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Title	Paracetamol overdose: limiting the potential for harm

Authors:

	Title	First name	**Mid inits**	Last name	Postnom (eg, PhD)	Position1	Address1	Position2	Address2	Tel	Email
1	Prof.	Andis		Graudins	MB BS (Hons), PhD, FACEM, FACMT	Clinical Toxicologist and Director, Monash Clinical Toxicology Unit	1	Professor of Emergency and Toxicology Research (Adjunct)	2	03 9594 6666 / 042041 9420	Andis.Graudins@monashhealth.org
2	Dr.	Anselm		Wong	MBBS, FACEM, DipTox	NHMRC Research Fellow	2	Clinical Toxicologist and Emergency Physician	3		anselm.wong@austin.org.au

Number of corresponding author:	1
Number of alternative corresponding author:	

Addresses:

	Institution	Postal address	City	State	Post Code	Nation
1	Monash Health	Department of Emergency Medicine, Monash Dandenong Hospital	Melbourne	VIC	3175	
2	Monash University	Department of Emergency Medicine, Monash Dandenong Hospital	Melbourne	VIC	3175	
3	Victorian Poisons Information Centre, Austin Hospital	Studley Road	Melbourne	VIC	3084	

Postal address of first corresponding author (if different from the institutional address given above)	

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Paracetamol overdose: limiting the potential for harm

Paracetamol remains one of the drugs most frequently implicated in deliberate self-poisoning overdoses in Australia

Paracetamol is the pharmaceutical agent most frequently taken for deliberate self-poisoning by adults and adolescents in Australia, the United Kingdom, and other developed countries.[1] It is primarily taken in overdose by younger women, in most cases for deliberate self-harm. Toxicity can also result from accidental repeated supra-therapeutic ingestion, particularly by people at higher risk of hepatotoxicity.[2]

In this issue of the *MJA*, Cairns and her colleagues[3] highlight the increasing frequency and size of paracetamol overdoses from deliberate self-poisoning in Australia during 2004–2017. Paracetamol pack sizes sold in Australian supermarkets are limited to a maximum of 20 tablets (10 grams), but pharmacies sell packs of up to 100 tablets (50 grams). Given the impulsive nature of many paracetamol overdoses, access to larger pack sizes increases the risk of ingesting larger, toxic amounts and therefore the numbers of people who must be admitted to hospital for treatment with acetylcysteine.

Consequently, preventive measures that reduce the size of paracetamol overdoses have been of great interest. One measure employed overseas, restricting pack sizes, has had variable success. Despite tighter restrictions on pack sizes in Ireland, the size of paracetamol overdoses in Ireland and the United Kingdom were found to be similar.[4] In Scotland, the rate of and mortality from paracetamol overdoses did not drop after pack sizes were limited,[5] but mortality and the frequency of paracetamol-related liver transplantation declined in England and Wales.[6] The question of pack size restriction and its implementation still needs to be discussed in Australia.

Another emerging problem highlighted by Cairns and colleagues[3] is the increasing use of modified release paracetamol in overdoses in Australia, which increases the challenges for treating physicians. Modified release paracetamol is available over the counter in packs of 96 caplets, so that 63.8 grams can be ingested from one box. Compared with immediate release paracetamol, overdose with the modified release preparation is associated with delayed and erratic absorption, prolonged elevation of serum paracetamol concentration, and delayed development of liver injury.[7] Overdose treatment guidelines do not adequately cover all paracetamol ingestion scenarios;[8] liver injury can ensue despite increasing antidote dosing to treat massive ingestion of modified release paracetamol.[7] Notably, as Cairns and her co-authors also point out, the convenience from a therapeutic perspective of three-times-a-day dosing (instead of four times a day for

immediate release formulations) is of debatable significance. The Therapeutic Goods Administration recently proposed interim re-scheduling of modified release paracetamol, removing it from behind-the-counter sales to pharmacist-only access from October 2019.[9] However, the approach of the European Medicines Authority, which recently removed modified release paracetamol products from the market altogether,[10] is another option that might be considered in Australia.

While Cairns and colleagues found that the size of paracetamol overdoses and the incidence of related liver injury each increased across the study period, mortality had not risen.[3] This may, in part, be a testament to the effectiveness of acetylcysteine as an antidote to paracetamol poisoning and in preventing or modifying the degree of liver injury. For several decades, paracetamol overdose has been treated with intravenous acetylcysteine in a three-bag regimen over 20–21 hours, or longer in patients with liver injury. Acetylcysteine is highly effective in averting progression to liver injury and fulminant hepatic failure, and in reducing mortality. However, adverse drug reaction rates are high and may lead to treatment being interrupted or ceased prematurely.[11] Recent Australian studies found that simplifying this regimen to a two-bag infusion significantly reduces the incidence of adverse reactions, with no change in therapeutic effectiveness.[12] This advice is being adopted by many toxicology treatment centres in Australia, but further investigation is required to determine best practice acetylcysteine dosing. Given the variability in overdose sizes, formulations, and post-ingestion time of presentation, a one-dose-fits-all approach is inappropriate, and treatment should be tailored to the specific paracetamol overdose scenario. For example, patients with a massive paracetamol ingestion are most likely to benefit from increased acetylcysteine dosing,[13] while abbreviated treatment regimens may be suitable for some patients at low risk of liver injury.[14]

As well as refining treatment regimens for individual paracetamol overdose types, improving recognition of mental health problems and the primary prevention of deliberate self-poisoning by adolescents and adults, together with changes in policy on paracetamol pack sizes and access, are also important preventive avenues that should be explored. In the long term, combining these strategies may improve the toxico-epidemiology of paracetamol poisoning in Australia.

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Author details

Andis Graudins[1,2]
Anselm Wong[2,3]
1 Monash Health, Melbourne, VIC.
2 Monash University, Melbourne, VIC.
3 Victorian Poisons Information Centre, Austin Hospital, Melbourne, VIC.
Andis.Graudins@monashhealth.org

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See Research (Cairns)

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