Opioid Potency and Equianalgesia: Critical facts

1. **Opioid heterogeneity**: Not all opioids are created equal. There are variations in
   - Metabolism
   - Potency
   - Available routes of administration
   - Toxicity
   - Side effect profile
   - Presence or absence of ceiling effect
   - Interaction with the opioid receptors in the body—referred to incomplete cross-sensitivity or incomplete cross-tolerance.

2. **Switching opioids**: It is common in clinical practice to find that it is necessary to change either the route or the drug in a patient receiving opioid analgesics. Examples include:
   - Patient has become NPO, must switch from oral to parenteral
   - Patient is transitioning from post-op parenteral to a different drug given orally
   - High or escalating doses of one opioid are causing unacceptable side effects and must be changed
   - Insurance coverage favors one drug over another
   - A medication taken in the community is not on formulary in the institution

3. **Potency**: Potency refers to the amount of drug required to produce an effect. A major difference among opioids is the difference in potency: the same mg amount of one opioid will have different analgesic effects and side/toxic effects than a different opioid. When differences in potency are not taken into consideration, especially when changing routes or changing drugs, significant dosing errors can occur.
   - Patient may be under medicated and in severe pain
   - Patient may be over medicated and experience sedation, significant respiratory depression, and even death

4. **Relative potency**: Morphine 30 mg PO is the reference drug against which the others are measured. Relative potencies can be easily viewed on equianalgesic tables (see below).

5. **PO vs IV potency**: Because of differences in metabolism between oral and parenteral routes, the parenteral opioid is always more potent than the same mg amount of the oral opioid.

6. **Common potency-related errors**: The most common hospital-based source of error involving issues of potency is when a patient is switched from morphine to hydromorphone (Dilaudid). **Hydromorphone by any route is significantly more potent than morphine**.
   - <u>Oral</u> hydromorphone is **4** times more potent than <u>oral</u> morphine:
     7.5mg hydromorphone PO = 30mg morphine PO
   - <u>Parenteral</u> hydromorphone is **7** times more potent than <u>parenteral</u> morphine:
     1.5 mg hydromorphone IV = 10mg morphine IV
   - <u>Parenteral</u> hydromorphone is **20** times more potent than <u>oral</u> morphine:
     1.5 mg hydromorphone IV = 30mg morphine PO

7. **Opioid rotation**: changing from one opioid to another is referred to as "opioid rotation" or "opioid switching."
   - Indications for switching from one opioid to another include
     - Opioid-induced intractable and intolerable side effects
     - Inadequate analgesia despite appropriate dose escalation
   - The primary goal of opioid rotation protocols is to find a safe starting dose of the new opioid
   - The regimen is then titrated to the individual patient's needs using a combination of a scheduled dose and liberal use of PRN "rescue" doses

8. **Principles of opioid rotation**: Safe opioid rotation adheres to the following principles:
   - Use a consistent method or protocol
   - Consistently use the same equianalgesic table for calculating doses (there may be slight differences from one table to another)
   - In most cases, reduce the calculated dose by a standard percentage (25 – 50%) to account for:
     - Incomplete cross-tolerance
     - Variations in patient metabolism
     - Limitations of equianalgesic tables
     - ❖ Reducing the calculated dose may not be necessary when route alone is being changed
   - When rounding, round downward
   - Use a PRN rescue dose of 10% of the 24-hour dose, and available q 1 hour.
   - Adjust the scheduled dose after 24 hours based on total opioid intake (scheduled + PRN) over the previous day

9. **Using an equianalgesic table**: An equianalgesic table accounts for differences in potency by providing the approximate equivalent dose, by route, of multiple opioids compared to morphine 30 mg PO.
   - All values on an equianalgesic table represent doses that are equivalent to each other in terms of potency
   - The values on the table may be used to create simple ratio equations for calculating equianalgesic doses of any drugs in the table

Opioid Equianalgesic Doses		
Oral (mg)	**Drug**	**Parenteral (mg)**
30	Morphine	10
20	Oxycodone	N/A
7.5	Hydromorphone	1.5
N/A	Fentanyl	0.1 (100mcg)
200	Codeine	130
20	Hydrocodone	N/A

Step 1: set up the equation

Values from the table		Patient opioid values		Solve for *X*
Value of opioid 1 / Value of opioid 2	=	24-hour dose of current opioid (opioid 1) / *X* amt. of new opioid (opioid 2)	=	Equianalgesic 24-hour dose of opioid 2

Step 2: Reduce calculated 24-hour dose by 25 – 50% = 24-hour starting dose
Step 3: Divide 24-hour starting dose by number of doses per day = scheduled dose
Step 4: Order liberal "rescue" dose (10-15% of 24-hour starting dose) and titrate to comfort
Step 5: Monitor patient closely for balance of analgesia, function, and side effects
Step 6: After 12 – 24 hours recalculate scheduled dose:
Total opioid in 24 hours (scheduled + rescue) ÷ doses per day = new scheduled dose

Example 1: Mr. J. is on stable dose of sustained release oral morphine, but is now NPO. He has been taking MS Contin 60 mg q 12 hr plus 20 mg morphine solution 1 – 2 times per day for breakthrough pain. What is the appropriate starting dose of IV morphine?

Values from the table		Patient opioid values		Solve for *X*
Morphine 30 mg PO / Morphine 10 mg IV	=	120 mg morphine PO / morphine *X* mg IV	=	Equianalgesic 24-hour dose of opioid 2

(Note that a conservative estimate of 24 hour intake was used, and did not include the PRN doses)

Solve for *X* by cross-multiplying:
(MS 30 mg) x (*X*) = (MS 10 mg) x (MS 120 mg) =

30*X* = 1200, *X* = 40 mg. Divide by 24 to calculate the infusion rate = 1.6 mg/hr

Example 2: Ms A. has advanced endometrial cancer. Ms. A's abdominal pain is well controlled (range: 0 – 3/10) with 100 mg MS Contin q8 hours. She has a rescue dose of immediate release morphine 30 mg PO ordered, but rarely needs it. Co-morbid conditions require a change of drug and route.

Doing the math:

a. First calculate the 24 hour basal dose: morphine 100 mg x 3 doses per day = 300 mg.
b. Set up the simple proportion equation:

Values from the table		Patient opioid values		Solve for *X*
Morphine 30 mg PO / Dilaudid 1.5 mg IV	=	Morphine 300 mg PO / Dilaudid *X* mg IV	=	15 mg Dilaudid IV/24 hr

c. Reduce dose by 25%: 15 x .75 = 11.25 mg IV to be deliver over 24 hours by continuous infusion.
d. The hourly rate is 11.25 ÷ 24 = 0.5 mg/hour.
e. The rescue dose is 10 – 15% of the 24 dose: 11 x .1 = 1.1 mg. Suggested rescue dose: 0.5 – 2 mg IV q 1 hour as needed for breakthrough pain.