Toxicology Update: A Review of the Most Recent Articles That Should Change Your Practice

Robert S. Hoffman, MD, Professor of EM and IM, Director, Division of Medical Toxicology
Can medical students identify a potentially serious acetaminophen dosing error in a simulated encounter? a case control study

Robert A Dudas* and Michael A Barone
Health care use and serious infection prevalence associated with penicillin “allergy” in hospitalized patients: A cohort study

Eric Macy, MD, MS, and Richard Contreras, MS

San Diego and Pasadena, Calif

Facts

- Penicillin “allergy” is the most common drug-class “allergy” noted in the medical records of subjects using health care, including US hospitals.
- Most subjects with a history of penicillin “allergy” are not allergic and tolerate future penicillin use.
- In Kaiser over a 4 years period, less than 2% of subjects with a history of penicillin “allergy” had a positive penicillin allergy test result.
Analysis

• 2 years of Kaiser data
• Match of 51,582 hospitalized subjects with penicillin “allergy” to 2 unique discharge diagnosis–matched, sex-matched, age-matched, and date of admission–matched control subjects each
• Cases with penicillin “allergy” averaged more total hospital days compared with control subjects
• Cases were treated with significantly more fluoroquinolones, clindamycin, and vancomycin for each antibiotic compared with control subjects
More

- Cases had 23.4% more C *difficile*, 14.1% more MRSA, and 30.1% more VRE infections than expected compared with control subjects
- Cost to test 51,582 for PCN allergy = $6,776,327
- Over the 3-year study, 30,433 extra hospital days at $2,123.56/day = $64,626,630.48
- Cost $2,987,091.06 to test the 22,738 female cases >50 years old they accounted for 18,190 (59.8%) of the extra hospital days
Take Home Message

- PCN allergy is not as benign as most think
- Not giving PCNs when really acceptable:
  - Costs money
  - Increases hospital stay
  - Breeds antimicrobial resistance
- Test people with unconfirmed PCN allergy
ORIGINAL CONTRIBUTION

Underuse of Pregnancy Testing for Women Prescribed Teratogenic Medications in the Emergency Department

Monika K. Goyal, MD, MSCE, Adam L. Hersh, MD, PhD, Gia Badolato, MPH, Xianqun Luan, Maria Trent, MD, MPH, Theoklis Zaoutis, MD, MSCE, and James M. Chamberlain, MD

ACADEMIC EMERGENCY MEDICINE 2015;22:192–196
**Figure 1.** Pregnancy testing frequency by FDA pregnancy risk category.
A Randomized Trial of Icatibant in ACE-Inhibitor–Induced Angioedema

Murat Baş, M.D., Jens Greve, M.D., Klaus Stelter, M.D., Miriam Havel, M.D., Ulrich Strassen, M.D., Nicole Rotter, M.D., Johannes Veit, M.D., Beate Schossow, Alexander Hapfelmeier, Ph.D., Victoria Kehl, Ph.D., Georg Kojda, Pharm.D., Ph.D., and Thomas K. Hoffmann, M.D.
Bottom Line(s)

• Icatibant works
• It is very expensive
• FFP works as well
• There are no good comparisons between FFP and Icatibant
“Prophylactic antibiotics do not improve the outcome in children with mild respiratory illness after kerosene ingestion.”
The therapist and computer BIs significantly reduced consumption at 3 months, consequences at 3 and 12 months, and prescription drug use at 12 months; the computer BI reduced the frequency of DUI at 12 months; and the therapist BI reduced the frequency of alcohol-related injury at 12 months.
No statistically significantly increased risk for a major malformation was found. The risks for a cardio-vascular defect and notably a cardiac septum defect were increased and statistically significant (OR = 1.62, 95% CI 1.04–2.14, and RR 2.05, 95% CI 1.19–3.28, respective).
Adolescents admitted to hospital for self-poisoning were also more likely to die from accidents (5·2, 4·1–6·6) and from all causes (3·9, 2·8–5·4) during follow-up.
HR 32.1 (95% CI 23.6–43.6)

Number at risk
Reference group: 1023487  940141  784256  612828  433874  221595  571
Self-poisoning cohort: 20471  18730  15585  12149  8596  4401  10
Postcards from the EDge: 5-year outcomes of a randomised controlled trial for hospital-treated self-poisoning

Gregory L. Carter, Kerrie Clover, Ian M. Whyte, Andrew H. Dawson and Catherine D’Este
Association of Emergency Department Opioid Initiation With Recurrent Opioid Use

Jason A. Hoppe, DO*; Howard Kim, MD; Kennon Heard, MD, PHD

*Corresponding Author. E-mail: jason.hoppe@ucdenver.edu, Twitter: @drjhoppe.
Figure. Patient inclusion diagram.
Increasing Incidence of the Neonatal Abstinence Syndrome in U.S. Neonatal ICUs

Veeral N. Tolia, M.D., Stephen W. Patrick, M.D., M.P.H.,
Monica M. Bennett, Ph.D., Karna Murthy, M.D., John Sousa, B.S.,
P. Brian Smith, M.D., M.P.H., M.H.S., Reese H. Clark, M.D.,
and Alan R. Spitzer, M.D.
A  Admissions for the Neonatal Abstinence Syndrome

No. per 1000 Admissions


Discharge Year
PEDIATRICS/ORIGINAL RESEARCH

Color-Coded Prefilled Medication Syringes Decrease Time to Delivery and Dosing Error in Simulated Emergency Department Pediatric Resuscitations

Maria E. Moreira, MD; Caleb Hernandez, DO; Allen D. Stevens, BA, CCRC; Seth Jones, BS, NREMTP; Margaret Sande, MD, MS; Jason R. Blumen, BA, NREMTP; Emily Hopkins, MSPH; Katherine Bakes, MD; Jason S. Haukoos, MD, MSc*

*Corresponding Author. E-mail: jason.haukoos@dhhha.org.

256 doses administered

Conventional Syringe | Color-Coded Syringe

11 doses excluded
- 2 Atropine
- 1 Bicarbonate
- 1 Calcium
- 4 Epinephrine
- 2 Etomidate
- 1 Succinylcholine

129 doses

118 (92%) doses

Incorrect Dose | Correct Dose

31 (26%) doses

Critical Error | Non-Critical Error

20 (65%) doses

11 (35%) doses

127 doses

123 (97%) doses

Incorrect Dose | Correct Dose

5 (4%) doses

Critical Error | Non-Critical Error

0 (0%) doses

4 doses excluded
- 2 Epinephrine
- 1 Ketamine
- 1 Succinylcholine

118 (96%) doses

Critical Error | Non-Critical Error

5 (100%) doses
We found no overall adverse association between prenatal MeHg exposure and neurodevelopmental outcomes.
Bx. boy nearly died after pharmacy dispensed METHADONE instead of Ritalin: suit

By DOUGLAS MONTERO and JEANE MACINTOSH

He was supposed to get Ritalin. Instead, a Bronx pharmacy filled out a potentially lethal dose of synthetic heroin to a 7-year-old boy, a lawsuit claims.

Little Adrien Hernandez went limp and stopped breathing in July, shortly after taking the third pill in what his mother believed was a new Ritalin prescription, still-shaken mom, Christina Torres told The Post yesterday.

The mom of four was in the shower when her older kids began shouting that her youngest had collapsed.

"They were screaming, 'Mommy! There's something wrong with Adrien!' " Torres, 31, who filed the suit yesterday, recalled.

Rushing to his side, she found him facedown, eyes rolling back in his head.

"He looked blue," Torres said.

She called 911, and — as the operator told a hysterical Torres to calm down — neighbors ran into their Bronx apartment and rushed Adrien and his mom to Jacobi Hospital.

As doctors worked feverishly to
13-Month-Old Boy Overdoses On Prescription Pills From Bottle Given To Him As A Rattle

The Huffington Post | Dean Praetorius
First Posted: 10/14/11 05:00 PM ET | Updated: 10/14/11 05:39 PM ET
Mother Charged After 6-Year-Old’s Death

By ANDY NEWMAN

A Bronx woman has been charged with reckless endangerment after her 6-year-old son died from ingesting methadone that the authorities said she had stored in a cold medicine bottle. But Bronx prosecutors said Friday that they were deferring prosecution pending the outcome of an autopsy, indicating that more serious charges are possible.

“We need a cause of death,” a spokesman for the Bronx district attorney’s office said.

The boy, Carlos Rios Jr., went into cardiac arrest on Saturday at his apartment on East 147th Street in Mott Haven, the police said. He had complained of feeling sick, and his father had given him a teaspoon of liquid from a DayQuil bottle, unaware that the boy’s mother, Raquel DeLeon, had put her methadone in the bottle, the father told the police.
Facts

• OD deaths have increased steadily in the US since 1979
  • In the past 3 decades, drug OD deaths have tripled
• In 2008, poisoning deaths exceeded motor vehicle deaths for the first time since 1980
• Of drug OD deaths in the US in 2010, 60% were related to pharmaceuticals, with 75% of them involving prescription opioids
• Heroin deaths have risen 55% in the last decade
More Facts

• Between 1996 and 2010, community based overdose prevention programs may have saved as many as 10,000 lives, according to a US CDC report (MMWR.2012;61:101)
• Cost as little as $8 a vial for injection use to and $50 dollars for a nasal administration kit
• The new FDA approved spring loaded kit will cost almost $600 but most wont pay full price
Back From the Brink
Groups Urge Wide Use of Opioid Antidote to Avert Overdoses

Bridget M. Kuehn, MSJ

Cost-Effectiveness of Distributing Naloxone to Heroin Users for Lay Overdose Reversal

Phillip O. Coffin, MD, and Sean D. Sullivan, PhD
Fuzzy Math

- Probabilistic analysis:
  - 6% of overdose deaths were prevented with naloxone distribution
  - 1 death was prevented for every 227 naloxone kits distributed
- Naloxone distribution increased costs by $53 and quality-adjusted life-years by 0.119 for an incremental cost effective ratio of $438
- Worst estimate is about $14,000
Comparison QALYs

- Passenger-side airbags, compared with driver’s-side only, cost $61,000 per QALY.
- Pap smear every 4 years for women 20-75, compared with no screening at all, is $16,000.
- The cost per QALY to go to annual pap smears from every other year is $1,600,000.
- For breast cancer, the cost per QALY for annual mammography for women 55-65 is $150,000; for women 40-50, it’s $240,000.
Take Home Messages

• Adult drug abuse kills adults
• Adult drug abuse kills children too
• Prevention is essential
  • Limited prescribing
  • Safe storage
• Home naloxone might be one component of a harm reduction strategy with the potential to save kids' lives
Gastrointestinal Decontamination: Common Sense vs. Limited Science
Multiple Position Papers on Gastrointestinal Decontamination:
J Toxicol Clin Toxicol

• Gastric lavage should not be employed routinely, if ever, in the management of poisoned patients.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Presentation GE Time</th>
<th>Followup GE Time</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricyclics</td>
<td>103</td>
<td>46</td>
<td>&lt;0.002</td>
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<tr>
<td>Acetaminophen</td>
<td>98</td>
<td>42</td>
<td>&lt;0.018</td>
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<tr>
<td>Opioid-acetaminophen</td>
<td>115</td>
<td>34.5</td>
<td>&lt;0.017</td>
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<tr>
<td>Carbamazepine</td>
<td>164</td>
<td>53</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>52</td>
<td>27</td>
<td>0.069</td>
</tr>
<tr>
<td>Total</td>
<td>99.5</td>
<td>40</td>
<td>&lt;0.001</td>
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</tbody>
</table>
CRITICAL CARE

Retained drugs in the gastrointestinal tracts of deceased victims of oral drug overdose

Z. LIVSHITS,¹ B. A. SAMPSON,² M. A. HOWLAND,³,⁴ R. S. HOFFMAN³, and L. S. NELSON³

A Prospective, Observational Study

Masato Miyachi, MD, Makiko Hayashida, PhD, and Hiroyuki Yokota, MD

(Medicine 94(4):e463)
FIGURE 2. Typical photographs showing stomach during the 3 phases of digestion: tablet/food phase (A), soluble/fluid phase (B), and reticular/empty phase (C).
GI Decontamination Summary

• Many (most) patients can be managed without GI decontamination
• Position Papers and Consensus Statements are based on a poor evaluation of limited and outdated evidence
• Common sense must prevail
• Try to identify people who are likely to benefit from decontamination and do it!
Steroids?

Definitively beneficial in animal models
Only useful when combined with antibiotics
Suggestive human case reports
Limited scientific data
A CONTROLLED TRIAL OF CORTICOSTEROIDS IN CHILDREN WITH CORROSIVE INJURY OF THE ESOPHAGUS

KATHRYN D. ANDERSON, M.D., THOMAS M. ROUSE, M.D., AND JUDSON G. RANDOLPH, M.D.

Abstract Background. It is controversial whether treatment with corticosteroids reduces stricture formation in the esophagus after the ingestion of caustic material.

Methods. We conducted a prospective study over an 18-year period in which 60 children (median age, 2 years) with esophageal injury from the ingestion of caustic material were assigned randomly to treatment either with or without corticosteroids. The corticosteroids were given initially as prednisolone (2 mg per kilogram of body weight per day intravenously) and then as prednisone orally to complete a three-week course. All patients were evaluated by esophagoscopy within 24 hours of the ingestion. Those with moderate or severe esophageal injury had repeat esophagoscopy and barium swallow at follow-up.

Results. Esophageal strictures developed in 10 of the 31 children treated with corticosteroids and in 11 of the 29 controls (P not significant). Four children in the steroid group and seven in the control group eventually required esophageal replacement (P not significant). All but 1 of the 21 children with strictures had severe circumferential burns on initial esophagoscopy.

Conclusions. There appears to be no benefit from the use of steroids to treat children who have ingested a caustic substance. The development of esophageal stricture was related only to the severity of the corrosive injury. (N Engl J Med 1990; 323:637-40.)
Anderson: NEJM 1990

Randomized, controlled study

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<th></th>
<th>Steroids</th>
<th>No steroids</th>
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<tbody>
<tr>
<td>Patients</td>
<td>31</td>
<td>29</td>
</tr>
<tr>
<td>Strictures</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Need for surgery</td>
<td>4</td>
<td>7</td>
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</tbody>
</table>
High Doses of Methylprednisolone in the Management of Caustic Esophageal Burns

Merve Usta, Tülay Erkan, Fugen Cullu Cokuğras, Nafiye Urganci, Zerrin Onal, Mahir Gulcan and Tufan Kutlu

*Pediatrics* 2014;133;e1518; originally published online May 26, 2014;
DOI: 10.1542/peds.2013-3331
Design

- 83 children grade IIb esophageal burns
- 42 got methylprednisolone (1 g per 1.73 m$^2$ per day for 3 days), ranitidine, ceftriaxone, and TPN
- 41 children got the same regimen excluding methylprednisolone.
Results

- Strictures by endoscopy:
  - 4 patients (10.8%) in the study group
  - 12 controls (30%) ($P = 0.038$).

- Strictures by barium meal:
  - 14.3% vs 45.0% ($P = 0.004$)

- TPN duration shorter in the study group ($P = 0.001$)

- No steroid side effects
Safety, tolerability, and efficacy of idarucizumab for the reversal of the anticoagulant effect of dabigatran in healthy male volunteers: a randomised, placebo-controlled, double-blind phase 1 trial

Stephan Glund, Joachim Stangier, Michael Schmohl, Dietmar Gansser, Stephen Norris, Joanne van Ryn, Benjamin Lang, Steven Ramael, Viktoria Moschetti, Fredrik Grünenfelder, Paul Reilly, Jörg Kreuzer
Fluctuations in serum ethanol concentration in the treatment of acute methanol poisoning: a prospective study of 21 patients

Sergey Zakharov\textsuperscript{a}, Tomas Navratil\textsuperscript{b,c}, Tomas Salek\textsuperscript{d}, Ivana Kurcova\textsuperscript{e}, Daniela Pelcova\textsuperscript{f}
Fomepizole *versus* ethanol in the treatment of acute methanol poisoning: Comparison of clinical effectiveness in a mass poisoning outbreak

SERGEY ZAKHAROV,1 DANIELA PELCLOVA,1 TOMAS NAVRATIL,1,2 JAROMIR BELACEK,3 MARTIN KOMARC,3 MICHAEL EDDLESTON,4 and KNUST ERIK HOVDA5
THANKS