# NSW Clinical Mass Spec Forum

# MS Applications in Clinical Toxicology

**Date:** 20th April, 2023

**Location:** University of Technology, Sydney, CB04.05.430

**Online link:**
https://zoom.uts.edu.au/j/88346142764

**Meeting Chair:**
Dr Jay Ramanathan MBBS MPH BN AFRACMA FRACP
*RPA & Liverpool Hospitals, WSU School of Medicine*

**5:30 – 6:00pm**
Arrival and refreshments

**6:00 – 6:25pm**
Dr Rowena Penafiel
*Quantitating methadone partitioning in erythrocytes to inform the interpretation of whole blood methadone concentrations*

**6:30 – 6:55pm**
A/Prof Angela Chiew
*Paracetamol metabolites on presentation following an acute paracetamol overdose (ATOM-7)*

**7:00 – 7:25pm**
A/Prof Darren Roberts
*Toxic tales about thebaine*

**7:30 – 8:30**
*Refreshments and Networking*

## |6:00 - 6:25pm| Quantitating methadone partitioning in erythrocytes to inform the interpretation of whole blood methadone concentrations

**Dr Rowena Penafiel** is an Advanced Trainee in Clinical Pharmacology, Toxicology and Addiction Medicine at Royal Prince Alfred Hospital. She previously completed a Bachelor of Science with First Class Honours in Pharmacology at the University of Sydney before proceeding to a Bachelor of Medicine and Bachelor of Surgery at the Australian National University.


**Abstract**

Methadone is commonly implicated in unexpected deaths. Forensic laboratories report methadone blood concentrations but clinical studies report methadone plasma concentrations, and the relationship between results in these different matrices is poorly defined. Our pilot study investigated recovery and matrix effects in whole blood when using an existing clinical solid phase extraction protocol designed for plasma samples before analysis by LC-MS/MS. This method was then employed to compare methadone concentrations in whole blood and plasma in patients on oral methadone.


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## |6:30 - 6:55pm| Paracetamol metabolites on presentation following an acute paracetamol overdose (ATOM-7)

**Associate Professor Angela Chiew** is a Clinical Toxicologist and Emergency Medicine Physician at Prince of Wales Hospital, Randwick and a Clinical Toxicologist for the NSW Poison's Information Centre. She completed her PhD in Paracetamol Poisoning in 2020 through Sydney University. She performs research into paracetamol poisoning and her major contribution has been the establishment of the Australian Toxicology Monitoring (ATOM) Study. She is on the editorial boards of Emergency Medicine Australasia, British Journal of Clinal Pharmacology and Clinical Toxicology, and is the lead author of the Australian and New Zealand Paracetamol Guidelines published in 2015 and 2019. She has just been appointed the Lead Clinical Toxicologist overseeing and managing the NSW Poisons Information Centre Research Portfolio. She is also chair of the International Clinical Toxicology Recommendations Collaborative into paracetamol poisoning.


### Abstract

**Introduction:** Paracetamol is commonly taken in overdose and can cause acute liver injury (ALI) via the toxic metabolite NAPQI formed by cytochrome(CYP) P450 pathway. We aimed to evaluate the concentrations of paracetamol metabolites on presentation following an acute paracetamol poisoning and whether these predicted the subsequent onset of ALI.

**Method:** The Australian Toxicology Monitoring (ATOM) study is a prospective observational study, recruiting via the NSW and QLD PICs and 4 toxicology units. Patients(>14y) following an acute paracetamol ingestion presenting < 24h post-ingestion were recruited from Sept 2013 until Dec 2016. Initial samples were analysed for paracetamol metabolites by liquid chromatography, tandem mass spectrometry. Metabolites measured were the nontoxic glucuronide (APAP-Glu) and sulfate (APAP-Sul) conjugates and NAPQI (toxic metabolite) conjugates APAP-cysteine (APAP-Cys) and APAP-mercapturate (APAP-Mer). The primary outcome was hepatotoxicity (ALT>1000U/L).

**Results:** 200 patients were included, median age 25y and a median ingested dose of 20g. 191 received acetylcysteine at a median time of 5.8h post-ingestion. 26 developed hepatotoxicity, one had hepatotoxicity on arrival (excluded from analysis). Those who developed hepatotoxicity had significantly higher total CYP metabolite concentrations: [36.8µmol/L (IQR: 27.8 – 51.7) vs 10.8µmol/L (IQR:6.9 – 19.5)] and these were a greater proportion of total metabolites [5.4% (IQR:3.8 – 7.7) vs 1.7% (IQR:1.3 – 2.6)(p<0.001)]. Furthermore, those who developed hepatotoxicity had lower APAP-Sul concentrations [49.1µmol/L (IQR: 24.7 – 72.2) vs 78.7µmol/L (53.6 – 116.4)] and lower percentage of APAP-Sul [6.3% (IQR: 4.6 – 10.9) vs 13.1% (9.1 – 20.8)(p<0.001)].

**Conclusion**: This study found that those who developed ALI had higher paracetamol metabolites derived from CYP pathway and lower sulfation metabolite on presentation. Paracetamol metabolites may be utilised in the future to identify patients who could benefit from increased acetylcysteine or newer adjunct or research therapies.

## |7:00 - 7:25pm| Toxic tales about thebaine

**Associate Professor Darren Roberts** is the Medical Director of the NSW Poisons Information Centre and Staff Specialist in clinical toxicology/pharmacology and addiction medicine at Royal Prince Alfred Hospital. His clinical training is in clinical pharmacology/toxicology, nephrology and addiction medicine. He has a PhD in clinical toxicology and has completed fellowships in nephrology/vasculitis (Cambridge UK) and anti-infectives in critical illness (University of Queensland).


**Abstract**

Drinking poppy seed washings as a tea can give opiate effects. In late 2022, a non-food grade poppy seed high in the neurotoxic alkaloid thebaine entered the food market and people consuming this as a tea experienced thebaine toxicity. This talk will discuss what we knew about thebaine before this cluster, the clinical effects of patients in NSW, the importance of laboratory testing to confirm the presence of thebaine, and the pharmacokinetics of thebaine in patients providing serial samples


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