PATHOPHYSIOLOGY OF OPIOID WITHDRAWAL

R. COREY WALLER MD, MS
PRINCIPAL, HEALTH MANAGEMENT ASSOCIATES
FACULTY, INSTITUTE FOR HEALTHCARE INNOVATION (IHI)
CHAIR, LEGISLATIVE ADVOCACY COMMITTEE, ASAM
THE DOPAMINE EFFECT

THE DAYS OF “NORMAL PAST”  CRAVING OUT OF CONTROL  THE NEW NORMAL
TOLERANCE

Initial phase
- MOR
- cAMP
- Epigenetic effect

Stable phase
- Impact on emotion
- Impact on neonate
  - Special case for methadone
## WITHDRAWAL

| **The Locus Coeruleus** | Increased NE activity (hyperactivity)  
Indirect increase in RAS activity (poor sleep architecture) |
|-------------------------|---------------------------------------------------------|
| **PAG**                 | • Opioid dependence induces coupling of mu-receptors to  
                          presynaptic inhibition in GABAergic nerve terminals in the  
PAG  
• The removal of the opioid decouples this interaction |
TREATMENT

1. Opioids
   - Buprenorphine
   - Methadone
   - Morphine

2. Alpha 2 agonists
   - clonidine
   - dexmedetomidine
   - lofexidine

3. Benzo’s
   - Diazepam
   - Chlordiazepoxide
REFERENCES


• Handong Ouyang, 1 Shue Liu, 1,2 Weian Zeng, 3 Roy C. Levitt, 2 Keith A. Candiotti, 2 and Shuanglin Hao 1,2; An Emerging New Paradigm in Opioid Withdrawal: A Critical Role for Glia-Neuron Signaling in the Periaqueductal Gray The Scientific World Journal, Volume 2012, Article ID 940613, 9 pages