Childhood poisoning in the developing world--just snakes, spiders, paraffin and pesticides?

G. Randall Bond, MD
No conflict to declare
Special Thanks

Joanna Tempowski
Kalle Hoppu
Michael Eddleston
<table>
<thead>
<tr>
<th>Terms and terms…</th>
<th>Developing countries</th>
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<td>You get the idea</td>
<td>Low income countries</td>
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<td>Low resource settings</td>
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Proportion of all people living on US$10 or less (PPP) / day
In Africa, injuries are 2% of childhood mortality*. From WHO, poisoning is 3.9% of injury mortality worldwide†.

* under 6 y - Global, regional and national causes of child mortality in 2008: a systematic analysis  Black Lancet 2010  † Under 18y world- WHO
Mortality rates due to poisoning per 100,000 children by WHO region and country income level, 2004

Source: WORLD REPORT ON CHILD INJURY PREVENTION, WHO, 2008
Context: Total Sub-Saharan under 5 mortality is 17,100 per 100,000
WHO--worldwide

- 125 children die from poisoning every day.
- The rate of poisoning is highest for children under 1 year, but peaks again at 15 years and older as adolescents begin experimenting with substances.
- Fatal poisoning rates are 4 times higher in LMICs than HICs.
- The most common poisoning agents in LMICs are paraffin, household products and pharmaceuticals.
- In HICs the most common poisons are over-the-counter medications, household products, and prescription drugs.
Pediatric Poisonings

Environmental—natural: snakes, spiders, plants
Environmental—chemical: kerosene, caustics, pesticides
Environmental*—pollutants: air and soil
Pharmaceutical—unintentional, therapeutic*

*Not counted as poisoning by WHO
Environmental—natural: snakes, spiders, plants

Snakebite—5M bites, 100-200,000 deaths/yr all Indian experience evaluating 122,848 deaths
Snakebite 0.5% of all deaths
For age 0-4, 52 of 23,630 deaths age 0-4
Age 0-4 were 52/562 snakebite deaths: 9.2%
Only 8/52 died at hospital
Extrapolation: about 14,000 ped deaths/yr world
Spiders? Plants? Likely far less.

WHO Poisoning, & Mohapatra B: Snakebite in India ...2011
Environmental—chemical: kerosene, caustics, pesticides

Poisons may be up to 7% of ped admissions
Paraffin (Kerosene)–up to 50% of all poisons admissions in low resource economies. Deaths still a small portion.
Pesticides—6% to 16% of ped poisons admissions. May be 1/3 of OP exposures.

Environmental—pollutants: air

Indoor air pollution from biomass and coal fuels affects one half of the world population, and about 80% in low-income countries of Africa and South Asia.

Outdoor air pollution levels are highest in cities in low resource countries, especially in Asia.

http://cherg.org/projects/air_pollution.html
Environmental—pollutants: air

Ozone linked to ED visits, URI, asthma and LRI in those under 5y. As asthma management and LRI management is delayed or limited in low resource economies and treatment less effective increased morbidity and mortality may result.

$\text{PM}_{10}$ linked to excess mortality in lower SES infants

WHO estimates

Indoor air pollution attributable deaths in children under 5 year in LREs:
870531  (really?)

Outdoor air pollution attributable deaths in children under 5 year in LREs:
30342

http://apps.who.int/ghodata/?vid=34100#
Environmental—pollutants: soil and water

Remember Bangladesh

Depending on the standard, 35-85 million of 125 million people drink arsenic-contaminated water!
Environmental—pollutants: soil and water

Deaths of 400 children and very high levels in a few thousand more in Zamfara State Nigeria get our attention, but lead is many places
Environmental—pollutants: soil and water
the impact of lead is widespread but not high:
DALY’s per 100,000 children under 5y (WHO)

<table>
<thead>
<tr>
<th>Low- and middle- income countries by WHO region</th>
<th>Year 2004 est.</th>
<th>@ 50 years/life</th>
</tr>
</thead>
<tbody>
<tr>
<td>African</td>
<td>765</td>
<td>15.3 lives/100,000</td>
</tr>
<tr>
<td>Americas</td>
<td>866</td>
<td>17.3 lives/100,000</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>1860</td>
<td>37.2 lives/100,000</td>
</tr>
<tr>
<td>South East Asia</td>
<td>1723</td>
<td>34.5 lives/100,000</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>1128</td>
<td>22.6 lives/100,000</td>
</tr>
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</table>

The *disability-adjusted life year (DALY)* is a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death.
Unintentional child self-exposure to medications is infrequent in low resource economies as few toxic medications are in the home. Isoniazide maybe but not with DOT. Contaminated medications result in intermittent low volume “mass” exposures (e.g., several DEG outbreaks, contaminated herbal medications).
Let’s return to the mortality pie chart and consider therapeutic medication errors

* Under 6y- WHO † under 18 y -Global, regional and national causes of child mortality in 2008: a systematic analysis Black Lancet 2010
In Africa alone there are 3M non-neonatal deaths. Malaria, pneumonia and diarrhea each account for 500,000 deaths. It is easy to attribute any death or adverse event to the primary disease.

Proposition:
In low resource settings there are a number of environmental stresses and common practices that result in significant uncounted morbidity and mortality due to medication error. The impact may be much larger than all poisonings. These deserve to be evaluated and addressed systematically by world health bodies.
Medication Error

“Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.” *

*United States Coordinating Council for Medication Error Reporting and Prevention
Aspects of medication use

Efficacy

Availability

Safety  (failure = “poisoning”)
How does medication administration work in low resource economies?

Efficacy: Many, many papers have summarized poor choice of medications, particularly in outpatients

Examples
Osterholdt DM et al. Predictors of treatment error for children with uncomplicated malaria seen as outpatients in Blantyre district, Malawi 2006
How does medication administration work in low resource economies?

Availability: In spite of pediatric essentials medicines list and research in low resource countries, essential medicines are often not available.

See Hoppu K et al. Realities of pediatric pharmacotherapy in the developing world. Archives of Disease in Childhood 2011;96:764-768
How does medication administration work in low resource economies?

Cost saving policy may mean that some of the best/least toxic medications may not be available or implementation is delayed: e.g., artemether v. quinine in pediatric malaria.


- Intravenous artesunate should be used in preference to quinine for the treatment of severe *P. falciparum* malaria in children. *Strong recommendation, high quality evidence*
Only two articles seem directly relevant to error and safety

In 4 months on a well staffed 60 bed Ped Unit, only 407 patients were treated, all awake and eating, most errors were timing of administration.


22 year retrospective review of poisonings in the first 28 days of life—few were med errors.

Two others indirectly relevant

Survey of nurses: Medication errors were under-recognized and underreported.


India as a model for developing systems for addressing the issue of medication errors and ADRs.

In 2000, in the United States, “To Err is Human” was greeted with shocked disbelief.

Medication safety is clearly a neglected topic and I believe the published data massively underestimate the frequency and significance of errors in inpatient pediatric patients in low resource settings.
The “rights” of medication safety

Right patient
Right drug—chosen for indication
Right drug—available in formulary
**Right drug**—administered
Right dose—chosen
Right dose—administered
Right time
**Right route**
Context: Inpatient medicine is not the same in high and low resource settings

89 patients in 36 beds with at least one guardian per patient in a room 35 M x 15 M
How does medication administration work in low resource settings?

Chaotic environment (busy, loud, no space, meds not in proximity to patients)

Meds given under stress (convulsions, fever, coma, multiple simultaneous sick patients, overwhelming patient:clinician and patient:nurse ratio)
Improved work environment
Ease of access to key meds is prized
Common injectable medications “readily available”

- Paraldehyde
- Diazepam
- Phenobarbitone
- Glucose D50
- Lignocaine
- Frusemide
- Adrenalin
- Atropine
- Dexamethasone
- Quinine
- Ceftriaxone
- Benzyl Penicillin
- Gentamicin
- Metronidazole
Oral medications in use
Common oral medications “on the table”

<table>
<thead>
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<th>Common Medication</th>
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<tr>
<td>Digoxin</td>
<td>Cotrimoxazole</td>
</tr>
<tr>
<td>Captopril</td>
<td>Amoxicillin</td>
</tr>
<tr>
<td>Methyldopa</td>
<td>Flucloxacillin</td>
</tr>
<tr>
<td>Frusemide</td>
<td>Lumefantrine/Artemether</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>Paracetamol</td>
</tr>
</tbody>
</table>

Common oral medications “off the table”

ARVs
TB meds
Africa, Africa and Asia oral med trolleys
Medication storage is suboptimal

IV/IM medications pictured include:
- Frusemide
- Phenobarbitone
- Quinine
- Diazepam
- Atropine
- Paraldehyde
- Vitamine K
- Glucose
- Lignocaine

African nation #1
Medication availability in the neonatal unit at a hospital in African nation # 2
A close-up of the neonatal unit at a hospital in Africa nation #2
Never waste a limited resource…but

May 2, 2012 CDC Position statement:
Protect Patients Against Preventable Harm from Improper Use of Single-dose/Single-use Vials
How does medication administration work in low resource settings?

Not all patients have an actual weight, many have estimates. Worse with small infants.

Some drugs may have a narrow therapeutic window—quinine, digoxin, gentamicin, paracetamol.

Some drugs (e.g., gentamicin) are given once per day to minimize staff time—high peaks.

No electrolytes, no creatinine, no drug levels are available.

Adult tablets are split for pediatric dosing.
How does medication administration work in low resource settings?

Doses are handwritten, often on a variety of papers. Not all one time doses may be recorded or recorded in the same place. Abbreviations are common. Handwriting?
How does medication administration work in low resource settings?

Doses are drawn up by a variety of personnel—particularly in an emergency e.g., convulsion—physicians, clinical officers, nurses and often students in these disciplines.
How does medication administration work in low resource settings?

Per kg dosing requires multiplication. Volume dosing and mg dosing may be confused. Labels may be per vial not per mL. Translation of mg dose to the correct volume may be confusing.

Dosing of some drugs like diazepam, which may be given IV (0.1 mg/kg) or PR (0.5 mg/kg) may be confused.
Fluids and additives to fluids are administered at rates and for totals by drop counts without pediatric buretrols.

End points are the initial volume in the bottle.
Additives are infrequently labeled

When labeled may not reflect all additives.
Two common medications: D50W (glucose) and Lignocaine 2%

Therapeutic D50W dose = 1 mL/kg (0.5g/kg)
But 1ml/kg lignocaine is 20mg/kg IV push = lethal
Is D5W a poison?

WHO guidelines for malaria management suggest giving quinine in 10 mL/kg D5W.

But numerous patients have severe anemia, prolonged convulsions and coma …

Hypoglycemia can occur but that is a lot of free water to give an injured brain
How important is the absence of D5W in the outcome of the AQUAMAT trial?


230 (8·5%) patients assigned to artesunate treatment died compared with 297 (10·9%) assigned to quinine treatment (odds ratio [OR] stratified for study site 0·75, 95% CI 0·63–0·90; relative reduction 22·5%, 95% CI 8·1–36·9; p=0·0022)

The development of coma (65/1832 [3·5%] with artesunate vs 91/1768 [5·1%] with quinine; OR 0·69 95% CI 0·49–0·95; p=0·0231), convulsions (224/2712 [8·3%] vs 273/2713 [10·1%]; OR 0·80, 0·66–0·97; p=0·0199), and deterioration of the coma score (166/2712 [6·1%] vs 208/2713 [7·7%]; OR 0·78, 0·64–0·97; p=0·0245) were all significantly less frequent in artesunate recipients
“Poisonings” 0,04% of deaths…but how many of the others are really poisonings?

Global, regional and national causes of child mortality in 2008: a systematic analysis  Black Lancet 2010
Conclusion 1

The morbidity and mortality attributable to medication safety errors likely dwarfs that of “poisoning” in the usual sense in low resource economies.
Conclusion 2

Environmental stresses and common medication practices result in significant mis-attributed morbidity and mortality. The causes of these errors deserve to be evaluated and addressed by academics and world health bodies with attention to systems solutions.
Conclusion 3

Proposed solutions must 1) address system issues, not individual error, 2) be practically and culturally acceptable to those who work in under-resourced economies 3) fit the budgets of the Ministries of Health in these nations.