 15:45 Section 3: Natural Toxin and Special Lecture

Moderator: Dr. Jou-Fang Deng, TVGH, *Taiwan* & Dr. Dong-Zong Hung, CMUH, *Taiwan*

13:30 – 14:00 POLES Point of Care Ultrasonography (POCUS) for local envenomation from snakebite
[30 min]
Dr. Cheng-Hsuan Ho, TSGH, *Taiwan*

14:00 – 14:40 The neurology of snakebite
[40 min]
Prof. Sir David A. Warrell, University of Oxford, *UK*

14:40 – 15:20 Marine stings
[40 min]
Prof. Sir David A. Warrell, University of Oxford, *UK*

15:20 – 15:45 Characteristics of clinical manifestations of botulism in Vietnam between 2020-2023
[25 min]
Dr. Doãn Uyên Vy Vanessa, Cho Ray Hospital, *Vietnam*

15:45 – 16:00 Panel Discussion & Closing remarks

1-bromopropane (1-BP) poisoning

正溴丙烷中毒

Dr. Te-Hao Wang 王德皓醫師

Visiting staff,
Department of Emergency Medicine,
National Yang Ming Chiao Tung University Hospital,
Yilan, Taiwan
國立陽明交通大學附設醫院急診醫學科主治醫師

1-bromopropane (1-BP) is an alternative to ozone-depleting solvent that is used in degreasing, dry cleaning, spray adhesives, and aerosol solvents. Occupational exposure to 1-BP is associated with adverse peripheral sensory, motor, and central nervous system effects. We report our Health Hazard and Medical Evaluation of 6 patients with neurotoxicity associated with occupational exposure to 1-BP in Taiwan.

正溴丙烷(1-BP)自 2007 年美國政府公告為合法使用於金屬清洗、電子產品清洗及精密儀器清洗，用來替代破壞臭氧層物質包括三氯乙烷和氯氟烴碳化物的新興溶劑，並曾於台灣使用作為替代新興溶劑；臺北榮民總醫院毒藥物諮詢中心曾於接獲南部醫院諮詢，檢查追蹤發現為有機溶劑正溴丙烷造成之神經毒性，並後續建立職業病診斷指引；研討會藉由此群聚中毒事件介紹溴丙烷的中毒病患的特性及暴露危害。

Neurotoxicity of 1-bromopropane

正溴丙烷之神經毒性

Professor Gaku Ichihara 市原 学 教授

Professor,
Department of Occupational and Environmental Health,
Faculty of Pharmaceutical Sciences,
Tokyo University of Science,
Tokyo, Japan

In 1995, case series of reproductive and hematopoietic disorders were reported in Korea after replacement of freon with an alternative of 2-bromopropane. Subsequently to animal studies revealing reproductive and hematopoietic toxicity of 2-bromopropane in rats, a comparative study of 2-bromopropane and 1-bromopropane demonstrated more potent neurotoxicity of 1-bromopropane compared to 2-bromopropane. The first case of 1-bromopropane intoxication was reported in United States, and the report referred to our animal experiment showing 1- bromopropane neurotoxicity. Human cases of peripheral neuropathy or encephalopathy after exposure to 1-bromopropane were reported also in North Carolina and Utah, USA, Taiwan and Japan. Biopsy of sural nerve from a human case demonstrated degeneration of myelin sheath, which was very similar to the change in peripheral nerve of the rats exposed to 1-bromopropane. As the workers reported depression and cognitive dysfunction after exposure to 1-bromopropane, we investigated the effect of 1-bromopropaen on the density of noradrenergic or serotonergic axons in the brain of rats and revealed that exposure to 1-bromopropane specifically reduced the density of noradrenergic axons int the brain. We further compared proteomic profiles between 1-bromopropane and acrylamide, as both chemicals have similar toxicities, as shown by human case reports, histopathological studies, and similar chemical reactivities as soft electrophiles. The study revealed similar proteomic profiles between them, thus the study on 1-bromopropane can be generalized into understanding neurotoxicity of variety of environmental electrophiles. Further studies also revealed role of microglia in 1-bromopropane or acrylamide-induced encephalopathy and role of inflammatory signals in induction of electrophile-induced encephalopathy.

Key words: 1-brompopane, neuropathy, encephalopathy, electrophile

1995 年，在韓國以異溴丙烷(2-BP)替代氟利昂之後，出現了一系列生殖和造血系統疾病的個案報告。在許多的動物研究發現異溴丙烷對大鼠的生殖和造血系統毒性後，進一步的研究比較了正溴丙烷(1-BP) 和異溴丙烷的神經毒性，結果顯示正溴丙烷的神經毒性比異溴丙烷更強。在美國報告的第一例人類正溴丙烷中毒的案例中，引用了我們所發表的正溴丙烷造成的神經毒性研究。接著在美國的北卡羅納州、猶他州、台灣及日本，陸續報告了人類因暴露正溴丙烷而出現周邊神經病變或腦病變的報告。其中一中毒案例的腓腸神經切片組織中，出現髓鞘的退化；這與大鼠動物實驗中周邊神經的變化非常相似。在部分職業暴露正溴丙烷的個案中，曾出現憂鬱和認知功能障礙，因此我們研究了正溴丙烷對大鼠腦部正腎上腺素神經元或血清素神經元軸突密度的影響，並發現暴露於正溴丙烷時會特別降低其密度。接著我們進一步比較了正溴丙烷和丙烯醯胺之間的蛋白質體學，因為這兩種化學物質在人類病例報告、組織病理學研究以及親電子反應中，表現出相似的化學反應及毒性。該研究顯示了它們之間的蛋白質體學相似，因此對正溴丙烷的研究可延伸至各種環境親電體的神經毒性。研究還顯示微膠細胞在正溴丙烷或丙烯醯胺導致的腦病變中之作用角色，以及發炎訊號在親電體引起的腦病變誘導中的作用。

Death as a blue man: refractory methemoglobinemia after N,N-dimethyl-p-toluidine ingestion

N, N - 二甲基對甲苯胺中毒引起的變性血紅素血症

Dr. Chih-Yang Mao 毛志揚醫師

Emergency chief resident,
Linkou Chung Gung Memorial Hospital,
Taoyuan, Taiwan
林口長庚紀念醫院急診醫學部急診醫學科總醫師

Introduction:

N,N-Dimethyl-p-toluidine (DMPT) is a widely used high-production-volume chemical that serves as a polymerization accelerator in the production of bone cements and dental materials. Despite its common use, there is limited information available regarding human DMPT poisoning.

Case report:

A 27-year-old Thai man attempted suicide by ingesting 30 mL of a DMPT solution (Thermo Scientific Chemicals 99%, CAS 99-97-8). He rapidly developed dyspnea and was promptly taken to a local hospital emergency department (ED). Upon arrival, he was conscious but cyanotic, and his vital signs were: body temperature 36.9℃, heart rate 132 beats/min, blood pressure 213/122 mmHg, respiratory rate 18 breaths /min, and oxygen saturation (measured by pulse oximetry, SpO2) at 88%. An immediate administration of a non-rebreathing mask was initiated. Blood gas analysis revealed: pH 7.47, PaO2 367 mmHg and calculated oxygen saturation 99.8%. Laboratory results indicated a methemoglobin level of 25.1%. Due to the unavailability of methylene blue, the patient was intubated, administered activated charcoal, and transferred to a medical center, where he received 150 mg of methylene blue (approximately 2 mg/kg) in the ED. The methemoglobin level just prior to methylene blue administration was 48%. After antidote therapy, his cyanosis diminished, and SpO2 improved to 99% within10 min. However, he experienced a recurrence of cyanosis, and his methemoglobin level rebounded to 30% in three hours. Glucose-6-phosphate dehydrogenase activity was assessed and found to be within normal range. Additional methylene blue treatment was administered, cumulating to a total dose of 7 mg/kg, but the methemoglobin level went even

higher to a peak of 73%. Subsequently, exchange transfusion was initiated, and a high dose intravenous vitamin C (1g every 6 hours) was administered; however, the patient's response was inadequate. He subsequently developed acute liver injury, acute kidney injury, hemolysis, hypotension, and died 3 days after ingestion.

Discussion:

The precise mechanism underlying DMPT toxicity remains incompletely elucidated. In vitro studies have suggested that induction of methemoglobinemia could be attributed to the biochemical transformation of DMPT into a toxic metabolite p-methylphenylhydroxylamine, an analog of aniline's metabolite phenylhydroxylamine which is considered responsible for methemoglobinemia observed in aniline poisoning. Information regarding the pharmacokinetics of DMPT is also limited. The refractory methemoglobinemia observed in our patient is probably due to the high toxic burden and redistribution of DMPT.

Conclusion:

Ingestion of DMPT can lead to refractory methemoglobinemia. Further research should prioritize exploring the mechanism of its toxicity and its pharmacokinetics to deepen our understanding of DMPT-related toxicity.

簡介：

N,N-二甲基對甲苯胺（N,N-Dimethyl-p-toluidine, DMPT）是一種工業化學用品，通常用作骨水泥和牙科材料製造過程中的加速聚合劑。過往極少有 DMPT 中毒的案例。

案例：

一名 27 歲的泰國男性企圖自殺，他攝入了 30 毫升的 DMPT 溶液（Thermo Scientific Chemicals 99%，CAS 99-97-8）。隨即出現呼吸困難，被送往當地醫院急診室。到達時意識清醒但呈現發紺狀態，生命徵象：體溫 36.9℃，心率 132 次/分鐘，血壓 213/122 毫米汞柱，呼吸率 18 次/分鐘，血氧飽和度（SpO2）88%。立即給予非再吸入型面罩。動脈血氧分析顯示：pH 7.47, PaO2 367 mmHg，計算的血氧飽和度為 99.8%。實驗室數據顯示變性血紅素數值為 25.1%。由於缺乏甲烯藍解毒劑，經插管及給予活性碳治療後，被轉送至醫學中心，到院後給予 150mg 甲烯藍（約 2mg/kg）。給藥前變性血紅素的數值為 48%。治療後 10 分鐘內，他的發紺改善，SpO2 達到 99%。然而，3 小時後再度出現發紺，變性血紅素之數值再次上升至 30%。Glucose-6-phosphate dehydrogenase(G6PD)活性檢查結果顯示正常。我們給予了更

多的甲烯藍，累積劑量到達 7mg/kg，但變性血紅素的數值持續上升，甚至高達 73%。我們後續進行交換輸血並給予高劑量維生素 C 治療（每 6 小時靜脈注射 1 克），但治療效果仍不佳。病患後續發生急性肝損傷、急性腎衰竭、溶血、低血壓，最終在攝入 DMPT 後的第 3 天死亡。

討論：

關於 DMPT 毒性的確切機制尚未完全了解。體外研究顯示，引起變性血紅素血症可能是由於其轉化為有毒代謝物 p-methylphenylhydroxylamine，此化合物與被認為在苯胺中毒中導致變性血紅素血症的代謝物 phenylhydroxylamine 極為相似。DMPT 的藥物動力學資訊仍有限。此案例觀察到的頑固性變性血紅素血症可能是由於 DMPT 的高毒性和毒藥物的再分布所致。

結論：

攝入 DMPT 可能導致反覆且難以治療的變性血紅素血症。未來可針對其作用機制和藥物動力學進行相關研究，以加深我們對 DMPT 毒性的認識。

E-commerce causing new poisoning from cyanide to gold cyanide

引起罕見中毒的網購商品：氰化物與氰化金

Professor Winai Wananukul

Professor of Medicine,
Head, Department of Medicine,
Director, Ramathibodi Poison Center,
Division of Clinical Pharmacology and Toxicology,
Department of Medicine,
Faculty of Medicine Ramathibodi Hospital, Mahidol University
Bangkok, Thailand

The availability of toxic substances through e-commerce poses a challenge for the prevention and management of poisoning cases. This abstract reports on four incidents of gold cyanide poisoning in Thailand, which is a rare and previously unknown type of poisoning in this country. The patients acquired gold cyanide online after the authorities restricted the access to cyanide products following a series of 14 suspected homicides by cyanide. The clinical manifestations and treatment of gold cyanide poisoning differ from those of cyanide poisoning and will be discussed in detail. Two of the patients died despite timely intervention. It highlights the need for health care professionals to be prepared for new and uncommon forms of poisoning due to e-commerce.

透過網購取得有毒物質並引起中毒案件，對於預防和管理中毒事件帶來了很大的挑戰。本文摘要了泰國發生的四起氰化金中毒案件，這在泰國是一種罕見且先前未知的中毒型別。在發生了 14 起懷疑使用氰化物的殺人案後，政府限制了氰化物產品的購買可及性。然而，本報告的案例是透過網路購買了氰化金，氰化金中毒的臨床表現和治療方法與氰化物中毒有所不同，詳細內容將在本演講中進一步討論。儘管進行了及時的處置，仍然有兩名患者因此而死亡。因此，醫療專業人員需要做好準備，以應對由網購引起的新興和不常見的中毒情況。

Glyoxylate treatment restores redox balance and rescues mitochondrial toxicity

乙醛酸治療：恢復細胞氧化還原平衡並解救粒線體因中毒造成的失能

Professor Randall T. Peterson

L. S. Skaggs Presidential Endowed Chair,
Professor, Pharmacology and Toxicology,
Adjunct Professor, Biochemistry,
Dean, College of Pharmacy, University of Utah,
Salt Lake City, Utah, U.S.A.

Compounds with cyanide antidote activity have been identified previously, but all function via stoichiometric reaction with free cyanide to form a less-toxic cyanide complex. As such, these cyanide scavengers work at stoichiometric doses and only prior to cyanide interacting with its target proteins. Furthermore, existing cyanide antidotes are delivered intravenously over 15-20 minutes, reducing their utility for field deployment. A cyanide countermeasure that did not rely solely on scavenging of free cyanide would be a highly valuable addition to the countermeasure arsenal because it could potentially 1) be effective at sub-stoichiometric doses, 2) be used in combination with existing scavenging agents, and 3) provide benefit even after cyanide had bound to its cellular targets. The endogenous metabolite glyoxylate was found in a phenotypic screen to rescue zebrafish from cyanide toxicity. Glyoxylate was also found to be effective in preventing cyanide-induced death in established cyanide assays in mice, rabbits, and pigs. Unlike approved cyanide countermeasures, glyoxylate can be delivered by intramuscular injection in a small volume compatible with future autoinjector delivery. Glyoxylate appears to be well tolerated and to function via a novel mechanism involving transformation by lactose dehydrogenase (LDH) to normalize the disrupted mitochondrial and cytoplasmic NADH:NAD^+ ratios in cyanide-exposed animals. Therefore, glyoxylate represents a promising new type of countermeasure that functions via metabolic modulation and holds potential for development as an effective, rapidly-delivered cyanide countermeasure.

過去已確認出具氰化物解毒劑活性的化合物，但均需透過與遊離氰化物進行化學反應形成較低毒性的氰化物複合物來發揮作用。這些化合物除了需在化學當量劑量下才能起作用，並且需在氰化物與其目標蛋白質相互作用之前起作用。此外，目前的氰化物解毒劑需要透過靜脈注射 15-20 分鐘時間才能發揮作用，這降低了在戰場上使用這些解毒劑的實用性。因此，若有不完全依賴清除游離氰化物的輔助治療方式具有潛在的優勢。這種新型對策可以帶來以下幾個潛在的好處：(1) 可以在低於化學當量劑量下發揮作用 (2) 可與現有解毒劑併用 (3) 即使在氰化物與其細胞標靶結合後也能提供益處。在表型篩選中我們發現了內源性代謝物乙醛酸，可以援救斑馬魚免受氰化物毒性。乙醛酸在小鼠、兔子和豬的氰化物測試中也被發現可以有效預防氰化物中毒導致的死亡。與現有的氰化物治療對策不同，乙醛酸可以透過以小劑量肌肉注射，適用於自動注射器的給藥方式。乙醛酸似乎具有良好的耐受性，並透過乳酸脫氫酶轉化為新的機制發揮作用，改善了暴露氰化物的動物中受損的粒線體和細胞質的 NADH : NAD^+比值。因此乙醛酸透過代謝調節發揮作用，可作為一種新型、有效且可以快速給予的氰化物中毒治療對策，具有十足的發展潛力。

Metformin acidosis

Metformin 引起的乳酸血症

Dr. Chien-Lin Chang 張建林醫師

Chief Resident,
Department of Gastroenterology Medicine,
Taipei Veterans General Hospital,
Taipei, Taiwan
臺北榮民總醫院內科部胃腸肝膽科總醫師

Metformin associated lactic acidosis (MALA) is a rare complication characterized by nausea, vomiting, abdominal pain, dyspnea, dizziness, and general malaise. Its presentation is usually acute. Usually seen in patients with acute-on-chronic kidney disease, the presentation of MALA in healthy patients is rare. We present metformin-associated lactic acidosis in a 64-year-old woman with an underlying disease of hypertension, type 2 DM, and chronic kidney disease who suffered from acute nausea, vomiting, abdominal pain, and respiratory failure. After admission, the blood test revealed metabolic acidosis and hyperlactatemia. The patient underwent continuous veno-venous hemodiafiltration (CVVH) and received intubation for respiratory failure. Recovery was observed after the above supportive treatment and then the endotracheal tube was successfully removed. The patient was discharged under stable conditions.

Metformin 相關乳酸中毒是一種罕見的併發症，在臨床上其症狀通常表現為急性的噁心、嘔吐、腹痛、呼吸急促和全身虛弱。併發症通常發生在患有慢性腎臟疾病並突然出現急性腎功能惡化的患者身上，對於一般健康的人來說比較少見。本次演講中，將分享一名 64 歲女性的病例，她患有高血壓、糖尿病和慢性腎臟病，在使用 metformin 後產生了乳酸中毒。因急性的噁心、嘔吐、腹痛和呼吸衰竭接受住院治療。血液檢查結果顯示代謝性酸中毒和高乳酸血症。為了治療此併發症，患者接受了連續靜脈血液過濾透析並因呼吸衰竭，需要插管治療。在接受了上述的支援性治療後，患者逐漸康復，並成功拔管、脫離呼吸器。她的病情穩定後順利出院。

"Lactic acidosis" construct

乳酸中毒的正確觀念

Dr. Luke Yip

Medical Officer & Senior Advisor for Medical Toxicology,
US Department of Health and Human Services,
Centers for Disease Control and Prevention,
Office of Non-communicable Diseases, Injury, and Environmental Health,
National Center of Environmental Health/ATSDR,
Atlanta, Georgia, U.S.A.

Hyperlactatemia and *metabolic acidosis* are the hallmark of anaerobic metabolism, a reflection of mitochondrial exhaustion or failure, which is often perverted to "lactic acidosis." The construct of "lactic acidosis," lactate production releases net protons and causes acidosis/academia, is a misleading concept. In actuality cellular metabolism produces the acid salt form of lactate, not the acid form that releases a net H^+. Thus, lactate is not a source of H^+ and does not cause or contribute to metabolic acidosis. To better understand this, we begin with a review of the biochemistry and metabolic pathways involved in lactate metabolism, discuss the genesis of net H^+ production, H^+ handling in steady state, and biochemical reality of "lactic acidosis".

典型的細胞無氧代謝會產生高乳酸血症和代謝性酸中毒，這反映了線粒體的功能障礙，這類型的酸中毒通常被稱為「乳酸中毒」，但此觀念並不完全正確。因酸中毒或酸血症非因乳酸產生後釋放氫離子所引起。實際上，細胞代謝產生的乳酸是乳酸鹽型態，並不是可釋放氫離子的乳酸型態。因此，在酸血症的患者中，乳酸並不是釋放氫離子的來源，也不是引起或促成代謝性酸中毒的原因。本次演講旨在介紹乳酸代謝的生物化學和代謝途徑，討論酸血症中氫離子的來源及處理方式，並探討「乳酸中毒」的實際化學機轉。

Use of a semi-quantitative urine drug testing method to aid in the diagnosis of suspected tramadol overdose

使用半定量尿液藥物測試方法協助診斷懷疑 Tramadol 過量

Dr. Chun-Man Chan Jones 陳俊文醫師

Deputising chief of service,
Department of Medicine & Therapeutics,
Prince of Wales Hospital Poison Treatment Centre, Hospital Authority
Honorary Clinical Supervisor,
Hong Kong College of Family Physicians,
Honorary Clinical Associate Professor,
The Chinese University of Hong Kong,
Hong Kong SAR, China

Objectives:

To describe a semi-quantitative urine drug testing method to aid in the diagnosis of drug overdose when serum drug concentration measurement is unavailable.

Case Report:

A 30-year-old female nurse presented with unexplained episodes of acute impaired consciousness, type-2 respiratory failure, miosis, and convulsions along with mixed metabolic and respiratory acidosis requiring multiple ICU admissions over the course of one year. Her past medical history included idiopathic intracranial hypertension which was resolved with a ventriculoperitoneal shunt. She had chronic headaches and mood disorder without neurological impairment between episodes of impaired consciousness. Repeated cranial imaging studies and lumbar punctures were unremarkable. Comprehensive drug screening of urine samples collected during hospital admissions detected presence of tramadol (Table 1). Repeated episodes of CNS and respiratory depression raised the suspicion of intoxication of substances with opioid-like activity such as tramadol. However, quantitative tramadol measurement of serum sample was unavailable in our hospital, a semi-quantitative method was developed to aid in diagnosis of suspected tramadol overdose.

Table 1. Drugs / metabolites detected by urine drug screening tests (LCMS)

Date	Clinical manifestations	Drugs	Metabolite(s) of drug
31/07/2018	ICU admission	Lamotrigine, paracetamol, tramadol, trazodone, fexofenadine	Clonazepam, tramadol, trazodone, paracetamol
15/06/2018	Asymptomatic	Lamotrigine, paracetmaol, tramadol, piracetam	Clonazepam, trazodone
04/06/2018	ICU admission	Lamotrigine, paracetamol, tramadol, levetiracetam, acetazolamide, amoxicillin	Clonazepam, tramadol
30/05/2018	ICU admission	Lamotrigine, paracetamol, tramadol, levetiracetam, acetazolamide, lidocaine	Cloazepam, tramadol, lidocaine
08/10/2017	Convulsion	Paracetamol, fexofenadine, tramadol, ciprofloxacin	Tramadol

Methods:

A total of 177 convenience urine samples, including the patient's samples, with tramadol/metabolites detected positive by Waters® UPLC® Xevo G2-S TOF Toxicology Screening System during 2017-2018 were reviewed. Methapyrilene was added to all samples as an internal standard. Results were reported as positive when the response count (RC) was ≥3500. The RC is positively correlated with the drug/metabolite concentration although specific calibration was not performed for concentration measurement. The RCs of tramadol were normalized against the RCs of methapyrilene and to urine creatinine level (RCtramadol). A case of known tramadol overdose (500 mg) in which the urine sample collected 13 hours after ingestion was identified from the laboratory database as a comparison.

Results:

The RCtramadol of all urine samples ranged from 0.005 to 14.6. The urine samples of said patient in instances with convulsions and requiring ICU admission were found to have relatively high RCtramadol values (13.7, 7.9, 3.9,

and 3.4); while the RCtramadol of the urine sample was low when she was asymptomatic (0.03). The RCtramadol of the known case of acute tramadol overdose was 8.4.

Conclusion:

This semi-quantitative urine drug testing method may be useful to aid in diagnosis of suspected drug overdose when the serum drug measurement is unavailable. This method is simple and requires no additional demand on the human and laboratory resources.

目的：

描述一種半定量尿液藥物測試方法，以協助在無法進行血清藥物濃度測量時診斷藥物過量情況。

案例：

一名 30 歲的女性護理人員出現了不明原因的急性意識障礙、第 2 型呼吸衰竭、瞳孔縮小和抽搐等症狀，並伴有混合的代謝性和呼吸性酸中毒，一年內反覆多次入住加護病房。她曾患原發性顱內高壓，透過腦室腹膜分流術(V-P shunt)已改善。在多次的意識障礙發作期間，她患有慢性頭痛和情緒障礙，但無神經功能損傷。除此之外，患者進行了多次腦部影像學檢查和腰椎穿刺，結果均無發現異常。住院期間的尿液樣本進行了全面的藥物篩檢，發現了 Tramadol（Table 1）。反覆發作的中樞神經系統和呼吸抑制，引起了我們對類鴉片物質（例如 Tramadol）中毒的懷疑。然而，本院內無法進行血清樣本 Tramadol 的定量檢測，因此開發了一種半定量方法來輔助診斷疑似 Tramadol 過量。

方法：

回顧了 2017 年至 2018 年期間使用 Waters® UPLC® Xevo G2-S TOF 毒物篩檢系統檢測的共 177 個尿液樣本，其中包括該患者的樣本，均呈現 tramadol 及其代謝物陽性反應。為了內部標準化，將 methapyrilene 新增到所有樣本中。當反應計數（response count, RC）大於或等於 3,500 時，結果被報告為陽性。雖然未進行特定校準以測量濃度，但 RC 與藥物及其代謝物濃度呈正相關。RCtramadol 則以 methapyrilene 的 RC 以及尿液中肌酸酐的水平作為標準化。選取了一例已知 tramadol 過量（500 毫克）的病例，使用其服用 tramadol 後 13 小時收集的尿液樣本作為比較。

結果：

所有尿液樣本的 RCtramadol 值範圍從 0.005 到 14.6。在該患者出現抽搐並需要入住加護病房治療時，尿液樣本 RCtramadol 值較高（13.7、7.9、3.9 和 3.4）；而在無症狀時，尿液樣本的 RCtramadol 值較低（0.03）。已知的急性 tramadol 過量病例

的 RCtramadol 值為 8.4。

結論：

當無法進行血清藥物檢測時，這種半定量尿液藥物檢測方法可能有助於懷疑藥物過量的診斷。該方法簡單易行且不需要額外的人力和實驗室資源。

Over-the-counter (OTC) drug dependence and overdose among young generations in Japan

日本年輕世代非處方藥物濫用中毒趨勢

Professor Yoshito Kamijo 上條 吉人 教授

Professor & Head of Clinical Toxicology Center
Department of Clinical Toxicology,
Faculty of Medicine, Saitama Medical University,
Saitama Medical University Hospital,
Saitama, Japan

OTC drugs available in Japan are characterized by a cocktail of various ingredients, including acetaminophen, ibuprofen, dihydrocodeine, dextromethorphan, methylephedrine, diphenhydramine, bromovalerylurea, caffeine, etc. For any of these products, prescription is not required, face-to-face sales by pharmacists are not required, and internet purchases are also available. The Corona Disaster has made it difficult to visit a hospital despite symptoms such as fever and cough, and demand for OTC drugs has increased. Meanwhile, the number of patients dependent on OTC drugs has rapidly increased especially among young generations. Among patients with drug-related disorders who visited psychiatric facilities in Japan, the ratio of patients who were primarily dependent on OTC-drugs increased approximately six-times between 2012 and 2020. Among patients with drug-related disorders who presented at psychiatric facilities in 2020, younger generations were more dependent on OTC-drugs, while older generations were more dependent on hypnotics or anxiolytics mainly including benzodiazepine receptor agonists. Among patients with drug-related disorder who were treated in psychiatric facilities in Japan, about half of patients were dependent on novel psychoactive substances (NPSs) and few patients were dependent on OTC-drugs in 2014. Afterward, the ratio of patients dependent on NPSs decreased rapidly mainly because of enhanced enforcement, but that of patients dependent on OTC-drugs increased rapidly. In 2020, more than half of patients were dependent on OTC-drugs and few patients were dependent on NPS. Among patients who were transported to our center after overdosing drugs, the ratio of patients who overdosed OTC-drugs increased markedly, especially among teenagers. In 2020, 60% of teenage patients overdosed OTC-drugs.

We studied the degree of drug-dependence and suicidality, and socio-psychological characteristics of patients transported to our center after overdosing OTC-drugs between April 2021 and October 2022. As a result, 64% of patients participated were females. The mean age of patients was 24.3 years and median age was 21.0 years. So, most patients were in their teens and twenties. The results of the DAST-20, which assesses the severity of OTC-drug dependence, showed 64% were mildly dependent on OTC-drugs. While 36% were moderately or severely dependent, requiring outpatient or hospitalized care. In addition, 28% routinely overdosed OTC-drugs, suggesting that their dependence on OTC-drugs had progressed considerably. A total score of 10 or higher on the "Suicide Risk" section of the M.I.N.I. is considered "high suicide risk." The results of this survey showed a very high mean score of 25.6 points and median score of 29.0 points, suggesting that their suicide tendency is so serious. Questioned about social activities, 52% were students, and 32% were full-time workers, meaning that most patients (80%) were socially active. Questioned about triggers or motives that lead to overdosing OTC-drugs, health problems were the most common (30%), followed by work problems (20%), school problems (15%), love affair problems, and economic problems. This study suggests that young people who had difficulty living with various psychosocial problems but somehow managed to lead a social life overdosed OTC-drugs as a means of suicide, to relieve discomfort, or to forget about their painful situation. It is important to understand that an "overdose of OTC-drugs" is a psychological condition at high risk of suicide and to provide support for the diverse psychosocial problems faced by young people.

日本市面上的非處方藥物具有混合多種藥物的特性，可能成分包含乙醯胺酚(acetaminophen)、布洛芬(ibuprofen)、二氫可待因(dihydrocodeine)、右美沙芬(dextromethorphan)、甲基麻黃鹼(methylephedrine)、苯海拉明(diphenhydramine)、溴化纈草酸尿素(bromovalerylurea)、咖啡因(caffeine)等成份，無需處方、不需由藥師實體販售，可透過網路進行購買。新冠疫情期間，民眾即使有發燒、咳嗽等症狀，也很難就醫，對非處方藥物的需求因而增加；同時，特別是年輕世代中，非處方藥物濫用人數也迅速攀升。於 2012-2020 年間，日本因藥物相關問題於精神科機構就診的患者中，非處方藥物濫用的比例增加約六倍。2020 年的數據顯示：年輕世代多依賴非處方藥物，而年長世代多依賴安眠藥或抗焦慮藥物（主要為作用於「苯二氮平受體」的安眠藥物/BZRAs)。因藥物相關問題於精神科機構接受治療的患者中，有一半以上與濫用新興影響精神物質（NPS）有關，2014 年間幾乎沒有濫用非處方藥物患者，後因對 NPS 濫用問題加強執法之故，NPS 濫用人數急速下降，而非處方藥物濫用人數則迅速增加，2022 年時，一半以上的患者為非處方藥物濫用，而 NPS 濫用人數則很少。

在我們毒物中心過量服用藥物的患者中，過量服用非處方藥物過的比例顯著增加，尤其是在青少年之間（2020 年時有 60%青少年因過量服用非處方藥物前來就診）。調查於 2021 年 4 月至 2022 年 10 月之間，因過量服用非處方藥物而被送至中心的患者在藥物濫用程度、自殺傾向及社會心理特質等情形，結果顯示：參與研究的患者中有 64%為女性，患者的平均年齡為 24.3 歲，中位數年齡為 21.0 歲，大多數患者處於 10 到 20 多歲之間。使用藥物濫用篩檢量表（DAST-20）評估對非處方藥物濫用程度結果顯示：64%患者濫用情形輕微，而 36%為中度或嚴重濫用患者，需要門診追蹤或住院診療。此外，28%患者經常過量服用非處方藥物，顯示嚴重依賴非處方藥物。經過自殺危險因子評估會談（M.I.N.I. – Mini International Neuropsychiatric Interview）後，這些患者的平均分數為 25.6 分，中位數為 29.0 分，自殺風險相當高（M.I.N.I.評估分數大於等於 10 分表示「高自殺風險」）。問及社交活動部分，52%的患者是學生，32%是全職工作者，這意味著大多數患者（80%）在社交方面是活躍的。至於導致過量使用非處方藥物的觸發因素或動機，健康問題最為常見（30%），其次是工作問題（20%）、學校問題（15%）、感情問題和經濟問題。本研究表明：年輕人在面對生活中各種心理社會問題時，雖然努力維持社交生活，有些人會以過量使用非處方藥物，作為一種自殺、緩解不適或忘卻痛苦處境的方式。理解「過量使用非處方藥物」是一種高自殺風險的心理狀態，並為年輕人所面臨的多種心理社會問題提供支持，這一點至關重要。

Occupational intoxications in the Czech Republic in the past 50 years

捷克過去 50 年職業中毒趨勢

Professor Daniela Pelclová

Physician & Professor,
Toxicological Information Centre,
Department of Occupational Medicine, General University Hospital
First Medical Faculty of the Charles University,
Prague, Czech Republic

Objective:
To describe trends in occupational intoxications in the Czech Republic (population 10.5 million) in the view of a historical perspective.

Methods:
The numbers of occupational intoxications, acknowledged in the Czech Republic by Departments of Occupational Medicine were searched in the records of the Institute of Statistics in the years 1973-2022.

Results:
The number of occupational intoxications declined from 345 in 1973 (10% from all occupational diseases) to 3 cases in 2022 (0.3% of occupational diseases). Main causes in the first decade were poisonings with carbon monoxide (32%), solvents (19%), pesticides (18%), Pb (13%), methemoglobinizing agents (6%), Hg, Cr, CS2, H2S, cyanides or other agents (all 2%). In 2022, two workers were intoxicated by CO, one by isopropyl alcohol. Nowadays, antidotal treatment for metals or pesticides poisonings is needed exceptionally. In the past, two groups of workers were severely intoxicated with permanent chronic consequences, both due to a political pressure. First group were 80 chemical workers, producing defoliant (trichlorophenoxyacetic acid) in 1965-1968, used in Vietnam; and exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) due to a higher working temperature and pressure. They developed chloracne, neuropsychological impairment, hyperlipidemia and/or porphyria. Last 14 workers, examined in 2016, with blood 2,3,7,8-TCDD level still 112 pg/g lipids (population level 12 pg/g lipids) were compensated for chronic metabolic changes due to 2,3,7,8-TCDD, including atherosclerosis, hypertension, diabetes, and neuropsychological impairment. Second group concerned 50

toluene-exposed rotogravure printers of press exported to Soviet Union in the years 1977-1989, with 3fold excess of workplace toluene concentration above limits (average 1970 mg/m3), who experienced acoustic and visual hallucinations in the workshop; 5 printers were compensated for toxic encephalopathy.

Conclusion:

In past 5 decades, thanks to preventive measures and no political pressure on the factories after 1989, the number of occupational poisonings declined. Occupational medicine was transformed into an outpatient medical field.

Key words: Occupational, intoxications, carbon monoxide, lead, toluene, dioxin

目的：

回顧捷克的職業中毒趨勢（人口 1050 萬）。

方法：

檢索 1973 年至 2022 年間，職業醫學部記錄的職業中毒案例統計資料。

結果：

過去 50 年中，捷克職業中毒的案例數從 1973 年的 345 例（佔所有職業疾病的 10%）下降到 2022 年的 3 例（佔職業疾病的 0.3%）。前十年職業中毒主要原因為一氧化碳中毒（32%）、溶劑中毒（19%）、農藥中毒（18%）、鉛中毒（13%）、會引起變性血紅素的物質中毒（6%）以及汞、鉻、二硫化碳、硫化氫、氰化物或其他物質中毒（皆為 2%）。2022 年時有兩名一氧化碳中毒及一名異丙醇中毒案例。現今，金屬或農藥中毒極需要解毒劑。過去曾經因為政治壓力的緣故，有兩起工人集體中毒事件，最終產生了慢性併發症。其中一起為 1965-1968 年間，於生產越南使用的除草劑（三氯苯氧基醋酸）工廠中的 80 名工人，於高溫及高壓的工作環境下，暴露了 2,3,7,8-四氯雙苯環戴奧辛(2,3,7,8-TCDD)，因而出現了氯痤瘡、神經心理障礙、高血脂症或紫質症。有 14 名工人在 2016 年時，血中 2,3,7,8-TCDD 數值仍達 112 pg/g lipid（平均值為 12 pg/g lipid）獲得了賠償，因 2,3,7,8-TCDD 造成他們有慢性代謝問題，如動脈粥狀硬化、高血壓、糖尿病和神經心理障礙等。第二起事件為 50 名暴露甲苯的凹版印刷工人，該印刷廠的出版品在 1977-1989 年間出口至蘇聯。其工作環境中的甲苯濃度超標 3 倍（平均為 1970 mg/m^3），工人們有視、聽幻覺情形；其中 5 名因中毒導致的腦病變最終獲得賠償。

結論：

過去 50 年裡，受惠於預防措施的實施推廣，加上 1989 年後工業不再受壓於政治因素，職業中毒案例數量有所下降。職業醫學現已轉變為門診醫學領域。

Occupational intoxications in Taiwan

臺灣職業中毒

Dr. Jou-Fang Deng 鄧昭芳醫師

Physician,
Taiwan Poison Control Center,
Department of Occupational Medicine and Clinical Toxicology,
Taipei Veterans General Hospital,
Director, Foundation for Poison Control
Taipei, Taiwan
臺北榮民總醫院職業醫學及臨床毒物部毒藥物防治諮詢中心醫師
毒藥物防治發展基金會董事長

Modern clinical toxicology started in Taiwan in 1985 when both the National Poison Center of Taiwan (PCC-Taiwan) and the Division of Clinical Toxicology located at the Taipei Veterans General Hospital (TVGH) were founded together. The primary function and role of PCC-Taiwan was designed and charged to answer phone inquiries regarding any related exposure to potential toxicants. In 37 years, it provides 24 hours on line answering services to more than 160,000 phone calls made by medical professionals and general public through a designated hotline (+886-2-28717121). In addition to the primary function, the PCC-Taiwan also exercises efforts in carrying out the activities of: (1). Information providing and data collection; (2). Technical assistance in diagnostic identification for toxic substance and its active ingredients; (3). Providing clinical toxicology analytic laboratory service; (4). Technical support to assist the medical care of poisonings; (5). Medical surveillance for poisoning trends; (6). Research and training of clinical toxicology; (7). Creation of antidote supply network; (8). International collaboration. PCC-Taiwan also has been involved in the investigation and research of numerous major poisoning events in Taiwan.

The handling of poisonings related to occupational exposures is one of the important areas which the PCC-Taiwan has been engaged with. Acute toxic gas exposures, heavy metal exposures, organic solvent exposures, aggressive chemical splashes and silica exposures are several fields which have gained more attention in our daily practice. Cases of N-Hexane polyneuropathy, CO poisoning, Hydrogen sulfide poisoning, Chlorine gas poisoning, Ammonia gas poisoning, 1-BP poisoning Dimethylacetamide poisoning, Acetonitrile

poisoning, Caprolactam poisoning, Hydrogen fluoride poisoning and Tetramethylammonium hydroxide poisoning will be demonstrated very briefly and brought up for discussion.

In summary, in daily operation, PCC-Taiwan can serve as a surveillance center in detecting any poisonings related to occupational exposures whether it is chronic or acute. In any situation, as demanded, PCC-Taiwan will exercise technical assistance in the way of diagnosis making and treatment providing as well as an outbreak investigation of occupational poisoning.

History and functions of the Toxicological Information Centre in the Czech Republic

捷克毒物中心歷史及任務角色

Dr. Kateřina Kotíková

Director,
Toxicological Information Centre,
Department of Occupational Medicine, General University Hospital,
Prague, Czech Republic

Established in 1962 at the Department of Occupational Medicine of the General University Hospital in Prague, our Toxicological Information Centre (TIC) is the only toxicological consultation service for the Czech Republic (10.5 million inhabitants).

Initially, it was opened for toxicological consultations from health care professionals, since 1989 it has been also providing telephone advice on poisonings to the public. Czech TIC is a 24/7 service available 365 days a year. The Centre is staffed with trained professionals including physicians and pharmacists answering inquiries about potential poisonings from different sources - pharmaceuticals, chemicals, consumer products, plants, mushrooms, animal toxins, substances of abuse, etc. The total number of full-time positions is 5, divided among 7 employees. Night and weekend services are also provided by colleagues from the Department of Occupational Medicine.

Telephone calls to the TIC are recorded, and data are stored electronically. For answering toxicological inquiries, we use either our own toxicological database created and updated by the staff of the TIC, containing currently more than 70 000 items, or toxicological databases with charged annual subscriptions, (e.g., Toxbase, TOXINZ).

The number of toxicological calls is increasing every year. TIC provided 8 934 consultations in 2002, 14 697 ten years later, in 2012, and 26 601 twenty years later, in 2022. The majority of the calls concern child exposure (58.3 % in 2022). The most frequent cause of poisoning is medication (39.0 % in 2022). Since 2021, we have registered a significant increase in reported self-poisonings in children (up to the age of 15 years) and adolescents (from 16 to 19 years).

Of the total number of 3 270 self-poisonings caused by drugs, paracetamol was most frequently used in children and antidepressants in adolescents. In 2022, 54.7 % of the toxicological calls came from the public, 37.2 % from healthcare professionals, and the rest from various institutions.

In cooperation with the Ministry of Health of the Czech Republic, TIC is responsible for the availability and stocking of unlicensed antidotes, antiinfectives, and antisera for Czech patients. TIC also provides education to students of the Faculty of Medicine of Charles University in Prague. The research findings of Czech TIC are presented at international congresses; since 1964 at EAPCCT (European Association of Poison Centres and Clinical Toxicologists).

Keywords: toxicological centre; the Czech Republic; inquiries; database; antidotes; self-poisoning

捷克共和國於 1962 年在布拉格總醫院的職業醫學科成立毒物諮詢中心(TIC)，並提供全國 1050 萬人民專業之毒物諮詢服務。

起初，TIC 僅對醫護專業人員提供諮詢服務，自 1989 年起，增加服務對象為全國人民，並且 24 小時、全年無休提供諮詢服務。TIC 的組成為受過訓練的專業人員，包括醫生及藥師，可提供不同中毒問題的諮詢，包括處方藥物、化學品、生活用品、植物、蕈類、動物毒素、濫用物質等。全職員額為 5 位，分配給 7 位員工；非上班時段則會由布拉格總醫院職業醫學科的醫事人員提供諮詢服務。

任何打至 TIC 的電話諮詢都會以電子檔記錄。提供毒物諮詢服務的資料庫包括 TIC 創建和更新的毒理資料庫，內含超過七萬種物質的資料；或者使用付費年度訂閱的毒物資料庫(例如 Toxbase, TOXINZ)。

每年的毒物諮詢電話數量都在增加。2002 年，TIC 提供了 8,934 人次之諮詢服務；2012 年為 14,697 人次；2022 年則達到了 26,601 人次。大部分的諮詢與兒童中毒有關（2022 年佔全部諮詢之 58.3%），藥物中毒是最常見的原因（2022 年佔 39.0%）。自 2021 年以來，我們注意到兒童（15 歲以下）和青少年（16 至 19 歲）自殺中毒案例顯著增加。在 3,270 起藥物自殺中毒案例中，兒童暴露物質最常見為解熱鎮痛藥（尤其是乙醯胺酚），而青少年則主要暴露抗憂鬱藥物。2022 年，54.7%的毒物諮詢來自民眾，37.2%來自醫護專業人員，其餘的則來自其他各種單位。

TIC 與捷克共和國的衛生部合作，負責儲備及管控國內無許可證的解毒劑、抗感染藥物以及抗血清。TIC 也提供布拉格查理大學醫學院(the Faculty of Medicine of Charles University)教育訓練。捷克 TIC 的研究成果自 1964 年起，每年發表在如歐洲毒物中心及臨床毒理學家協會（EAPCCT）的會議上。

The function and role of Taiwan Poison Control Center

臺灣毒藥物防治諮詢中心的功能與角色

Professor Chen-Chang Yang 楊振昌教授

Chair,
Taiwan Poison Control Center,
Department of Occupational Medicine and Clinical Toxicology,
Taipei Veterans General Hospital,
Distinguished Professor,
Institute of Environmental & Occupational Health Sciences,
Joint Professor,
Institute of Public Health, Institute of Food Safety and Health Risk Assessment, and Institute of Emergency and Critical Care Medicine,
School of Medicine, National Yang Ming Chiao Tung University
Taipei, Taiwan
臺北榮民總醫院職業醫學及臨床毒物部主任

In response to the rapidly increased poisoning incidents in Taiwan, and in line with the international trend, under the auspices of Ministry of Health & Welfare, Taiwan's first and only national poison control center (PCC-Taiwan) was founded in Taipei Veterans General Hospital in July 1985. It is the first 24-hour consultation center for poison and drug information in Taiwan and Asia, serving healthcare professionals at all levels and the general public. The 24/7 hotline is 02-28717121.

The services provided by Taiwan PCC include the following: assisting the emergent analysis, identification, diagnosis and treatment of various poisonings, providing help in poisoned patients' referral, and establishing a reporting system for tracking and collective reporting of acute poisoning cases to reduce the waste of medical resources. With the epidemiologic data collected by the PCC and the collaboration with various governmental agencies, PCC has played a significant role in the early warning of acute poisonings in Taiwan. Taiwan PCC is also responsible for the procurement, control, and distribution of specific antidotes through the National Antidote Network, ensuring that responsible emergency hospitals nationwide have access to designated antidotes. In addition, Taiwan PCC organizes training courses on poisoning prevention and management as well as domestic and international conferences to enhance the level of toxicology healthcare in Taiwan.

Starting in 2022, Taiwan PCC has developed an artificial intelligence-assisted query system for poison diagnosis, aiming to improve the prediction of poisoning exposure by collecting epidemiological data and collaborating with government agencies in the early stages of acute poisoning. The development of this system is expected to provide more comprehensive consultation services to healthcare professionals and the public in Taiwan.

為了應對台灣中毒事件的快速增加並與國際趨勢保持一致，毒藥物防治諮詢中心（以下簡稱中心）在衛生福利部的支持下，於 1985 年 7 月在臺北榮民總醫院成立。為國內及亞洲第一個 24 小時提供各級醫療人員及全國民眾諮詢之毒藥物防治諮詢中心。

中心 24 小時諮詢專線：02-28717121，提供的服務包括：協助緊急分析、鑑定、診斷和治療各種中毒症狀，提供中毒患者轉介的幫助，建立病人追蹤及集體中毒的通報系統，可有效降低病人重症率，並減少醫療資源浪費。透過中心收集的流行病學數據以及與政府機構的合作，在急性中毒早期發揮預警功能。此外，中心下轄全國解毒劑儲備網，負責採購、管控及配置特定解毒劑於全台各急救責任醫院，每年定期舉辦中毒教育訓練、國內與國際中毒相關研討會，以促進學術交流，提升國內有關中毒的醫療水準。

隨著科技不斷進步，中心於 2022 年開始發展中毒診斷人工智慧輔助查詢系統，完整的收集國內中毒案例資料，期望能更好地預測中毒暴露情況。希望透過該系統之發展，能夠提供全台醫療專業人員和民眾更完善的諮詢服務。

Trends in use of antidotes and antisera from Toxicologic Information Centre for the Czech Republic

捷克毒物中心解毒劑與抗蛇毒血清的使用趨勢

Mgr. Milada Běhounková

Pharmacist,
Toxicological Information Centre,
Department of Occupational Medicine, General University Hospital,
Prague, Czech Republic

Objective:
Toxicologic Information Centre (TIC) in Prague is the only TIC in the Czech Republic. It is responsible for purchasing, controlling and distribution of specific antidotes, anti-infectives and antisera. Majority of antidotes, some anti-infectives and antisera are not authorized in the Czech Republic and could not be available in time. Specific Therapeutic Programme (STP) is the only way how to ensure ready stock of the lifesaving agents. State Institute for Drug Control (SÚKL) issues an opinion on STP. The fund for purchasing of antidotes, anti-infectives and antisera is guaranteed by the Ministry of Health of the Czech Republic.

Methods:
The number of antidotes and antisera that were used for the treatment between 2013 and 2022 were summarised. The trends were evaluated.

Results:
Antidote ANTICHOLIUM was used for 1-2 patients per year for the intoxication with Datura stramonium, Atropa belladonna or drugs with central anticholinergic effect. During past 10 years, ANTIVIPMYN TRI and SNAKE VENOM ANTISERUM were used for 3 patients. All of them were snake keepers and they were bitten accidentally. DIGIFAB was given to maximum 5 patients per year in digoxin overdose or for treatment of *Taxus baccata* poisoning. Chelating antidote DIMAVAL cps or inj. was used for 1-2 patients every year, most frequently for cobalt/chromium intoxication from a damaged hip prosthesis. Peak of FOMEPIZOL use in 2013 caused treatment of acute methanol poisoning during Czech mass methanol outbreak 2012-2013.

Intoxication with *Amanita phalloides* and the consumption of LEGALON SIL relates to picking mushrooms, very popular hobby in the Czech Republic. The number of treated patients has seasonal variations 0-15 per year. Lead intoxications and use of SUCCICAPTAL is decreasing. The European viper (*Vipera berus*) is the only life-threatening snake living in the nature, and the use of antivenom VIPERATAB is continuously increasing, with maximum 19 patients in 2020.

Conclusion:

The trends in exposure to heavy metals, cyanides and insecticides are decreasing in the Czech Republic. The number of used antidotes during the period of last ten years is low (Cyanokit, Dimaval, Succicaptal, Natriumthiosulfat) or zero (Toxogonin). The most frequently used drugs were Legalon SIL and ViperaTab. The number of poisonings treated depends on meteorological conditions and human activities.

Keywords: antidotes, treatment, poisoning, intoxication

目的：

捷克共和國唯一的布拉格毒物中心（TIC）在解毒劑、抗生素和抗血清的採購、管理和分發上演著重要的角色。然而，由於許多解毒劑以及部分抗生素和抗血清製劑在捷克共和國尚未獲准使用，因此確保及時獲得這些藥物可能面臨困難。為確保庫存充足，捷克共和國藥物監管機構（SÚKL）負責制定特定治療計劃（STP），相關經費由捷克共和國衛生部承擔。

方法：

本研究針對 2013 年至 2022 年間使用的解毒劑和抗蛇毒血清製劑進行了資料整理，並評估其使用趨勢。

結果：

每年有 1 至 2 名患者因曼陀羅、風信子或具有中樞抗膽鹼作用的藥物中毒而使用 ANTICHOLIUM 解毒劑。在過去的 10 年中，有 3 名蛇飼養者因意外被蛇咬傷而使用了 ANTIVIPMYN TRI 和抗蛇毒血清。每年最多 5 名患者使用 DIGIFAB，用於毛地黃過量或紅豆杉（*Taxus baccata*）中毒。每年有 1 至 2 名患者使用重金屬螯合劑 DIMAVAL 膠囊或注射劑，主要用於人工髖關節引起的鈷或鉻中毒事件。FOMEPIZOL 使用在 2013 年達到高峰，主因為 2012 至 2013 年發生了大規模甲醇中毒事件。LEGALON SIL 的使用與捷克共和國人民對採摘蘑菇的嗜好有關，每年因誤食毒鵝膏(*Amanita phalloides*)導致中毒的治療人數依季節性變化，範圍在 0 至 15 人之間。鉛中毒和 SUCCICAPTAL 的使用正在減少。而對於歐洲蝰蛇（*Vipera berus*）咬傷引起的中毒，使用抗蛇毒血清 VIPERATAB 的情況不斷增加，僅在 2020 年就有 19 名患者使用。

結論：

捷克共和國在重金屬、氰化物和殺蟲劑暴露方面的趨勢呈下降趨勢。在過去十年中，使用的解毒劑數量相對較少（Cyanokit、Dimaval、Succicaptal、Natriumthiosulfat），甚至有一些解毒劑未被使用（Toxogonin）。而使用最廣泛的解毒劑是 LEGALON SIL 和 VIPERATAB。接受解毒劑治療的人數，依氣候和人類活動有所變化。

The antidote preparedness and network supply in Taiwan

臺灣解毒劑儲備網介紹

RPh. Hsiang-Ling Chen 陳香齡藥師

Pharmacist & Special poison information,
Taiwan Poison Control Center,
Department of Occupational Medicine and Clinical Toxicology,
Taipei Veterans General Hospital,
Taipei, Taiwan
臺北榮民總醫院職業醫學及臨床毒物部毒藥物防治諮詢中心藥師

Antidotes play a crucial role in the medical management of acute or chronic poisoning cases. Administering the correct antidote in a timely manner can be a lifesaving intervention. Therefore, the establishment of an antidote supply system is essential to respond to sudden poisoning emergencies and prevent fatalities. Taiwan Poison Control Center (PCC-Taiwan) fund of The Ministry of Health and Welfare (MOHW) has been procuring antidotes that are not available domestically since 2000. These antidotes are supplied to designated hospitals throughout Taiwan. PCC-Taiwan is responsible for the management and distribution of antidotes, as well as providing 24-hour consultation and real-time updates on antidote availability.

On the basis of the investigation in the early stage of the establishment of the antidote supply system. In 2000, PCC-Taiwan purchased antidotes for cyanide poisoning (Cyanide Kit and hydroxocobalamin), anticholinergic poisoning (Physostigmine), digitalis toxicity (DigiFab), heavy metal poisoning (Ca-EDTA/DMSA/DMPS), methanol poisoning (Fomepizole), methemoglobinemia (Methylene blue), etc. During the past 22 years, more than 721 patients have received antidotes provided by the antidote supply network. Now there are 70 designated hospitals participating in the program.

Due to the reduction in government funding and the availability of domestically produced pharmaceuticals, certain antidotes have been removed from the supply list. Currently, PCC-Taiwan provides antidotes for cyanide poisoning (Cyanide Kit), anticholinergic poisoning (Physostigmine) and digitalis toxicity (DigiFab). The total number of cases using these antidotes has been 134 for the cyanide antidote, 265 for Physostigmine, and 74 for DigiFab, retrospectively. PCC-Taiwan assesses the quantity of antidotes needed by each hospital for the following year based on usage reports provided by hospitals,

and it adjusts the allocation accordingly. The antidote review committee is convened to discuss on antidote procurement related matters irregularly. It is hoped that these efforts will contribute to providing a more comprehensive medical environment for patients affected by poisoning.

解毒劑在中毒的醫療處置上扮演了相當重要的角色，特定急慢性中毒的病患，如能給予正確的解毒劑，將可及時拯救病患性命，因此建立必要的解毒劑儲備系統對於因應中毒突發事件，預防無藥可救有其重要性及必要性。衛福部暨臺北榮總院臨床毒藥物諮詢中心自 2000 年起定期採購國內無法取得之解毒劑，提供給全台特定醫院使用，負責解毒劑採購、管理及分配，並提供 24 小時諮詢與即時解毒劑庫存狀況。

依據解毒劑儲備系統建置前期之調查，2000 年採購氰化物中毒解毒劑(Cyanide Kit 及 hydroxocobalamin)、抗膽鹼作用劑中毒解毒劑(Physostigmine)、毛地黃解毒劑(DigiFab)、重金屬中毒解毒劑(Ca-EDTA/DMSA/DMPS)、甲醇中毒解毒劑(Fomepizole)、變性血紅素血症解毒劑(Methylene blue)等，為解毒劑儲備項目。在過去 22 年間，已超過 721 位病患，曾接受過解毒劑儲備網提供之解毒劑，目前解毒劑配置醫院涵蓋全台各區共 70 家醫院。

由於政府經費逐年減少，部分解毒劑已納入全民健保給付或國內可取得，這些品項則退出儲備項目。現今僅採購氰化物中毒解毒劑(Cyanide Kit)、抗膽鹼作用劑中毒解毒劑(Physostigmine)及毛地黃解毒劑(DigiFab)，其歷年使用總個案數分別為 Cyanide Kit 134 人，Physostigmine 265 人，DigiFab 74 人。毒藥物諮詢中心每年根據解毒劑使用者提供之報告書，統計使用數量及評估使用成效，再依使用狀況調整下年度分配予各醫院解毒劑之儲備量。不定期召開解毒劑審議委會，針對採購解毒劑相關議題討論決策。期望可以提供中毒病人更完善的醫療環境。

Selected addictive substances in the Czech Republic – trends recorded by Toxicological Information Centre

捷克毒物中心非法藥物和尼古丁產品的中毒趨勢

Mgr. Michal Čečrle

Pharmacist,
Toxicological Information Centre,
Department of Occupational Medicine, General University Hospital,
Prague, Czech Republic

Objective:
To analyze Toxicological Information Centre (TIC) calls after exposure to addictive substances (mainly illicit and nicotine) since the beginning of the recent version of electronic records (2005).

Methods:
The calls were searched from January 2005 to May 2023, divided into following categories: hallucinogens, cocaine, marijuana and hashish, morphine and derivatives, amphetamine derivatives, nicotine, and others.

Results:
Total number of calls to TIC related to all potentially toxic agents steadily increases, from 9 495 in 2005 to 26 599 in 2022. In the years 2005-2022, there were total 297 131 calls to TIC, and 2 959 calls related to addictive substances (i.e. 1% of total calls). Among them, most frequent was nicotine (662 calls; 22,4%) and amphetamine derivates, especially metamphetamine, called pervitin (608 calls; 20,5%), then marijuana and hashish (508 calls; 17,2%), morphine and derivates (84 calls; 2,8), hallucinogens (71 calls; 2,4%), cocaine (69 calls; 2,3%). The rest were other, combination or unknown (957 calls; 32,3%). In 2022, calls due to addictive substances reached 424 (1,59%). In 227 calls concerning nicotine, the children prevailed (79%) with mostly accidental ingestions (92%), there were 40 adults (18%), and 3% animals or uncategorized subjects. Nicotine "chewing" pouches appeared first in 2019 and have an increasing trend. Relatively recently, kratom and hexahydrocannabinol (HHC) appeared on the Czech market. We recorded first call concerning kratom in 3/2017 and HHC in 5/2022. The median age of the users was 19.3 (3-65) years.

These products can still be purchased from vending machines publicly located (e.g., shopping centers), and their regulation is being prepared at the governmental level.

Conclusion:
The abuse of psychoactive substances is a social-wide problem. The number of calls due to addictive substances is gradually increasing a little. There is an increase in new substances, kratom and HHC, especially among adolescents.

目的：

分析自 2005 年起，捷克毒物諮詢中心接獲涉及暴露成癮性物質（主要為非法濫用物質和尼古丁產品）的諮詢紀錄。

方法：

我們檢索了 2005 年 1 月至 2023 年 5 月的電話諮詢紀錄，並把暴露的成癮物質分為以下幾類：迷幻劑、古柯鹼、大麻和濃縮大麻脂、嗎啡及其衍生物、安非他命衍生物、尼古丁以及其他類別。

結果：

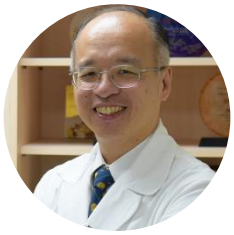
捷克毒物諮詢中心中毒諮詢電話數量逐年增加，從 2005 年的 9,495 人次增加到 2022 年的 26,599 人次。在 2005 年至 2022 年間，捷克毒物中心總共接獲了 297,131 人次的諮詢電話，其中 2,959 人為成癮物質之諮詢（佔總諮詢電話的 1%）。尼古丁產品為諮詢人次最多的成癮物質（662 次；佔 22.4%），其次是安非他命衍生物，特別是甲基安非他命，也稱為 Pervitin（608 次；佔 20.5%），接著分別為大麻和濃縮大麻脂（508 次；佔 17.2%）、嗎啡及其衍生物（84 次；佔 2.8%）、迷幻劑（71 次；佔 2.4%）、古柯鹼（69 次；佔 2.3%），其他類別和併用物質或未知成份的諮詢電話共計 957 次（佔 32.3%）。於 2022 年，成癮物質相關的總諮詢電話共 424 通（佔總諮詢電話的 1.59%）。在 227 通尼古丁暴露案件中，79%為兒童誤食（意外暴露佔兒童尼古丁中毒原因的 92%），而成年人共有 40 名個案（佔 18%），動物佔 3%及其他未知族群。尼古丁咀嚼袋產品在 2019 年首次出現，並且使用量呈現增加的趨勢。近年來，卡痛和六氫大麻酚也陸續出現在捷克。第一個卡痛諮詢電話出現在 2017 年 3 月，而第一個六氫大麻酚的諮詢電話則是在 2022 年 5 月。使用者的平均年齡為 19.3 歲（年齡最小和最大的個案分別為 3 和 65 歲）。這些產品目前可從公共場所（如購物中心）的自動販賣機取得，政府也在制定相關法規。

結論：

濫用成癮物質是一個社會性議題。捷克毒物諮詢中心接到的相關諮詢電話數量逐漸增加。此外，卡痛和六氫大麻酚等的新興影響精神物質使用量也有所增加，特別是青少年族群。

Recreational use of New Psychoactive Substances (NPS) in Taiwan

臺灣新興濫用藥物監測



Dr. Cheng-Chung Fang 方震中醫師

Division Head,
Division of Traumatology and Toxicology,
Department of Emergency Medicine,
National Taiwan University Hospital,
Clinical Associate Professor,
Department of Emergency Medicine,
College of Medicine, National Taiwan University,
Taipei, Taiwan
台大醫院急診醫學部外傷及毒物科主任

Recreational Use of New Psychoactive Substances (NPS) is a growing problem in these years. More and more NPS are entering into the market and it is difficult for emergency physicians to identify the patients using NPS and manage them properly. We performed a comprehensive analysis on patients' urine samples by liquid chromatography tandem-mass spectrometry to identify the illicit drugs. Furthermore, we established Taiwan Emergency Department Drug Abuse Surveillance (TEDAS) Project in 2019, and provides a nationwide epidemiological profile of recreational drug use in Taiwan. This speech will present the clinical characteristics of NPS use patients at emergency departments in Taiwan and the results of TEDAS project.

近年來，新興影響精神物質（NPS）的濫用問題日益加劇。越來越多的 NPS 進入市場，對急診醫師而言，辨識使用 NPS 的患者並給予適當的處置面臨困難。為確定非法藥物的使用情況，我們使用液相層析串聯質譜法對患者的尿液樣本進行全面分析。此外，我們於 2019 年成立了臺灣全國急診監測計畫(TEDAS)，旨在提供臺灣全國濫用藥物使用的流行病學調查。本演講將介紹臺灣濫用 NPS 的患者至急診就醫時的臨床特徵以及 TEDAS 的調查結果。

Identification of small molecules rescuing doxorubicin induced cardiomyopathy

改善 Doxorubicin 所引發心肌病變的分子化合物

Professor Randall T. Peterson

L. S. Skaggs Presidential Endowed Chair,
Professor, Pharmacology and Toxicology,
Adjunct Professor, Biochemistry,
Dean, College of Pharmacy, University of Utah,
Salt Lake City, Utah, U.S.A.

Doxorubicin is a highly effective chemotherapy drug, but its usage is limited by its cardiotoxic effect. The most effective chemotherapy doses cause high levels of heart failure, and even when used at “safe” dosages, doxorubicin causes heart failure among a significant number of patients. Therefore, a drug capable of countering the cardiac toxicity of doxorubicin but preserving its anti-tumor potency would be of high clinical value.

To tackle this problem, we established a doxorubicin-induced heart failure model in zebrafish that recapitulates the cardiomyocyte apoptosis and contractility decline observed in treated humans. Using this model, we screened 3,000 compounds and discovered that visnagin (VIS) rescues cardiac performance and circulatory defects caused by doxorubicin treatment in zebrafish.

VIS reduces doxorubicin-induced apoptosis in cultured cardiomyocytes and in zebrafish. We further show that VIS mediated apoptosis reduction results in improved cardiac contractility in doxorubicin-treated mice. Using medicinal chemistry, we developed a series of VIS analogs, some possessing ~1000X greater potency than VIS. These VIS analogs appear to be well tolerated in mice and provide potent cardio protection against doxorubicin, without diminishing its anti-tumor efficacy. Mechanistically, the compounds appear to function via dual action on the targets MDH2 and Cyp1. Together, these data suggest that VIS and VIS analogs may potentially have therapeutic utility as adjuvants for doxorubicin chemotherapy.

Doxorubicin 是一種非常有效的化療藥物，即使在最有效的化療劑量下使用，它也可能導致嚴重的心衰竭。即使以所謂的「安全」劑量使用，許多患者仍可能出現心衰竭的情況。因此，開發能減輕 doxorubicin 心臟毒性並保留其抗癌效果的藥物具有很高的臨床價值。

為此，我們使用斑馬魚建立了 doxorubicin 誘導心衰竭模型，這個模型展示了在治療過程中心肌細胞凋亡和收縮力下降的情況。我們利用這個模型篩選了 3,000 種化合物，結果發現 visnagin（VIS）可解決 doxorubicin 引起的心臟毒性。

VIS 能夠減少斑馬魚和培養皿中，心肌細胞因 doxorubicin 誘發的凋亡現象。進一步的研究證實，使用 VIS 能減少細胞凋亡，並改善接受 doxorubicin 治療的小鼠心肌收縮能力。後續利用藥物化學開發了一系列的 VIS 類似物，在小鼠實驗中，這些類似物表現出良好的耐受性，並且對 doxorubicin 有有效的心臟保護作用，並且不會減弱其抗癌功效。以機轉而言，這些化合物似乎對 MDH2 和 Cyp1 靶點的雙重作用發揮效用。綜上所述，這些數據顯示：VIS 及其類似物可能為 doxorubicin 療程的潛在輔助藥物。

Thallium

鉈中毒

Dr. Luke Yip

Medical Officer & Senior Advisor for Medical Toxicology,
US Department of Health and Human Services,
Centers for Disease Control and Prevention,
Office of Non-communicable Diseases, Injury, and Environmental Health,
National Center of Environmental Health/ATSDR,
Atlanta, Georgia, U.S.A.

Thallium, a bluish-white, soft, heavy, inelastic metal found in trace amounts in the earth's crust, was independently discovered by William Crookes and Claude Auguste Lamy. Thallium (Greek, thallos, "a green shoot" or "twig"), name comes from thallium's bright green spectral emission lines, was named by Crookes. Thallium tends to form the +3 and +1 oxidation states with the latter being far more common and found geologically mostly in potassium-based ores. Commercially, thallium is produced as a byproduct from refining of heavy-metal sulfide ores. Majority of thallium production is used in the electronics industry, and the remainder is used in the pharmaceutical industry, glass manufacturing, and used in infrared detectors. Soluble thallium salts (many of which are nearly tasteless) are highly toxic, and they were historically used as a rodenticide and insecticide. Because of their nonselective toxicity, use of these compounds has been restricted or banned in many countries. Thallium also gained historic popularity as a murder weapon; "the poisoner's poison" and "inheritance powder" (alongside arsenic).

Historically, medicinal use of thallium salts included treatment of ringworm, a depilatory agent, and reduction of night sweating of tuberculosis patients. Current medical use of thallium include radioisotope thallium-201 (as the soluble chloride) in nuclear medicine scan; cardiac stress test. We will discuss thallotoxicosis based on a case study.

鉈是一種呈青白色、柔軟、重量沉重且不具彈性的金屬，在地殼中以微量存在。它由威廉·克魯克斯和克勞德·奧古斯特·拉米所發現。鉈這個名字來自於希臘語中的「thallos」，意為「綠色的嫩芽」或「小枝」，是根據鉈的亮綠色光譜發射線命名的。鉈通常形成 3 價和 1 價的氧化態，其中 1 價的氧化態更常見，主要存在於含鉀的礦石中。商業上，鉈是作為重金屬硫化礦石的精煉過程的副產物而生產的。大部分的

鉈用於電子工業，其餘則用於製藥業、玻璃製造業和紅外線探測器。可溶性的鉈鹽（多數幾乎無味）具有高毒性，曾被廣泛用作滅鼠劑和殺蟲劑。由於其非選擇性的毒性，許多國家限制或禁止使用這些化合物。鉈作為一種殺人武器在歷史上廣為人知；與砷並列被稱為「下毒首選」或「遺產之粉」*。

在醫療上，過去使用鉈鹽來治療癬、作為脫毛劑和減輕結核病患者夜間出汗的症狀。目前，醫療上仍會在核子醫學檢查中使用鉈，例如放射性同位素鉈-201（以可溶性氯化物形式）和心臟壓力測試。本次報告將以一個案報告來討論鉈中毒。

*譯註：如此稱呼是因為藉由謀殺以獲得他人遺產。

Sulfur mustard – case report

芥子氣中毒個案報告

Colonel Professor Kai Kehe

Colonel & Professor,
Bundeswehr Medical Service Headquarter,
Head of Division A VI - Public Health,
Koblenz, Germany

Sulfur mustard (SM) is a chemical warfare agent (CWA) that was first used in World War I and in several military conflicts afterwards. The threat by SM is still present even today. SM has been used by the Islamic State and more recently in Syria. Additionally, old stockpiles as well as remainders all over the world are still a threat. CWA are banned by the Chemical Weapons Convention (CWC).

The present case report describes an accidental exposure of three workers that occurred during the destruction of SM. All exposed workers presented a characteristic SM-related clinical picture that started about 4h after exposure with erythema and feeling of tension of the skin at the upper part of the body. Later on, superficial blister and a burning phenomenon of the affected skin areas developed. Similar symptoms occurred in all three patients differing severity. One patient presented sustained skin affections at the gluteal region while another patient came up with affections of the axilla and genital region. Fortunately, full recovery was observed on day 56 after exposure except some little pigmentation changes that were evident even on day 154 in two of the patients. SM-exposure was verified for all three patients using bioanalytical GC MS and LC MS/MS based methods applied to urine and plasma.

芥子氣（SM）是一種化學戰劑（CWA），首次在第一次世界大戰及之後幾次的軍事衝突中使用。芥子氣的威脅至今仍然存在。芥子氣曾被伊斯蘭國使用，最近也在敘利亞使用。此外，世界各地的庫存和殘留物仍然是一個威脅。根據化學武器公約（CWC），化學戰劑是禁止被使用的。

本個案報告描述了三名工人在芥子氣摧毀過程中意外暴露的情況。所有受到暴露的工人在暴露後約 4 小時出現了典型的芥子氣中毒的臨床症狀，包括皮膚紅斑和上半身的緊繃感。隨後，暴觸芥子氣的皮膚區域出現了水泡和燒灼感。三名患者都出現了類似但嚴重程度不同的症狀。其中一名患者在臀部區域出現持續性的症狀，而另一名

患者在腋下和鼠蹊部出現症狀。幸運的是，所有患者在暴露後的 56 天內康復，兩名患者在第 154 天還有些微的色素變化。患者的尿液和血漿經氣相層析質譜儀（GC-MS）和液相層析串聯質譜儀（LC-MS/MS）檢測，證實了本報告中的三名患者皆曾受到芥子氣暴露。

Sulfur mustard poisoning – picture linked to molecular toxicology

芥子氣中毒－從分子毒理學看毒物臨床表現

Colonel Professor Kai Kehe

Colonel & Professor,
Bundeswehr Medical Service Headquarter,
Head of Division A VI - Public Health,
Koblenz, Germany

Sulphur mustard (SM) is one of the major chemical warfare agents developed and used during World War I. Large stockpiles are still present in several countries. It is relatively easy to produce and might be used as a terroristic weapon. Sulphur mustard is a vesicant agent and causes cutaneous blisters, respiratory tract damage, eye lesions and bone marrow depression. The clinical picture of poisoning is well known from the thousands of victims during World War I and the Iran-Iraq war.

SM is a strong alkylating agent, which produces subepidermal blisters, erythema and inflammation after skin contact. Despite the well-described SM-induced gross and histopathological changes, the exact underlying molecular mechanisms of these events are still a matter of research. As part of an international effort to elucidate the components of cellular signal transduction pathways, a large body of data has been accumulated in the last decade of SM research, revealing deeper insight into SM-induced inflammation, DNA damage response, cell death signaling, and wound healing. SM potentially alkylates nearly every constituent of the cell, leading to impaired cellular functions. However, SM-induced DNA alkylation has been identified as a major trigger of apoptosis. This includes monofunctional SM-DNA adducts as well as DNA crosslinks. As a consequence, DNA replication is blocked, which leads to cell cycle arrest and DNA single and double strand breaks. The SM-induced DNA damage results in poly (ADP-ribose) polymerase (PARP) activation. High SM concentrations induce PARP overactivation, thus depleting cellular NAD(+) and ATP levels, which in consequence results in necrotic cell death. Mild PARP activation does not disturb cellular energy levels and allows apoptotic cell death or recovery to occur. SM-induced apoptosis has been linked both to the extrinsic (death receptor, Fas) and intrinsic (mitochondrial) pathway.

Additionally, SM upregulates many inflammatory mediators including interleukin (IL)-1alpha, IL-1beta, IL-6, IL-8, tumor necrosis factor-alpha (TNF-

alpha) and others. NF-kappaB activation is linked to this inflammatory response. Recently, the SM-induced senescence of cells has been identified as a potential target of pharmaceutical investigation.

芥子氣（SM）為第一次世界大戰期間開發和使用的主要化學戰爭劑之一，至今在多個國家仍然存在大量庫存。它相對容易生產，可以被用作恐攻武器。芥子氣是一種發疱劑，中毒表現包括皮膚水泡、呼吸道損傷、眼部病變和骨髓抑制。在第一次世界大戰和兩伊戰爭中，我們在數以千計的受害者身上可見其中毒症狀。

芥子氣是一種強烷化劑（alkylating agent），與皮膚接觸會產生皮下水泡、紅斑和發炎。儘管對於芥子氣引起的組織和組織病理學變化已有詳細描述，但其與生物體間的分子學機制，仍然是值得研究的議題。過去十年間，國際間對於芥子氣細胞訊息傳導途徑的研究已累積了大量的相關資料，對於芥子氣引起的炎症、DNA 損傷反應、細胞死亡信號和傷口癒合等方面有更深入的了解。芥子氣可烷基化細胞中幾乎每個部分，導致細胞功能受損；而芥子氣引起的 DNA 烷基化，是誘發細胞凋亡的主要觸發因素。這包括單官能基的 SM-DNA 加合物(monofunctional SM-DNA adducts)以及 DNA 交聯(DNA crosslinks)，造成 DNA 複製被阻斷，進而導致細胞週期阻滯，以及 DNA 單股和雙股斷裂等結果。芥子氣引起的 DNA 損傷導致聚腺苷二磷酸核糖聚合酶（PARP）的活化。而高濃度的芥子氣引起 PARP 過度活化，從而耗盡細胞的 NAD+和 ATP 濃度，進而導致壞死性細胞死亡(necrotic cell death)。輕度 PARP 活化不會干擾細胞能量水平，也不影響正常的細胞凋亡或恢復過程。芥子氣誘導的細胞凋亡既與外在途徑（death receptor, 死亡受體，例如 Fas）有關，也與內在途徑（粒線體）有關。

此外，SM 會上調許多發炎介質，包括白介素（interleukin , IL）-1α、IL-1β、IL-6、IL-8、腫瘤壞死因子-α（TNF-α）等。NF-κB(nuclear factor kappa-light-chain-enhancer of activated B cells, NF-κB)的活化與這種發炎反應有關。最近，人們已將芥子氣誘導的細胞衰老認為是一個潛在的藥物發展研究目標。

Inorganic mercury exposure following Indian indigenous (Siddha) medicine intake - a rare cause of anti-VGKC antibodies-associated acquired neuromyotonia

Anti-VGKC 抗體陽性致神經性肌強直症之罕見原因：印度悉達醫學治療引起的無機汞中毒

Professor Ravikar Ralph

Professor & Head,
Poisons Information Center,
Department of Internal Medicine, Christian Medical College
Vellore, Tamil Nadu, India

Acquired neuromyotonia (Isaac's syndrome) is an autoimmune disorder characterised by peripheral nerve hyperexcitability. It is clinically defined by myokymia, neuromyotonia, fasciculations, cramps and muscle-stiffness. While dysautonomia (hyperhidrosis, arrhythmia and blood pressure lability) and pain (neuropathic or muscular) are other common additional manifestations, sensory symptoms like paraesthesias are rare. Important findings on needle electromyography (EMG) include continuous single motor unit discharges occurring as doublet, triplet and multiplet single-unit discharges firing at higher rates (150-300 Hz; neuromyotonic discharges) and at lower rates (less than 60 Hz; myokymic discharges). The strong autoimmune basis of this syndrome is evidenced by its association with elevated titres of antibodies targeting specific components of the voltage-gated potassium channel (VGKC) including leucine-rich glioma-inactivated 1 (LGI1), contactin associated protein 2 (CASPR2) and contactin 2.

While this condition is often idiopathic or secondary to neoplasms, it can also rarely follow exposure to heavy metals like lead, silver, mercury and gold. We describe a series of five patients with inorganic mercury toxicity following indigenous (Siddha) medication intake who presented with acquired neuromyotonia, based on their clinical and autoantibody profile and discuss pathogenic aspects of mercury-induced autoimmunity. We also highlight a rare subset of patients in our series who were positive for dual anti-VGKC-autoantibodies (LGI1 and CASPR2). While several reports of anti-CASPR2

antibody positive acquired neuromyotonia exist, there is only one other report of dual-antibody positive neuromyotonia following chronic mercury exposure in the literature.

後天神經性肌強直症(Isaac’s syndrome)是一種持續性周邊神經病變引起的自發性連續性肌肉活動的自體免疫疾病。臨床上可見肌纖維顫動(myokymia)、神經性肌肉強直(neuromyotonia)、肌肉束顫動(fasciculations)、痛性痙攣(cramps)、以及肌肉僵硬。自律神經失調(多汗、心律不整、血壓不穩)以及疼痛(神經性或肌肉性)是常見之臨床症狀，而感覺異常如麻痺感較為少見。針極肌電圖檢查可見連續單一運動單位放電，以成對、三個一組、或多個單位連續放電，高頻電磁波(150-300 赫茲)可見神經性肌肉強直，以及低頻電磁波(小於 60 赫茲)可見肌纖維顫動。診斷這個症候群的證據為其相關的抗體濃度升高，例如 VGKC (voltage-gated potassium channel)、LGI1 (leucine-rich glioma-inactivated 1)、CASPR2 (contactin associated protein 2)、以及 contactin 2。

雖然通常發生原因不明，或與腫瘤的發生有關，但仍有少部分的機率為鉛、銀、汞或金等重金屬暴露。我們呈現了五位接受印度悉達醫學*治療的個案，出現神經性肌肉強直之臨床表現，同時出現自體抗體異常，以討論無機汞暴露導致自體免疫疾病之致病機轉。在這些個案系列中，我們也強調部分病人的罕見表現，亦即出現雙重自體抗體異常(LGI1 及 CASPR2)。文獻上後天神經性肌肉強直的案例中，有 CASPR2 抗體陽性的報告；但僅有一篇慢性汞中毒之個案，出現雙重自體抗體異常之後天神經性肌肉強直表現。

*譯註：根據維基百科，Siddha medicine「悉達醫學」起源自印度南部坦米爾納德邦的傳統醫學，為古印度三大傳統醫學之一，也是官方承認的合法傳統醫學療法之一。

Severe subacute inorganic arsenic poisoning caused by a folk medicine for treatment of psoriasis: A case series

民間藥物治療乾癬引起的嚴重亞急性無機砷中毒：案例系列報告

Dr. Chun-Man Chan Jones 陳俊文醫師

Deputising chief of service,
Department of Medicine & Therapeutics,
Prince of Wales Hospital Poison Treatment Centre, Hospital Authority
Honorary Clinical Supervisor,
Hong Kong College of Family Physicians,
Honorary Clinical Associate Professor,
The Chinese University of Hong Kong,
Hong Kong SAR, China

Introduction:

Inorganic arsenic poisoning is rare in Hong Kong. Arsenic poisoning usually occurs in settings of acute intentional overdose, chronic occupational exposure, or environmental exposure from consumption of drinking water with high inorganic arsenic content in some parts of the world. Arsenic intoxication resulting from consumption of pharmacotherapeutics is uncommon. In August 2015, a group of patients with chronic psoriasis presented with a variety of clinical features after a medical tourism in China. Their presenting clinical features and biochemical findings were compatible with subacute arsenic poisoning of various degrees after repeated exposures to a folk medicine allegedly made of realgar (Xiong Huang). Our aim was to describe the clinical features and laboratory findings of the subacute arsenic poisonings. We also described the initial therapeutic response to the chelation therapies with Dimercaptosuccinic acid (DMSA) and 2,3-dimercapto-1-propanesulfonic acid (DMPS).

Methods:

From August to October 2015, we prospectively collected data on all consecutive cases of folk medicine exposure in adults reported to our poison centre by using a standard assessment form. By using the result of arsenic and mercury contents measured from a folk medicine sample obtained from the index patient (arsenic 42657 microgram/mg; mercury 6.59 microgram/gram),

the quantity of folk medicine exposure of all patients were estimated. The frequency of the presenting clinical features and laboratory abnormalities were observed. Symptomatic patients or asymptomatic patients with elevated urine arsenic levels for spot urine samples (>68 nmol/mmol Cr) were treated with DMSA 30 mg/kg/d orally for 5 days in October 2015. Twenty four-hour urine samples were collected for arsenic measurements on the day before (D0DMSA) and on the first day after the commencement of DMSA (D1DMSA). In light of the reported effectiveness of DMPS in literature, patients were further treated with DMPS 400 mg/d orally for 7 days after a drug holiday of 3-week period in November 2015. Similarly, 24-hour urine samples were collected for arsenic measurements before (D0DMPS) and on the first day after commencement of DMPS (D1DMPS). Patients were advised to restrict their seafood intake during the treatment and urine measurement. A comparison of mean changes of the 24-hour urinary arsenic excretions with DMSA and DMPS was made using the Wilcoxon-rank sum test.

Results:

Thirty-one patients exposed to the folk medicine were recruited to our centre for management of suspected arsenic poisoning. The estimated mean daily inorganic arsenic exposure was 259.8 mg/day (range: 90.6 – 494.5 mg/day). The mean duration of exposure was 132.9 days (range: 7 – 1098 days). Common adverse reactions and laboratory abnormalities among patients following exposure to the folk medicine were as follows: nausea/vomiting (55%); significant weight loss (40%); facial swelling (30%); melanosis (60%); keratosis (25%); macrocytosis (50%); sensory neuropathy (50%); and elevated 24-hour urine arsenic (65%). The mean spot urine arsenic/Cr level was 578.9 nmol/mmol Cr (range: 68 – 4730 nmol/mmol Cr). The mean 24-hour urine arsenic level was 4337.3 nmol/day (range: 959 – 15026 nmol/day). There were 18 and 15 patients treated with DMSA and DMPS respectively. The 24- hour urine samples of 12 patients were available for measurement and comparison of urinary arsenic excretion pre- and post-chelation therapies with DMSA and DMPS. The mean changes of 24-hour urinary arsenic excretion with DMSA and DMPS were -32.9 ± 375.5 nmol/day and 221.6 ± 258.8 nmol/day respectively ($p = 0.24$).

Conclusion:

Subacute arsenic poisoning following use of therapeutic agents is rare. We reported a case series of subacute arsenic poisoning after repeated exposures of a folk medicine allegedly made of realgar. The adverse reactions were

common. Response to chelation therapy with DMPS appeared more effective than with DMSA. Further studies are needed to confirm the findings.

前言：

在香港，無機砷中毒並不常見。砷中毒通常是由於急性蓄意過量、長期職業暴露，或在某些地區的飲用水含有高濃度的無機砷所引起。而因藥物副作用導致的砷中毒則相對罕見。2015 年 8 月，一群慢性乾癬患者在前往中國進行醫療旅遊後出現了多種砷中毒症狀。他們的症狀和生化檢查結果與反覆接觸一種含有雄黃的民間藥物相關，而導致了不同程度的亞急性砷中毒。我們的目的是描述亞急性砷中毒的臨床特徵和實驗室檢查結果。同時，本報告也描述了使用重金屬螯合劑 DMSA(Dimercaptosuccinic acid)和 DMPS(2,3-dimercapto-1-propanesulfonic acid)進行治療的成效。

方法：

從 2015 年 8 月到 10 月，我們前瞻性地收集了所有向香港毒物中心報告的系列成人民間藥物暴露病例的資料，並使用標準評估表進行評估。從指標患者的民間藥物樣本中測定了砷和汞含量（砷：42657 μg/mg；汞：6.59 μg/g），以估算出所有患者的民間藥物暴露量，並觀察了臨床特徵和實驗室異常的頻率。在 2015 年 10 月，對有症狀的患者或尿液中砷濃度升高的無症狀患者（> 68 nmol/mmol Cr）進行了口服 DMSA 的治療，劑量為每日每公斤體重 30 毫克，為期 5 天。在 DMSA 開始治療的前一天（D0DMSA）和第一天（D1DMSA）收集了尿液樣本進行砷濃度測量。根據文獻報告的 DMPS 的效果，在患者停止 DMSA 治療的三週後，我們給予口服 DMPS 每日 400 毫克的劑量治療，為期 7 天。同樣地，在 DMPS 治療開始的前一天（D0DMPS）和第一天（D1DMPS）收集了尿液樣本進行砷測量。在治療和收集尿液的期間，建議患者限制食用海鮮。統計分析則使用 Wilcoxon 檢定，比較 DMSA 和 DMPS 治療過程中 24 小時尿液中砷排泄量的平均變化。

結果：

香港毒物中心招募了 31 位曾使用民間藥物的患者，進行疑似砷中毒的治療。估計平均每日無機砷暴露量為 259.8 毫克（範圍：90.6 – 494.5 毫克/天）。平均暴露天數為 132.9 天（範圍：7 – 1098 天）。在使用民間藥物後，患者可能出現的常見不良反應包括噁心或嘔吐（55%）、明顯體重減輕（40%）、面部腫脹（30%）、黑色素沉著（60%）、角化症（25%）、巨細胞貧血（50%）、感覺神經病變（50%）以及尿液中 24 小時砷濃度升高（65%）。平均單點尿液中砷濃度/肌酐為 578.9 nmol/mmol Cr（範圍：68 – 4730 nmol/mmol Cr）。平均 24 小時尿液中砷濃度為 4337.3 nmol/天（範圍：959 – 15026 nmol/天）。其中，18 名患者接受 DMSA 治療，另有 15 名患者接受 DMPS 治療。共有 12 名患者的 24 小時尿液樣本可用於測量和比較螯合治療前後的尿液砷排泄量。DMSA 治療後，24 小時尿液砷排泄量的平均變化為-32.9 ± 375.5 nmol/天，而 DMPS 治療後的平均變化為 221.6 ± 258.8 nmol/天（p = 0.24）。

結論：

使用治療藥物後發生亞急性砷中毒的情況很少見。我們報告了一系列因反覆接觸雄黃製成的民間藥物而導致的亞急性砷中毒病例，不良反應很常見。與 DMSA 相比，使用 DMPS 進行螯合治療的反應似乎比使用 DMSA 更為有效，需要進一步的研究進行確認。

Role of poison information centers in management of complex snakebite envenoming cases in India through remote consultation: an illustrative case-series from a national-level poison center

印度毒物諮詢中心處理複雜蛇咬傷案例中的角色：國家級毒物諮詢中心的蛇傷案例系列報告

Dr. Jambugulam Mohan

Physician & Assistant Professor,
Poisons Information Center,
Department of Internal Medicine, Christian Medical College
Vellore, Tamil Nadu, India

Most medically-significant snakebites in India are caused by four species namely, *Daboia russelii, Echis carinatus, Naja naja* and *Bungarus caeruleus* (the "big-four"). However, some lesser-known, range-restricted pit-viper species, are also being identified from parts of north-eastern and southern India, as being capable of causing medically-important bites. The identification of these snakes and management of their envenoming can be challenging for Indian physicians due to limited awareness and the potential ineffectiveness of Indian polyspecific antivenom in neutralizing venoms of species other than the "big-four".

Poisons information centers can play an important role in assisting with the diagnosis and management of snakebite envenoming through the provision of remote expert opinion by telemedicine. However, despite their immense potential in supporting snakebite management in India, the concept of poison centers is yet to catch-on. We aim to highlight the role of PICs in the diagnosis and management of challenging cases of snakebite in India through a series of pit-viper bite cases managed by a national-level poison information center.

在印度，蛇咬傷中具有臨床意義的大多由四種毒蛇引起，即 *Daboia russelii*、*Echis carinatus*、*Naja naja* 和 *Bungarus caeruleus*（通稱為「四大毒蛇」）。然而，一些鮮為人知且分佈有限的蝰蛇物種，發現分佈於印度東北部和南部地區，也可能引發臨床上重要的蛇傷案例。鑒於印度醫師對此類蛇種的認識有限，且印度多價的

抗蛇毒血清對於「四大毒蛇」以外的蛇毒中和效果可能有所不足，因此對於這些蛇種的鑒別與咬傷的臨床處置成為印度醫護人員面臨的一大挑戰。

中毒諮詢中心透過遠程專業意見提供蛇咬傷的診斷與處置建議，在印度蛇咬傷治療處置中扮演重要的角色。然而，儘管中毒諮詢中心在印度蛇咬處置方面具有重大潛力，但該概念尚未普及。我們旨在透過一系列由國家級中毒諮詢中心處理的蝰蛇咬傷案例報告，凸顯中毒諮詢中心在印度複雜蛇咬案例的診斷與臨床處置中所扮演的角色。

Role of Taiwan Poison Control Centre in snakebite envenomation

臺灣毒物中心蛇咬傷諮詢

Dr. Kai-Wen Cheng 鄭凱文醫師

Chief resident,
Taiwan Poison Control Center,
Department of Occupational Medicine and Clinical Toxicology,
Taipei Veterans General Hospital,
Taipei, Taiwan
臺北榮民總醫院職業醫學及臨床毒物部總醫師

In Taiwan, there've been four types of antivenom available to treat the six most medically significant snakebite envenomation for 14 years. However, the management of snakebite envenoming is still challenging for healthcare providers. According to the registry data related to snakebites, reasons to consult PCC-Taiwan in the past years include advice on initial management, progressing symptoms despite administration of antivenom, identification of biting species, and exotic snakebites. The role of PCC-Taiwan in snakebite envenomation in the future would be focused on knowledge translation, not only bridging the basic science and the daily practice of managing snakebites but also sharing invaluable clinical experience among practitioners.

在台灣，過去 14 年雖有四種抗蛇毒血清可供治療六種較嚴重的毒蛇咬傷，但蛇傷診治及處置對臨床醫護人員而言依然相當棘手。據臺灣毒藥物防治諮詢中心統計資料，歷年蛇傷案件的諮詢原因包括初步處置建議、個案於注射抗蛇毒血清後症狀仍持續惡化、辨識咬傷物種、以及非本土蛇類咬傷。未來面對蛇傷處置，毒藥物防治諮詢中心將側重於知識轉譯，除推廣傳播蛇毒基礎研究進展及其臨床應用，亦將持續協助臨床醫護人員分享、交流寶貴的臨床經驗。

POLES: Point of Care Ultrasonography (POCUS) for local envenomation from snakebite

重點式照護超音波應用於局部蛇咬傷治療

Dr. Cheng-Hsuan Ho 何政軒醫師

Director,
Division of Surgical Emergency,
Tri-Service General Hospital,
Taipei, Taiwan
三軍總醫院急診醫學部急診外科主任

The clinical procedure for managing snakebite patients at the Emergency Department of Tri-Service General Hospital involves the five-step NIAPS protocol: 1) Notification of the patient's condition, 2) Identification of snake species, 3) Selection of appropriate antivenom, 4) Monitoring of the patient's response using ultrasound POLES, and 5) Evaluation of risk factors for surgical intervention.

To monitor changes in local tissue swelling following snakebite, our hospital developed an ultrasound monitoring process known as Point of Care Ultrasonography (POCUS) for Local Envenomation from Snakebite (POLES). The POLES procedure consists of three steps. In step one, Localization, ultrasound is used to observe the condition of interstitial edema in the tissue. In step two, RPP measurement (rate of proximal progression), the boundary between the inflamed tissue and the normal tissue is identified and marked on the patient's skin. Recordings are taken at regular intervals to track the swelling progression rate (cm/hour) by dividing the distance between the two marks by the time interval. If this rate decreases, the antivenom administration can be withheld. In step three, Doppler ultrasound, an artery within the swollen area is selected and the ultrasound is adjusted to the Doppler mode. The vessel is then adjusted longitudinally, and the Pulse Wave mode is used to observe the systolic and diastolic waveforms of the artery. If there is a diastolic retrograde arterial flow (DRAF), it indicates that the compartment pressure is greater than the patient's diastolic pressure, and acute compartment syndrome is likely to occur. This non-invasive and repeatable procedure enables emergency clinical physicians to quickly and objectively evaluate local tissue changes caused by snakebites. It provides immediate information on swelling location, whether

additional serum is needed, and whether compartment syndrome is likely to occur. Emergency clinical physicians can provide appropriate treatment with antivenom therapy and ultrasound (POLES) monitoring.

Key words: snakebite, Taiwan, Point of Care Ultrasonography, Local Envenomation

三軍總醫院急診醫學部處理蛇咬傷患者的臨床程序涉及五步驟- NIAPS 準則：(1)告知患者病情 (2)識別蛇的種類 (3)選擇適當的抗蛇毒血清 (4)使用重點式照護超音波監測患者的反應 (5)評估手術介入的危險因素。

為了監測蛇咬傷後局部組織腫脹的變化，我們醫院發展使用超音波監測程序，稱為重點式照護超音波應用於蛇局部咬傷(POLES)。過程由三個步驟組成。 第一步定位，利用超音波觀察組織間質水腫情況；第二步，使用 RPP(近端進展率)測量，識別發炎組織和正常組織之間的邊界並在患者皮膚上標記。需定期進行記錄，透過將兩個標記之間的距離除以時間間隔來追蹤腫脹進展速率(單位:公分/小時)。若該速率下降，則可以停止注射抗蛇毒血清；第三步，使用都卜勒超音波，選擇腫脹區域內的動脈，並將超音波調整為都卜勒模式。然後調整血管為縱向，使用脈搏波模式觀察動脈的收縮和舒張波形。如果出現 diastolic retrograde arterial flow，則指出筋膜室壓力大於患者的舒張壓，很可能發生急性腔室症候群。這種非侵入性且可重複執行的程序幫助急診臨床醫生能夠快速、客觀地評估蛇咬傷引起的局部組織變化。它提供有關腫脹位置、是否需要額外血清以及是否可能發生腔室症候群的即時資訊。急診臨床醫生可以通過抗蛇毒血清治療和超音波(POLES 重點式照護超音波應用於局部蛇咬傷)監測提供適當的治療。

The neurology of snakebite

毒蛇咬傷對神經系統的影響

Professor Sir David A. Warrell KCMG

Emeritus Professor,
Nuffield Department of Clinical Medicine,
University of Oxford,
Oxford, UK

Snake venoms evolved to immobilise the snakes' prey or deter their enemies by targeting receptors crucial for vital physiological functions, notably neuro-muscular transmission.

Ptosis: in human patients the earliest symptom is usually bilateral palpebral ptosis, as in some other intoxications (e.g. botulism), and auto-immune and metabolic neurological conditions (myasthenia gravis, Lambert-Eaton and Miller-Fisher syndromes). Why are external ocular muscles (EOMs) so vulnerable to neuro-muscular blockade? They differ from other skeletal muscle in many respects, consisting of diverse myosin and nicotinic AChR (αβεδ- and δβγδ-) isoforms, being innervated singly (rapid twitch) or multiply (tonic) at rapid firing frequency. Twitch fibres have less prominent synaptic folds, with fewer AChRs incurring lower safety factor (difference between endplate potential and minimal depolarisation needed to trigger propagated action potential), and increases vulnerability to reduction in synaptic depolarisation caused by snake venom neurotoxins. They have a rich blood supply, a high metabolic rate, and show decreased inhibition of complement deposition at neuro-muscular junctions making them targets of auto-immune disease.

Descending paralysis: the classic clinical progression of snakebite neurotoxicity is descending symmetrical flaccid paralysis. It starts with muscles innervated by cranial nerves; then cervical nerves (causing the "broken neck sign" and diaphragm paralysis); then thoracic and lumbar nerves. The end-point of descending snakebite paralysis is near-total flaccid paralysis, the patient being apparently unresponsive patient, with GCS 3, fixed dilated pupils, and mis-diagnosis of "locked-in" syndrome or "brain death". The possible explanation of this descending pattern of paralysis raises the question: "Why do some progressive paralyses descend (snake venom neurotoxins, puffer fish – tetrodotoxin - poisoning, paralytic shellfish – saxitoxin - poisoning, botulism,

myasthenia gravis and Lambert-Eaton Syndrome) and others ascend (Guillain-Barré Syndrome – Landry, hyperkalaemic paralysis, tick bite paralysis, rabies encephalomyelitis, neuromyelitis optica spectrum disorder)? Ascending patterns have been explained by the vulnerable of longest axons, and the greater exposure of lumbar roots to toxins or antibodies in cerebro-spinal fluid before they exit the spinal canal. However, there has been no explanation for descending paralysis.

Other possible direct neurotoxic effects of snake venom toxins: these are muscle hyper-excitability (fasciculations, myokymia), autonomic nervous system stimulation, overwhelmingly-painful envenoming, and acute and persistent anosmia. More controversial effects are drowsiness, seizures, and other possible CNS effects, acute neuropathy, and delayed persistent neurological disturbances (resembling post-poliomyelitis syndrome).

Indirect neurological effects of snakebite envenoming: these result from intra-cranial haemorrhage or thrombosis complicating coagulopathic envenoming, profound hypoglycaemia from acute hypopituitarism caused by anterior pituitary infarction (Russell's viper), optic neuritis, Guillain-Barré Syndrome, cerebellitis, acute disseminated encephalomyelitis (ADEM), acute haemorrhagic leukoencephalitis (AHLE), posterior reversible encephalopathy syndrome (reversible posterior leukoencephalopathy syndrome) (PRES), and peripheral neuropathies caused by compression by haematomas, or by tight tourniquets.

The use of snake venom neurotoxins in neurology research: In 1963: α-bungarotoxin was isolated from *Bungarus multicinctus* venom by Taiwanese scientists and shown to bind to muscle-type nAChRs. Labelled toxin proved invaluable for localising nAChRs in tissues, and investigating normal and disturbed cholinergic synaptic transmission, notably, in the pathophysiology of myasthenia gravis.

蛇毒蛋白演化進展成以影響重要生理功能的關鍵受體為目標，特別是神經肌肉傳導，麻痺固定其獵物或威嚇敵人。

眼瞼下垂：雙側眼瞼下垂是蛇咬傷患者常見的早期症狀，同樣的症狀也出現在某些中毒（如肉毒桿菌中毒）及自體免疫和代謝性神經疾病（重症肌無力、Lambert-Eaton 和 Miller-Fisher 症候群）患者中。為何眼外肌如此容易受到神經肌阻斷劑影響呢？在許多方面與其他骨骼肌不同，眼外肌由多種肌凝蛋白（myosin）和菸鹼型乙醯膽鹼受體（αβεδ- 和 δβγδ-）異構體組成，在高神經激發頻率下，單一（rapid twitch / 快速收縮）或多重（tonic / 強直）受神經支配。收縮纖維的突觸摺疊較不明顯，且乙醯膽鹼受體較少，導致較低的安全係數（即終板電位和觸發傳播動作電位所需的最小去極化之差），這使其容易受神經性蛇毒蛋白引起的突觸去極

化減少的影響。因血液供應豐富、代謝率高，對神經肌肉接合處補體沉積的抑制減少，使其成為自體免疫疾病的靶點。

下行性麻痺：神經性蛇毒蛋白造成之典型臨床進展為下行、對稱且無力性麻痺狀態。首先影響受腦神經支配之肌肉，接著是頸椎神經（產生如頸椎骨折的症狀和橫膈麻痺），然後是胸椎神經和腰椎神經。蛇咬傷所導致之下型性麻痺的最終階段為近乎癱瘓，患者呈現無反應、GCS 3 分，瞳孔散大、對光無反應，可能被誤診為閉鎖症候群（Locked-in syndrome (LIS), pseudocoma）或腦死。探討對於此類下行性麻痺症狀的可能導因引出了一個問題：「為什麼有些進行性麻痺會呈現下行性模式（如神經性蛇毒蛋白、河魨毒素（tetrodotoxin, TTX）、麻痺性貝毒（paralytic shellfish poison, PSP）、雪卡毒素（ciguatoxin, CTX）及肉毒桿菌中毒、重症肌無力和 Lambert-Eaton 症候群），而有些則呈現上行性模式（如 Landry-Guillain-Barré症候群、高血鉀性麻痺、蜱蟲咬傷急性麻痺、狂犬病腦脊髓炎和泛視神經脊髓炎）？」造成上行性麻痺可能得導因與較長軸突容易受傷、腰椎神經根在毒素或抗體仍存於腦脊髓液中時較大程度地暴露到該毒素或抗體；然而對於下行性麻痺，則尚無明確解釋。

蛇毒毒素可能產生其他直接的神經毒性反應：肌肉過度興奮（抽搐、肌肉顫動）、自律神經刺激、極度疼痛的中毒症狀，以及急性和持續性的嗅覺喪失。較具爭議的影響包括嗜睡、癲癇和其他可能的中樞神經症狀、急性神經病變，以及延遲地持續性神經系統疾患（類似於小兒麻痺後症候群）。

間接神經毒性：由顱內出血或血栓導致，可能加重凝血異常毒性反應，由於腦下垂體前葉梗塞所致急性腦下垂體功能減退造成嚴重低血糖（鎖鏈蛇），視神經炎，Guillain-Barré症候群，小腦炎，急性瀰漫性腦脊髓炎（ADEM），急性出血性白質炎（AHLE），可逆性後腦病變症候群（PRES），及因血腫壓迫或止血帶過緊引起的周邊神經病變。

神經性蛇毒蛋白於神經學研究中的應用：1963 年，台灣科學家從雨傘節蛇毒中分離出α-bungarotoxin（α-BuTX，一種突觸後神經毒素），並證實其與肌肉型菸鹼型乙醯膽鹼受體（muscle-type nAChRs）結合。標記的毒素對於在組織中定位菸鹼型乙醯膽鹼受體，以及研究正常和受干擾的膽鹼性突觸傳遞機制非常有價值，特別是在重症肌無力的病理生理學研究中，這一技術具有重要意義。

Marine stings

海洋生物螫/刺傷

Professor Sir David A. Warrell KCMG

Emeritus Professor,
Nuffield Department of Clinical Medicine,
University of Oxford,
Oxford, UK

Fish Stings: are extremely painful (needing urgent hot water treatment!). Symptoms are local swelling, discolouration, sweating, paraesthesia, local lymphadenopathy, necrosis, and less commonly, nausea, vomiting, hypotension, cardiac arrhythmias, cardiac arrest, respiratory distress, convulsions, and autonomic stimulation. Wounds may be infected by marine or fresh-water *Staph., Strep.* spp*., Vibrio vulnificus, Mycobacterium marinum, Aeromonas hydrophila*). Fatalities are very rare (from reef stonefish *Synanceia verrucosa* in Polynesi).

Echinoderms (starfish and sea urchins): painful stings from venomous spines and grapples leave diagnostic dark-blue/black staining around the wound. Early aggressive surgical removal of spines is recommended, before they have a chance to work down into a joint or to the periosteum.

Jellyfish, Portuguese man o' war and other cnidarians (formerly called "coelenterates"): stings cause intense pain, linear wheals (in diagnostic patterns), swelling, erythema, vesiculation, necrosis, scarring, and with *Physalia* vasospasm causing peripheral gangrene. Systemic symptoms are cough, nausea, vomiting, abdominal colic, diarrhoea, rigors, severe musculoskeletal pains, syncope, profuse sweating, cyanosis, generalised convulsions, and pulmonary edema. ***Irukandji syndrome*** caused by 1cm diameter transparent cnidarians produces minimal local signs with hyper-catecholaminaemia delayed by mins-hours.

Sea bathers' eruption is caused by tiny thimble Jellyfish (*Linuche unguiculata*) producing itching of scalp and skin underneath swimming costumes in tropical waters, or afterwards while showering. An itchy maculo-papular eruption may persist for days, sometimes with mild systemic symptoms. Wash body and swimwear preferably with sea water. Antihistamines and antipruritics may be needed.

Treatment for all marine stings: first, remove victim from the water to prevent drowning. For fish, sea urchin and jellyfish stings, immerse the stung part in hot, not scalding, water (<45°C). Shave off tentacles or wash off with sea water. Vinegar/acetic acid, alcoholic sun tan lotion, and pressure-immobilisation, are no longer recommended because they stimulate further nematocyst discharge! Topical lignocaine HCl spray may relieve pain of jellyfish stings and prevent further nematocyst discharge. Prevention is by obeying warning notices, looking out for washed-up jellyfish before entering the sea, not swimming alone, and wearing protective clothing (wet suit, nylon tights). Stings, especially by Portuguese men o' war, may hypersensitise so that re-exposure will cause anaphylaxis. *Chironex fleckeri* "sea wasp" antivenom, and Scorpion fish antivenom are available in Australia.

魚刺傷：非常疼痛，需要緊急使用溫熱水浸泡！中毒症狀如局部腫脹、變色、流汗、感覺異常、局部淋巴腫脹、壞死，較少見的症狀有噁心、嘔吐、低血壓、心律不整、心跳停止、呼吸困難、抽搐和自主神經興奮。傷口可能會被海洋或淡水中的細菌感染，例如葡萄球菌屬(*Staph.* spp.)、鏈球菌屬(*Strep.* spp.)、創傷弧菌(*Vibrio vulnificus*)、海洋分枝桿菌(*Mycobacterium marinum*)、親水性產氣單孢菌(*Aeromonas hydrophila*)。死亡的案例非常少見(來自玻里尼西亞的玫瑰毒鮪*Synanceia verrucosa*)。

棘皮動物(海星及海膽)：帶毒液的硬棘刺傷相當疼痛，傷口周圍會有明顯的深藍色或黑色痕跡。建議盡早積極手術以移除棘刺，以免毒液有機會進入關節或骨膜。

水母、葡萄牙戰艦(僧帽水母)和其他腔腸動物：螫傷引起劇烈疼痛、線狀鞭痕（特殊臨床特徵）、腫脹、紅斑、水泡形成、壞死、瘢痕，尤其僧帽水母（*Physalia*）引起的血管痙攣，可能導致末梢壞死。系統性症狀包括咳嗽、噁心、嘔吐、腹痛、腹瀉、寒顫、嚴重的肌肉骨骼疼痛、暈厥、大量出汗、發紺、全身性抽搐和肺水腫。**伊魯康吉症候群**(*Irukandji syndrome*)是由約只有 1 立方公分的透明小水母螫傷導致，局部症狀輕微，但可能數分鐘或數小時後引發兒茶酚胺大量釋放，而引起嚴重系統毒性症狀。

海水浴疹：是由微小的頂針水母（*Linuche unguiculata*）引起的，在熱帶水域游泳時，或事後淋浴時，會在頭皮和穿著游泳衣下的皮膚上引起搔癢。搔癢的斑丘疹性皮疹可能會持續數天，有時會伴隨輕微的全身症狀。上岸前最好用海水清洗身體和泳衣，若出現症狀可能需要抗組織胺以及止癢藥物使用。

海洋生物螫/刺傷治療通則：首先，將病人帶離水中，以防止溺水。對於魚、海膽和水母螫傷，可將被螫傷的部位浸泡於<45°C 的溫熱水中。可以移除水母觸手或用海水沖洗；但使用醋酸、酒精性防曬乳液和壓迫固定，則會刺激更多刺絲胞釋放毒液，因此都已不再建議。局部使用止痛麻醉劑(如 lignocaine HCl)可以減少水母螫傷時的疼痛，並防止刺絲胞繼續釋放毒液。預防方法包括遵守警告標語、在進入海水前注意潮間帶的水母、不要獨自游泳、並穿著有適當防護之服裝（潛水衣、防寒衣）。

螫傷，尤其是僧帽水母，再次暴露會引發嚴重過敏反應。在澳洲有俗稱”海黃蜂”的箱型水母*(Chironex fleckeri)*、以及鮪科魚類之抗毒血清可使用。

Characteristics of clinical manifestations of botulism in Vietnam between 2020-2023

越南肉毒桿菌中毒臨床表徵：2020-2023 年

Dr. Doãn Uyên Vy Vanessa

Physician,
Internal Medicine,
Medical Toxicology, Cho Ray Hospital,
Ho Chi Minh City, Vietnam

Overview:
Botulinum toxin food poisoning causes life-threatening disease characterized by a flaccid descending paralysis. Botulinum Antitoxin (BAT) must be given at the right time to prevent respiratory failure requiring prolonged mechanical ventilation.

Methods:
This was a retrospective study. All nationwide cases of botulism were from 7/2020 to 6/2023 were reviewed. All reviewed cases were followed until the patients were completely recovered.

Results:
From 7/2020 to 6/2023, there were a total of 57 cases admitted to 8 different regional hospitals from different provinces, of which 24 were in Kontum. The sources of botulism were: vegetarian pate, vegetarian sausage, mouse meat, and fermented fish. There were 3 cultured food specimens that showed *C.botulinum* type B in 2 samples and type E in one sample. Stool cultures were performed on 13 cases. The results showed 1 sample each of *C. botulinum* type A and B, 3 samples were type B, and 7 samples were negative. There were 16 cases of botulism given BAT after patients had already developed respiratory failure and were receiving mechanical ventilation. None of these cases showed any improvement in muscle weakness or paralysis after treatment. Plasma exchange was performed in 12 cases. Electromyography showed axonal damage to motor nerves and testing for myasthenia gravis was negative. The time for complete recovery depended on the degree of paralysis, and ranged from 1 to 6 months for patients who had *C. botulinum* type A and B, and 2

weeks for all patients who had C. botulinum type E. The mortality rate of botulism was 8.7%.

Conclusion:

BAT administration at the correct time is critical to prevent the progression to respiratory failure. This improves patient outcome and avoids the needless use of an expensive antidote.

About us

Taiwan Poison Control Center

In response to the rapidly increased poisoning incidents in Taiwan, and in line with the international trend, under the auspices of Ministry of Health & Welfare, Taiwan's first and only national poison control center (PCC) was founded in Taipei Veterans General Hospital in July 1985. It is the first 24-hour consultation center for poison and drug information in Taiwan and Asia, serving healthcare professionals at all levels and the general public.

Foundation for Poison Control

The foundation was established in 1994 with the aim of promoting research, education, training, and assistance in the prevention and control of drugs, pharmaceutical, and chemical poisonings. We hold annual international conferences on toxicology to facilitate the exchange of knowledge with scholars from different countries, enhance our international capabilities, and facilitate communication and collaboration among poison control centers from around the world.

Contact us

(+886) 02-2871-7121
(+886) 02-2875-7525#821

d3-pcc@vghtpe.gov.tw
pccvgh@gmail.com

5F., Chih-The Building, No.322,
Sec. 2, Shih-Pai Rd., Beitou Dist.,
Taipei City 112062, Taiwan

https://wd.vghtpe.gov.tw/CT/Index.action
https://www.pcc-vghtpe.tw/tc/
http://www.fpc.org.tw/

Taipei Veterans General Hospital
臺北榮民總醫院 職業醫學及臨床毒物部
Department of Occupational Medicine and Clinical Toxicology