

Acute Pain

normal, predictable, protective, psychologic response

- An unpleasant sensory (biologic) and emotional (psychologic) experience associated with actual or potential <u>tissue damage</u>
- Usually easily localized
- "nociceptive"
- Somatic vs. Visceral
- Perception vs. Tolerance
 - Attitudes, beliefs, personalities, culture
 - Anxiety, depression, sleep deprivation, substance use disorder

Celsus De Medicina, 0 BC

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Inflammation

- Normal process to protect and promote healing
 - Vascular 5 cardinal signs of inflammation
 - Calor, Rubor, Tumor, Dolor, Functio Laesa
 - Vasodilation and increased vascular permeability

 Histamine, bradykinin, prostaglandins
 - Cellular diapedesis



- Pain without apparent biological value that has persisted beyond normal tissue healing time, usually 3 months.
 - Chronic back pain
 - Fibromyalgia
 - Headaches, migraines
 - Post-traumatic, post viral

Neuropathic pain

- Burning, freezing
- Lesion or disease of the nervous system
- Can be chronic (> 3 months duration)
- Central "sensitization"
- Usually responds to TCA's, anti-convulsants

Pain responses

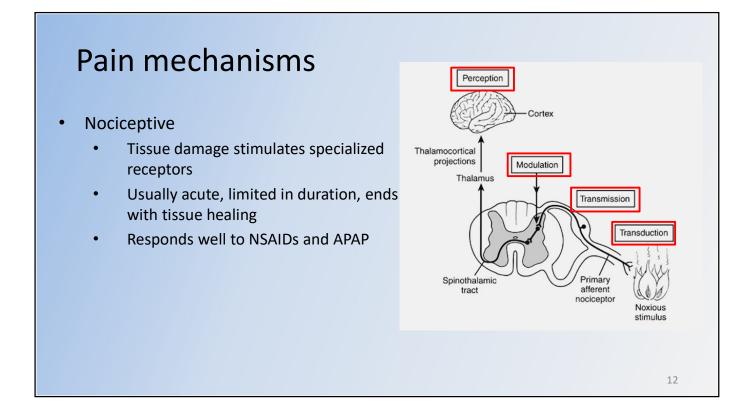
- Genetics
- Gender
- Culture
- Psychological factors
- Social factors
- Past experiences

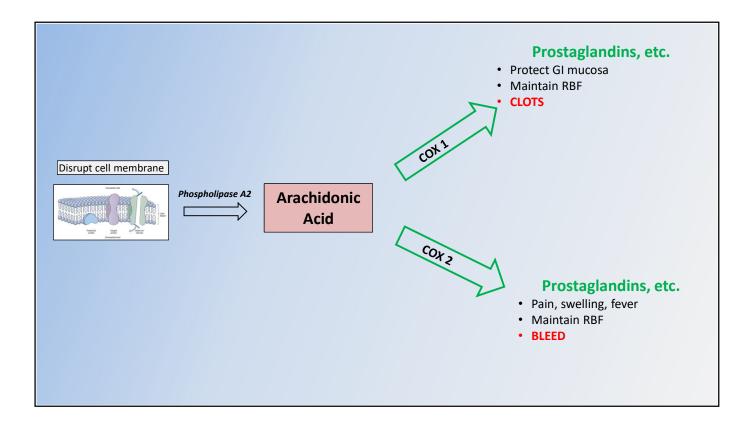
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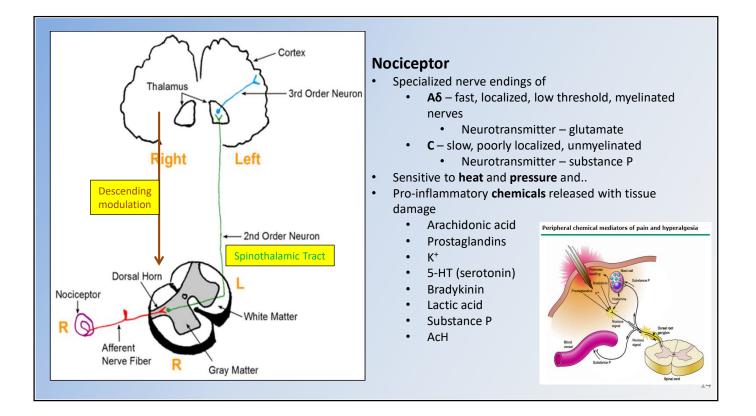
Pain Catastrophizing

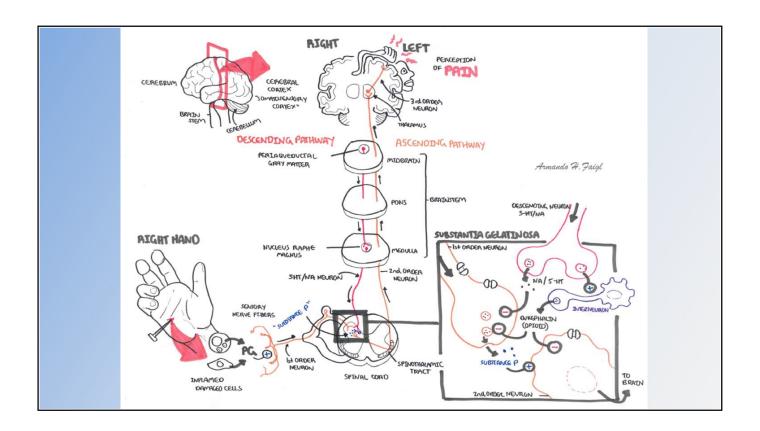
- A heightened emotional response to anticipated or actual pain
- "exaggerated" pain experience causes the patient to "feel" more pain
- Or.... Does more pain trigger a heightened response????

Quartana PJ, et. al. Pain catastrophizing: a critical review. Expert Rev Neurother 9:745-58, 2009.









Definition of terms analgesia – diminished pain sensation without LOC

- Preventive Analgesia (preferred term vs. pre-emptive)
 - Any anti-nociceptive regimen that will attenuate pain-induced sensitization
 - Before pain starts and continuous until pain stops (?)
 - Round the clock dosing
 - NSAID's inhibit PG formation, no effect on PG already there

Multimodal Analgesia – target different sites in pain pathway / synergy

- Reduce opioid requirements, better analgesia, less side effects
- Analgesics opioid, non-opioid
- Long acting local anesthesia
- Gabapentinoids
- Avoid inflammation cold packs, steroids, keep head elevated
- Careful manipulation / antibiotics when indicated

Non-Opioid Approach (multimodal) – different agents, different sites of action Opiods, α2 agonists TCAs, SSRIs NSAID's – ASA* • Acetaminophen Descending noradrenergic and serotoninergic inhibitory fibers Anticonvulsants spinothalm fibers Local anesthetics, Gabapentin* a2 agonists Opiods, ketamine gabapentinoids Local anesthetics, NSAIDs Pregabalin* • Ŷ Dorsal root ganglion Dorsal horn Anti-inflammatories ∜ Local anesthetics Nerve Temperature therapy Primary Steroids* afferen Long acting local anesthetics

Analgesic drug options for pain management

interrupt impulses / depress CNS interpretation

• Non-opioids

* pre-emptive

- interrupt prostaglandin synthesis by inhibiting COX
 - NSAIDs (reversible)
 - Acetaminophen (APAP)
 - Aspirin (ASA) (irreversible)
- enhance descending inhibitory neural traffic modulate ascending traffic
 - Gabapentinoids / Tricyclic anti-depressants / Tramadol

Opioids

activate specific receptors - Mu

Prostaglandins

- Inflammation, pain, fever (COX2)
- Protect stomach mucosa (COX1)
- Maintain kidney function (COX 1 / 2)
 Stop blooding (constriction, ophance B.) CO
- Stop bleeding (constriction, enhance P.) COX1
 Enhance blood flow (dilation, inhibit P.) COX2

Non-drug related options for pain management (post-op) "multi-modal"

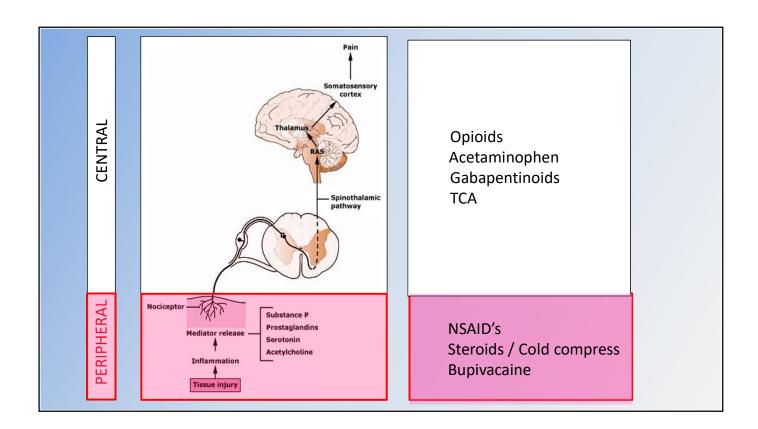
- Minimize inflammation
 - RICE rest, ice, compression, elevation
 - Steroids dexamethasone, methylprednisolone
 - Decadron[™], Medrol Dose-pak[™]
 - Avoid with active fungal or viral infection
 - GI upset, sleep disturbance, psychiatric challenge, diabetes
 - Careful surgical manipulation
- Adequate / long acting local anesthesia

Multi-modal Analgesia NNT

<u>N</u>umber <u>N</u>eeded to <u>Treat</u>

A measure of efficacy of a specific dose of an analgesic: the # of patients needed to get a 50% reduction in maximal pain for 4-6 hours.

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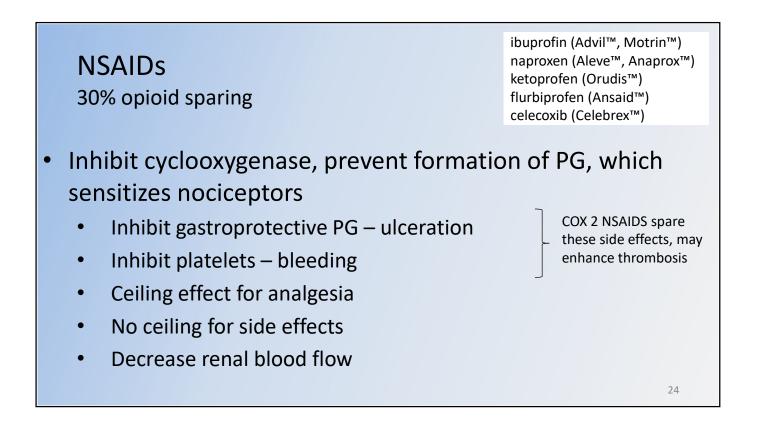


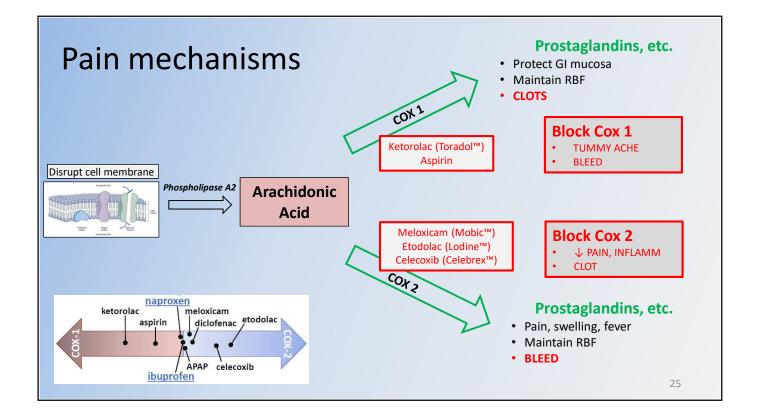
Acetaminophen (20% opioid sparing)

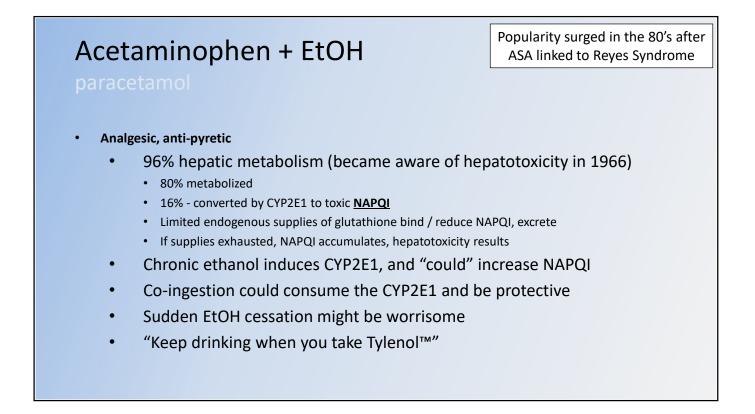
APAP = N-acetyl-para-aminophenol

- COX-3 inhibition central
- Analgesia, antipyretic
- No effect on inflammation
- Minimal GI irritation
- "safer" than ASA

	Ibuprofen	Acetaminophen
Analgesia	Peripheral PG blockade (inhibit Cox 1 Cox 2)	Central PG blockade (inhibit Cox 3)
Anti-pyretic	+++	++
Anti- inflammatory	++	-
Toxicity	Renal, HTN, clots (< 10 days duration)	Liver toxicity Large or prolonged dosing
Side Effects	GI upset, bleeding (?)	few







Non-opioids

summary

- NSAID should be first line Rx
 - Anti-inflammatory component : dose
 - Use before pain PREVENTIVE
- NSAID and acetaminophen are synergistic and should be used together
- Unlike opioids, there is a ceiling effect for analgesia
 - 400mg for ibuprofen
 - 1000mg for acetaminophen

Analgesic Use According to Acute Pain Level		
Mild	Ibuprofen 200-400mg prn q4-6°	
Mild to Moderate	Ibuprofen 400-600mg q6° x 4 fixed doses, Then Ibuprofen 400mg prn q4-6°	
Moderate to SevereIbuprofen 400-600mg PLUS acetaminophen 500mg q6° x 4 fixed dose Then Ibuprofen 400mg + acetaminophen 500mg prn q6°		
Severe	Ibuprofen 400-600mg PLUS acetaminophen 650mg with hydrocodone q6° x 4-8 fixed doses, Then Ibuprofen 400-600mg + acetaminophen 500mg prn q6°	
Moore, PA, Hersh, EV. Combining ibuprofen and acetaminophen for acute pain management after third- molar extractions: translating clinical research to dental practice. J AM Dent Assoc 144:898-908, 2013.		

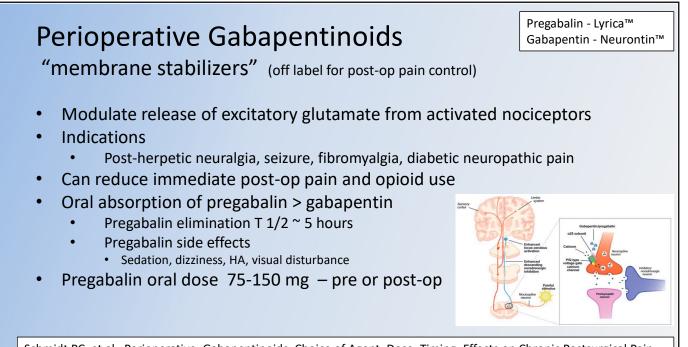
Contraindications - review

absolute / relative

Acetaminophen

- Allergy / intolerance / lack of efficacy
- LIVER DISEASE
- **Ibuprofen**
 - Allergy / intolerance / lack of efficacy
 - PEPTIC ULCER DISEASE or RENAL DISEASE
 - Coagulopathy disease or medications
 - Relative contraindications (if Rx > 5 days)
 - Patients taking sulfonylureas for type II DM glipizide, glyburide
 - Poorly controlled HTN
 - Prolonged use can interfere with anti-hypertensive medication (except CCB)
 - Cardiovascular disease
 - Lithium, high dose methotrexate
 - Pregnancy

Clinically Significant Drug Interactions with NSAIDs			
Diuretics, anti-HTN	Antagonized by NSAID	\uparrow Na ⁺ , H ₂ O retention with increased BP	
Alcohol	Enhanced by NSAID	个 GI irritation	
Warfarin	Enhanced by NSAID	个 bleeding risk	
Anti-platelet drugs	Enhanced by NSAID	\uparrow bleeding risk, competes with ASA, \uparrow clot risk	
DAOC	Enhanced by NSAID	个 bleeding risk	
K ⁺ sparing diuretics, K ⁺ suppl. Triamterene, Spironolactone, Amiloride	Enhanced by NSAID	Possible hyperkalemia	
Chemotherapeutic Agents	Enhanced by NSAID	个 risk of GI ulceration	
SSRI's Fluoxetine, sertraline, paroxetine	Enhanced by NSAID	\uparrow risk of GI ulceration and bleeding	
Corticosteroids	Enhanced by NSAID	个 Na ⁺ , H ₂ O retention with 个 BP, 个 risk of GI ulceration	



Schmidt PC, et al. Perioperative Gabapentinoids. Choice of Agent, Dose, Timing, Effects on Chronic Postsurgical Pain. Anesthesiol 119: 1215-21, 2013.

Steroids

- Anti-inflammatory and immunosuppressive
- Decrease nociceptive input
- Single dose does not increase wound infection

Narcotics:

- Opioids all drugs that act at mu receptor
 - Partially derived from poppy
 - Synthetic in the lab
 - Codones, morphones, fentanyls

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- There is no ceiling effect
- Opiate natural <u>derivative</u> of poppy
 - Morphine, heroin, codeine





Papaver somniferum

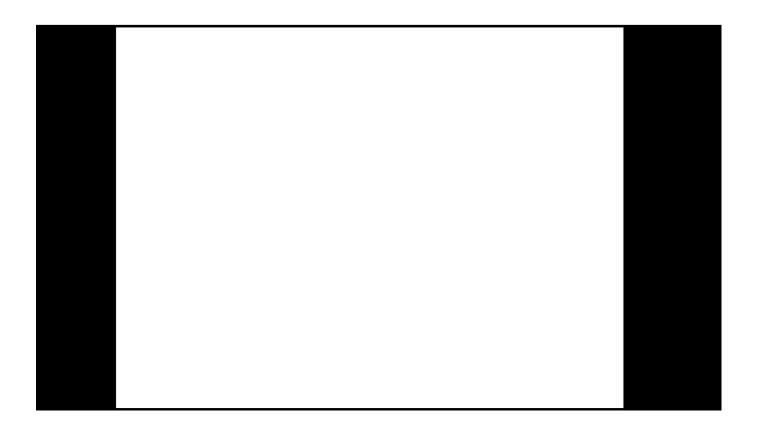


Opium

Heroin



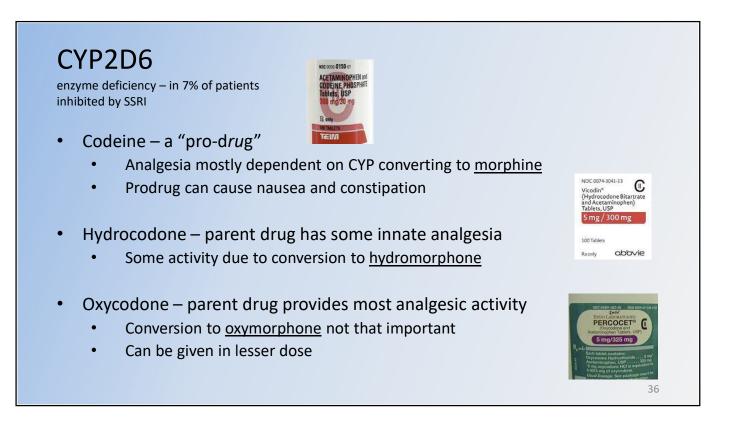
- Released during exercise, eating, socializing, panic, fight for flight
 - runner's high, frantic parent
- Attach to same receptors
 - Suppress pain / calm / slow breathing



Tylenol #3 = 300 mg acetaminophen
Codeine 30mg
NORCO – all tablets have 325mg acetaminophen
5, 7.5 OR 10mg hydrocodone
LORTAB – liquid
15ml = 7.5mg hydrocodone + 325mg acetaminophen
Tisml = 7.5mg hydrocodone + 325mg acetaminophen
5, 7.5 or 10mg hydrocodone

PERCOCET - 325mg acetaminophen

Oxycodone 5mg



Codeine > hydrocodone are pro-drugs

% of activity depends on conversion of parent drug to active drug by CYP2D6

CYP activity is variable –

- Increased CYP activity (1-7% of general population) TOO MUCH
 - Especially children AVOID CODEINE IF < 12 YEARS
 - Concomitant dexamethasone induces CYP2D6
- Decreased CYP activity NOT ENOUGH
 - 10%+ of general population cannot convert
 - Concomitant SSRI's
 - Prozac[™] (fluoxetine)
 - Paxil[™] (paroxetine)
- Codeine (converts to morphine)
- Tramadol = Ultram[™] (converts to M1 opioid metabolite)
- Hydrocodone Vicodin[™], Norco[™] (converts to hydromorphone)
- Oxycodone = OxyContin[™], Percodan[™] (converts to oxymorphone)
- Hydromorphone = Dilaudid[™]
- Morphine

Tramadol

- Tramadol also a pro-drug requiring CYP conversion
 - 50mg tablet ~ 60mg codeine
 - Norepi and serotonin reuptake inhibitor
 - Like TCA's interrupts nociceptive impulses
 - Mood elevation
 - Centrally acting analgesic, used for chronic pain
 - Tremors / Seizures at high doses

Tricyclic Antidepressants

Amitriptyline (Elavil™) Imipramine (Tofranil™) Doxepin (Sinequan™) Desipramine (Norpramin™)



Pediatric Analgesic Dosing			
	Dose	Maximum Dose	Not to <u>Exceed</u>
Acetaminophen	10 – 15mg/kg q4-6h	5 doses / 24 hours Or 75mg/kg/day	4,000mg
Ibuprofen	4 – 10 mg/kg q6-8h	40mg/kg/day	3,200mg
Hydrocodone Always with APAP 5/325			
Lortab Elixir 7.5/500mg/15 ml	0.25ml/kg q4-6h	6 doses / day	
Oxycodone	0.1 – 0.2mg/kg q4-6h		

Oral Drug	Dose (mg)	Half-life (h)	Onset (h)	Analgesic action (h)	Peak Duration (h)
Codeine ¹	15-60	4	0.25-1	0.5-2	3-4
Hydromorphone	1-4	2-3	0.5-1	1	3-4
Hydrocodone	5-7.5	2-3	0.5	1.5	3-4
Oxycodone	5	3-5	0.5	1-2	4-6
Tramadol ²	50-100	5-6	0.5-1	1-2	4-6

	Federal Schedules of Opioid	Medications
	Codeine	
	<i>Hydrocodone</i> combos Vicoden™, Norco™, Lortab™, Vicoprofen™	Schedule II rules Require signed prescription
11	<i>Hydromorphone</i> - Dilaudid™	Must be filled in 30 days in Illinois (no federal law)
	Morphine - MSContin™	emergency situation ?
	<i>Oxycodone</i> combos OxyContin™, Percocet™, Percodan™ (+ASA)	 Schedule III rules Oral or fax Can be refilled only 5 times in 6
	Codeine Combos – Tylenol #3™	months
	Buprenorphine / naloxone: Suboxone [™] , Subutex [™]	
IV	Tramadol - Ultram™	
V	Codeine Cough Suppressant	
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Opioid Analgesics

therapeutic considerations

Hydromorphone	1.5mg
Oxycodone	4 mg
Hydrocodone	6 mg
Morphine	6 mg
Codeine	40 mg

- Equipotent doses are equi-analgesic
 - Successful pain control depends on dose, not drug
- Oral doses are attenuated by
 - Gastric degradation
 - First pass metabolism

Morphine equivalent doses

Hydromorphone	1.5mg
Oxycodone	4 mg
Hydrocodone	6 mg
Morphine	6 mg
Codeine	40 mg
Tramadol	60 mg

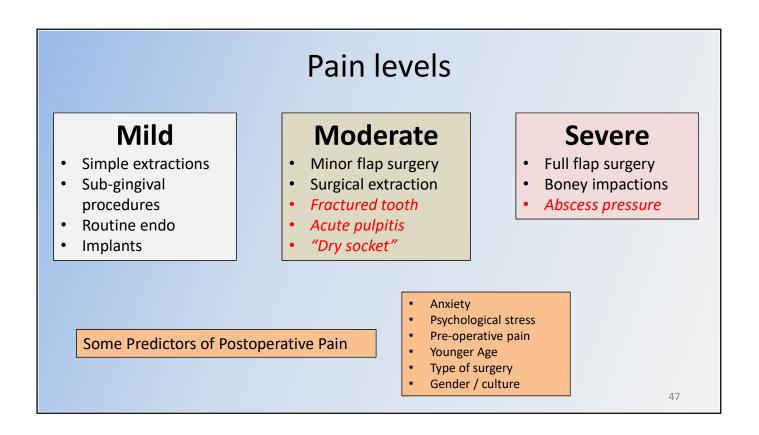
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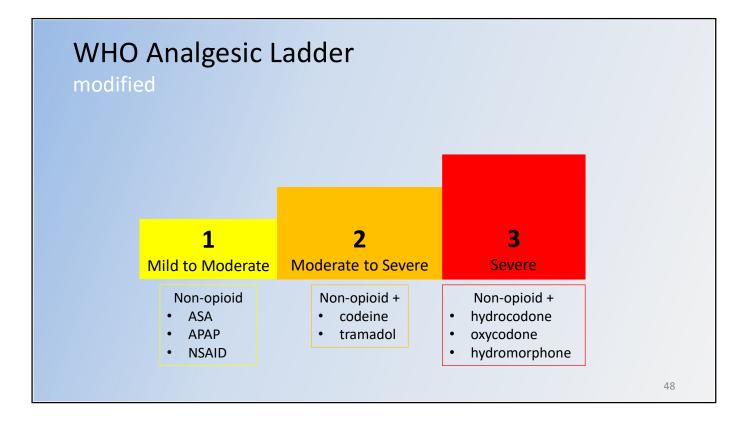
Are "weak" opioids safer? codeine, tramadol

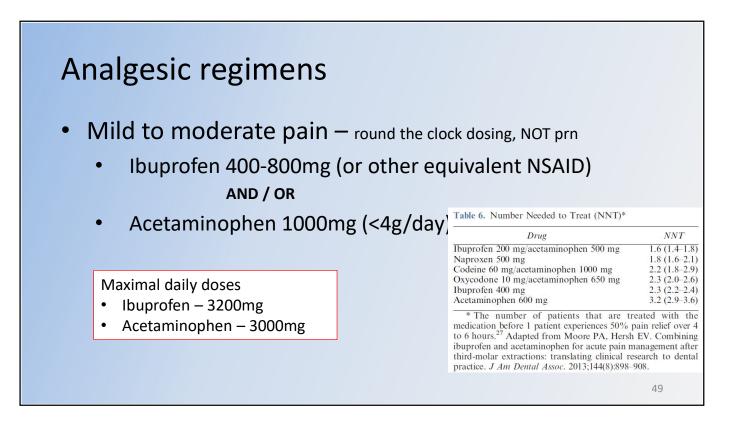
- Not necessarily
 - May not work
 - Can still be a substrate for addiction
 - Side effects present
 - Might trigger withdrawal with opioid dependence

Goals of perioperative pain management

- Relieve suffering
- Achieve early mobilization after surgery
- Achieve patient satisfaction







Analgesic regimens

- Add opioid COMBINATIONS for breakthrough pain
 - Hydrocodone 5 10mg
 - Norco[™] Lortab[™] Vicodin[™]
 - Oxycodone 5 10mg
 - Percocet[™] 5/325; 7.5/325; 10/325
- Tramadol 50-100mg

Opioid short term risks and adverse side effects

tolerance, dependence, hyperalgesia

Common

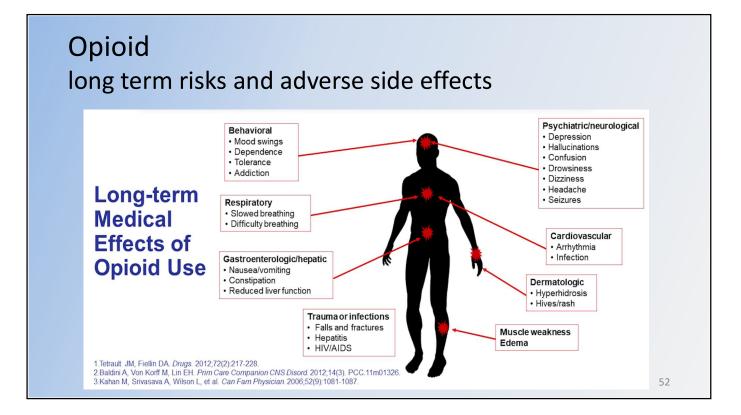
- N/V, sedation, constipation, urinary retention, sweating
- Pruritis (itching) histamine release
- Respiratory depression, loss of upper airway tone
- Rare
 - Allergy
- Serious
 - Overdose and death
 - When combined with other sedatives
 - Opioid use disorder

In elderly

- Drug-drug interaction
- Fall risk

Collateral risks

- Young children ingestion
- Adolescent experimentation



REMS

Risk Evaluation and Mitigation Strategy

- FDA drug safety program required for certain medication with serious safety concerns to help ensure benefits outweigh risks
- Reinforce medication use behaviors and actions that support the safe use of the medication

Opioid Analgesic REMS

- Drug makers must avail training to prescribers
- Boxed label warnings must appear
 - Overdose
 - Death
 - Neonatal opioid withdrawal
 - Drug interactions

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Types of REMS Requirements

REMS include a risk mitigation goal, and are comprised of information communicated to and/or required activities to be undertaken by one or more participants (e.g., health care providers, pharmacists, patients) who prescribe, dispense or take the medication. Together, the goal, communications and/or activities make up the safety strategy.

Each REMS is designed to help one or more of the key participants in a REMS address a specific safety concern. The most common role(s) of each of these key participants in a REMS are further described elsewhere. These roles may be similar across programs, but the specific requirements and risk messages of each REMS is tailored to each medication, the nature of its risks, and the likely setting in which the drug will be, or is being, used.

Original Contributions

Is it time US dentistry ended its opioid dependence?

Martin H. Thornhill, MBBS, BDS, PhD; Katie J. Suda, PharmD, MS; Michael J. Durkin, MD, MPH; Peter B. Lockhart, DDS

Thornhill MH, et. al. Is it time US dentistry ended its opioid dependence? JADA 150:883-889, 2019.

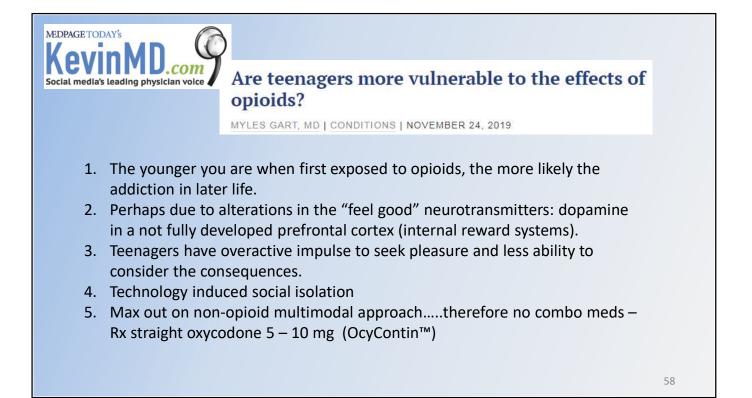


Would you give your child HEROIN to remove a wisdom tooth?

Ask Your Dentist How Prescription Drugs Can Lead to Heroin Abuse.



BEFORE THEY PRESCRIBE - YOU DECIDE. drugfreenj.org



Safe opioid prescribing

- Check IPMP
- Screen patients for opioid misuse risk
 - Current or hx of substance abuse disorders
 - Rx Opioid Misuse Risk factors
 - Personal or family hx of substance use disorder
 - Age between 16 45 years
 - Legal hx (DUI, incarceration)
 - Caucasian
 - Mental health challenges
- Do not mix with other sedatives, EtOH
- Minimize risk of diversion by educating patients about
 - Safe storage "locked box"
 - Proper disposal of unused medication

Ibuprofen – < 3,200mg/day Oral and maxillofacial surgeons: The experts in face, mouth and White Paper Acetaminophen - < 3,000 mg/day AAA an Association of Oral and Maxillofacial Surg No codeine to patients < 12 years Opioid Prescribing: Acute and Postoperative Pain Management Document everything Responsible Prescribing, uphold Dr-patient relationship Educate your patients Pre-op NSAID, steroid Long acting local • Avoid extended release opioids NSAID / acetaminophen – paired or sequential, round the clock • Short acting, lowest effective opioid dose for shortest duration for breakthrough pain Access PDMP – state Prescription Drug Monitoring Program Document need, safe storage and disposal

Pain control agreement

- Before treatment
- <u>Goal is to reduce, not eliminate pain</u>
- Alternatives to opioids what the studies show
- Discuss risks vs. benefits
 - Abuse, addiction, diversion, overdose
 - Hyperalgesia, sexual dysfunction
- How to take opioids
- Expectations from Rx
- 1 prescriber, 1 pharmacy
- Safe storage and disposal

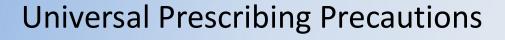
Is refilling an opioid prescription without seeing the patient legal?

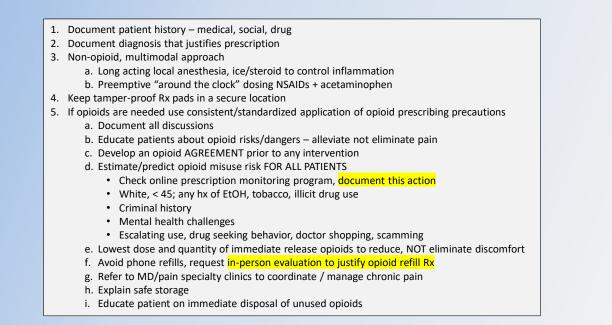
- "a prescription for a controlled substance must be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his/her professional practice."
- "the responsibility for the proper prescribing and dispensing of controlled substances rests on the prescribing practitioner, but a corresponding responsibility rests with the pharmacist who fills the prescription"

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Is refilling an opioid prescription without seeing the patient legal?

- Common themes
 - A valid provider-patient relationship must exist
 - The prescription must be issued for a valid medical purpose
 - The prescription must be therapeutic for the patient's condition



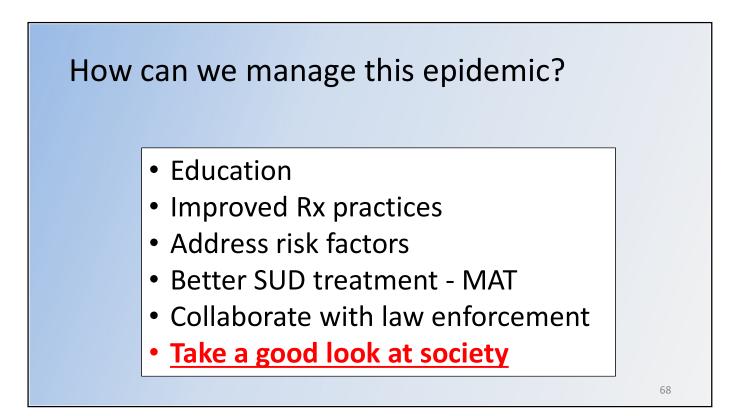


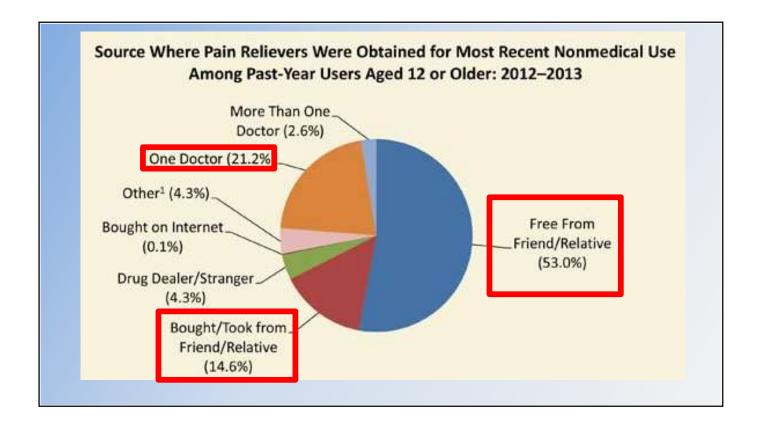
Summary

- Patients deserve pain relief
- Recognize that opioids have limited efficacy when used alone
- Prior to prescribing opioids, assess patients for opioid misuse risk
- Use universal precautions but individualize pain management based on risk
- Prescribe opioid in limited amounts with clear directions
- Educate patients on safe storage and disposal
- Use risk-benefit framework to guide clinical judgement.

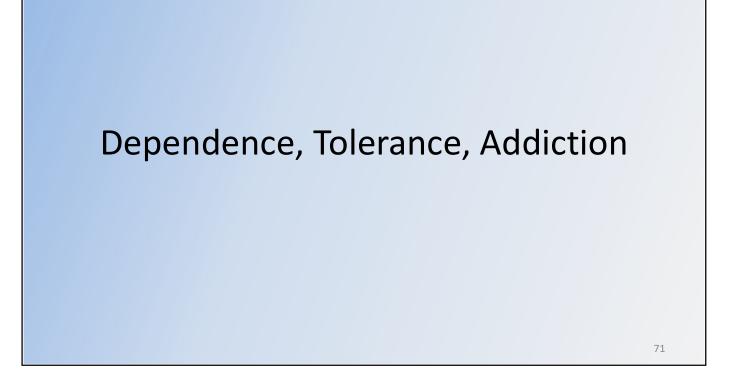








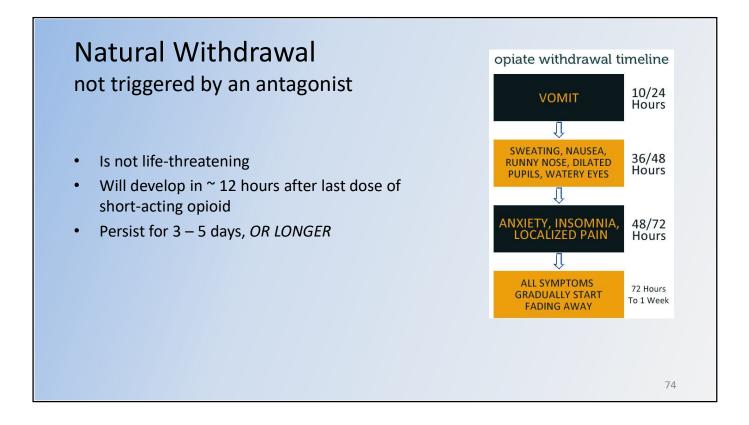
Opioid epidemic burden		
 Diversion, dependence, addiction Progression to heroin Overdose (death) Neonatal addiction / withdrawal Infection HIV; Hep B, C; staph Lost work, social failure 	 Health insurance expenditures ER visits Treatment of addiction Autopsies Treatment of related disease Payment for fraudulent / unnecessary Rx Loss of productivity in the work force Police / EMS 	
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Dependence, Tolerance, Addiction

- Physical dependence
 - A state of adaptation such that abrupt substance cessation triggers a withdrawal syndrome, generally reactions opposite to those produced by the drug. Can occur in 7 days of active intake. Abrupt cessation is more symptomatic than gradual tapering.

Mild	<u>Moderate</u>	<u>Severe</u>
Anxiety	Irritability / Agitation	Delirium, Violence
Nausea	Vomiting / cramping	Diarrhea / Incontinence
Wet runny eyes and nose sneezing, sweating		
Tremors	Muscle Cramping	Muscle Spasm
Loss of appetite		Dehydration
Piloerection	Hot and cold flashes	
Yawning	Hypertension / Tachycardia / Tachypnea	



IDEAS | ESSAY

The Perilous Blessing of Opioids

An injured bioethicist learned firsthand how desperately patients with severe pain need the relief of powerful drugs—and how little support they get to stop taking them.



Dependence, Tolerance, Addiction

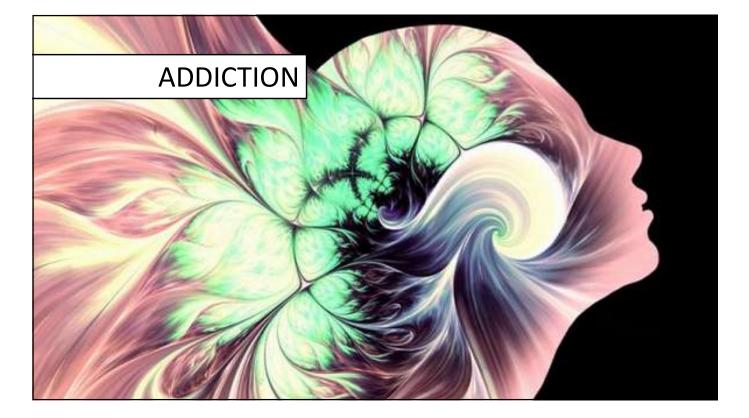
- Tolerance
 - Increasing amount of substance needed to achieve desired effect, attained by smaller doses in the past.
 - Occurs with analgesia, sedation and respiratory depression, <u>but not</u> <u>constipation or miosis</u>.
 - Gradually diminishes over time during abstinence



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Physical dependence ≠ addiction

- Tolerance and physical dependence are inevitable consequences of chronic opioid exposure
- Addiction is NOT an innate pharmacologic property of opioids.



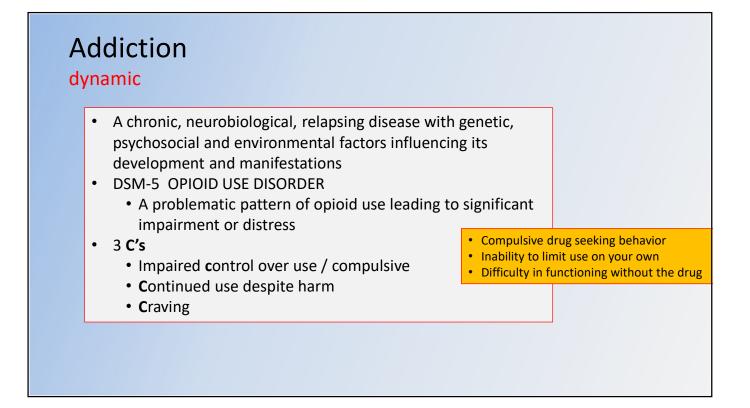


- 1. Characterize
- 2. Define
- 3. Manage

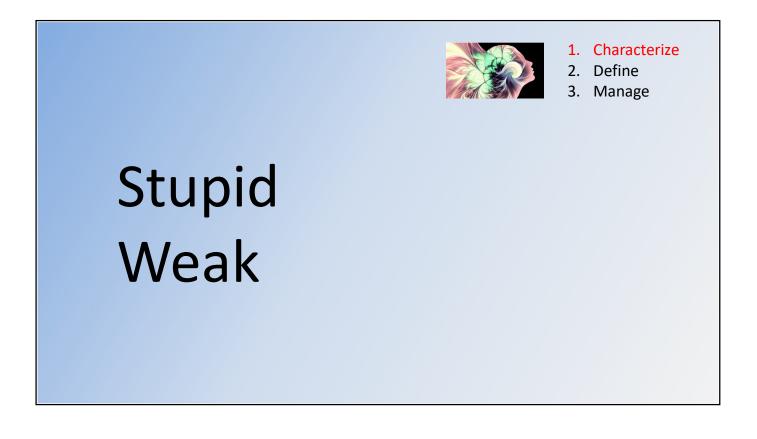
A dynamic, chronic, neurobiologic, relapsing disease with genetic, psychosocial and environmental factors influencing its development and manifestation.

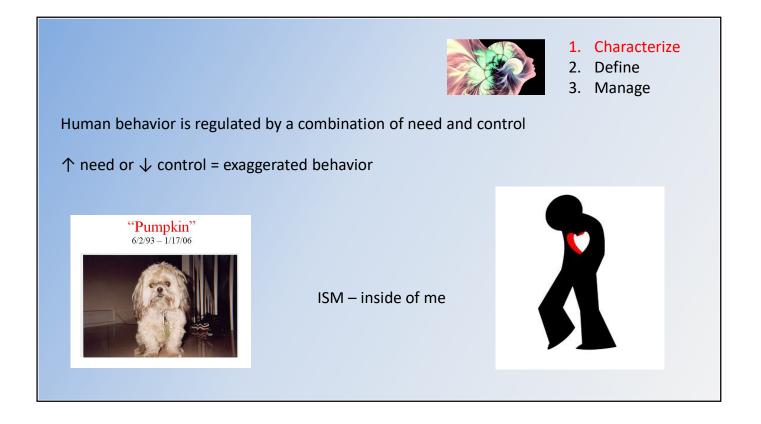
In SOME patients, a pathologic hijacking of the reward-related learning and memory areas of the brain

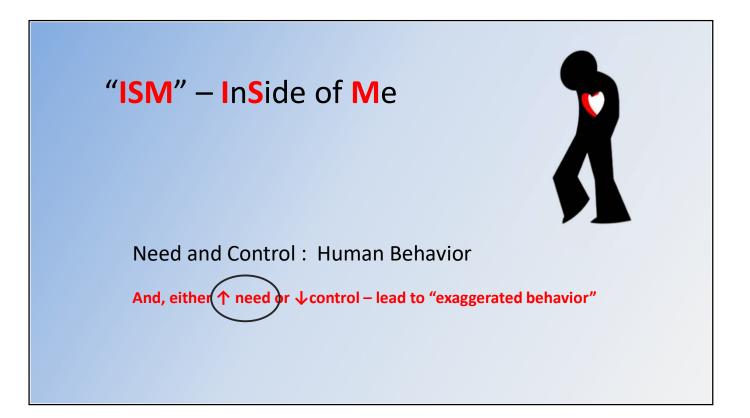
DSM -5 – OUD – a problematic pattern of opioid use leading to significant impairment or distress.



1. Characterize 2. Define 3. Manages 4. Why are addicts filled with shame / guilt 4. Why are family members filled with shame / blame / disappointment 5. Why did Nancy Reagan say – "Just Say No" 4. Why do we put addicts in JAIL 5. Why the STIGMA * "you did this to yourself, you miserable person" "you are now officially ostracized" * Disacterized * Disacterized<









"The first time I ever used an opioid, I felt the most confident and powerful I'd ever felt"......"So I said, this is it. I want to do this for the rest of my life"

"I didn't need 20 Vicoden when I got my wisdom teeth out," he says. "So I just saved them."

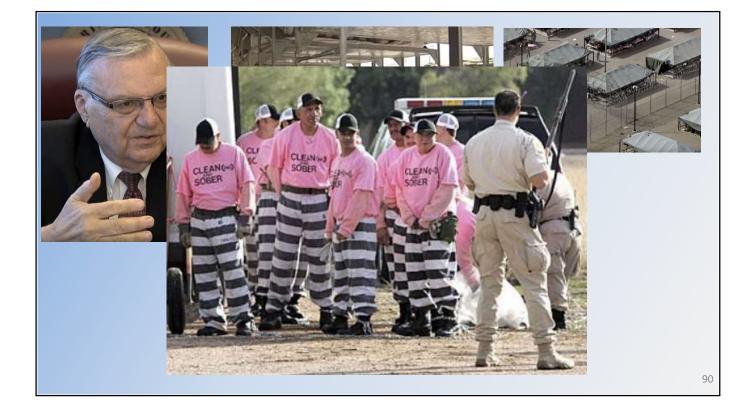
"The notion that people become addicted to drugs because they initially chose to take these drugs for pleasure is a belief that stems from a different time, in which we believed addiction to be a moral issue rather than a medical one."

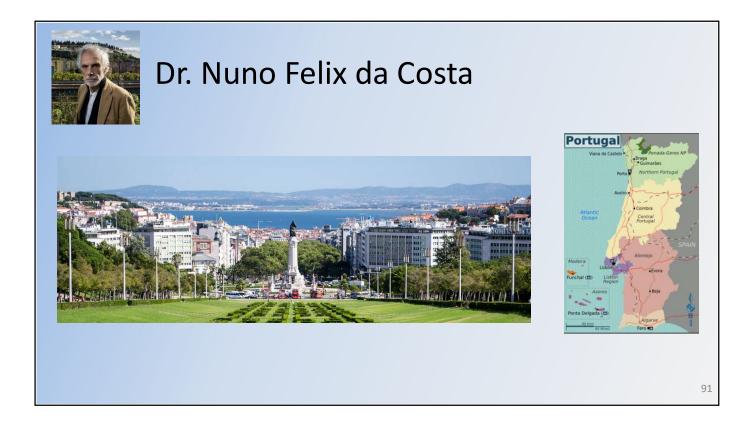


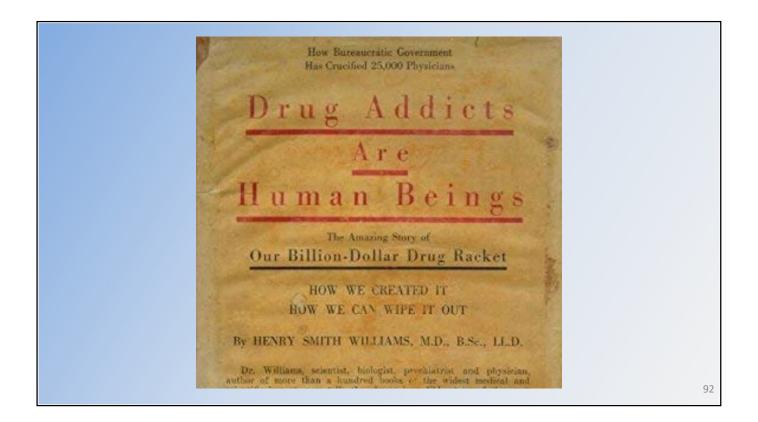


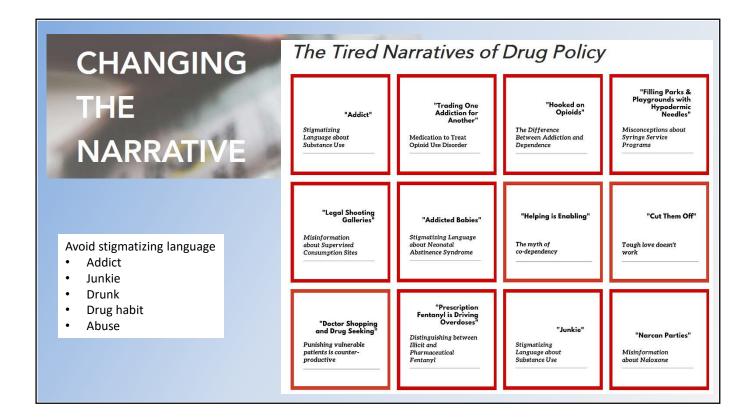
- McGill University Study in the 50's
- Alcohol does something FOR the addict
 - It fills a void,
 - They feel better, but they do not get better
- Alcohol does something TO the non-addicted
 - They drink to get high, loosen inhibitions

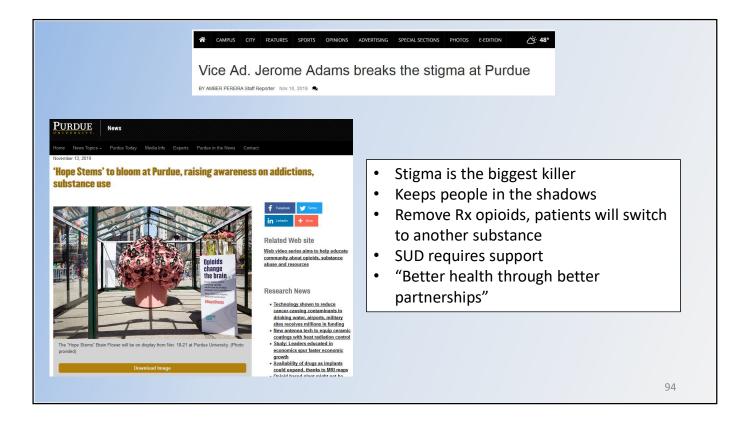




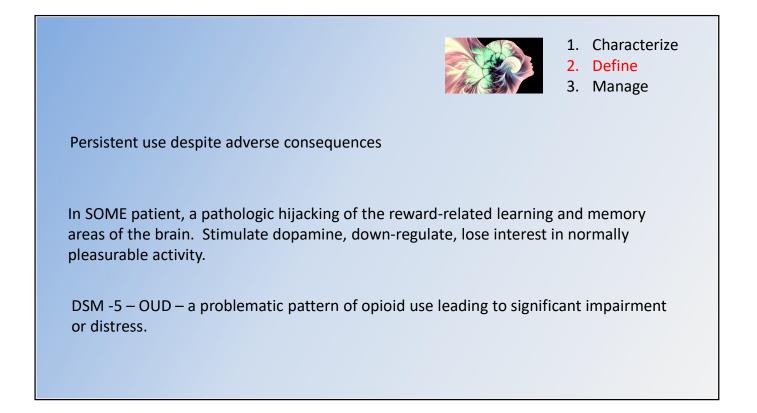




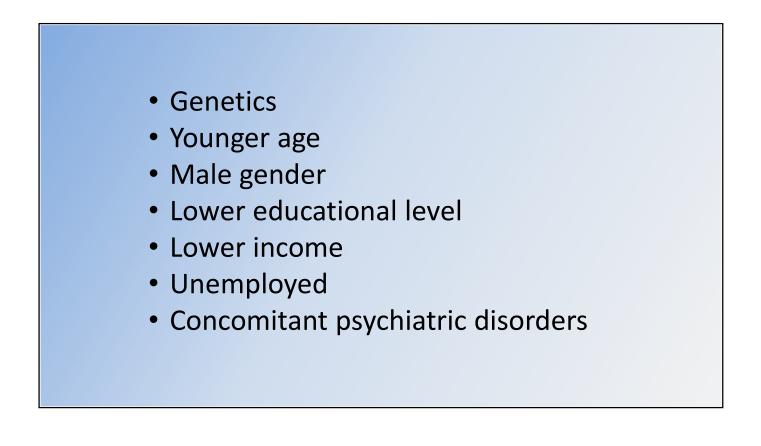












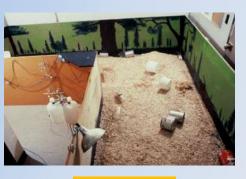






www.brucekalexander.com





"Rat Park"



Professor Peter Cohen

www.cedro-uva.org/cohen/



THE OPPOSITE OF ADDICTON IS CONNECTION.

Loneliness Is the Quiet Health Epidemic Impacting Your Heart, Brain, and Longevity

Here's what to know to protect ourselves, and one another

By Jannifer Wolff Nov 25, 2019

Lacking a social connection is considered more dangerous than smoking 15 cigarettes a day.

Being socially isolated, by contrast, hurts emotionally and psychologically, and its stresses take a physical toll. Persistent loneliness (lasting longer than two weeks) is linked to high blood pressure, depression, heart disease, and stroke among other conditions, including Alzheimer's disease. This appears to be due to increased inflammation; in excess, inflammation is associated with chronic disease.





Substance abuse disorder

A cluster of cognitive, behavioral and physiological symptoms indicating that the individual continues to use the substance despite significant substancerelated problems.

There exists an underlying change in brain circuits co-existent and possibly contributory to repeated relapse and/or craving.

- 1. Impaired control over substance use
- 2. Compulsive _____-seeking behavior
- 3. Inability to stop on your own
- 4. Social impairment difficulty in functioning without
- 5. Continued use despite harm

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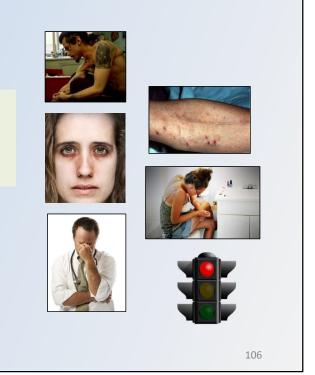
SUD, addiction, in general pandemic? Undetected?

All socio-economic strata, age, race

- ER physicians, dental sedation providers, anesthesiologists, psychiatrists
- DENIAL is UNIVERSAL

Concomitant

- Psychiatric disorders
- Infectious disease
- Criminal behavior



SUD, addiction, in general

- Prevalent, epidemic ? , but largely undetected
 - All socioeconomic strata, age, race
 - ER physicians, anesthesiologists, psychiatrists,
 - Denial is UNIVERSAL
 - Stigma, shame, failure of will
 - Concomitant
 - psychiatric disorders
 - infectious disease
 - criminal behavior

4 common characteristics of patients with drug use disorders

- Escalating use
- Drug-seeking behavior
- Doctor shopping
 - a routine of visiting several doctors complaining of similar symptoms in order to receive multiple prescriptions for the same condition
- Scamming
 - coercion or manipulation of the doctor in order to obtain medication.
 - Patient pressures dentist to Rx EVEN AFTER REQUEST DENIED, esp. when specific drug names is requested.

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Opioid use disorder

 Signs and symptoms that reflect compulsive, prolonged self-administration of opioid substances that are used for no legitimate medical purpose, or in doses greatly in excess of the amount needed for a medical condition.

	DSM-5 Criteria for Opioid Use Disorder
Check all that apply	Criteria (within a 12-month period)
	Opioids are often taken in larger amounts or over a longer period than was intended
	There is a persistent desire or unsuccessful efforts to cut down or control opioid use
	A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects
	Craving, or a strong desire or urge to use opioids.
	Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home
	Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids
	Important social, occupational, or recreational activities are given up or reduced because of opioid use
	Recurrent opioid use in situations in which it is physically hazardous
	Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance
	Exhibits tolerance*
	Exhibits withdrawal*
Total checked: f OUD is diagnosed	≥ 2 criteria met), assess severity as mild (2-3 criteria met), moderate (4-5 criteria met) or severe (≥ 6 criteria met).

Treatment options for opioid use disorder

to reduce HIV, death, etc.

- Long term out patient treatment
 - Medication-assisted treatment
 - Usually includes psychosocial intervention
 - Opioid agonists methadone, buprenorphine
 - Opioid antagonists naltrexone
- Inpatient/residential care
 - Supervised detoxification
- Psychosocial intervention (non-medication treatment)

Treatment options: Opioid Use Disorder

Psychosocial Treatment (no meds)

- Abstinence-based therapy dismal long term results
- Urine testing; incentives, group dynamics
- ↓treatment----个relapse

Maintenance medication: opioid agonists

- Methadone; buprenorphine
- "medication-assisted treatment"

Opioid antagonist treatment

Naltrexone

Treatment of opioid use disorder

Psychosocial Intervention

- "Contingency Management" 12 weeks
 - Behavioral intervention incentivize target behavior
 - Abstinence / reduction in drug use
 - Medication compliance
 - Treatment attendance
- Motivational Interviewing
 - Explore and resolve ambivalence to behavior change
 - Rapport / collaboration to effect change
- Cognitive-Behavioral Therapy
- Family Therapy
- 12 step facilitation
- Addiction counseling
- Mutual help groups

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Treatment of opioid use disorder

Maintenance medication

- <u>Agonists</u> -- "medication-assisted treatment"
 - <u>Methadone</u> SLOW, full μ opioid receptor agonist , NMDA antagonist
 - 80-160mg
 - Don't need or want other opioids, no euphoria, no withdrawal
 - Physiologic dependence persists
 - Regain societal productivity, safely drive a car
 - Monitored administration of liquid methadone clinics
 - Buprenorphine Sticky, partial μ opioid receptor agonist (weak), κ opioid receptor antagonist
 - Blocks all other drugs
 - Ceiling respiratory depression
 - 8-24 mg, sublingual

Maintenance medication: opioid agonists

- Methadone; buprenorphine
- "medication-assisted treatment"

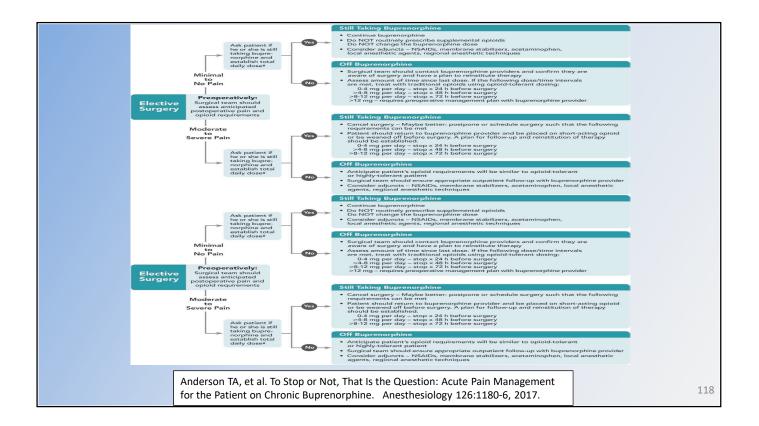
Methadone (analgesic effect)

- Don't need or want other opioids
- Full agonist, no "dopamine buzz"
- Prolonged onset, prolonged offset
- No craving, no withdrawal
- Physiologic dependence persists
- Can function in society
- MMT witnessed administration of liquid
- Prolonged QT interval with higher doses
- (300mg/day)
 - Elderly, ${\bf \downarrow}{\bf K}^{\scriptscriptstyle +},$ bradycardia, female, structural heart
- disease, arrhythmia
- Naloxone will reverse

Buprenorphine (little analgesia)

- Other opioids won't work
- High affinity for mu receptor
- Prevents other opioids/naloxone binding
- Partial (weak) agonist ceiling respiratory depression
- Overdose possible
- Less restriction on prescribing
- Suboxone[™] sublingual film (4:1 with naloxone)

Medications for OUD							
		Methadone	Buprenorphine	Naltrexone			
	Trade Name	Dolophine; Methodose	Subutex; Suboxone	Depade; Revia; Vivitrol			
	Class	Full agonist	Partial agonist	Antagonist			
	Use and Effects	Once daily, monitored P.O. liquid administration. Reduce craving and withdrawal, facilitate ADL.	Once daily, film tab, reduce craving and withdrawal, block effect of other opioids	P.O.; IM q 1 month, blocks mu receptor, diminish reinforcing effect of opioids			
	Advantage	Slow drug, careful and consistent dosing reduces euphoria	Greater availability, less risk of IV use with Suboxone	Not addictive or sedative			
	Disadvantage	"approved clinic", daily visits	Measurable abuse liability	Must achieve complete abstinence prior to use, patient compliance issues			



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Buprenorphine

- Subutex[™] = buprenorphine
- Suboxone[™] = buprenorphine + naloxone
- Sublocade[™]
 - Buprenorphine extended release injection SC
 - 100-300mg
 - Once a month dosing
- Probuphine implants 6 months

Buprenorphine Prescribing Restrictions have been relaxed.... Telehealth allowed no need for 8 hour federal education requirement

- New Rx have remained flat from 2019 to 2022
- Only 20% of patients managed with bup have stayed on it for > 6 months
- The new DEA 8 hour requirement may \downarrow the number of eligible prescribers
- 50% of patients presenting to ED with anaphylaxis get Rx for epi injection device
- 10% of patients presenting to ED with opioid overdose get Rx for buprenorphine

Chua, K., et. al. Trends in Buprenorphine Initiation and Retention in the United States, 2016-2022. JAMA 329:1402-1404, 2023.

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Treatment of opioid use disorder

- Maintenance medication
 - <u>Antagonists</u>
 - Need to withdraw first
 - Naltrexone
 - Blocks opioid receptors, nothing works
 - Prevents physiological dependence

Recovery – 3 choices

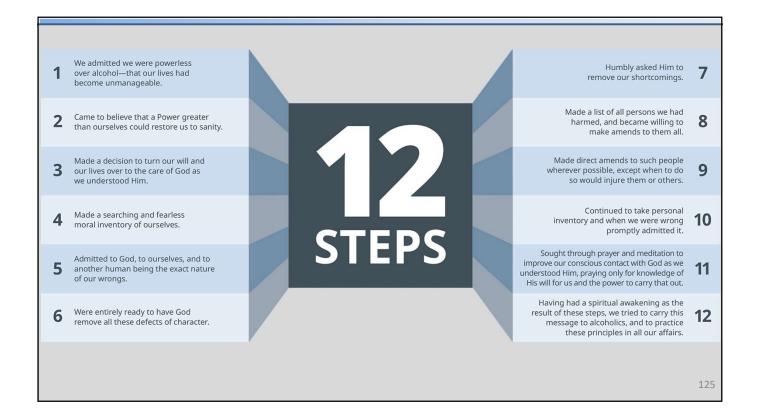
- Drunk
- Dry
- Spiritual Recovery
 - "get better, not feel better"

Recovery is not only possible, but it is assured if patients accept and apply themselves to the 12 step program.

Recovery requires a certain amount of character and pain

Willingness to take direction

Willingness because he(she) has suffered enough pain



12 step program.....

Turn over control to a "higher power"



The Human Brain Evolved to Believe in Gods

- 84% of world population
- Believe in higher power, spiritual force
- God (with a capital G)
- 20% of "atheists" accept higher power or spiritual forces

12 step program..... 9 Turn over control to a "higher power" 9 Admit to ourselves and others the exact nature of our wrongs 9 List people we have harmed and make amends 9 "spiritual awakening" 9 Etc....

12 step program.....

1. Admit you are powerless over the substance and that your lives have become unmanageable.



How to address a patient with suspected drug abuse disorder

- Non-judgmental
- Avoid confrontation
- Express empathy

Can you reliably identify patients with OUD?

- Regularly taking opioids more than prescribed doses for non-prescribed reasons, such as to improve mood or play better golf
- Taking opioids for fear of withdrawal
- Either high, craving or withdrawing
- Mood swings: agitated, skittish, exciting, euphoric
- Seeking opioids from multiple doctors
- Request a specific drug
- Losing interested / disengaging people, activities
- Engaging in high risk behaviors
- Generally, not interested in finding the "root of the problem"
- Doctor shopping
- Missed appointments
- Using more than 20 MME / day

- Unusual behavior in the waiting room
- Assertive personality, demanding immediate action
- Must be seen immediately
- Wants appointment at the end of the day
- Calls after regular business hours
- Claims non-opioids are not working
- Rx is lost
- Unusual appearance slovenliness or overdressed
- Fully clothed on hot weather, arms covered
- Pop-scars from subQ injections
- Needle tracts linear, hyper pigmented marks
- Raccoon eyes, yawning, fidgety withdrawal signs
- Unusual knowledge of controlled substances or disease entities, may exaggerate Sx
- No regular MD, no health insurance

How to address a patient with suspected drug abuse disorder

- Open ended questions
- 3 step interventional counseling
 - Feedback I am concerned about your Vicodin[™] use, may cause harm to body, work and social relationships
 - Advice try to cut dosage and use alternatives
 - Establish goals

Example		
"I understand that you are in pain and that this is causing you significant anxiety and distress."		
"What activities would you like to do that your pain is preventing you from doing?"		
"For some patients, continuous use of opioids can actually result in more pain by lowering the pain threshold.		
"A lower dose of opioids may make you less sedated and allow you to actually improve your ability to do the activities you want to do."		
"Would you be willing to try a lower dose of opioids or switch to a combination of nonopioid options?"		
"Would you be willing to meet every 2 weeks to discuss your progress?"		
Be calm, even-tempered, and nonjudgmental throughout the conversation		

Table 4. The "7 Es" to Remember When Engaging a Patient in

