

Medications in the Treatment of
Opioid Use Disorder:
Methadone and Buprenorphine –
What Really Are They?

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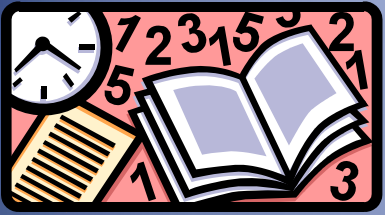
Cecil County Board of Health Workgroup Meeting
Elkton, MD
October 8, 2013

Objectives

1. Background information
2. How does opioid addiction develop?
3. Why are methadone and buprenorphine different from opioids of abuse?

BACKGROUND INFORMATION



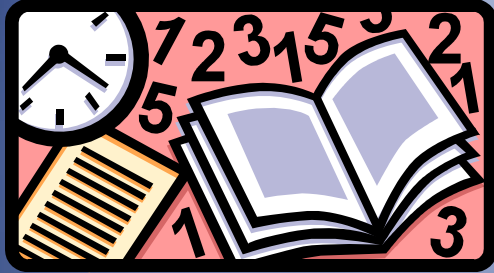


Basic Definitions

Addiction*

- A brain disease that affects behaviour. It is characterized by compulsive, continued use of a specific substance despite physical, psychological, or social harm
- The substance becomes a central and organizing feature of their life
- Represents a category of diseases called substance use disorders
- Are typically chronic, often relapsing diseases

*From the American Society of Addiction Medicine and the National Institute on Drug Abuse



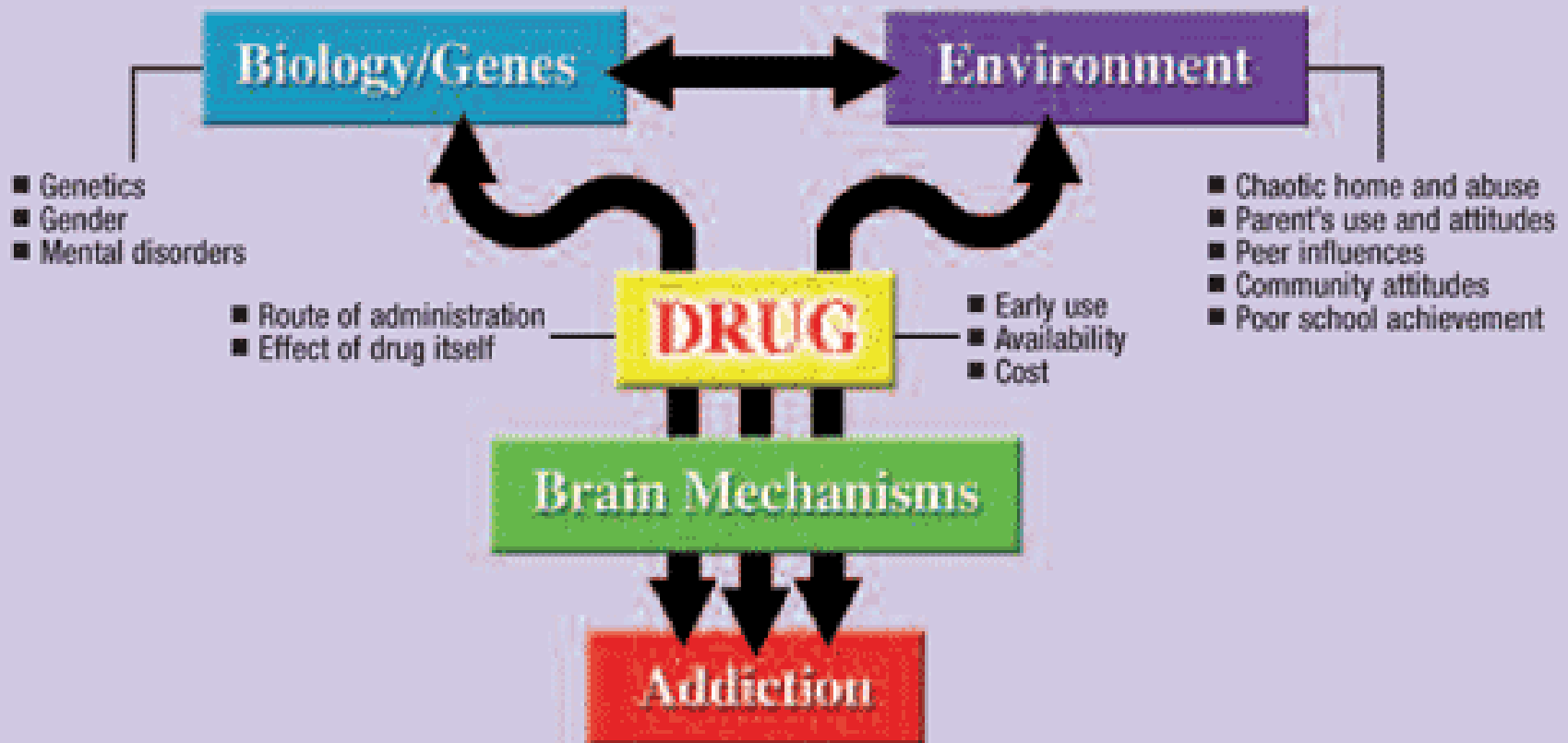
Basic Definitions

Physical Dependence

- An adaptation of the body to a specific substance so that in the absence of that substance a withdrawal syndrome develops. The withdrawal syndrome may be relieved in total or in part by readministration of the substance.

Why do some people develop addiction?

RISK FACTORS



Presence of Mental Illness

- 35% of people with alcohol use disorder and over 50% of those with drug use disorder have some type of other mental illness*
- Children with ADHD are at higher risk for cocaine abuse later in life
- In 2003, mutation in gene that regulates brain receptor sensitivity to dopamine discovered
- This mutation linked to bipolar disorder

*Regier et al., JAMA 264:2511-2518, 1990

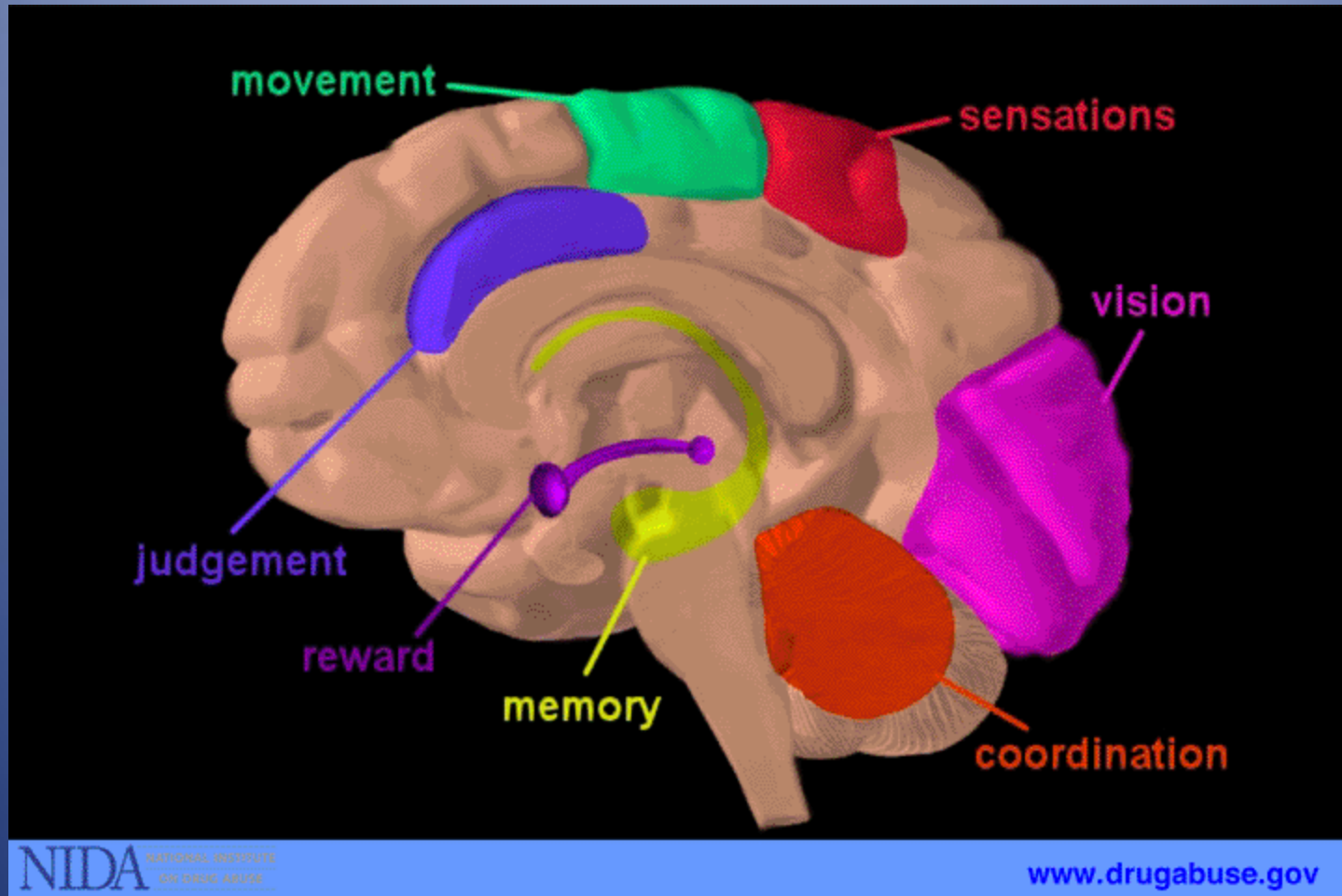
How does opioid addiction
develop?

Innate Opioid Receptor System

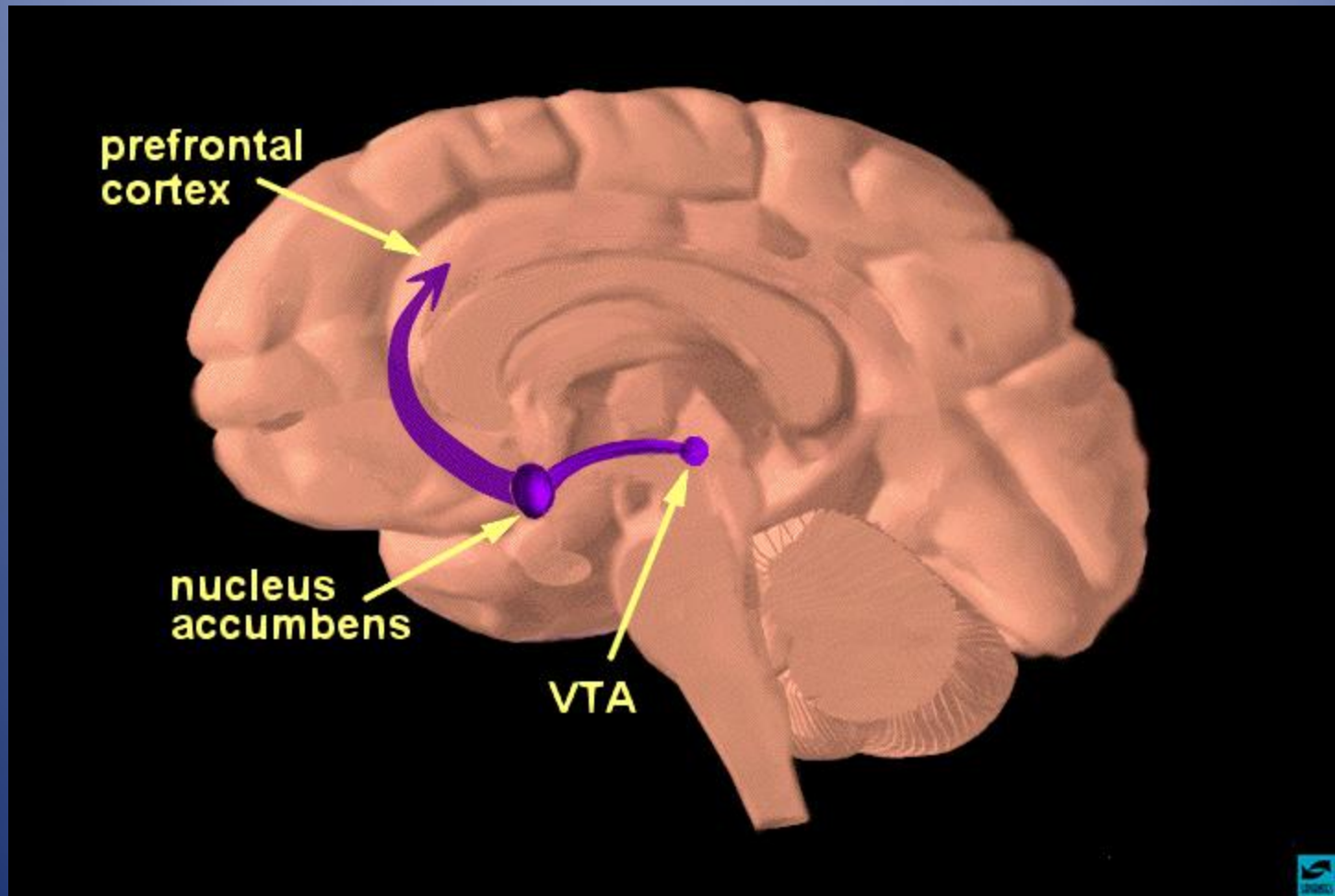
- Purpose
 - Regulate pleasure
 - Regulate pain



The Human Brain



The Reward Pathway



Here's how people communicate.



Transmitter

Receptor

Here's how brain cells communicate.



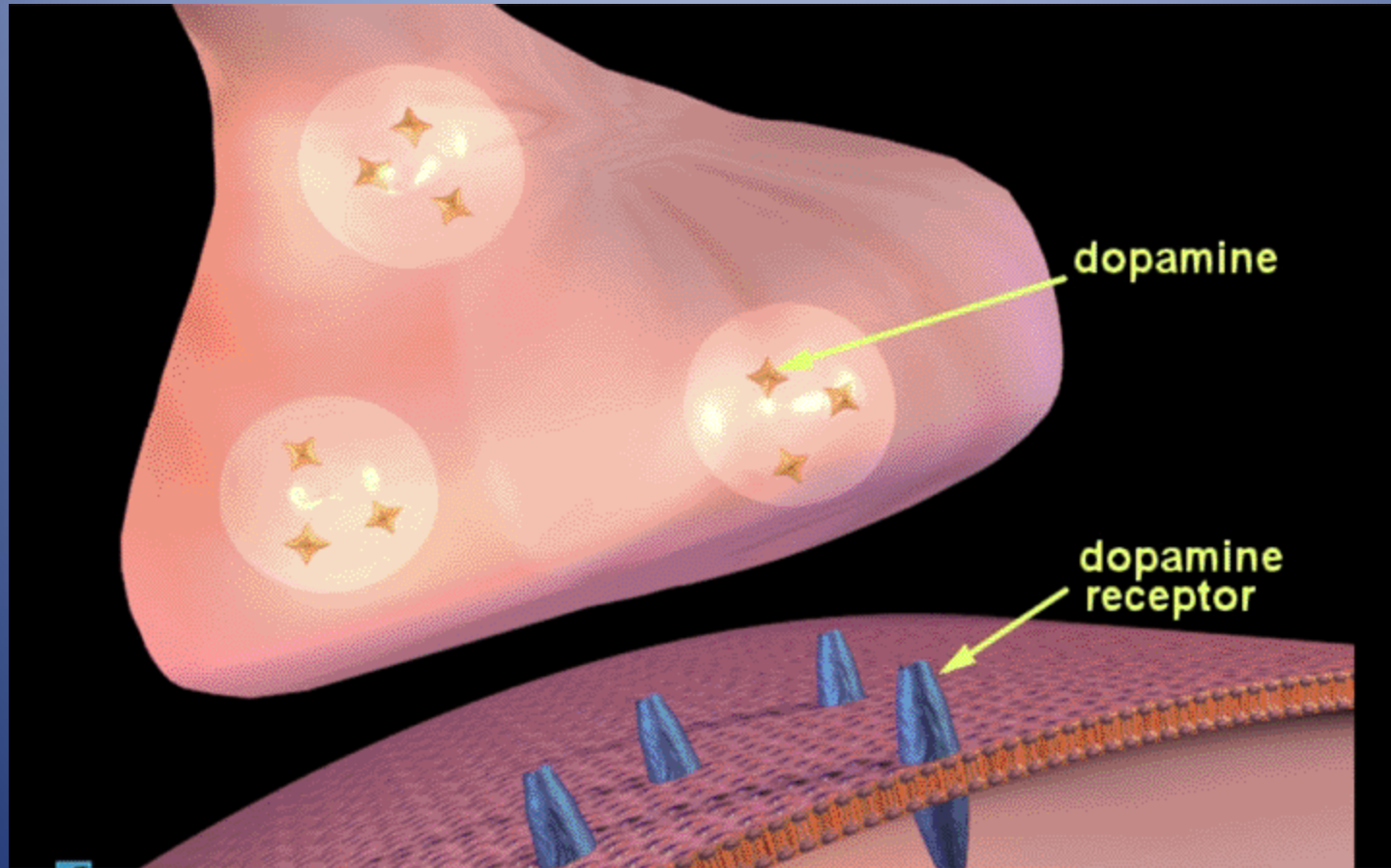
Neurotransmitter

Receptor

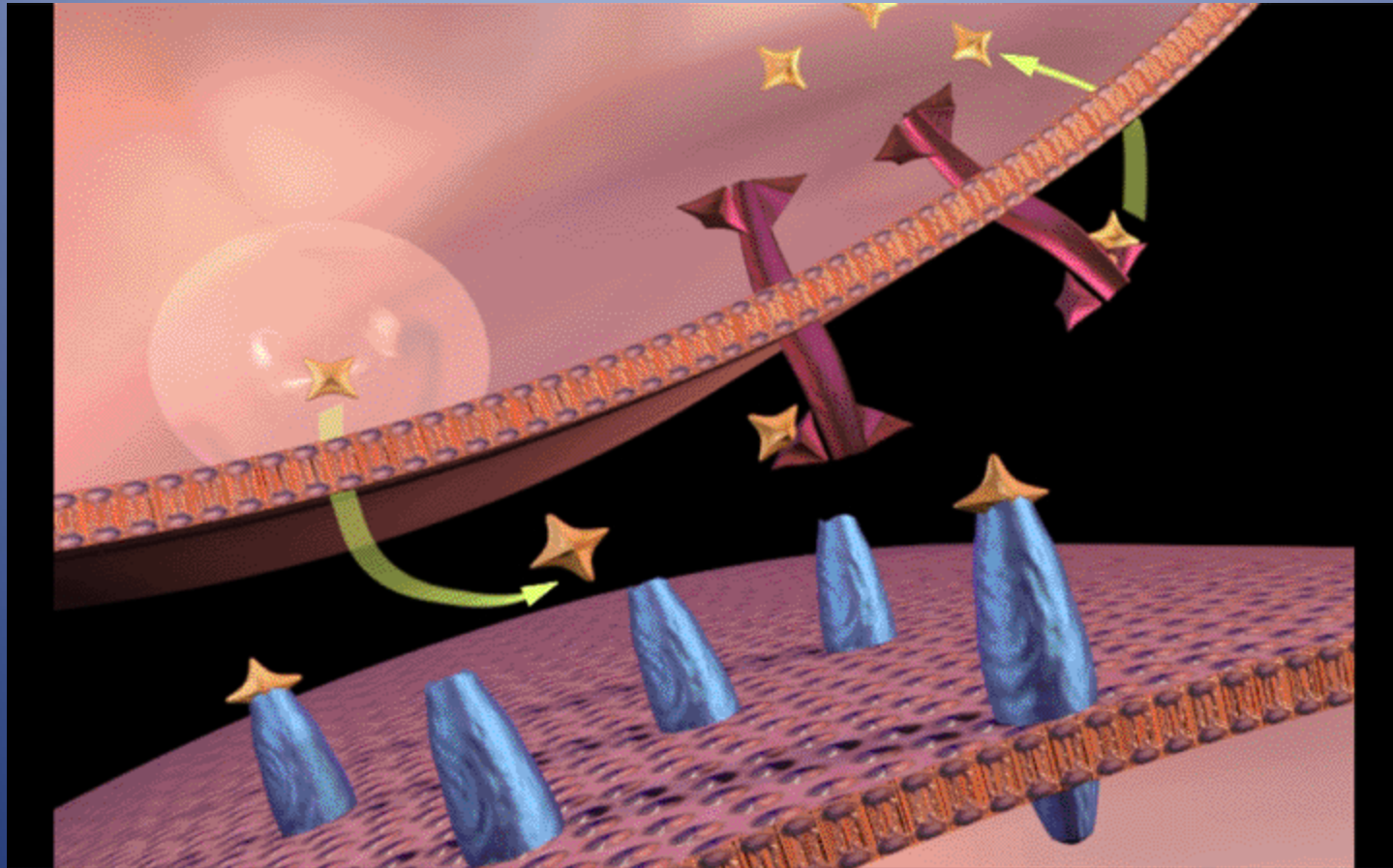
Concept courtesy: B.K. Madras

1. Neurotransmitter binds to receptor on second cell
2. This binding excites the second cell into action
3. The reward center in the limbic system contains thousands of nerves and many different neurotransmitters

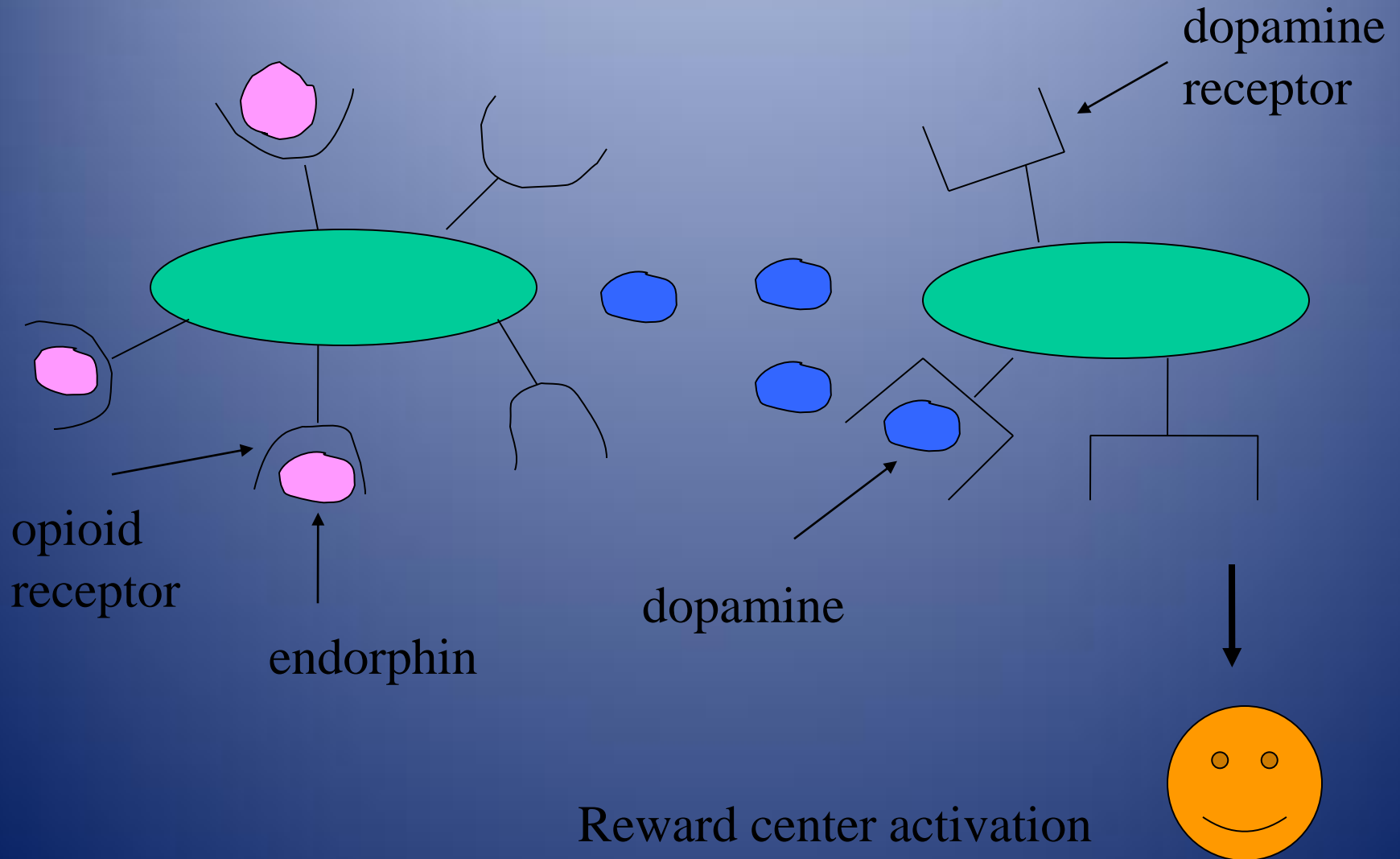
Dopamine



Dopamine



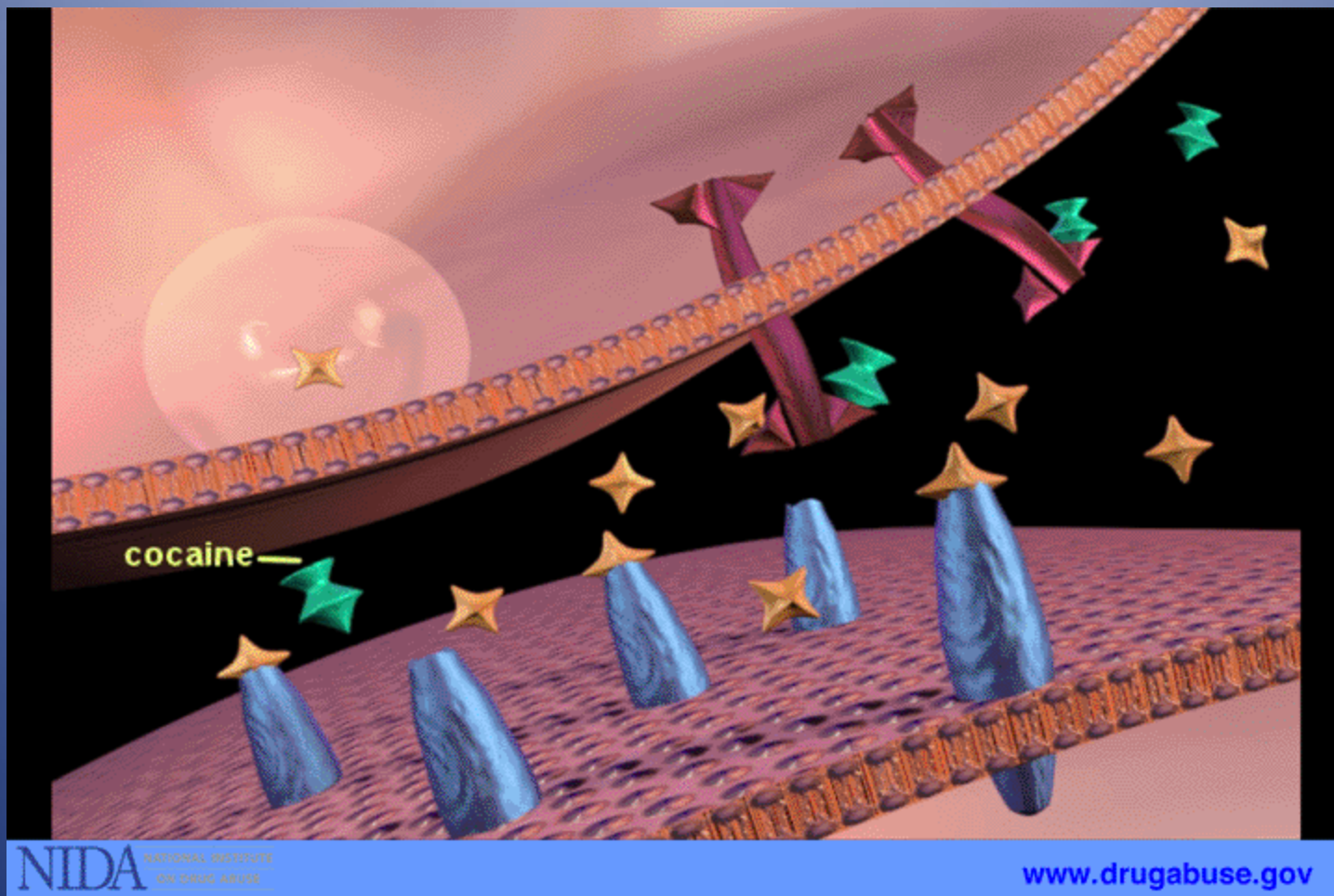
The Reward Center and Endorphins



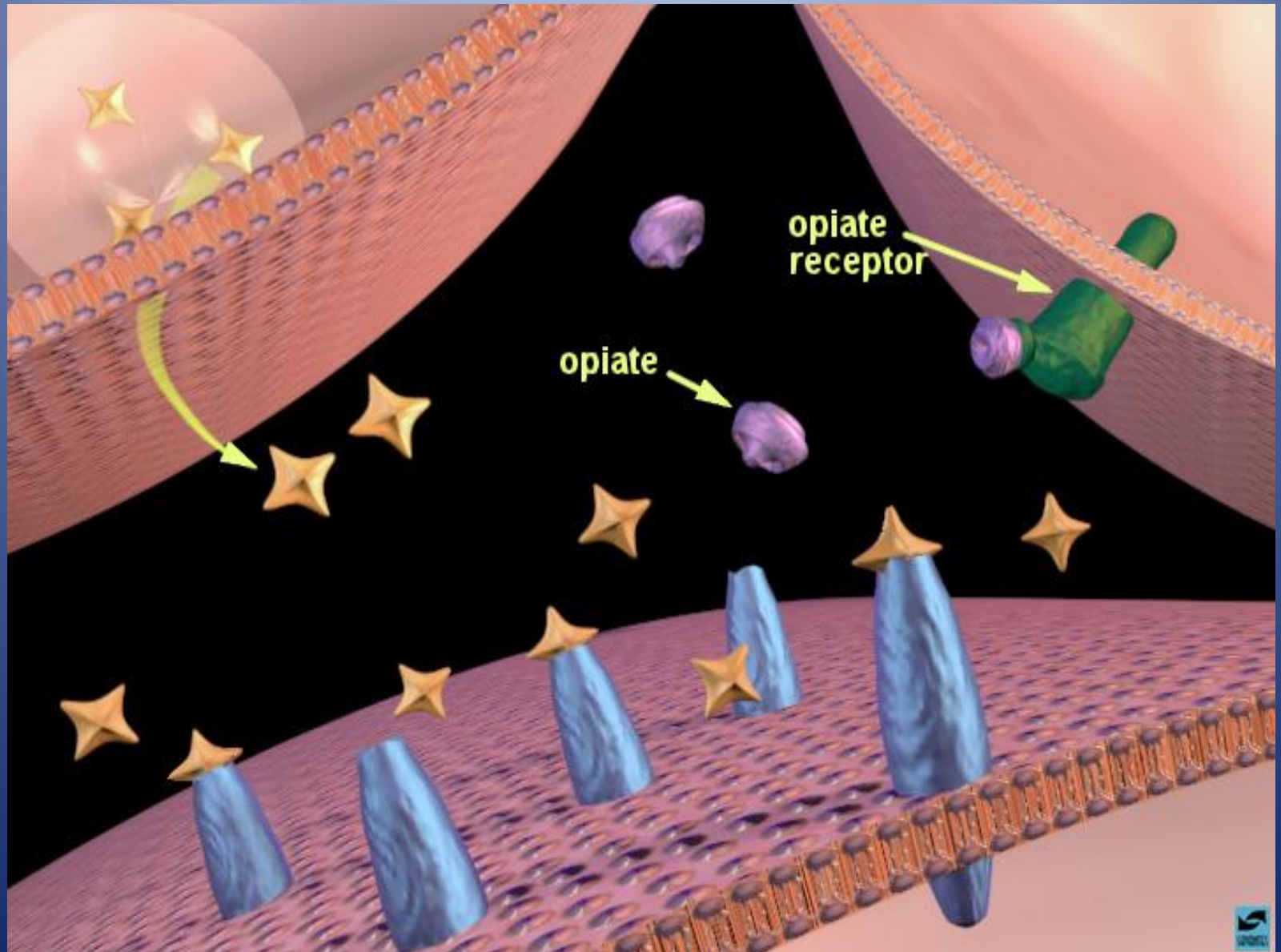
But.....

- All substances of abuse target the reward center and hijack it

Cocaine



Heroin



Why is euphoria from drugs a bad thing?

- Overwhelms natural process for feeling pleasure
- The brain remembers the intense pleasure brought about by drugs. These memories drive continued use and implicated in relapse

Receptor Changes

- Changes happen in the shape of the receptors with chronic, prolonged exposure
- These changes alter the way nerve cells in the reward center act
- These changes may be irreversible (or at least long-term)
- May be why so many people relapse after detox or after years of not using



Normal



Cocaine Abuser (10 days)



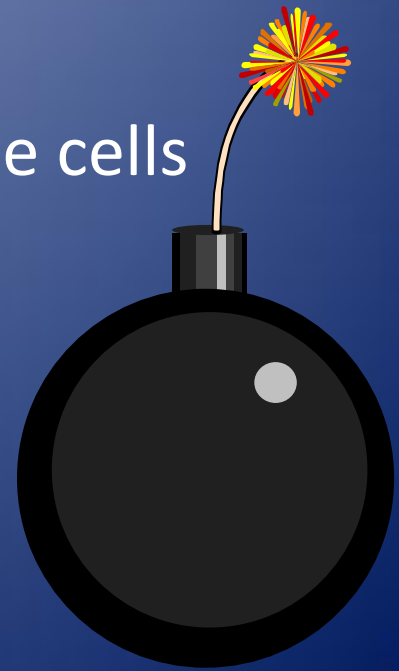
Cocaine Abuser (100 days)



Yellow and Red indicate the level of brain function

Opioid Withdrawal Syndrome

- With chronic exposure to opioids, the receptors and the cells get used to being activated by the opioid
- This means it takes more opioids to get the same feeling (tolerance)
- When suddenly the receptor is empty, the cells can't act and withdrawal occurs (physical dependence)



Symptoms of Opioid Withdrawal

- Dysphoria: anxiety, irritability, restlessness
- Hot and cold flashes
- Goose bumps
- Yawning
- Runny nose
- Watery eyes
- Diarrhea
- Abdominal cramps
- Joint and body pains and aches
- Headache
- Dilated pupils
- Nausea, vomiting
- Insomnia
- Fever

Summary

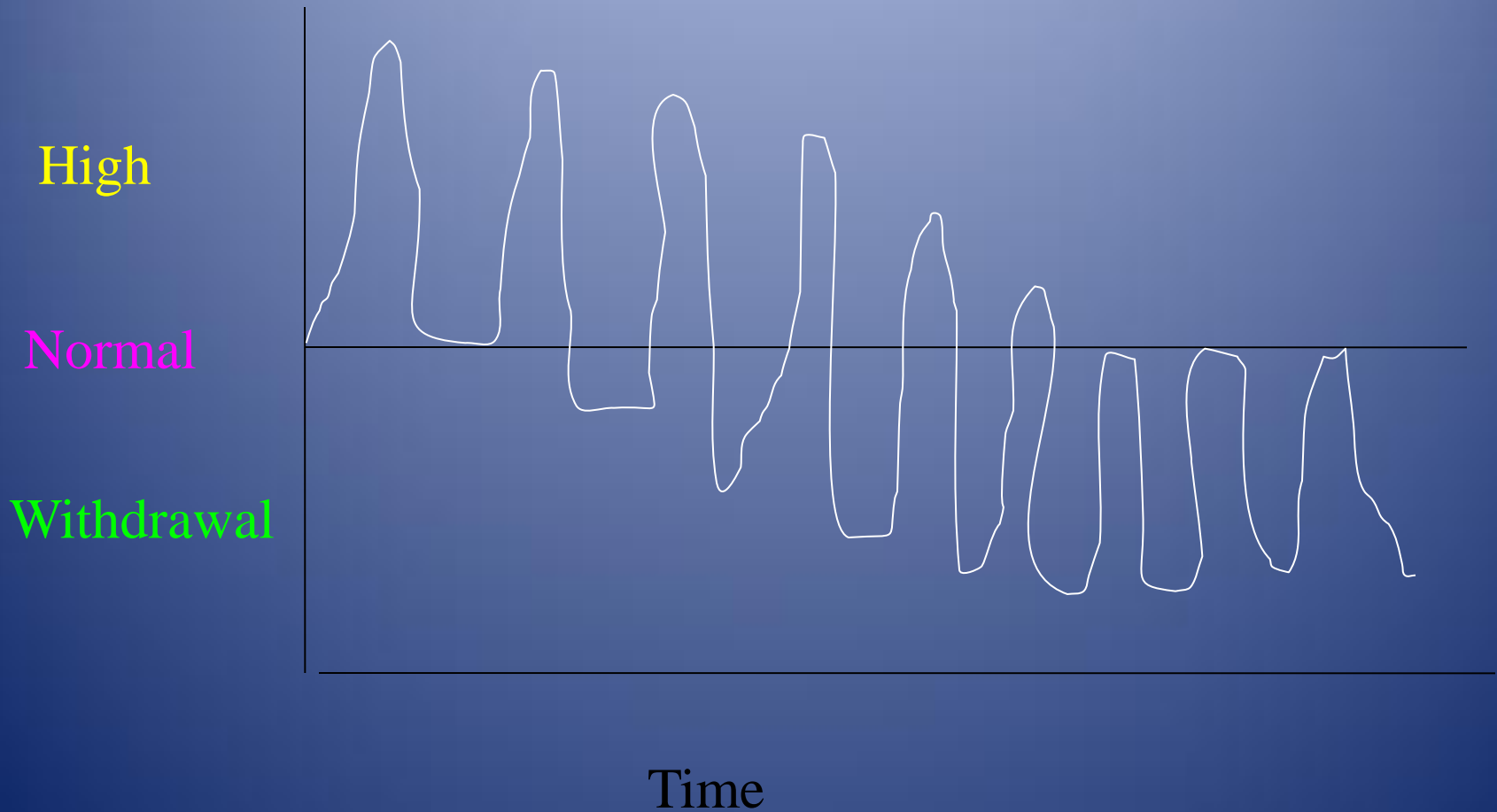
- All born with endorphin opioid system that helps us feel pleasure and regulate pain
- Too much opioids taken into body overstimulate the reward center
- With repeated exposure to opioids, the body adapts so that long-term changes happen to the receptors and cells in the reward pathway
- These changes are manifested by tolerance, withdrawal, and memory of overstimulation, all of which drive continued drug use

Why are methadone or buprenorphine then
different from opioids of abuse?

Pharmacologic Mechanism of Heroin

- Binds to opioid receptors in the reward center of the brain
- Produces intense euphoria
- Causes physical dependence
- Route of administration:
 - Snort
 - Injection
- Short-acting

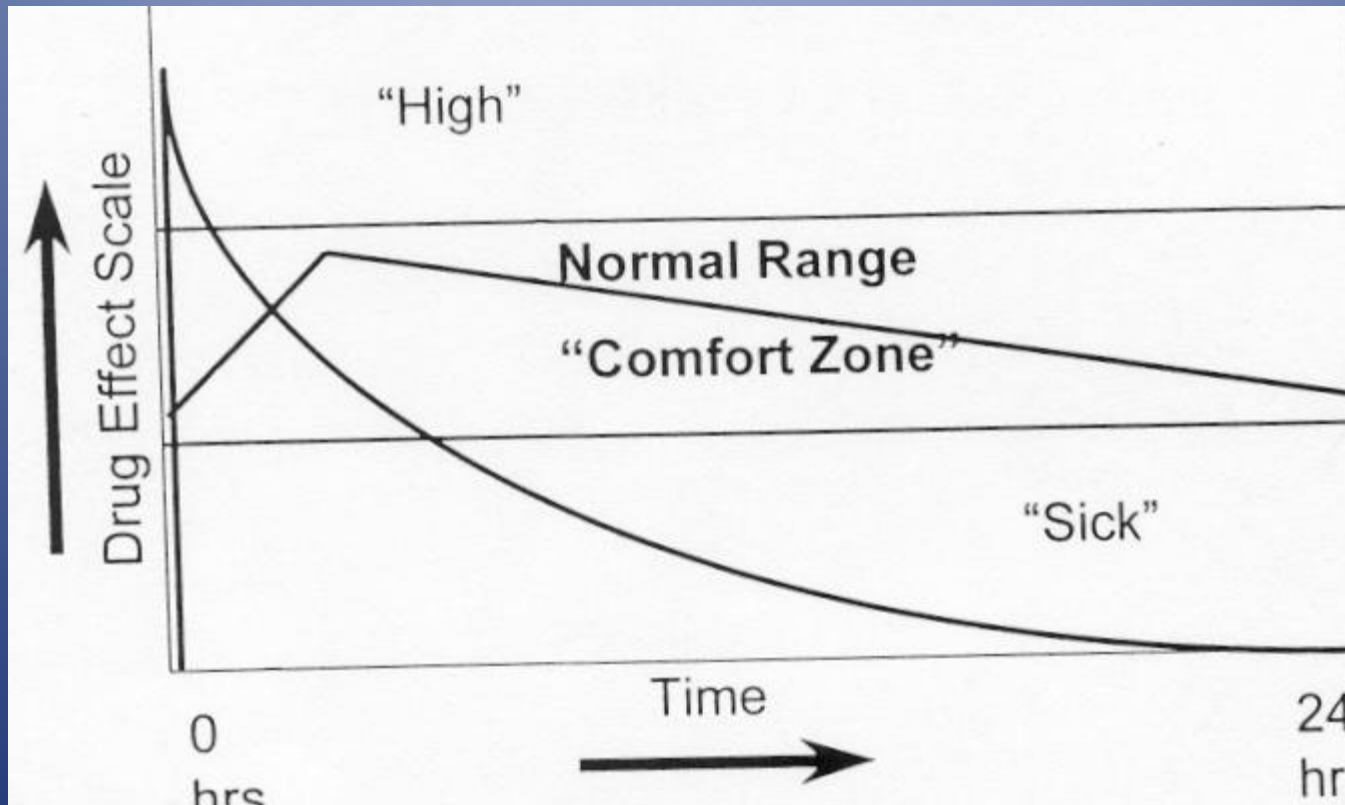
Pharmacologic Mechanism of Heroin



Pharmacologic Mechanism of Methadone

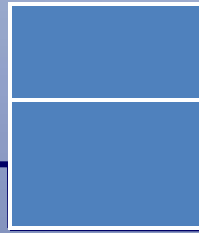
- Binds to opioid receptors in the reward center of the brain
- Causes physical dependence
- Route of administration: oral
- Long-acting
- In people with opioid addiction, at the correct dose, does not overstimulate the reward center

Methadone/Suboxone Dose-Response



Mu Opioid Receptor Activation

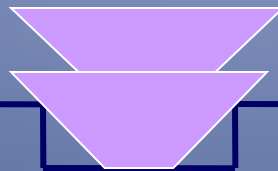
Full agonist



methadone

mu receptor site

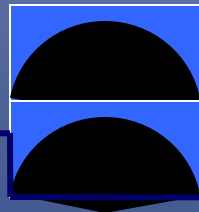
Partial agonist



buprenorphine

mu receptor site

Antagonist



naloxone

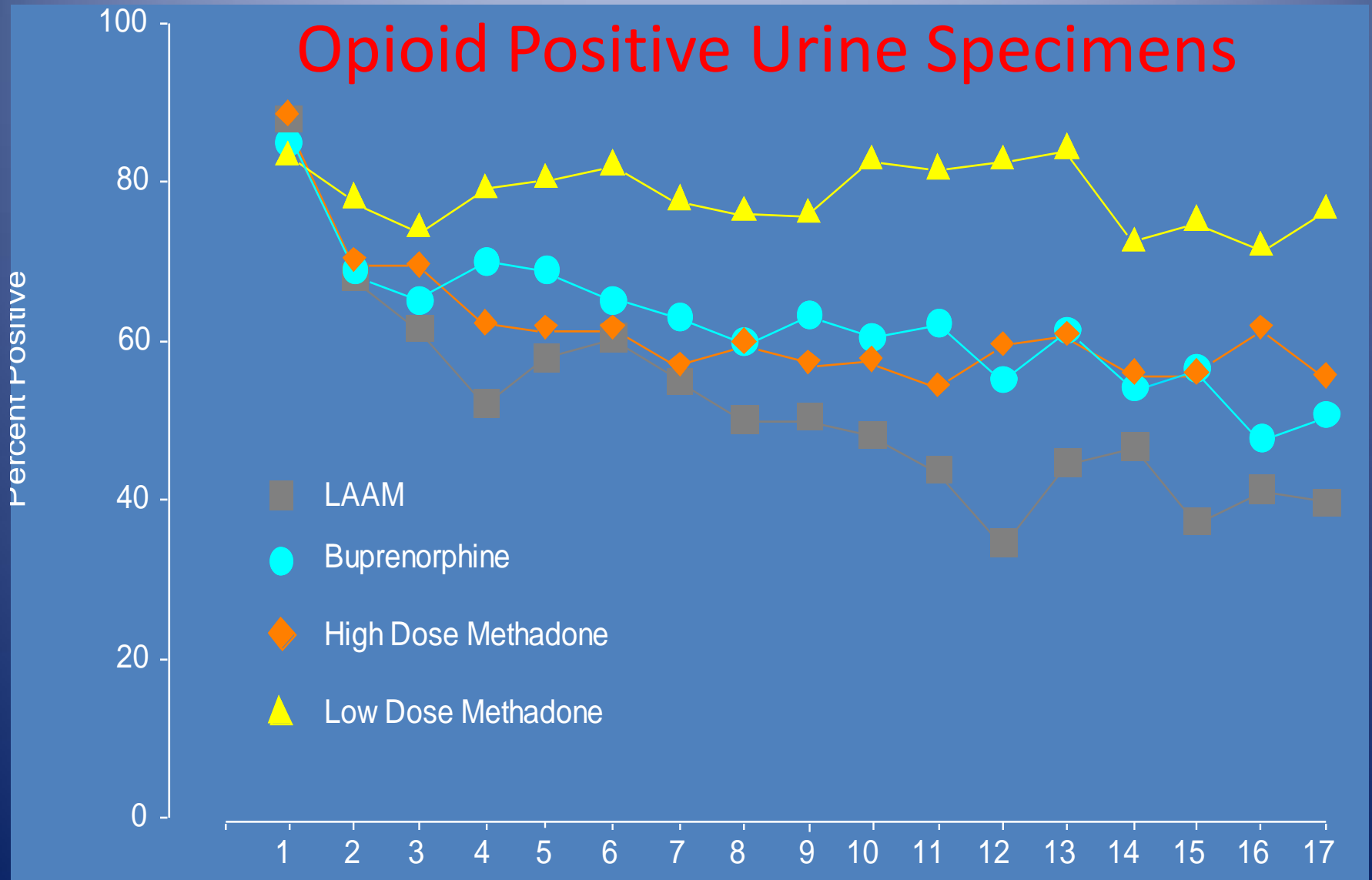
mu receptor site

Treatment Effectiveness

- Goal of treatment is to return to productive functioning
- Reduces drug use by 40-60%
- Drug treatment is as successful as treatment of diabetes, asthma, and hypertension
- Strongest predictor of recovery is retention in treatment

Effect of Medications on Opioid Use

Opioid Positive Urine Specimens



From: Johnson et al., 2000

Benefits Of Treatment

- Reduces risk of HIV infection
- Reduces risk of infection with hepatitis C and B
- Increases rates of employment among patients as a group
- Decreases crime
- Increases length of life



But.....

- Methadone and Suboxone can be abused
- People can overdose on methadone (not as easy on Suboxone)
- Lot of medication interactions with methadone
- Neither methadone nor Suboxone affect other drugs of abuse

Methadone and Other Substances

- Increases risk of acute opioid intoxication if mixed with alcohol
- Benzodiazepines potentiate sedative effects of opioids
- Overdoses have occurred in patients on buprenorphine and benzodiazepines
- Treatment may be needed for other substance use disorders but methadone should be continued with appropriate dose adjustment to minimize sedation while balancing risk of illicit opioid relapse

Side Effects of Methadone and Buprenorphine

- Sweating
- Respiratory depression
- Decreased libido and sexual dysfunction
- Sedation
- Constipation
- Insomnia
- Loss of appetite and dry mouth
- Heart arrhythmias (methadone at high doses)
- Headache (buprenorphine mostly)

How long is treatment needed?

- Individualized
- Less than 90 days in any treatment setting is of limited to no effectiveness
- Studies demonstrate that staying on medication in combination with counseling results in much better outcomes than detox

Treatment Outcomes for Detox

In methadone studies, 50-80% relapse within one year after detoxification

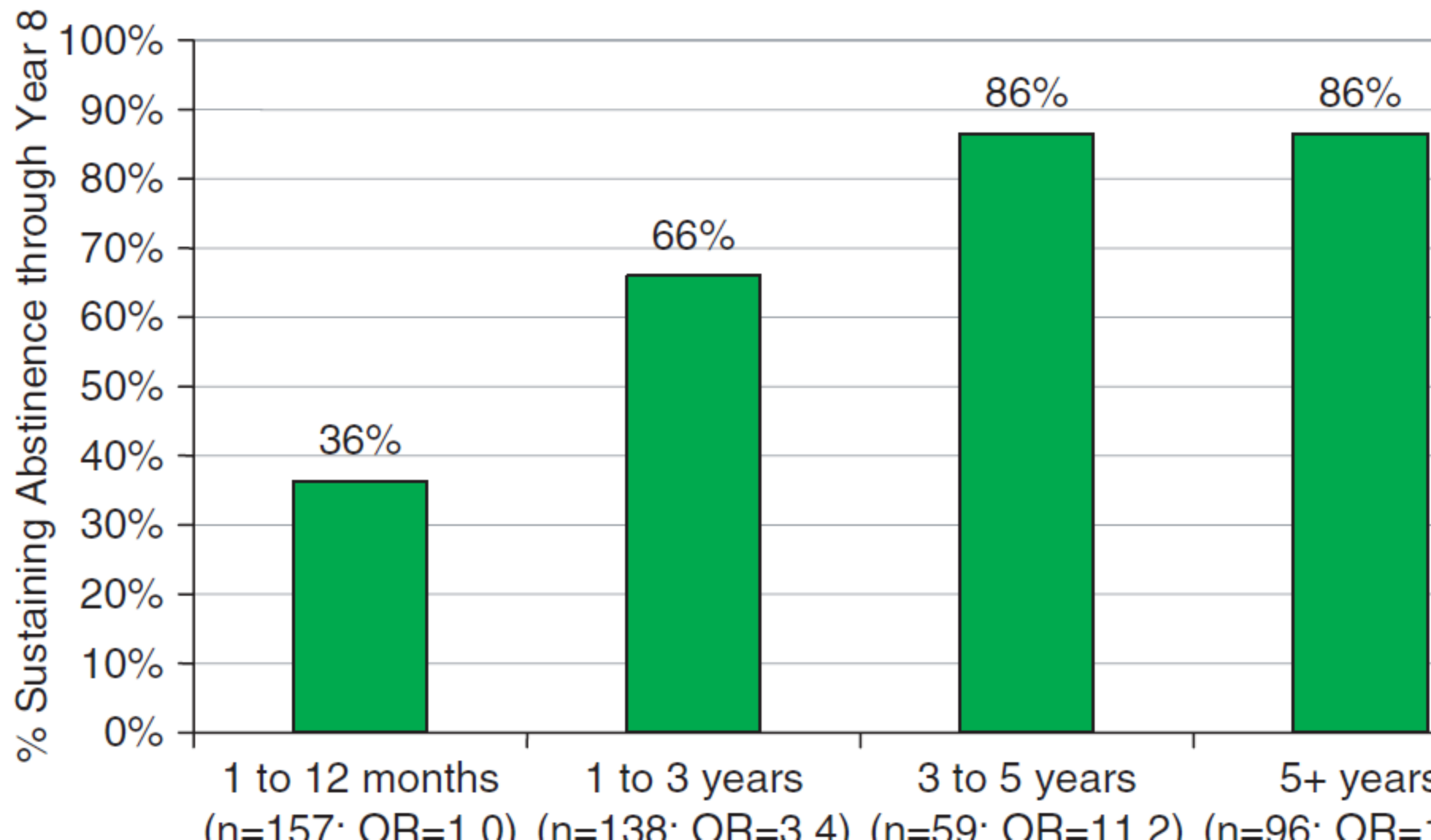
91% of patients receiving buprenorphine for 4 months had relapsed to prescription opioids within 2 months of taper*

*Weiss R. et al. NIDA CTN Prescription Opioid Treatment Study.
<http://www.medscape.com/viewarticle/722342>

Substituting one addiction for another?

- Suboxone treats withdrawal and physical dependence
- Medications and counseling treat opioid addiction
- On the right dose of medication, people function normally, are not getting high, and are not addicted

Figure 1
Percent Sustaining Abstinence Through Year 8
by Duration of Abstinence at Year 7



Components of Comprehensive Drug Addiction Treatment

