

Comedy of Errors: Methadone and Buprenorphine

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Disclosures

Nothing to disclosure

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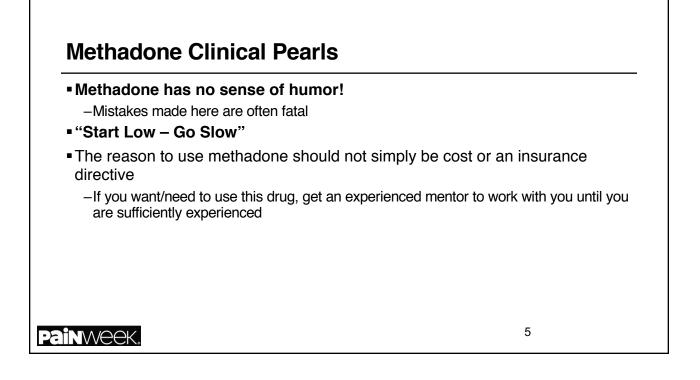
Learning Objectives

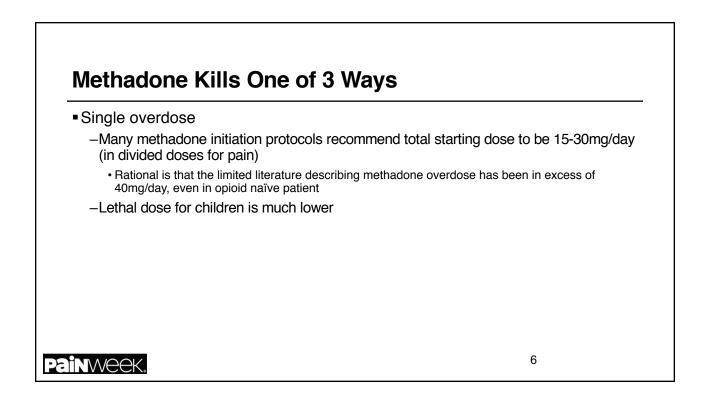
- Explain the pharmacology of methadone and buprenorphine
- Describe methadone and buprenorphine in a case-based model focusing on analgesic conversion

3

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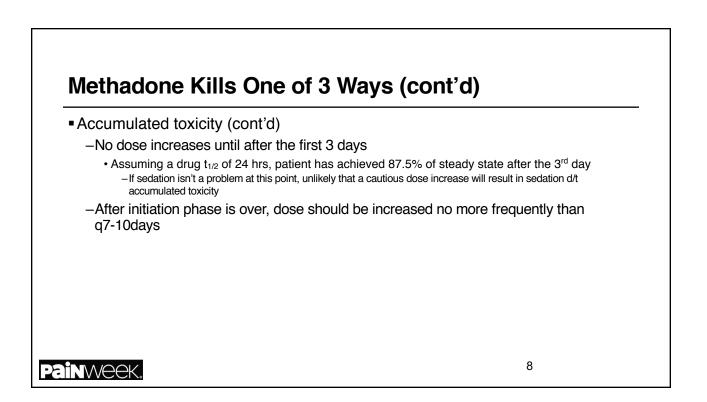


Methadone Kills One of 3 Ways (cont'd)

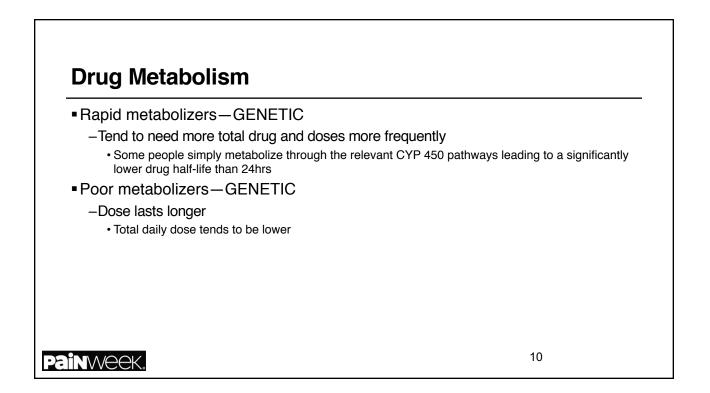
- Accumulated toxicity
 - "Today's dose isn't lethal; tomorrow's dose isn't lethal but all the 3rd days' dose PLUS ½ the 2nd days total dose PLUS ¼ of the 1st days dose *accumulates* to a fatal dose"
 - The most lethal period in methadone treatment is the first 7-10 days (induction phase)
 Over zealous dose increases are a big risk

7

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Drug Metabolism-latrogenic

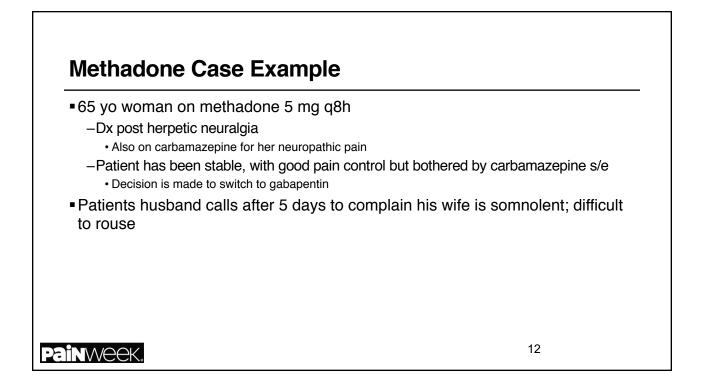
 While genetic variations tend to be fixed, CYP 450 active drugs can temporarily alter these pathways changing a normal metabolizer into a rapid or even poor metabolizer

11

-CYP 450 inducer-eg, phenytoin

-CYP 450 inhibitor-eg, macrolide antibiotics

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What's Happened?

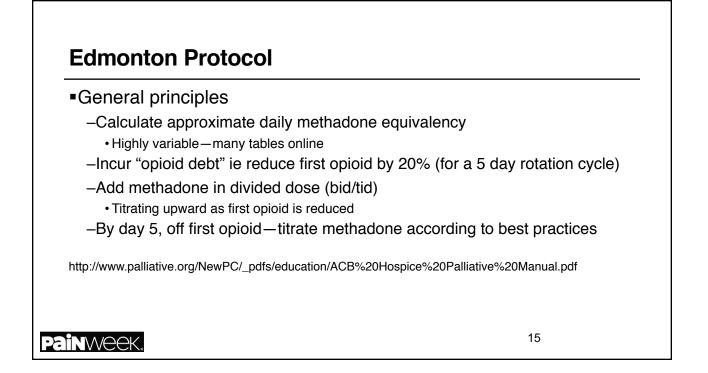
- Patient was on a stable dose of methadone, beyond the first 2 weeks of high risk initiation BUT
 - -A potent 3A4 inducer was discontinued
 - Gabapentin does NOT affect 3A4 pathway

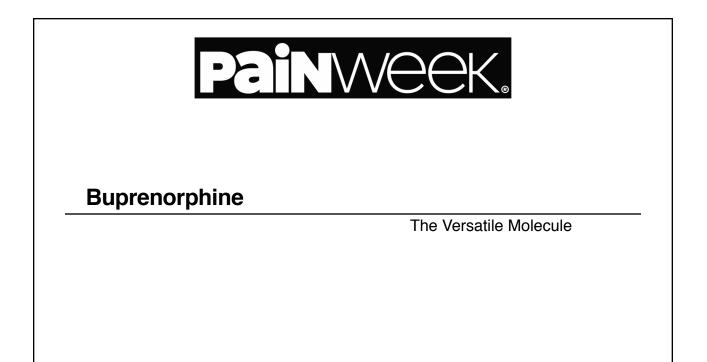
-So, in effect, the patient has had a significant effective increase in her methadone dose because she no longer rapidly metabolizes methadone

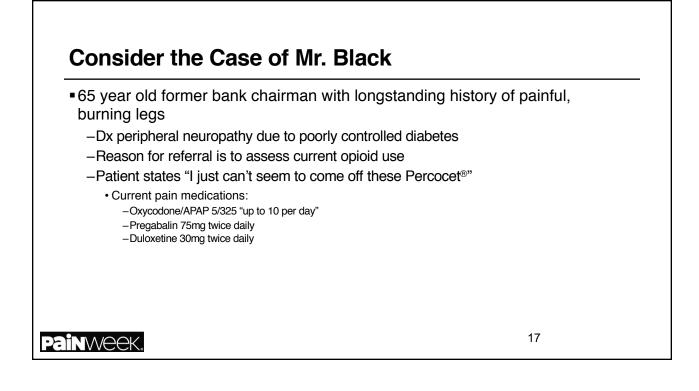
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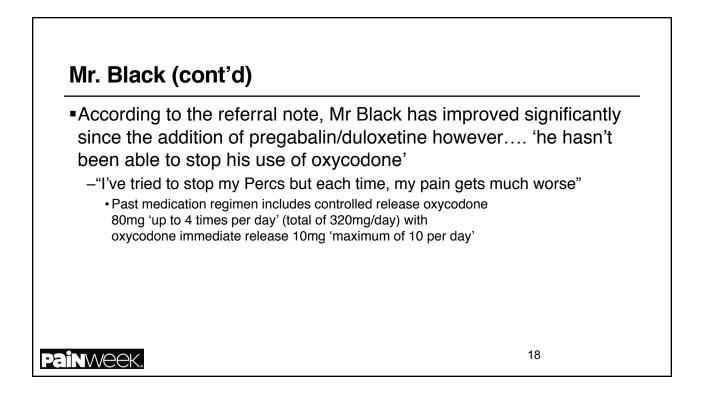
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Methadone Conversion Several things to consider Is the patient on lower dose morphine (<300mg/day MME) Methadone : morphine ~1:10 but varies! Do you want fast or slower conversion UK protocol vs Edmonton protocol Any concurrent disorders ie substance use? Age; resp illness etc

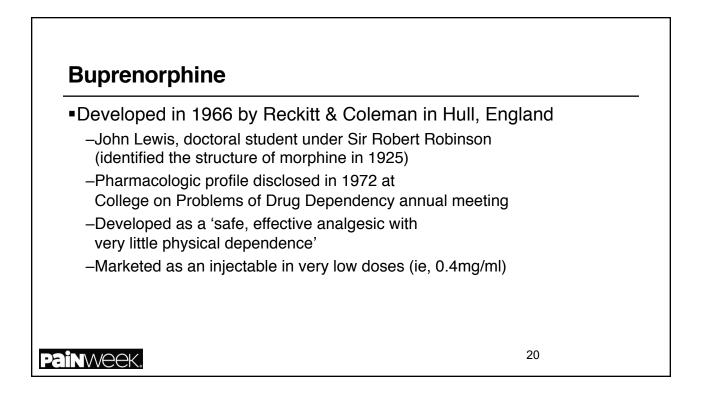








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Brief Overview: What We Thought

• Buprenorphine is a semisynthetic partial μ agonist (and κ antagonist)

- -Initially used as analgesic; now 1° maintenance agonist therapy (MAT)
- -Linear μ effect at lower doses
- -Morphine equivalency of ~40:1 over linear range
- -Improved safety profile due to "ceiling effect"
- -Available as SL mono/naloxone-combo tablet for DATA 2000

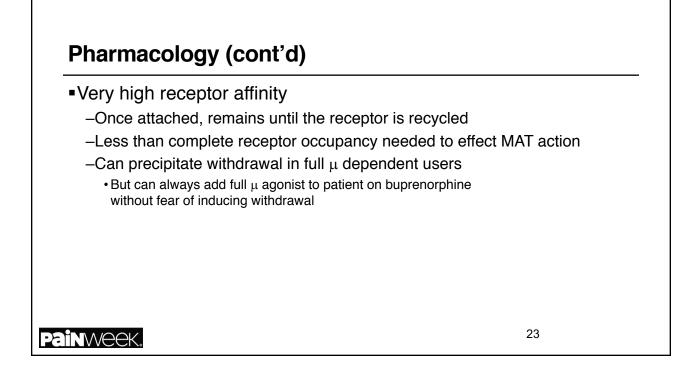
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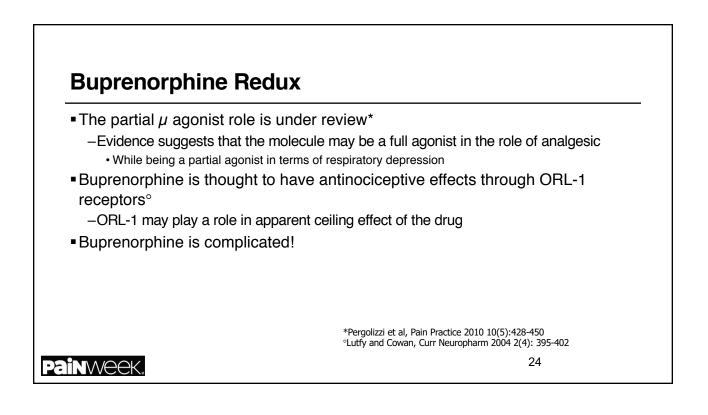
Pharmacology

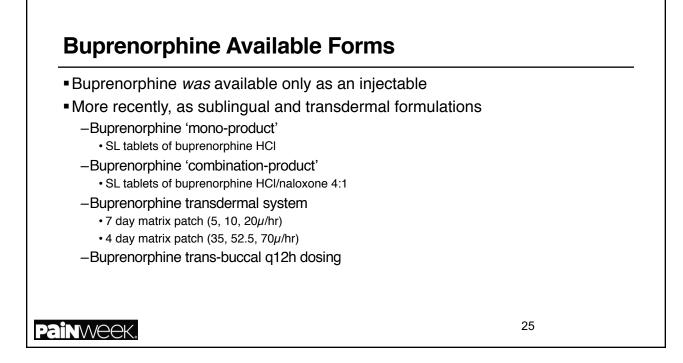
- Derived from opium alkaloid thebain
- Terminal elimination t¹/₂ ~24-60 hours but:
 - -Analgesic duration of action is ~6-8 hrs
 - -MAT duration of action is ~24-48 hrs
- Poor oral bioavailability but well absorbed by sublingual/parenteral/transdermal route
- CYP 450 3A4 (lesser 2C8) metabolism through N-dealkylation (like methadone)

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22







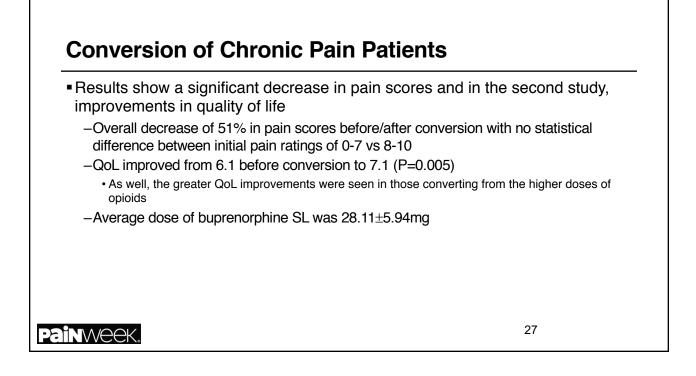


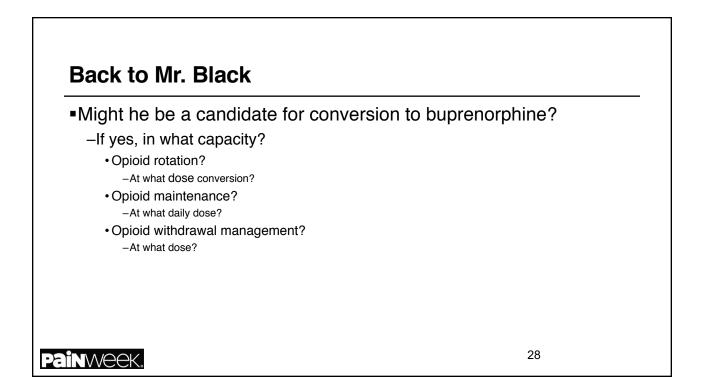
 2 papers outline the use of SL buprenorphine conversion in physically dependent pain patients – both were observational reports based on retrospective chart analysis

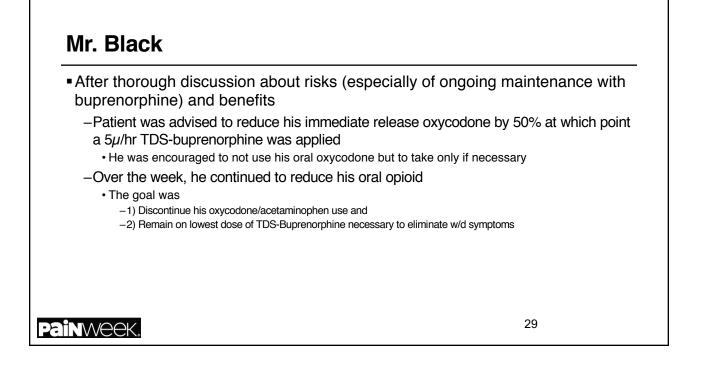
-Jonathan Daitch et al Pain Physician 2012 15:ES59-66

-Jonathan Daitch et al Pain Medicine 2014 15(12); 2087-2094









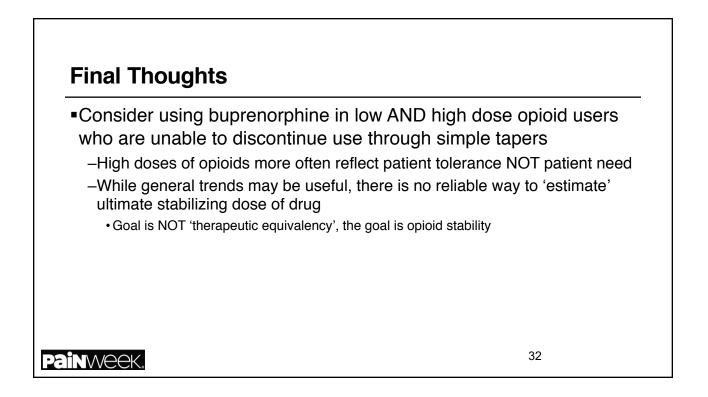
Mr. Black (cont'd)

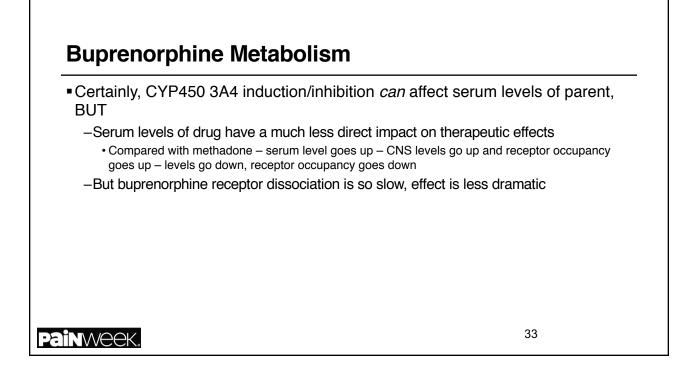
• On day 3, he was asked to call in to speak with our nurse regarding progress

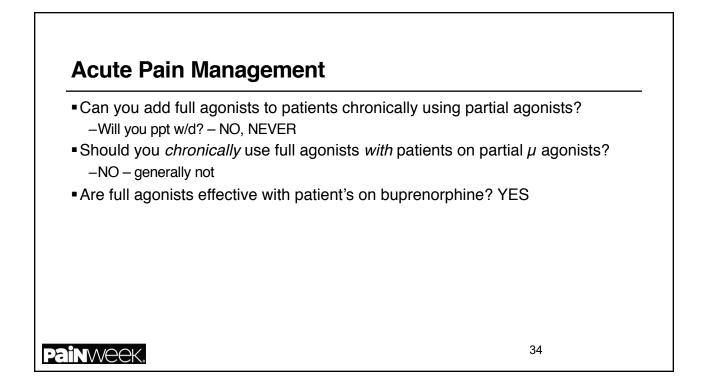
- –If necessary, the patch was increased to 10μ /hr after day 3
- -He was cautioned NOT to interpret a worsening of his pain symptoms as evidence of failure until he was on a steady (and optimal) dose of TDS-buprenorphine



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References

- Canadian Opioid Guidelines
 - <u>http://nationalpaincentre.mcmaster.ca/documents/Opioid%20GL%20for%20CMAJ_01may2017.</u>
- Transbuccal buprenorphine delivery system -https://www.belbuca.com/hcp/#
- Danielle Daitch MD1 et al Conversion from High-Dose Full-Opioid Agonists to Sublingual Buprenorphine Reduces Pain Scores and Improves Quality of Life for Chronic Pain Patients. Pain Medicine <u>Volume 15, Issue 12, pages 2087–2094</u>, December 2014
- Heit HA and D Gourlay, Buprenorphine: New tricks with an old molecule for Pain Management, Clinical J of Pain, 2008; 24:93-97
- dgourlay@cogeco.ca (Dr Douglas Gourlay feel free to contact)

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