Preventing Pharmaceutical Poisonings

Implementing poison prevention strategies to reduce the morbidity and mortality associated with poisonings can result in substantial health resource savings. This article reviews key strategies used to prevent poisonings, with the focus placed on reducing unintentional overdose in young children. Strategies to prevent harm associated with drug misuse/abuse and overdose are not addressed here.

Quantifying the actual pharmaceutical poisoning burden across the spectrum of degree of injury is an inexact science. Translation: we do not know exactly how many people are poisoned each year! Poisoned patients may die before reaching hospital or die in the Emergency Department prior to admission, and there can be overlap of the national hospital morbidity and mortality databases. Mortality statistics for any one year can be affected by the number of open coroner certified cases, as well as changes in coding practices.

Hospital poisoning statistics
Poisoning represents a common cause of hospital presentations and admissions for both adults and children. Data released by the Australian Institute of Health and Welfare (AIHW) for Australian public, private and psychiatric hospitals showed that during the year 2005 – 2006 [1]:

- Community injury accounted for 400,019 hospital separations = 5.5% of a total of 7,311,983 hospital separations from
- Pharmaceutical poisonings (2%) were the fifth most common reported identifiable cause of injury
- In children aged 4 years and under, pharmaceutical poisonings comprised 7% of the injuries resulting for hospitalisations.

On a positive note, the age-standardised rate of pharmaceutical poisonings resulting in hospital separations since the 1999 – 2000 12 month period showed a large downward trend (down from 100 to 63 per 100,000 population), mainly due to a reduction in rates in the 0–4 year age group (from 340 to 198 per 100,000) and the 15–49 year age group (from 116 to 63 per 100,000). (During the same period, the overall community injury rate for hospital separations had risen from 1,724 cases per 100,000 population in 1999 – 2000 to 1,790 cases per 100,000 in 2005 – 2006). The increased emphasis at the regulatory and community level on medication safety and poison prevention may account for this positive result.

Coronial Poisoning Statistics
Data from the Australian Bureau of Statistics [2] found that accidental poisoning (ICD-10 codes X40-X49, see below) accounted for 799 deaths registered in 2009 (0.6% of all registered deaths in 2009) and 8.9% of all external causes of death. More than twice as many males as females died from accidental poisoning in 2009; the median age being 41.5 years. Drugs accounted for 14.9% (n=566) of suicide deaths, followed by poisoning by other methods including by alcohol and motor vehicle exhaust (11.7%).
## Selected external causes of death, Mechanism by intent - 2009(a)(b) [2]

<table>
<thead>
<tr>
<th>Mechanism of death</th>
<th>Accidental death no.</th>
<th>Intentional harm(c) no.</th>
<th>self-Assault no.</th>
<th>Undetermined intent no.</th>
<th>Other intent(d) no.</th>
<th>Total no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poisonings (X40-X90, X60-X69, X85-X90, Y10-Y19)</td>
<td>799</td>
<td>566</td>
<td>3</td>
<td>345</td>
<td>0</td>
<td>1 713</td>
</tr>
<tr>
<td>Hanging (W75-W84, X70, X91, Y20)</td>
<td>220</td>
<td>1 093</td>
<td>6</td>
<td>127</td>
<td>0</td>
<td>1 446</td>
</tr>
<tr>
<td>Drowning &amp; submersion (W65-W74, X71, X92, Y21)</td>
<td>182</td>
<td>43</td>
<td>1</td>
<td>54</td>
<td>0</td>
<td>280</td>
</tr>
<tr>
<td>Firearms (W32-W34, X72-X74, X93-X95, Y22-Y24)</td>
<td>6</td>
<td>164</td>
<td>30</td>
<td>24</td>
<td>0</td>
<td>224</td>
</tr>
<tr>
<td>Contact with sharp object (W25-W29, X78, X99, Y28)</td>
<td>9</td>
<td>55</td>
<td>74</td>
<td>22</td>
<td>0</td>
<td>160</td>
</tr>
<tr>
<td>Falls (W00-W19, X80, Y01,Y30)</td>
<td>1 370</td>
<td>81</td>
<td>0</td>
<td>29</td>
<td>0</td>
<td>1 480</td>
</tr>
<tr>
<td>Other(e)</td>
<td>2 736</td>
<td>130</td>
<td>95</td>
<td>393</td>
<td>225</td>
<td>3 579</td>
</tr>
<tr>
<td>Total</td>
<td>5 322</td>
<td>2 132</td>
<td>211</td>
<td>994</td>
<td>225</td>
<td>8 884</td>
</tr>
</tbody>
</table>

(a) Causes of death data for 2009 are preliminary and subject to a revisions process.
(b) Data cells with small values have been randomly assigned to protect the confidentiality of individuals. As a result, some totals will not equal the sum of their components. Cells with a zero value have not been affected by confidentialisation.
(c) Includes ICD-10 codes X60-X84 and Y87.0. Care needs to be taken in interpreting figures relating to suicide.
(d) Includes Complications of medical and surgical care (Y40-Y84), Legal Intervention and operations of war (Y35-Y36), Sequelae with surgical and medical care as external cause (Y88) and Sequelae of other external causes (Y89).
(e) Includes sequelea, explosives, smoke/fire/flames, blunt object, jumping or lying before moving object, crashing of motor vehicle, other and unspecified means.

**International Classification of Diseases 10th version (ICD-10)**

Accidental poisoning by and exposure to noxious substances - X40-X49. (Evidence of alcohol involvement in combination with substances specified below may be identified by using the supplementary codes Y90-Y91).

**Includes:**
- accidental overdose of drug, wrong drug given or taken in error, and drug taken inadvertently
- accidents in the use of drugs, medicaments and biological substances in medical and surgical procedures
- poisoning, when not specified whether accidental or with intent to harm

**Excludes:**
• administration with suicidal or homicidal intent, or intent to harm, or in other circumstances classifiable to X60-X69, X85-X90, Y10-Y19
• correct drug properly administered in therapeutic or prophylactic dosage as the cause of any adverse effect (Y40-Y59)
• X40 Accidental poisoning by and exposure to nonopioid analgesics, antipyretics and antirheumatics
• X41 Accidental poisoning by and exposure to antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified
• X42 Accidental poisoning by and exposure to narcotics and psychodysleptics [hallucinogens], not elsewhere classified
• X43 Accidental poisoning by and exposure to other drugs acting on the autonomic nervous system
• X44 Accidental poisoning by and exposure to other and unspecified drugs, medicaments and biological substances
• X45 Accidental poisoning by and exposure to alcohol
• X46 Accidental poisoning by and exposure to organic solvents and halogenated hydrocarbons and their vapours
• X47 Accidental poisoning by and exposure to other gases and vapours
• X48 Accidental poisoning by and exposure to pesticides
• X49 Accidental

Poison Information Centre Statistics
For less severe poisoning exposures, some may be reported to the poisons information centre resulting in observation and treatment at home and/or at a medical centre; some may not be reported at all. In 2010, 218,217 calls were received by the four Poisons Information Centres collectively (NSW, Victoria, Western Australia and Queensland); just over 70% of these comprising poisoning exposures as against information queries. [3] The calls involved children (49%), adults (48%) and animals (3%). The “Top Ten” agents were:

1. Paracetamol-containing products (non-narcotics)
2. Benzodiazepines
3. Detergents
4. Ibuprofen
5. Ethanol
6. SSRIs
7. Spiders
8. Cleaners
9. Paracetamol+narcotic combination analgesics
10. Quetiapine.

Calls involving children (77% from the 3 years and under age group) were generally less serious, with victims advised to “stay at home” (80% child calls compared to 45% adult calls); adult calls were more likely to result in medical care (hospital, general practitioner).

WHO Poison Prevention Resolution
At the global level, in May this year, the 64th World Health Assembly adopted a landmark resolution on child injury prevention.[4] This followed on from the WHO/UNICEF World Report on Child Injury Prevention [5] and identified child injury as a “major child survival issue”. It urged Member States (Australia is one!) to prioritise the prevention of child injuries and implement the recommendations of the World Report. For poisoning, these recommendations focus on:

• Implementing reliable data collection
• Evaluating prevention interventions
• Supporting poisons information centres
• Using treatment protocols to assess and manage common child poisonings
• Regulating the manufacture, storage, distribution and disposal of toxic substances
• Mandating the use of child resistant packaging for medications and toxic substances
• Reducing environmental toxic contamination

A succinct summary of the risk factors for child poisoning is tabulated in the World Report [5]:

<table>
<thead>
<tr>
<th>Child</th>
<th>Agent</th>
<th>Physical environment</th>
<th>Socioeconomic environment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age and developmental factors (such as curiosity, judgement; gender; parental supervision)</td>
<td>Ease of opening package; attractiveness of substance; inadequate labelling; poor storage.</td>
<td>Cupboards within easy reach of children; absence of locking devices on cabinets; exposure to agents.</td>
<td>Lack of regulations and standards for toxic products and packaging; poverty; lack of awareness of toxicity and poisoning risks among caregivers.</td>
</tr>
<tr>
<td>Event</td>
<td>Occurrence</td>
<td>Toxicity of chemical; dose consumed; ease with which substance can be consumed (for instance, as liquid rather than solid).</td>
<td>Places where child can ingest substances without being seen.</td>
</tr>
<tr>
<td>Post-event</td>
<td>Child’s inability to communicate incident; lack of access to poison control centre.</td>
<td>Chemical agent without an antidote.</td>
<td>Lack of adequate pre-hospital care, acute care and rehabilitation.</td>
</tr>
</tbody>
</table>

The most effective strategies to prevent poisonings target high-risk populations (e.g., young children) and risk factors most amenable to change (e.g., “passive measures” such as using a less toxic agent, safer packaging and storage.)

Preventing poisoning – reducing the toxicity of the agent
A frequent suggestion is to include an antidote (methionine) in paracetamol tablets, and this was trialled in the UK in the late 1990s. However, this has not been a success since not all brands included the antidote, those that did were more expensive to purchase, and some people were allergic to the methionine. [6]

In the past decade, both Australia and New Zealand reduced the percentage of methanol included in methylated spirits as a denaturant, to reduce the methanol-associated toxicity of the commercially available product.

This year the U.S. Food and Drug Administration (FDA) announced a three year phase-in of limiting the paracetamol dose to a maximum of 325 mg/unit dose in prescription combination products, to reduce the potential for liver toxicity. Anecdotes rather than facts underpinned this decision. [7] Somewhat bizarrely, the advisory committees to the FDA also voted for non-prescription combination products retain their paracetamol 500mg/unit dose, as well as rejecting limits to be placed on the tubs of 1000 tablets of paracetamol sold in USA general stores.

Preventing poisoning – safe storage
Using locked cupboards and boxes, and fitting child resistant locks to cupboards and drawers, offer the most secure storage for medicines and poisons. The safety of unsecured storage depends on the supervision of the room (bedrooms and bathrooms fare least well), along with height, access and visibility to the child. Surveys generally show
that storage of medicines and poisons in the home is poor, with most products readily visible and accessible to children. [8]

Preventing poisoning - reducing the agent's attractiveness
Bitrex (denatonium sodium) is an extremely bitter agent added to non-pharmaceutical products such as the highly toxic pesticide paraquat, ethylene glycol (anti-freeze, a sweet-tasting liquid) and methylated spirits, to deter ingestion beyond the first mouthful. An emetic (ipecacuanha) was also added to paraquat to induce vomiting following ingestion. Stenching agents such as Rhodamine B have been added to a range of pesticides to deter ingestion, and to LPG to warn of its presence.

Liquids that resemble beverages (e.g., paraffin, ethylene glycol) may be mistaken for drinks especially if decanted into cups or drink bottles. Tablets and capsules can often be confused with lollies, whilst some medicines (phenolphthalein, pyrantel) may be formulated as chocolate squares. The formulation of medicines and poisons in the form of beverages, lollies, chocolates, toys and animal and cartoon characters is strongly discouraged in the preamble of the Australian and NZ Standards for Child Resistant Packaging. [9-12]

Preventing poisoning – removing/replacing the toxic agent
Removing a toxic agent, or restricting access to the agent, may result in other agents being sought out for overdose instead. During 1967 – 1976, replacing barbiturates with the markedly less toxic benzodiazepines resulted in reduced morbidity and mortality associated with hypnotic overdose. [13] Over the same time period, the decline in aspirin use (and overdose) was matched by an increase in paracetamol poisoning; mortality declined since paracetamol overdose was more readily managed with its specific antidote n-acetylcysteine.

The replacement of cresol with chlorocresol in vaporizing fluids during 1976 – 1978 resulted in dramatic reductions in both systemic and dermal toxicity following moderate ingestions. [14]

More recently, the use of the low toxicity serotonin re-uptake inhibitor antidepressants in favour of the cardiotoxic tricyclics antidepressants has significantly reduced antidepressant overdose mortality. In 1995, the overall relative mortality rate for tricyclic drugs was 34.14 (95% confidence interval 32.47 to 38.86; P < 0.001), monoamine oxidase inhibitors 13.48 (6.93 to 22.19; P < 0.001), atypical drugs 6.19 (4.04 to 8.80; P < 0.001), and selective serotonin reuptake inhibitors 2.02 (0.64 to 4.17; P < 0.001). [15]

Preventing poisoning – implementing poison prevention education
Educational approaches are most effective when used in conjunction with other strategies such as passive measures (e.g., child resistant packaging). Public awareness campaigns have a “feel good factor” but have not had a significant impact in changing behaviours and reducing poisonings. Poison prevention messages targeting caregivers may be most effective if they address changing behaviours of the caregivers. Home visits to re-inforce poison prevention education have been effective. [5] Perhaps home medication review visits could be used as poison prevention audit and education opportunities.

The WHO Report [5] identifies educational interventions with specific aims that are likely to be effective:
Pharmacy point-for-sale warnings on medicines dangerous in overdose, and that common household products and “healthy” or “natural” products such as essential oils and iron tablets can be dangerous to children

- Educating consumers that “child resistant” is not “child proof”
- Showing caregivers how to open and re-close correctly child resistant caps

Preventing poisoning – restricting access and using safer packaging

"Child resistant packaging" (CRP) is packaging that is significantly difficult for most children under five years of age to open or obtain a toxic amount of the substance within a reasonable time. It is not childproof packaging. CRP delays (but does not necessarily stop) access to the medicine or poison, so safe storage of products out of reach of children remains essential. The packaging should not be difficult for adults with no overt physical handicaps to use properly, i.e., CRP is also “senior friendly”. [9-12] Child resistant packaging includes packaging such as:

- child resistant closures (CRCs) or child safety caps (CSCs) that can, after opening, be reclosed with a similar degree of security, e.g., Clic-Loc, Snap-Safe, Pop-Lok, Palm-n-Turn, Arrow.
- non-recloseable packaging, such as strip foil or plastic blister unit (opaque or clear) packaging.

Child resistant packaging (CRP) has been effective in reducing both child and adult poisonings. In the USA, the use of CSCs was introduced in 1974, and their widespread use on medicines and toxic substances found in and around the home was associated with reductions of up to 80% in hospital admissions for children under five years of age. The use of CSCs over two decades in the USA reduced the mortality rate from the unintentional ingestion of oral prescription drugs by under five year olds by approximately 45%. [16]

A UK study found that medications involved in poisonings were most frequently packed in containers without child resistant closures (63%) or transparent blisters (20%). CSCs, foil strips, sachets and opaque blister packs had low associations with poisoning incidents. [8]

The benefits of using CRP have not been confined to child poisoning. Introducing non-recloseable CRP for carbamazepine and paracetamol resulted in substantial reductions in the number of tablets and amount ingested during adult intentional poisonings. [17, 18] In the case of carbamazepine the concomitant reduction in pack size more so than the change in packaging type appeared to have had the greater impact on the outcome of the overdose. Nonetheless, the use of non-recloseable CRP such as foil or plastic bubble packaging can slow down impulsive or spontaneous suicide attempts, allowing time for the person to rethink the situation. [19]

The CSCs used on medicines and poisons in Australia and New Zealand have been tested against each country’s Standard for Child Resistant Packaging (AS 1928-2007, NZS 5825, 1991). [9-12] Testing involves observing if panels of up to 200 children aged 42 to 51 months can gain access to the containers both before and after a non-verbal demonstration is given. To meet the Standard, not more than 15% and 20% of children can gain access prior to and after the demonstration respectively. Similarly, the Standard is met when 10% of panels of up to 100 adults aged 50 – 70 years are able to open and then re-close containers fitted with CSCs, having received only written (no verbal)
instructions. In New Zealand, this “senior friendly” test remains an optional addition, but it is a requirement of Standards used in Australia and the USA.

In the case of non-recloseable CRP, the Standard in current use (AS 1928-2007) describes the types of recommended packaging materials and contain physical test requirements relating to seal strength and integrity. The new Standard (AS 5014-2010) includes panel testing (children and adults) but has yet to be implemented. The recent problems in NZ where the new “child resistant foil packaging” used on Lanoxin tablets was completely resistant to adults attempting to access the tablets (the manufacturer advised pharmacists to re-pack the tablets into containers) may have been avoided had the packaging been tested using the new Standard AS 5014-2010.

The TGA is currently conducting a scoping exercise in relation to a review of the labelling and packaging regulatory framework. Once the scope and priorities have been determined, the TGA will engage with relevant stakeholders. It is anticipated that this will include consumer, professional and industry representative bodies, other government agencies and the jurisdictions. [20]


The medicines and poisons requiring CRP in Australia and New Zealand vary considerably, and these differences may now be addressed through the recently announced resurrection of the Australia New Zealand Therapeutic Products Agency (ANZTPA) [21]. This opens the way for authorities in both countries to work together to adopt a harmonised regulatory approach to enhance CRP to prevent poisonings. It is understood that there will be no diminution of regulatory standards in Australia. In New Zealand, an extremely limited and old list of medicines to be supplied in non-recloseable CRP appears in the Medicines Regulations (1984). However, because CSCs are excluded in the NZ definition of CRP (it refers only to non-recloseable packaging), the Standard is not encompassed by the regulations. Since 1995, a limited list of dispensed liquid medicines have, as part of a dispensing contractual requirement, been supplied with CSCs that do meet the Standard. This measure, along with a voluntary Code of Practice for Child-resistant Packaging of Toxic Substances (1998), has had an equivocal impact on preventing child poisonings in New Zealand, reflecting the limited and non-legislative nature of the intervention.

The Australian Therapeutic Goods Order 80 lists the medicines to be packaged at the manufacturer level in CRP meeting the relevant Standard [9-11] whilst those poisons requiring CRP appear as individual entries in the Standard for the Uniform Scheduling of Medicines and Poisons. These packaging requirements apply to the manufacturer’s original pack. While they do not apply to re-packaging by a pharmacist should it be decided that the original packaging is unsuitable for the patient, they do guide pharmacists in making professional decisions on what packaging is most appropriate to use to better ensure child safety.

In 2000 a Melbourne group investigated the poisoning risk associated with medicines not currently packaged in CRP. [22] They used the toxicity of a medicine along with its frequency and severity of poisonings as the basis for recommendations on not only those medicines requiring CRP but also on implementing strategies to support the wider use of CRP. In addition, they identified areas for further action, namely research into the failure
rates of CRP and improvements to poisoning surveillance systems to better determine how poisonings occur and how they might best be prevented.

In the UK, Ireland and Scotland, during the 1990s the sale of paracetamol (and aspirin) tablets were restricted to 16 tablets per person per purchase from retail outlets and 32 tablets per sale from pharmacies. [23, 24] The packaging was changed from a loose preparation to a blister pack and this additional measure resulted in an almost doubling of the price per tablet of both paracetamol and aspirin. These regulatory changes had substantial beneficial effects on mortality and morbidity associated with self poisoning using these drugs. In Scotland there was a dramatic 45% fall in deaths from paracetamol poisoning. However, the benefits were short-lived (lasting about two years), with deaths and admissions rising again.

**What of the “non-toxic” ingestions?**
The non-toxic ingestion by a child, whilst posing no immediate danger, can serve as a signal to enhance poison prevention practices. The pharmacist can take the opportunity, whilst reassuring the caregiver that no acute toxicity exists this time, to offer practical advice on “poison proofing” the home to prevent what may well be a toxic exposure next time.

**Low toxicity products [25-29]**

<table>
<thead>
<tr>
<th>Miscellaneous</th>
<th>Household cleaners</th>
<th>Cosmetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bird seed</td>
<td>Carpet cleaners</td>
<td>Baby oil</td>
</tr>
<tr>
<td>Blu Tack</td>
<td>Fabric conditioners</td>
<td>Baby wipes</td>
</tr>
<tr>
<td>Candles (beeswax or paraffin)</td>
<td>Fabric washing powders</td>
<td>Hair conditioner/ shampoo</td>
</tr>
<tr>
<td>Cat/dog food</td>
<td>Fabric washing flakes</td>
<td>Moisturiser cream/lotion</td>
</tr>
<tr>
<td>Chalk</td>
<td>Fabric washing liquids</td>
<td>Solid cosmetics</td>
</tr>
<tr>
<td>Coal</td>
<td>Scouring powders/creams</td>
<td>(lipstick, make-up)</td>
</tr>
<tr>
<td>Charcoal</td>
<td>Washing up liquid</td>
<td>Shaving cream</td>
</tr>
<tr>
<td>Crayons</td>
<td>(NOT machine dishwashing products)</td>
<td>Soaps</td>
</tr>
<tr>
<td>Dyes</td>
<td>Do It Yourself Products</td>
<td></td>
</tr>
<tr>
<td>Felt tip/ball point pen ink</td>
<td>Emulsion paint</td>
<td></td>
</tr>
<tr>
<td>Fish food</td>
<td>Putty</td>
<td></td>
</tr>
<tr>
<td>Houseplant food</td>
<td>PVA glue/superglue</td>
<td></td>
</tr>
<tr>
<td>Icepack fluid</td>
<td>Wallpaper paste</td>
<td></td>
</tr>
<tr>
<td>Pencil “leads”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Play-Doh and modelling clay</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silica gel</td>
<td>Garden</td>
<td></td>
</tr>
<tr>
<td>Silly Putty</td>
<td>Soil</td>
<td></td>
</tr>
<tr>
<td>Sweeteners (saccharin, cyclamates)</td>
<td>Faeces</td>
<td></td>
</tr>
<tr>
<td>Teething rings</td>
<td>Worms/slugs</td>
<td></td>
</tr>
<tr>
<td>Thermometers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toothpaste</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pharmacists and pharmacy staff are well-placed to identify potential poisoning hazards and dangerous medication management practices, and intervene in a practical way. The
websites of the Poison Information Centres in Australia and NZ provide ready access to attractive and useful resources that can be used in poison prevention activities in the pharmacy and during home medication review visits. The Centres may also supply brochures, stickers and magnets - they are only a telephone call away

Australia: 13 11 26

NZ: 1800 POISON

Professor Nerida Smith
Useful links to Australian and NZ Poisons Information

NSW Poisons Information Centre
http://www.chw.edu.au/poisons/

Queensland Poisons Information Centre

Victorian Poisons Information Centre
http://www.austin.org.au/poisons

Western Australian Poisons Information Centre

NZ Poisons Information Centre
http://poisons.co.nz/

NZ Poisons Information Database
http://www.toxinz.com/

Australian Wikitox Open Source Clinical Toxicology Curriculum (includes HyperTox)
http://curriculum.toxicology.wikispaces.net/Home+Page
References


