

# Opioid Pharmacology for Physical Therapists



**Allison Seiko Komirenko**

Doctor of Pharmacy Candidate, 2015

University of California, San Francisco

April 7, 2016

*Slides adapted from Tina Tran, PharmD (2014)*

- **What you (should) already know...** 😊

- Physiology of pain transmission pathways
- Neurotransmitters/modulators and receptors involved in the pain pathways

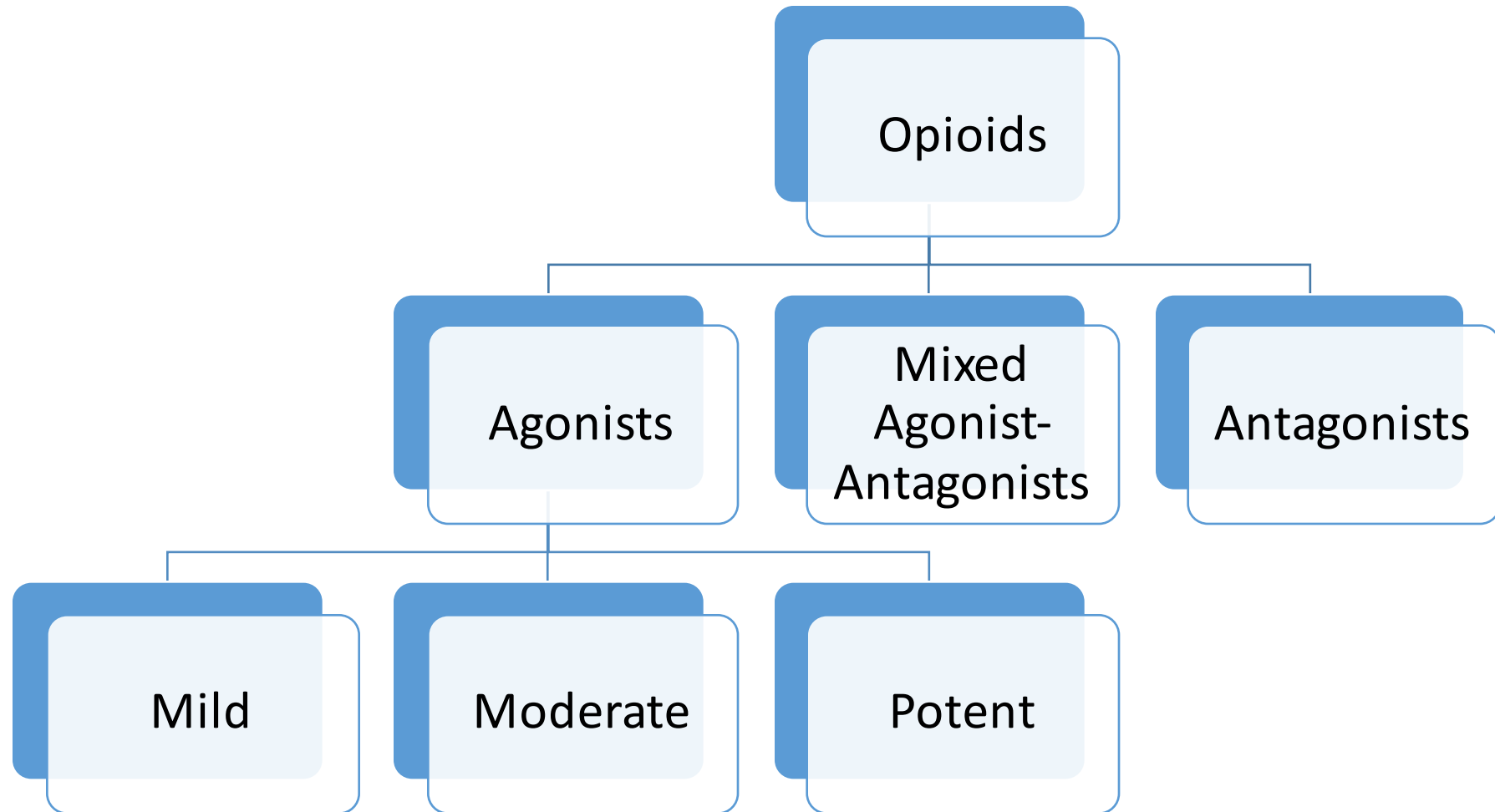
- **What we will discuss today...**

- Clinical uses of (1) **opioid agonists (aka opioid analgesics)**, (2) **mixed agonist-antagonist opioids**, and (3) **pure antagonist opioids**
- Mechanism of action (MOA)
- Acute effects on central and peripheral nervous system
- Different dosage forms and routes of administration
- Tolerance vs. Dependence vs. Addiction
- Adverse drug effects (ADEs) and toxicity

- **What you should be able to do after the lecture...**

- Explain the advantages of optimized pain control regimens for physical therapy treatments
- Explain how opioid adverse drug reactions could clinically interfere with physical therapy treatments

# Classification of Opioids



# Opioid Agonists (Opioid Analgesics)

| Mild Analgesics                                                              | Moderate Analgesics                                                               | Potent Analgesics                                                                                                                                                    |
|------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"><li>• Tramadol</li><li>• Codeine</li></ul> | <ul style="list-style-type: none"><li>• Hydrocodone</li><li>• Oxycodone</li></ul> | <ul style="list-style-type: none"><li>• Morphine</li><li>• Oxymorphone</li><li>• Hydromorphone</li><li>• Fentanyl</li><li>• Meperidine</li><li>• Methadone</li></ul> |

# Opioid Agonists – Clinical Indications

- Analgesia
- Cough Suppression
- Treatment of Diarrhea
- Anesthesia
- Opioid Dependence

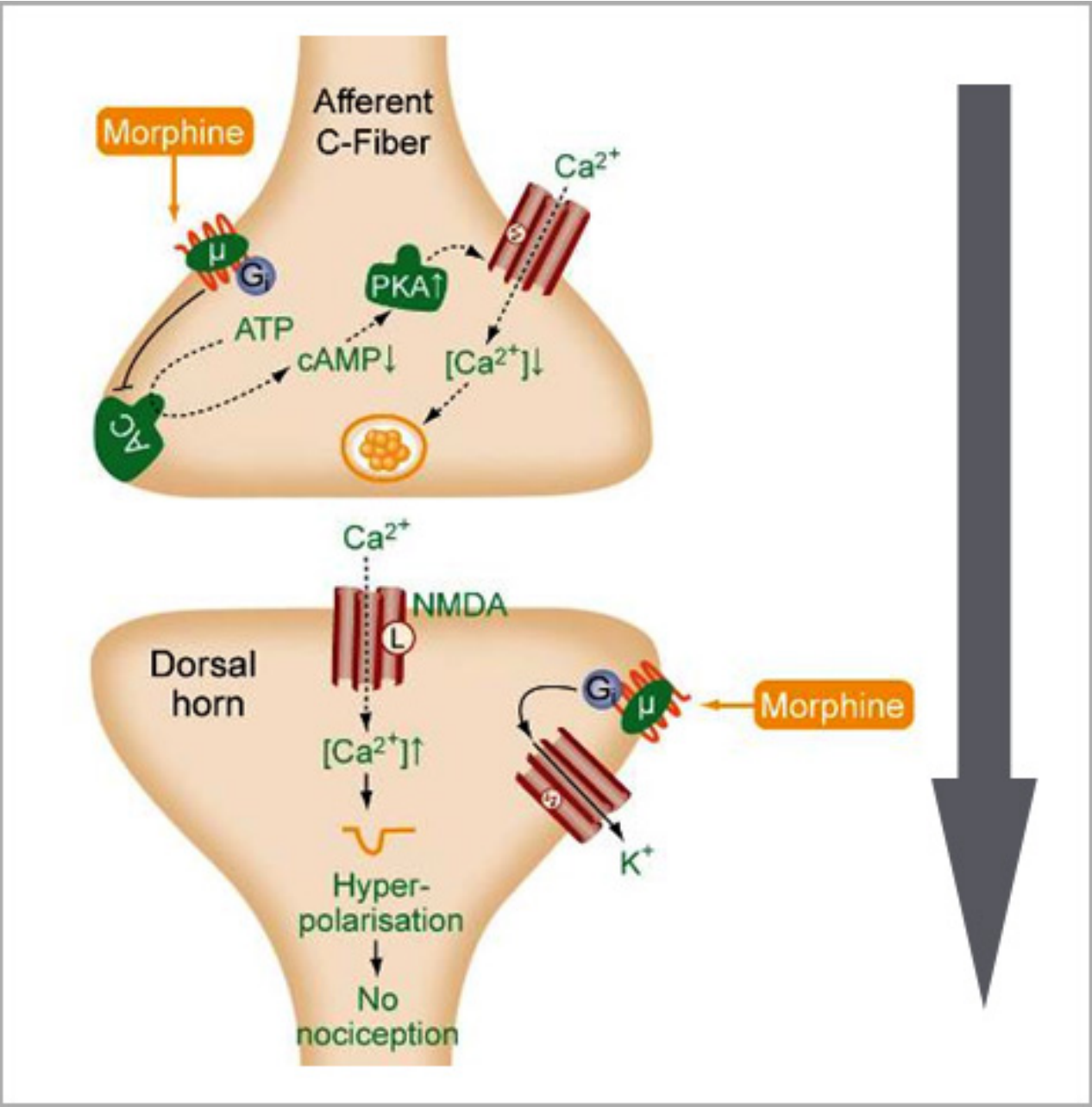


# Opioid Analgesics – Mechanism of Action

- Bind to specific G protein-coupled receptors in the brain and the spinal cord
- 3 subgroups of opioid receptors:
  - Mu
  - Delta
  - Kappa
- Alter transmission and modulation of pain

**PRESYNAPTIC ACTION**

- ↓  $\text{Ca}^{2+}$  influx
- ↓ transmitter release



**POSTSYNAPTIC ACTION**

- ↑  $\text{K}^+$  conductance  
(Hyperpolarization)

# Routes of Administration

- Oral
- Parenteral
- Transdermal
- Rectal suppositories
- Buccal trans-mucosal
- Patient-controlled analgesia (PCA)





# Adverse Effects and Toxicity

- **Central Nervous System**

- Sedation and Confusion
- Respiratory Depression
- Nausea and Vomiting

- **Peripheral Nervous System**

- Hypotension
- Pruritis
- Constipation



# Management of Opiate Adverse Effects

| Adverse Effect                                                                                                               | Management                                                                                                            |
|------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|
| Sedation and Confusion                                                                                                       | <ul style="list-style-type: none"><li>• Switch opiate</li><li>• Give smaller doses more frequently</li></ul>          |
| Respiratory Depression                                                                                                       | <ul style="list-style-type: none"><li>• Reduce dose</li></ul>                                                         |
| Nausea and Vomiting                                                                                                          | <ul style="list-style-type: none"><li>• Antiemetics</li></ul>                                                         |
| Hypotension <ul style="list-style-type: none"><li>• Most common with morphine</li><li>• Least common with fentanyl</li></ul> | <ul style="list-style-type: none"><li>• Maintenance fluids</li></ul>                                                  |
| Pruritis                                                                                                                     | <ul style="list-style-type: none"><li>• Antihistamines</li></ul>                                                      |
| Constipation                                                                                                                 | <ul style="list-style-type: none"><li>• Hydration</li><li>• “Mush and push”</li><li>• Suppositories, enemas</li></ul> |

# Tolerance, Dependence, and Addiction

- **Tolerance**

- With repeated use, efficacy decreases and a larger amount of drug must be used to produce the same analgesia effect

- **Dependence**

- Withdrawal symptoms occur if drug is discontinued

- **Addiction**

- Continued use of drugs despite harmful consequences related to health or daily activities

# Withdrawal Symptoms

*Extremely unpleasant, but not life-threatening*

- Dysphoria
- Diarrhea
- Rhinorrhea
- Muscle/bone pain
- Pupil dilation
- Piloerection
- Increased HR/BP
- Insomnia



# Mixed Agonist-Antagonists

- **Indication:**

- Treatment of opioid abuse by suppressing withdrawal symptoms

- **MOA:**

- Partial Agonist: Binds tightly to the Mu receptors but produces limited analgesic effect
  - Agonist in the absence of other opioids, but antagonist in the presence of other opioids

- **Example:**

- Buprenorphine (Suboxone®)

# Opioid Antagonists

- **Indication:**

- Management of acute opioid overdose

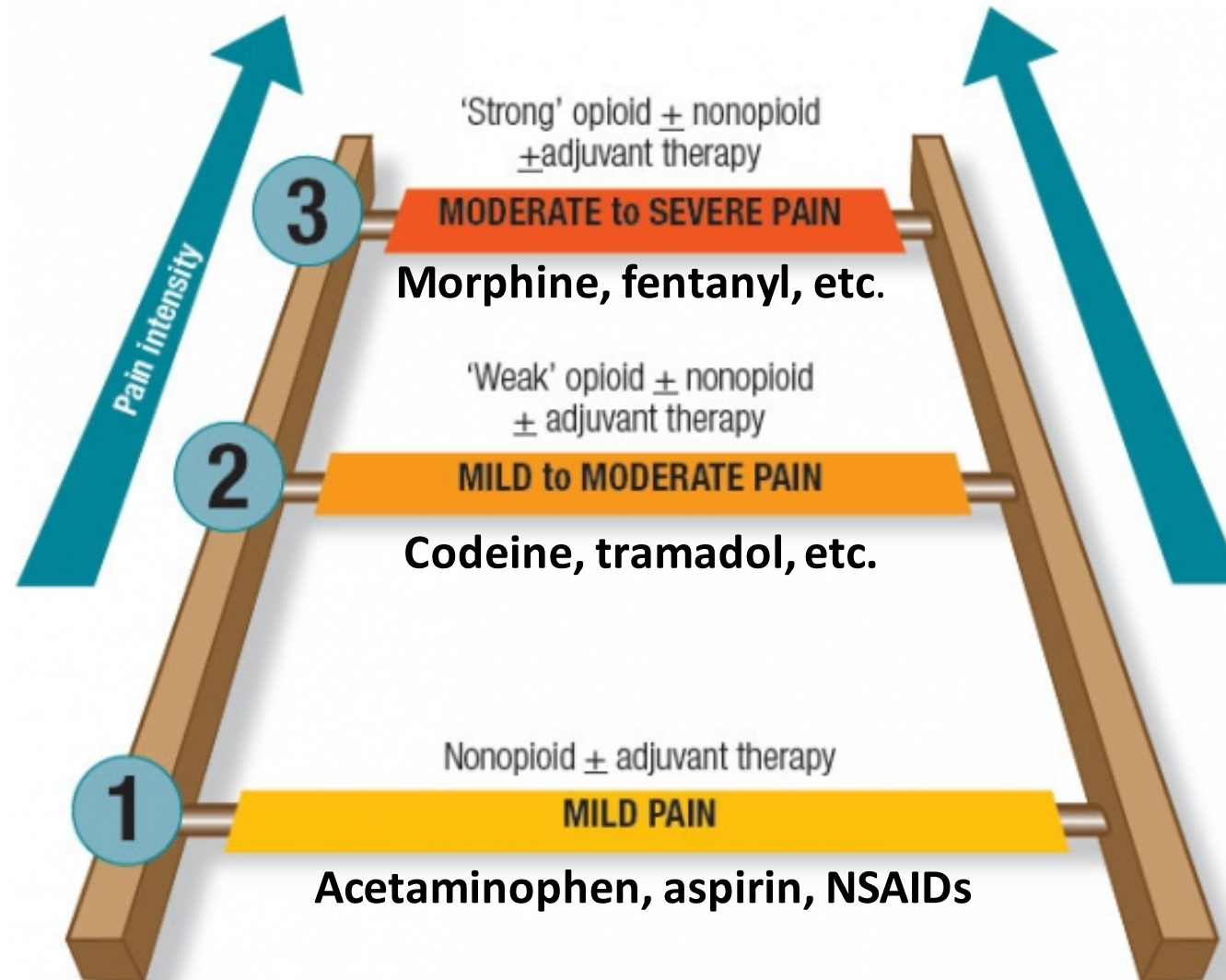
- **MOA:**

- Pure Antagonist: Binds with greatest affinity to the Mu receptors and reverse the effects of opioids

- **Example:**

- Naloxone (Narcan®)

# WHO's Pain Relief Ladder



# Clinical Relevance for Physical Therapy

- **Opioid analgesics**

- Reduce pain levels and facilitate patients' progress through various physical therapy treatments
- Use for acute pain relief (e.g., post-surgery) and chronic pain relief (e.g., cancer pain, chronic pain)

- **It is important for physical therapists to...**

- Monitor patients during physical therapy sessions and recognize opioid adverse effects
- Be aware of the high abuse potential and clinical presentations of opioid tolerance, dependence, and addiction



# Opioid Adverse Effects – Physical Therapy Focus

| Adverse Drug Effect                          | Effect on Rehabilitation                                                                  |
|----------------------------------------------|-------------------------------------------------------------------------------------------|
| Orthostatic Hypotension                      | May require a little extra time when assuming a more upright position                     |
| Respiratory Depression                       | May compromise patient's respiratory response due to hypoxia or hypercapnia               |
| Sedation and Confusion                       | May slow down patient understanding and response following instructions                   |
| Muscle Aches and Bone Pain during Withdrawal | May require heat, electrotherapy, massage, or relaxation techniques to relieve symptoms   |
| Constipation                                 | May benefit from patient/caregiver education on lifestyle and over-the-counter management |