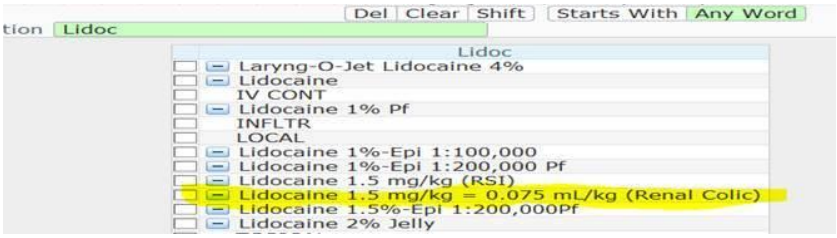
Emergency Department Pharmacist's Notes

August 2020

Lidocaine for Renal Colic | Prochlorperazine for Headache | Phenobarbital for Alcohol Withdrawal | Naloxone | Management of Bleeding from Oral Anticoagulants- ACC Guidelines

IV Lidocaine for Renal Colic

- 1.5 mg/kg in 100 mL NS over 10 min (Max 200 mg) is one of ALTO (Alternatives to Opioids for Pain Management)
- Meditech order string is available



Prochlorperazine for Migraine

- IM, IV: 10 mg once (available in ED Pyxis)
- Included in ED Headache order-set
- Some experts suggest adjunct use of diphenhydramine 25mg to prevent akathisia and dystonic reactions
- IV prochlorperazine appears to be as effective or more effective than IV metoclopramide or SubQ sumatriptan, and more effective than hydromorphone in the acute treatment of migraine

Reversal Agents for Oral Anticoagulants

- 2020 JACC published decision pathway on management of bleeding in pts on oral anticoagulants
  - https://www.onlinejacc.org/content/76/5/594
  - The guidelines include practical and simplified decision trees, definition of bleed severity (critical site bleed, hemodynamic instability, hemoglobin drop), management of major/non-major bleed, OAC (oral anticoagulants) reversal agents, timing of anticoagulation re-initiation etc.
  - Note there is a low fixed dose option of 4 factor PCC (Kcentra) for warfarin reversal vs. traditional dosing (INR and Wt based): See Figure 3. Some institutions use this low dose protocol (eg., Johns Hopkins)

- Swedish formulary reversal agents for oral anticoagulants
  - **Kcentra** for warfarin or Factor Xa inhibitors (eg., Eliquis, Xarelto)
  - **Praxbind** for Pradaxa
  - **Vitamin K** for warfarin
  - Andexxa (a reversal agent for Factor Xa inhibitors) is NOT available in Swedish
  - ED orderset, **ED Bleeding Reversal Agents** is available in Meditech

- Management of elevated INRs from warfarin (**V**itamin **K A**ntagonist, VKA)

INR	Clinical Setting	Recommendations
<4.5	No Bleeding	Hold warfarin until INR in therapeutic range
4.5-10	No Bleeding	Hold warfarin until INR in therapeutic range Consider vitamin K 2.5 mg PO if risk factors for bleeding
>10	No Bleeding	Hold warfarin until INR in therapeutic range Give vitamin K 2.5-5 mg PO or 1-2 mg IV Repeat every 24 hours as necessary

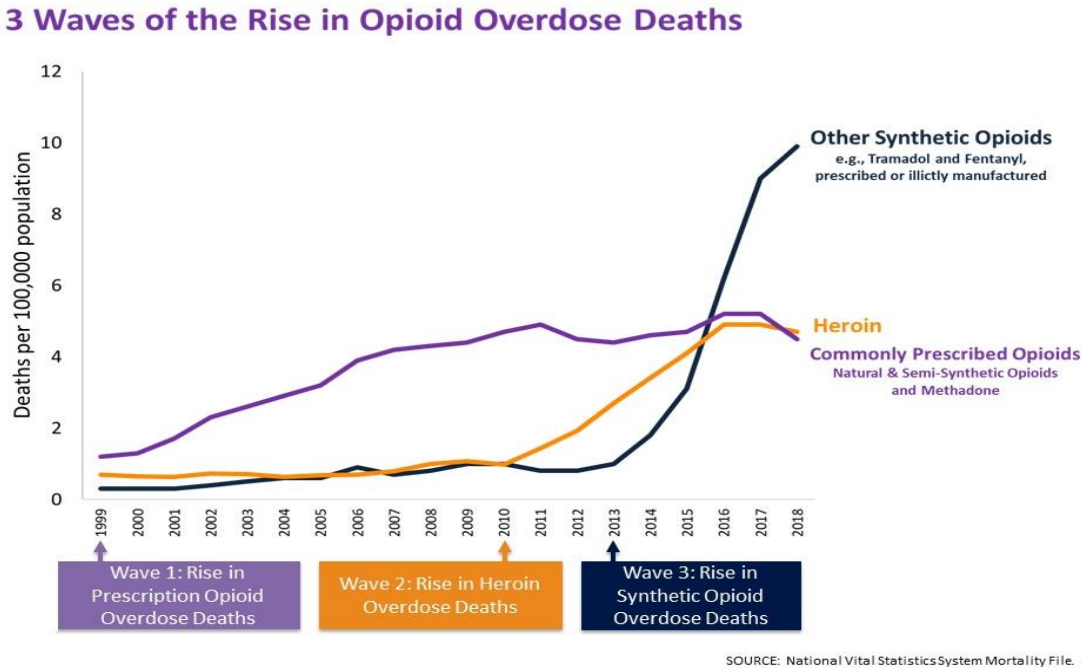
Any INR	Serious or life-threatening bleeding	Hold warfarin Give vitamin K 5-10 mg IV over 30 min Administer 4-factor PCC. Refer to Institutional Kcentra guideline Check INR 30 min after Kcentra administered If Kcentra is not available, or volume resuscitation necessary, consider FFP 15-20 mL/kg

Vitamin K (phytonadione)		
	Onset of action	Peak effect
Oral	6-12 hrs	24-48 hrs
IV	1-2 hrs	12-14 hrs
SQ	Not recommended due to unpredictable or delayed response	

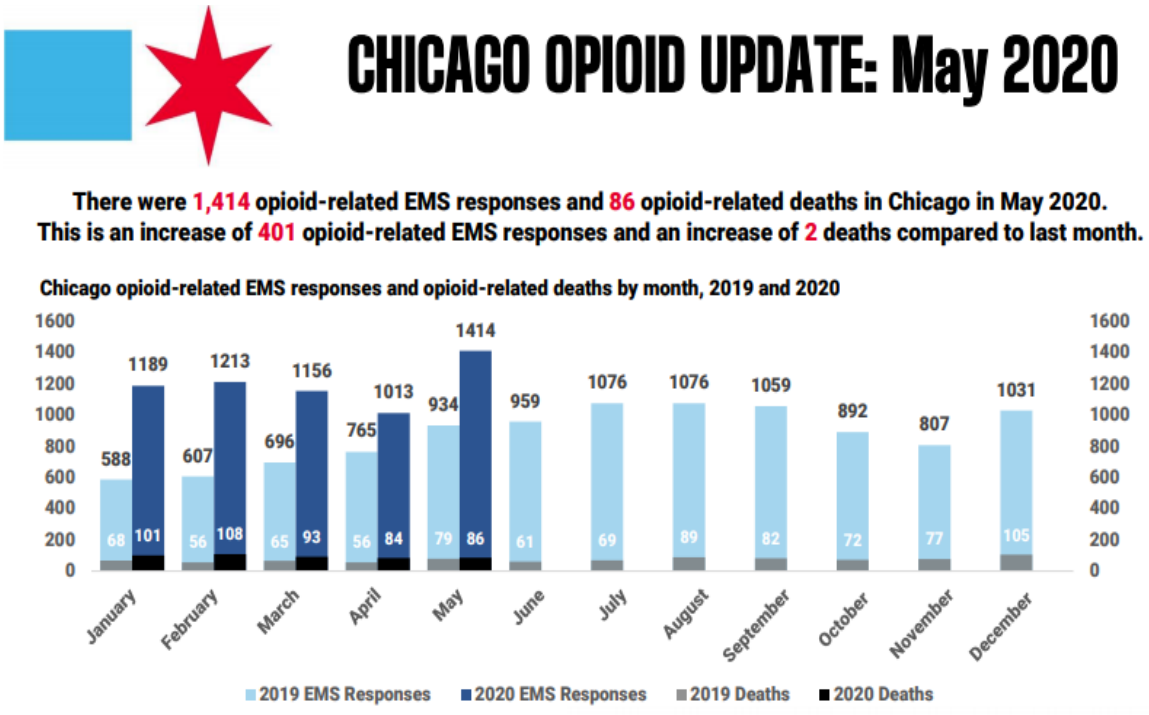
Naloxone

- July 23, 2020 FDA announced it is requiring that labeling for opioid pain medicine and medicine to treat opioid use disorder (OUD) be updated to recommend that health care professionals should discuss naloxone with patients and caregivers
  - Goal is to help reduce opioid overdoses and deaths
  - https://www.fda.gov/news-events/press-announcements/fda-requiring-labeling-changes-opioid-pain-medicines-opioid-use-disorder-medicines-regarding
  - The FDA is working with other federal, state and local officials as well as health care professionals, patients and communities nationwide to help increase availability of naloxone and combat opioid overdoses

- Naloxone can be prescribed by provider **or** can be obtained **without a RX** at a pharmacy that is using a **standing order** for the medication. Many outpt pharmacies such as Walgreens, CVS, and our GMP pharmacy use a **naloxone standing order**
  - **Illinois Naloxone Standing Order** it allows eligible entities, namely pharmacies and opioid overdose education and naloxone distribution (OEND) programs to provide naloxone to any requesting person with the intent to respond to a suspected opioid overdose without a direct prescription. With this standing order, insurers, such as Medicaid and Medicare, can be billed. Eligible entities must complete approved training and education on naloxone administration to access the order. Pharmacies utilizing the order should report naloxone dispensing information to the Illinois Prescription Monitoring Program.
- Next step: Developing plan for naloxone prescribing and dispensing in ED?



https://www.cdc.gov/drugoverdose/epidemic/index.html



Phenobarbital (vs. Benzodiazepines) for Alcohol Withdrawal Syndrome

- Benefits of phenobarbital use over benzodiazepines
  - Longer ½ life: 80-120 hrs vs. 14-20 hrs (lorazepam) but duration of sedation is similar (4-10 hrs vs. 6-8 hrs). Helps in treatment of severe AWS and prevents seizures and fatal DT. Less often drug administration (vs. lorazepam)
  - Better MOA: both benzodiazepines and phenobarbital work by inhibiting GABA receptors, but phenobarbital has an additional benefit of suppressing the excitatory glutamate receptors (NMDA receptor)-> less delirium and agitation
  - Studies found phenobarbital use is associated with less ICU admission, hospital stay, health care costs, and attention from nursing staff compared to benzodiazepines
  - Hepatic impairment: phenobarbital exposure is increased. Thus use with caution

- There are various dosing regimens for AWS (examples below)

Swedish (ICU/IMCU only)	Uptodate	By Mosley MD. (Emergency Medicine News)	By Parthvi et al. (Journal of clinical intensive care and medicine)
Only Severe AWS/High risk **Day1 - Loading 10mg/kg IM** (divided 40%, 30% and 30%) 3 hrs between Day2 – 64.8mg PO q12h Day3 – 32.4 mg po q12h Day4 – 32.4 mg po q24h *ICU/IMCU providers use phenobarbital as prn IV/IM adjunctive to Ativan and Librium	**IV**: Initial dose of **260 mg**, followed by subsequent doses of **130 mg** prn **Oral Fixed Dose Regimen** Day1 - 60 mg QID Day2 - 60 mg TID Day3 - 60mg BID Day4 - 30mg BID Additional 60 mg PRN for breakthrough withdrawal symptoms or 130 mg IM PRN for more substantial withdrawal (eg, HR, SBP marked agitation)	**In ED**: **Load 260 mg IV over 5 min**. Repeat 130 mg IV q30 min until symptoms abate (may use up to 10 mg/kg = 700-1000mg) **For outpt use**: 30 mg Tab x 8 tabs total Day1: 60mg po q12h Day2: 30mg po q12h Day3&4: 30mg po q24h Adjust dose/ treatment period as needed based on the stratification of risks	**#1 Load 10-15mg/kg over 30 min** (if no other sedative given) **#2** Forgo loading, **Mild sx**: give 130mg iv boluses over 3 min **Mode-severe**: 260 mg over 5min. Repeat 130mg Q30 min PRN (max 1040 mg in 24hrs)

- Cost/ Availability
  - Wholesale price: **$50** per 130 mg Injectable phenobarbital vs **50 cents** per 2 mg lorazepam inj.
  - Phenobarbital injectables are often on backorder
  - No significant cost difference between oral phenobarbital and chlordiazepoxide

- Use in our ED
  - For severe AWS pts who are refractory to benzodiazepine (use in conjunction with benzodiazepines for synergistic effect instead of phenobarbital monotherapy)?
  - Dose 130 mg or 65 mg IV/IM Q30 min as needed?
  - Monitoring tools of AWS
    - CIWA-Ar (revised Clinical institute withdrawal assessment of alcohol scale)
    - PAWSS (Prediction of Alcohol Withdrawal Severity Scale**)**

https://www.mdcalc.com/ciwa-ar-alcohol-withdrawal https://www.mdcalc.com/prediction-alcohol-withdrawal-severity-scale