Introduction to Addiction Psychiatry

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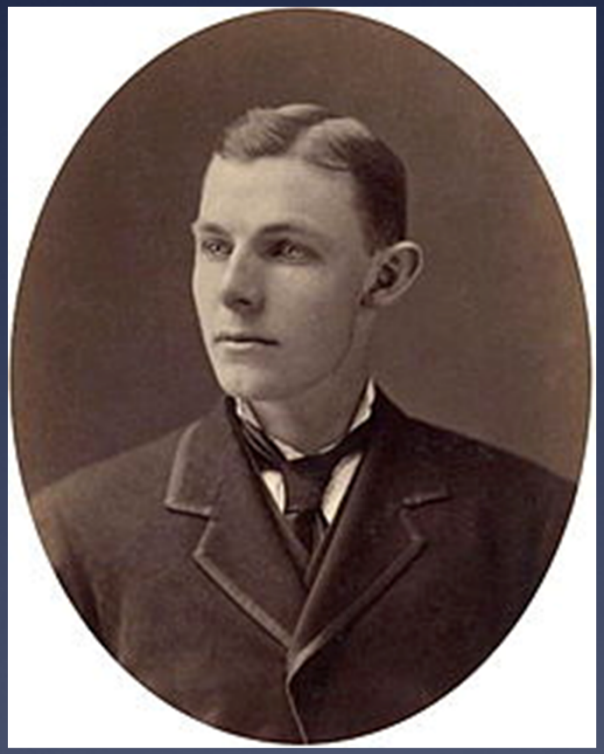
Disclosure

* I do not have any financial interest, relationships, or other potential conflicts, with respect to the material which will be covered in this presentation.

Who is this?



William Halsted, MD

* One of the founders of John Hopkins Hospital.
* A pioneering surgeon
* Developed aseptic techniques for surgical procedures.
* Struggled with severe addiction.

William Halsted, MD

Halsted the addict was a mess. He would disappear for long stretches (his summer vacations routinely lasted five months); no one knew quite where he went. His behavior was erratic; friendly to colleagues and patients one moment and hostile the next, he would bow out of operations at the last minute, and his residents pretty much ran his service without him. "The Professor" was often missing in action.

Addiction Definition

- A primary, chronic disease of brain reward, motivation, memory and related circuitry.
- Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations.
- This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

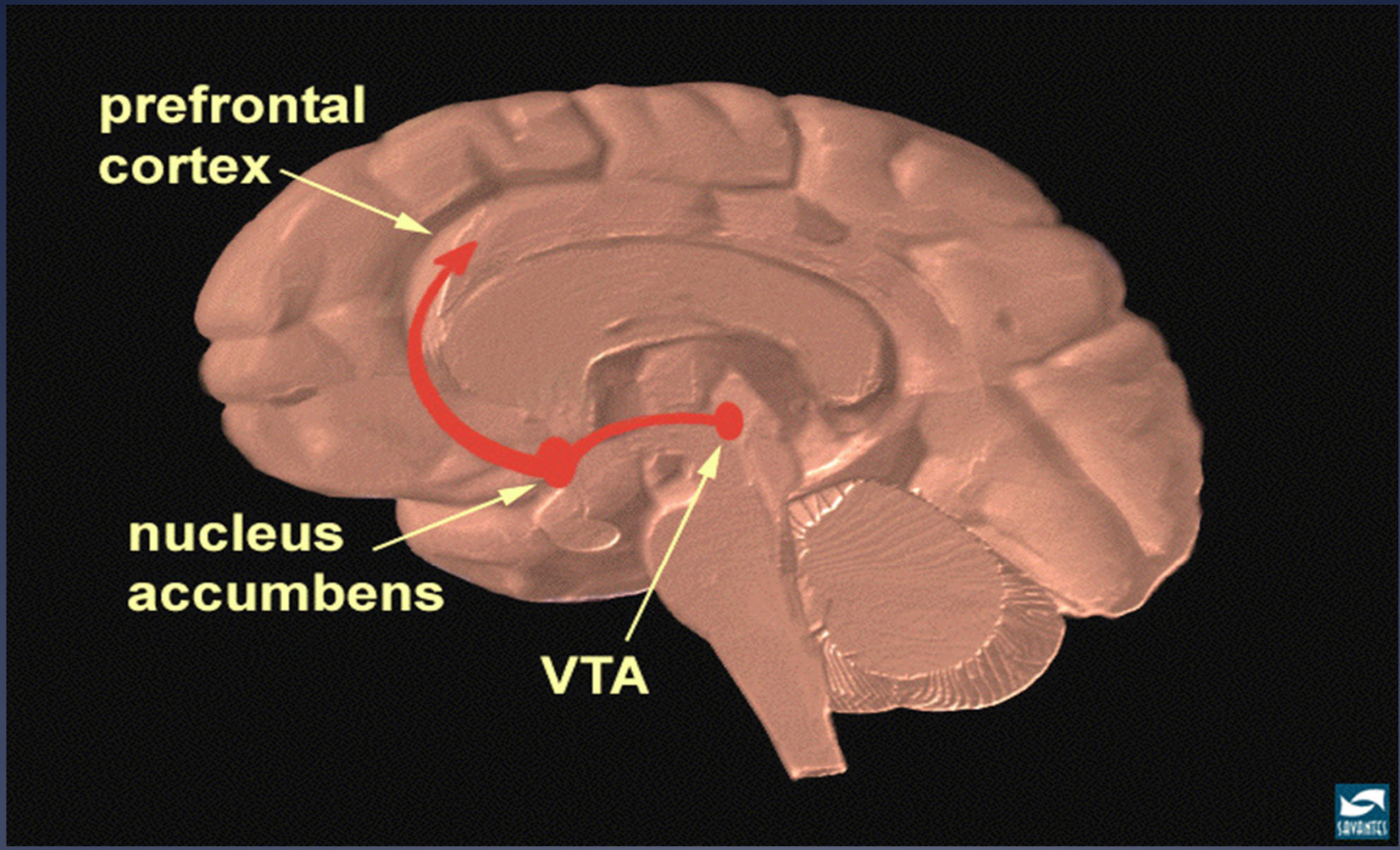
Addiction Definition (cont'd)

- Addiction is characterized by
  - inability to consistently abstain from drug use.
  - impairment in behavioral control.
  - craving.
  - diminished recognition of significant problems with one's behaviors and interpersonal relationships.
  - a dysfunctional emotional response.
- Like other chronic diseases, addiction often involves cycles of relapse and remission.
- Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.

Addiction Definition

- The 4 "C's"
  - Loss of **C**ontrol
  - **C**ompulsive use
  - Use despite **C**onsequences
  - **C**ravings

What Happening in the Brain?



Some clinical points

- Addiction is more than just the compulsive use of a drug.
- Addiction is a BEHAVIORAL SYNDROEM, which involves, personality changes, functional decline, and lapses in judgement, insight, and decision making.
- Addiction can be VERY DIFFICULT to diagnose. I much more than asking yes and no questions, and patients are very good at concealing behaviors.

Definitions

- DSM IV terminology
  - Addiction = Dependence
  - Do not confuse this definition of "dependence" with "physical dependence"
- DSM-V terminology
  - Addiction = Substance Use Disorder
- NOTE: The word "Addiction" is not used.

Physical Dependence

- An altered state of physiology resulting from prolonged drug exposure, resulting in tolerance and/or withdrawal.
  - Example: a patient experience opiate withdrawal after stopping morphine 72 hours ago.
- It is a normal physiological response, and is NOT indicative of addiction, by itself.
- Is NOT necessary to make a diagnosis of addiction (substance use disorder).

Substance Use Disorder

- Is simply another way of saying "addiction."
- Criteria are universal for ALL substances. (ex. Nicotine Use Disorder has the same diagnostic criteria as Cocaine Use Disorder).
  - The behavioral phenotypes of addiction are very similar, regardless of class of drug is being used.
  - Example: Behaviors associated with opiate addiction mirror those of cocaine addiction.
    - This indicates a central and common disease process or pathway.

Substance Use Disorder

- A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by 2 (or more) of the following, occurring within a 12-month period:
- 1. Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home.
- 2. Recurrent substance use in situations in which it is physically hazardous.
- 3. Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance.

Substance Use Disorder (cont'd)

* 4. Tolerance
* 5. Withdrawal
* 6. The substance is often taken in larger amounts or over a longer period than was intended.
* 7. There is a persistent desire or unsuccessful efforts to cut down or control substance use.
* 8. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.

Substance Use Disorder (cont'd)

- 9. Important social, occupational, or recreational activities are given up or reduced because of substance use.
- 10. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
- 11. Craving or a strong desire or urge to use a specific substance.

Substance Use Disorder (cont'd)

- Severity specifiers:
  - Mild: 2-3 positive criteria
  - Moderate: 4-5 positive criteria
  - Severe: 6 or more positive criteria

  Specify if:
  - With Physiological Dependence: evidence of tolerance or withdrawal (i.e., either Item 4 or 5 is present)
  - Without Physiological Dependence: no evidence of tolerance or withdrawal (i.e., neither Item 4 nor 5 are present)

What Drugs Can Cause Addiction?

- Only certain drugs are addictive, and are able to stimulate the addiction circuitry.
  - Opiates/opioids
  - Cannabinoids (marijuana)
  - Psycho-stimulants (Adderall, cocaine)
  - Sedative/hypnotics (Benzodiazepines)
  - Nicotine
  - Alcohol
- Relative very few chemical compounds can stimulate the addiction circuitry, in comparison to all the drugs know.

Historical Perspective

Historical Perspective

You can't set her free. But you can help her feel less anxious.

You know this woman.

She's anxious, tense, irritable. She's felt this way for months.

Beset by the seemingly insurmountable problems of raising a young family, and confined to the home most of the time, her symptoms reflect a sense of inadequacy and isolation. Your reassurance and guidance may have helped some, but not enough.

SERAX (oxazepam) cannot change her environment, of course. But it can help relieve anxiety, tension, agitation and irritability, thus strengthening her ability to cope with day-to-day problems. Eventually—as she regains confidence and composure—your counsel may be all the support she needs.

Indicated in anxiety, tension, agitation, irritability, and anxiety associated with depression.

May be used in a broad range of patients, generally with considerable dosage flexibility.

Contraindications: History of previous hypersensitivity to oxazepam. Oxazepam is not indicated in psychoses.

Precautions: Hypotensive reactions are rare, but use with caution where complications could ensue from a fall in blood pressure, especially in the elderly. One patient exhibiting drug dependency by taking a chronic overdose developed upon cessation questionable withdrawal symptoms. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose; excessive prolonged use in susceptible patients (alcoholics, ex-addicts, etc.) may result in dependence or habituation. Reduce dosage gradually after prolonged excessive dosage to avoid possible epileptiform seizures. Caution patients against driving or operating machinery until absence of drowsiness or dizziness is ascertained. Warn patients of possible reduction in alcohol tolerance. Safety for use in pregnancy has not been established.

Not indicated in children under 6 years; absolute dosage for 6 to 12 year-olds not established.

Side Effects: Therapy-interrupting side effects are rare. Transient mild drowsiness is common initially; if persistent, reduce dosage. Dizziness, vertigo and headache have also occurred infrequently; syncope, rarely. Mild paradoxical reactions (excitement, stimulation of affect) are reported in psychiatric patients. Minor diffuse rashes (morbilliform, urticarial and maculopapular) are rare. Nausea, lethargy, edema, slurred speech, tremor and altered libido are rare and generally controllable by dosage reduction. Although rare, leukopenia and hepatic dysfunction including jaundice have been reported during therapy. Periodic blood counts and liver function tests are advised. Ataxia, reported rarely, does not appear related to dose or age.

These side reactions, noted with related compounds, are not yet reported: paradoxical excitation with severe rage reactions, hallucinations, menstrual irregularities, change in EEG pattern, blood dyscrasias (including agranulocytosis), blurred vision, diplopia, incontinence, stupor, disorientation, fever, euphoria and dysmetria.

Availability: Capsules of 10, 15 and 30 mg. oxazepam.

To help you relieve anxiety and tension

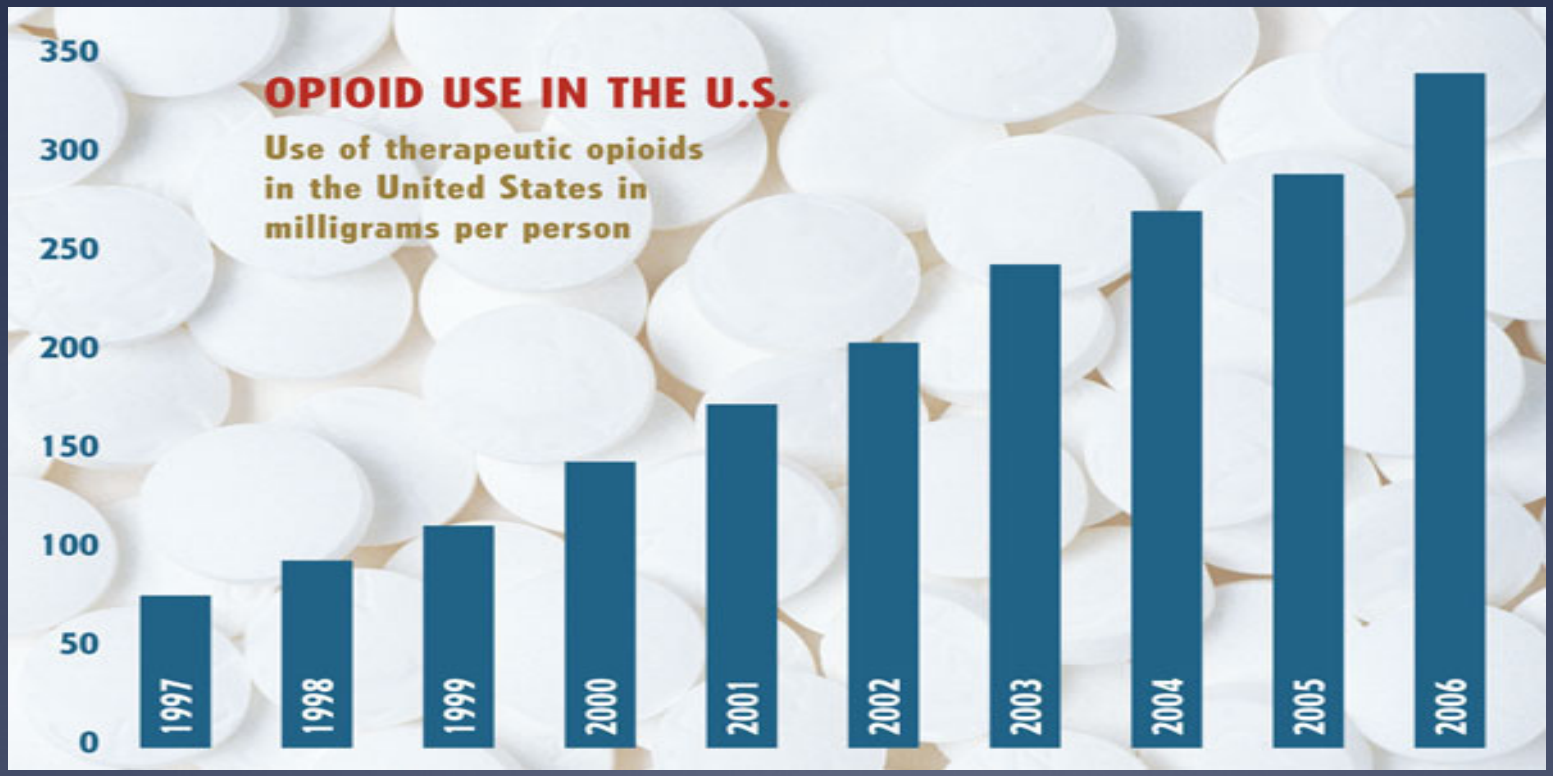
Serax®
(oxazepam)

Wyeth® SERVICE TO MEDICINE

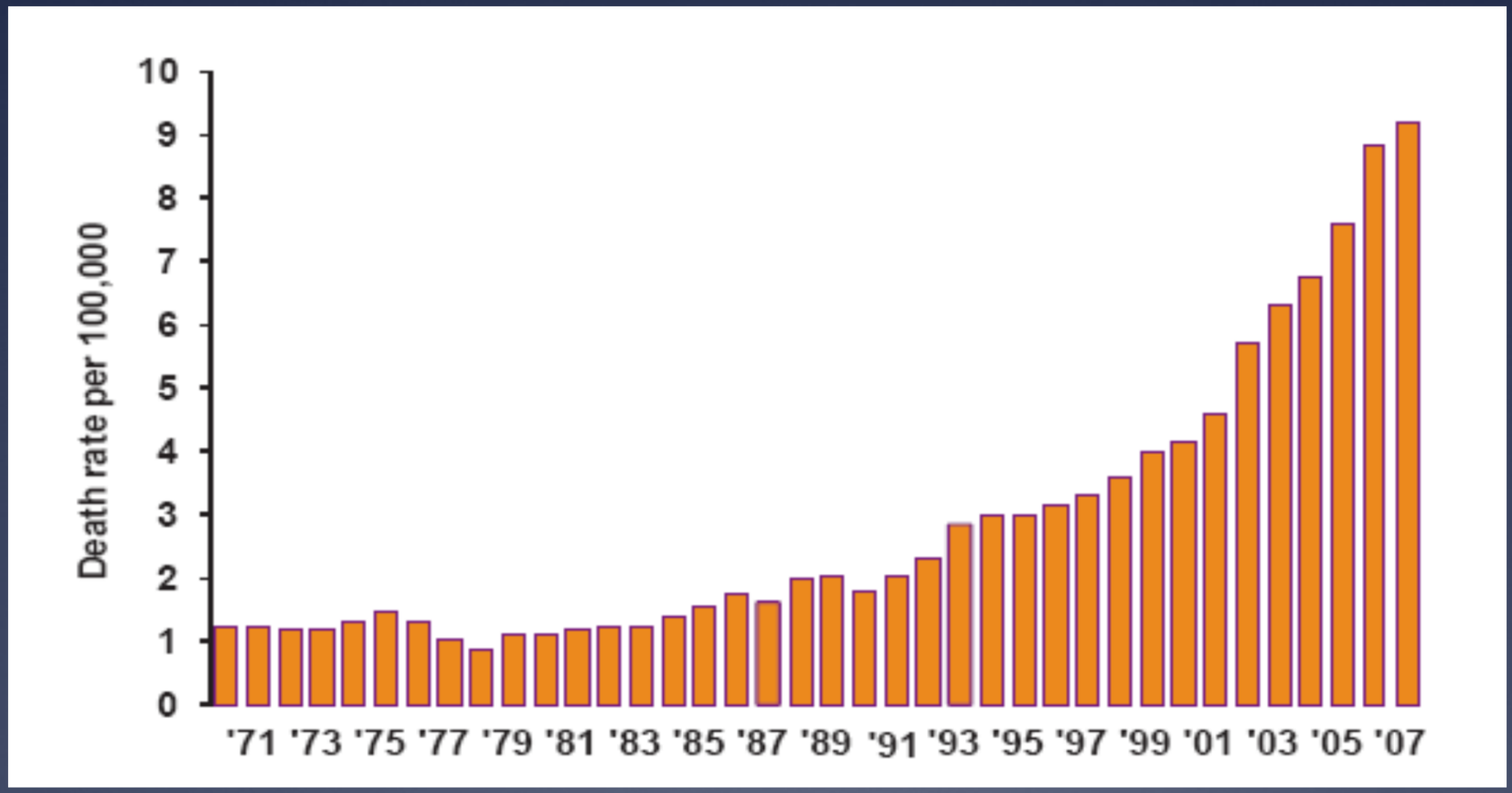
Wyeth Laboratories
Philadelphia, Pa.

Trends in Opiate Prescribing

* The use of therapeutic opioids-natural opiates and synthetic versions-increased 347% between 1997 and 2006, according to this U.S. DEA data.



Rate of Unintentional Drug Overdose Deaths in US 1970 - 2007



Patient Interpretation of the Problem

- They will minimize or deny the problem.
  - This is a SYMPTOM of the disease, and is to be expected.
  - Patients will "protect" their relationship with the drug, and will block any intervention that attempts to interfere with their drug use.
  - Addiction causes patients to undergo a **personality metamorphosis.**
  - They begin to manipulate, lie, and even steal, in order to satiate their drug craving.

Patient Assessment: What to look for

- Social cues:
  - Lying
  - Stealing
  - Manipulative behaviors
  - Various complaints from family members
  - Relationship turmoil/breakup
  - Family reports large amounts of money missing.
  - Decreased work performance or job termination.
    - If patient has lost their job, always ask: "What happened?" May help you identify a problem.

Patient Assessment: What to look for

- Physiologic signs:
  - Macrocytic anemia
  - Thrombocytopenia
  - Transaminitis
  - Other signs of possible liver disease
  - Mental status changes
  - Slurred speech
  - Withdrawal symptoms (tremor, autonomic dysfunction, etc).
  - Weight loss
  - Patient appears disheveled

Patient Assessment

Be empathetic, non-judgmental, and open ended.

Show you care

- "How do those around you feel about your drug use?"
- "You appear to be struggling to me. What do you think?"
- "It seems like your making some bad choices. What do you think is going on?"
- You don't seem like the type of person who will put others at risk when you drive. What do you think is going on?" (when questioning a patient about a DUI).

Treatment

- Levels of treatment
  - Out-patient treatment
    - Weekly therapy (individual or group, or both)
    - Psychiatric care, if needed.
  - Intensive out-patient program (IOP)
    - Day treatment program (daily 9AM -1PM)
    - Typically 3-5 weeks
  - Inpatient – detoxification
  - Inpatient/residential – long-term residential care.
    - May be 3-6 months

Treatment support

- Community Meetings
  - Alcoholics Anonymous/Narcotics Anonymous
    - Daily meetings: typically recommend "90 and 90" which is 90 meetings in 90 days, to those early in treatment.
    - Meetings are free
    - Offer support to patients, NOT treatment.
    - Can be a life-line for many patients.
    - Is quite helpful, despite what critics say.
    - Patients work through 12 steps.
    - Encourage patients to get a sponsor, which is essentially a mentor.

Pharmacotherapy for Addiction

Antabuse (disulfiram)

* Approved for use in 1949
* Typical dose: 250mg qd
* Inhibits aldehyde dehydrogenase, which converts acetaldehyde to acetic acid.
* Elevates blood acetaldehyde concentration, resulting in a disulfiram-ethanol reaction.
* Best used in a supportive or monitored environment.

Antabuse (disulfiram)

- Disulfiram-Ethanol Reaction (DER)
  - Warmness and flushing of the skin
  - Tachycardia, palpitations, hypotension
  - Sweating
  - Nausea/vomiting
  - Dizziness, blurred vision, confusion.

ReVia (naltrexone)

- Approved for use in 1994
- Typical dosing: 50mg qd
- Mechanism: Opioid antagonist
- Decreases the reinforcing effects of alcohol, and diminishes cravings.
- This is also used in the treatment of opioid dependence.

Naltrexone

- "Black-box warning for hepatotoxicity
  - Draw initial liver enzymes/LFT
  - On-going monitoring is necessary only if warranted.
- Should be started a the time psychosocial treatment is initiated
- Starting dose: 25mg daily: increase by 25mg increments every 3-7 days to a maximum dose of 150mg daily
  - Desire to drink is what your assessing for
  - No evidence for efficacy at doses greater than 50mg daily.

Naltrexone

- Side effects:
  - Nausea, and other GI side effects early in treatment
  - Liver toxicity
  - Neuropsychiatric side-effects are often transient, and include: headache, dizziness, light-headedness, and weakness.

Vivitrol (naltrexone)

- Approved for use in 2006
- Used for both alcohol dependence and opioid dependence
- Long acting, injectable formulation of naltrexone
- Typical dose: 380mg IM every month
- Increases adherences in non-compliant patients.
- Evidence suggests better outcomes than with oral naltrexone, possibly due to steady-state blood levels as opposes to daily fluctuations.

Campral (acamprosate)

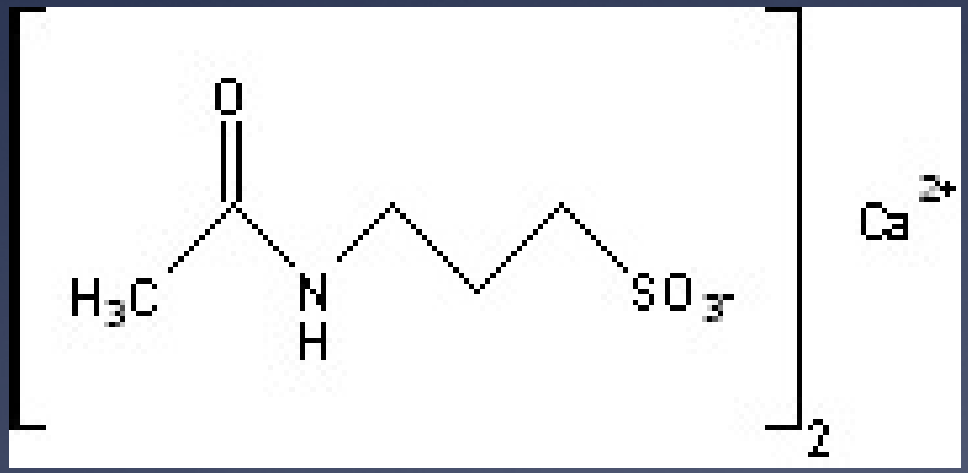
- Approved for use in 2004
- Is acetylhomotaurinate: an amino acid derivative.
- Typical dosing 666mg tid (2 capsule of 333mg)
- Used in patients who are abstinent from alcohol, and who are in psychosocial treaments.
- Mechanism of action is not well understood
- Thought to act as an antagonist at glutamate NMDA receptors. In doing so, restores homeostasis within the GABA and glutamate system.

Campral

- Typically not a first-line choice in treatment.
- Extensively studied in Europe with good results, but these findings have failed to be replicated in the US.
- Excreted unmetabolized through the kidney
  - Patients need to have good kidney function
  - Naltrexone and Antabuse are metabolized by the liver.

Campral

- Chemical structure
- acetylhomotaurinate



Other drugs for the Treatment of Alcohol Dependence

- Topomax (topirmate)
- Zofran (ondansetron)
- Baclofen

Buprenorphine

- A partial mu opioid agonist
- Used in opioid maintenance therapy (OMT)
- Is a potent analgesic
- Dispensed in two forms:
  - Suboxone (buprenorphine/naloxone)
    - 4/1 ratio
    - Naloxone has no bioavailability in the SL route. It is placed here to deter addicts from dissolving and injecting the tablet, which will result in precipitated withdrawal.
    - Starting dose typically 8mg/2mg; max daily dose is 32mg/8mg.
  - Subutex (buprenorphine)
    - Used in pregnant females on OMT
    - Can be used solely as an analgesic.

Buprenorphine

- Can be prescribed for OMT in an office, as opposed to methadone, which can also be given in designated methadone clinics.
  - This is a strong advantage, since it diminishes barriers to treatment.
    - Methadone clinic are plagued with strong negative social stigma.
- Providers wishing to give buprenorphine for OMT must have an "X" number from the DEA.
  - You must take an online course (8 CME credits), pass a post test, and pay $171 dollars.

Methadone

- Used in opioid maintenance therapy (OMT)
- Mechanism: full mu opioid agonsit
- It is also a very potent analgesic, and is used extensively in pain management.

- Prescribing guidelines:
  - You cannot prescribed methadone for OMT unless you are a physician in a methadone clinic. Exceptions occur during inpatient medical stays, when withdrawal poses a risk to the patient (i.e. a pregnant woman with opioid dependence going through withdrawal).
  - You can; however, prescribed methadone as an analgesic, for the management of pain.

Methadone Dosing

- Has a long elimination half-life, > 36 hours, yet a very short analgesic effect, about 6 hours
  - This difference can lead to unintentional overdose and possibly death.
  - BE CAREFUL when dosing this medication, and be aware of this principle.
- Dosing for OMT is typically qd
- Dosing as an analgesic is typically tid

Thank you!

- Question and Answer Session
- Please email me with any questions.
  - ejouney@med.umich.edu