“Houston we have a problem!”
The epidemic of non medical use of
prescription opioids

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Disclosure
• I have participated/consulted in funded
("sponsored") research by the following “pharmas”
  • Purdue (oxycodeone, oxycontin, hydromorphone)
  • Endo (oxymorphone)
• Since very few analgesic drugs have been studied
  in children, this lecture will include “off label” use
  of drugs.

Objectives
• Describe a process of discovery and
  quality improvement in the delivery of
  medical care that can be used in your
  own practice
• Describe how we went from the
  undertreatment of pain to an epidemic of
  opioid abuse and how this affects your
  practice
• What are the alternatives?

“The world is full of obvious things which
nobody by any chance ever observes.”
Sherlock Holmes - The Hound of the Baskervilles
Sir Arthur Conan Doyle

It all started with an observation

An Analysis of 34,218 Pediatric Outpatient Controlled
Substance Prescriptions
Jessica A. George, MD,* Paul S. Perk, BS,* Joanne Hunsberger, MD,* Joanne E. Shaj, MD,*
Christoph U. Urichson, MD,† Elizabeth D. White, RN,* Benjamin H. Lee, MD, MPH,*
and Myron Yaster, MD‡

Anesthesia and Analgesia. 2016;122(3):807-813
Analysis of Controlled Substance Prescriptions: Summary of Results

Regardless of the opioid prescribed, providers wrote for very large quantities of drug to be dispensed.

Research Study Questions:
- How well is post-op pain managed?
- How much of the controlled substance prescription remains after 10-14 days at home?
- Is opioid therapy required at 10-14 days? At 6 months post-discharge?
- What do parents know about safe disposal of unused opioids?
Research Study Questions:

- Were they given instructions on how to dispose of leftover meds?
- Who informed them (physician, nurse, pharmacist)?
- Did they dispose of unused meds?
- Are there at-risk individuals in the home? (Adolescents and risk of NMUPO; young children and risk of accidental ingestion.)
Storage and Disposal of Morphine at the End of Treatment

<table>
<thead>
<tr>
<th>Storage, n (%)</th>
<th>Room</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Kitchen</td>
</tr>
<tr>
<td></td>
<td>Bathroom</td>
</tr>
<tr>
<td></td>
<td>Parent’s bedroom</td>
</tr>
<tr>
<td></td>
<td>Child’s bedroom</td>
</tr>
<tr>
<td></td>
<td>Other</td>
</tr>
<tr>
<td></td>
<td>Open or closed space</td>
</tr>
<tr>
<td></td>
<td>Open</td>
</tr>
<tr>
<td></td>
<td>Closed</td>
</tr>
<tr>
<td>Disposal of morphine at the end of treatment, n (%)</td>
<td>Return to pharmacy</td>
</tr>
<tr>
<td></td>
<td>Throw away</td>
</tr>
<tr>
<td></td>
<td>Keep at home</td>
</tr>
<tr>
<td></td>
<td>Do not know</td>
</tr>
</tbody>
</table>


NMUPO and Adolescents

- 27% mistakenly believe that misusing and abusing prescription drugs is safer than using street drugs.
- 33% say they believe “it’s okay to use prescription drugs that were not prescribed to me to deal with an injury, illness or physical pain.”

2012 Partnership Attitude Tracking Study (PATHS)-MetLife Foundation
Opioids, Pain, and Surgery

- 51 million Americans undergo surgery/year
- For moderate to severe pain, opioids remain the gold standard for pain management

"Duh!"

- 80% of patients receive opioids after surgery
- > 80% receive either oxycodone or hydrocodone
- Surgical patients routinely receive the opioids most commonly implicated in overdose deaths

Haven’t we seen this before?

Pain is the 5th vital sign

Opioidphobia
We need DATA!

- Type of surgical procedure
- Preoperative patient characteristics
  - Age
  - Gender
  - Race
  - Language
  - Prior opioid or alcohol use/abuse
  - Preoperative medication use (antidepressants, benzodiazepines)

Strategies to limit opioid use after surgery

The “Usual Suspects”

- Regional and Neuraxial Anesthesia
- Multimodal analgesia
  - Acetaminophen
  - NSAIDs
  - Gabapentenoids
- Non pharmacologic approaches

PK it’s not just for exams

Acetaminophen AND Ibuprofen

After Surgery in Germany, I Wanted Vicodin, Not Herbal Tea

Current and Future Targets

- NMDA Receptor Blockade
  - Ketamine, Methadone, Dextromethorphan
- Opioid Receptor
  - Mu, Kappa, Delta, Neuropeptide nociception
  - Peripherally active agonists
  - Biased ligands
- Alpha 2 agonists
  - Clonidine, Tizanidine, Dexmedetomine

Peripherally restricted opioids

- Reduced side effect profile and minimum abuse and drug seeking behavior
- Kappa peripherally restricted agonists are in phase 2 and 3 trials and are effective for acute, chronic, inflammatory and visceral pain as well as pruritus

Biased Ligand Opioids

- Combine a classic mu agonist with a beta arrestin molecule modulating opioid side effects. Specifically reducing:
  - Tolerance
  - Respiratory depression
  - Pruritus
- In phase 2 trials

Cannabinoids

- Cannabinoid receptors (CB1 and CB2) are G protein coupled receptors (like opioids).
- CB1 receptors are in spinal cord neurons, particularly dorsal root ganglia
- CB2 are in spinal cord microglia
- Psychotropic and abuse potential effects are CB1, analgesia are CB1 and CB2

Cannabinoids

- There is NO postoperative data
- There is A LOT of anectodal data, particularly for opioid substitution
- There is evidence that it may be effective in neuropathic pain
- We NEED data but there are enourmous hurdles in studying a Class 1 drug
Conclusions Future Directions

- Need to identify reasons for overprescribing of these meds and mitigate risk to patient by behavior change and data-driven practices
- Develop new methods of disposal
- We can’t forget the need for humane pain management which for moderate to severe pain almost always requires opioids

BUT

A Journey of Discovery

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