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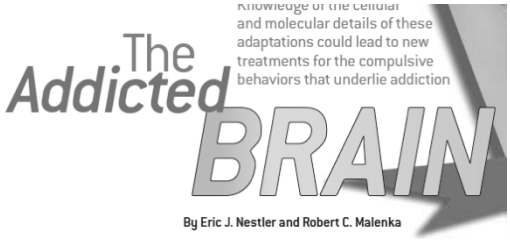
Physiology of Addiction

Disclaimers

- Consultant, DEA/FBI/ DOJ
- Consultant, BCBS
- Medical Director, HPRP
- Methadone provider, WSU
- Medical Director, Dawn Farm

Review article



What is Addiction?

- Physiologic Dependence?
- Lack of willpower?
- An "amoral" condition?
- A brain disease?

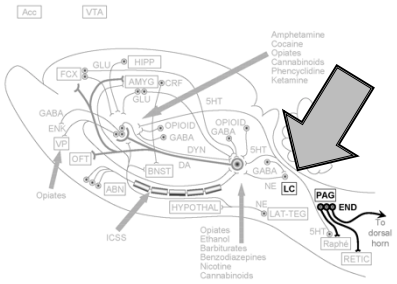
Physiologic Dependence: Tolerance and Withdrawal

- Tolerance: requiring increasing amounts of drug to get the same effect
- Withdrawal: the opposite effect of the drug when it is removed
- NEITHER of these imply chemical dependency (addiction)

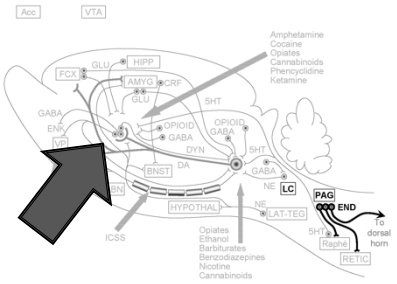
Physiologic Dependence: Tolerance and Withdrawal

- 100 people are treated with morphine for two weeks after an accident.
- Their insurance runs out, the morphine is suddenly stopped.
- 95 of them will have "the flu" (physical withdrawal) and will go on with their lives.
- 5 of them will start robbing party stores to get more morphine!!!!
  - = ADDICTION

Drug WITHDRAWAL: Gardner 2006

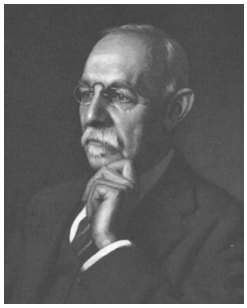


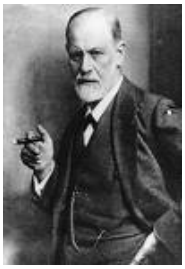
Drug ADDICTION: Gardner 2006



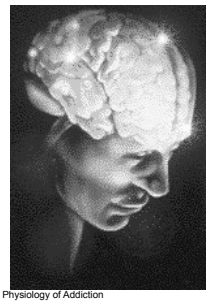
Lack of Willpower?

An "amoral" condition?

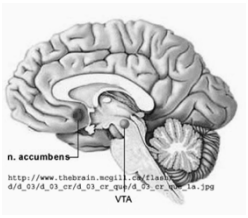




Brain disease?



Nucleus Accumbens = the Pleasure Center



- Responds to dopamine (DA)
- Part of the LIZARD BRAIN
- Responds to drugs
- Responds to food
- Responds to sex
- Sends signals to your frontal cortex
- THE PLEASURE CENTER IS ABNORMAL (DAMAGED) IN ADDICTION


NATIONAL ★ ★ ★ ★ FINAL

DAILY NEWS

NEW YORK'S HOMETOWN NEWSPAPER

STRAWBERRY TELLS JUDGE:

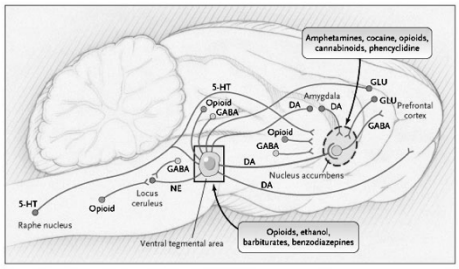
'MY BRAIN IS BROKEN'

SEE PAGES 4-5

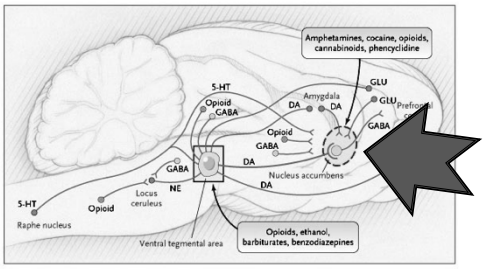
... AS YANKS GET ANOTHER 'W'

President Bush accepts autographed baseball from the World Champion Yankees while shaking hands with Roger Clemens at the White House yesterday.

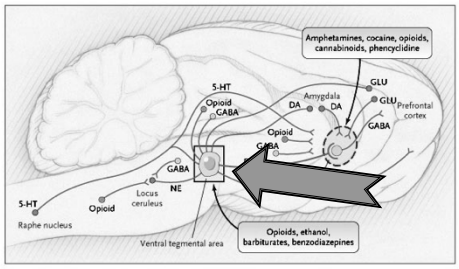
WHO'S IN CHARGE HERE?



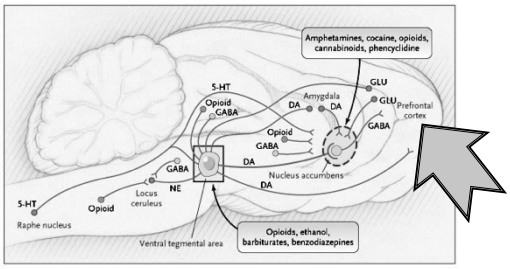
The Nuclues Accumbens: GO!!!

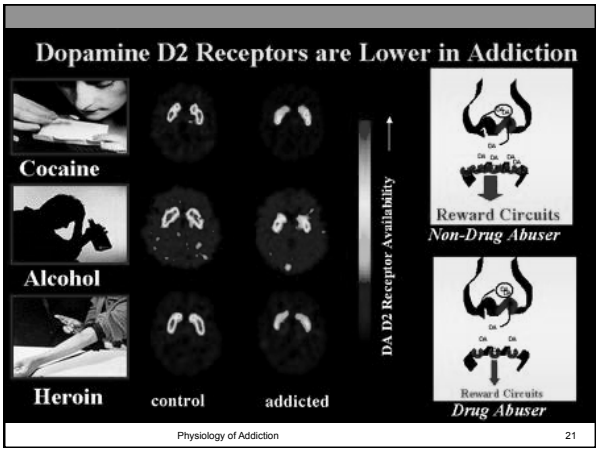


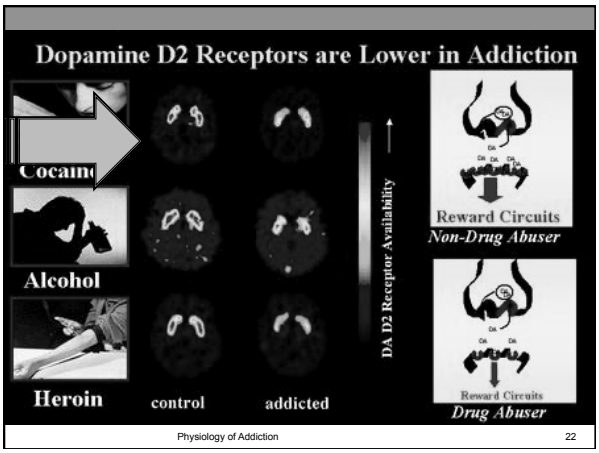
VTA: the "gas tank": supplies dopamine to the Nuclues Accumbens

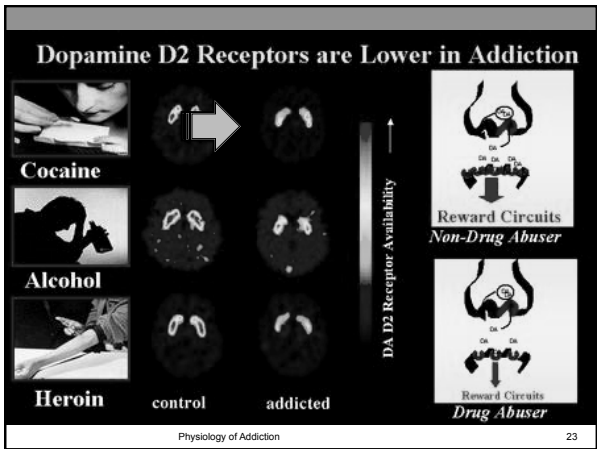


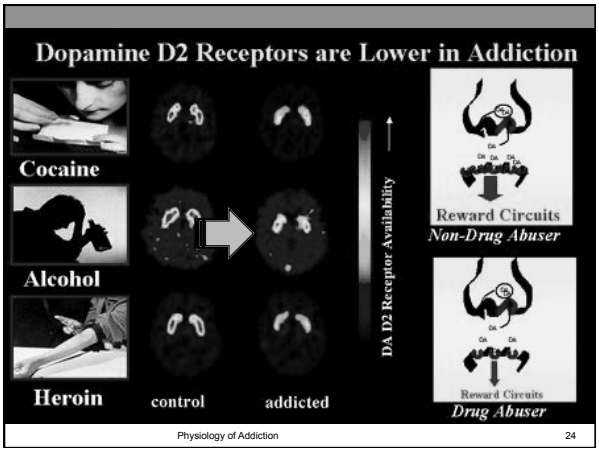
Frontal Cortex: STOP!!!!

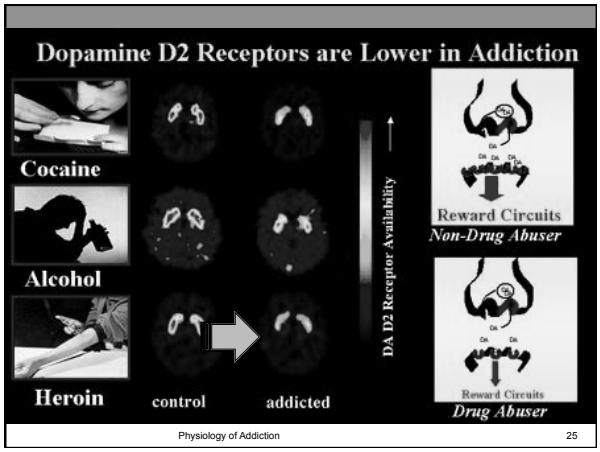










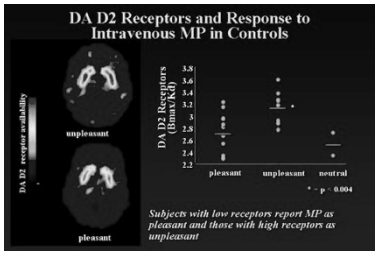


Which came first?

- Do some people develop addiction because they have "reward deficiency syndrome" (decreased dopamine) OR:
- Do people with addiction have low dopamine because they have "burned out" their pleasure centers?

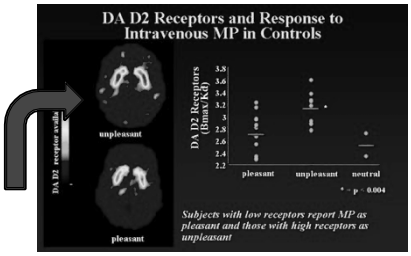
Physiology of Addiction 26

Abnormal response to Ritalin (methylphenidate) is due to abnormal brain chemistry

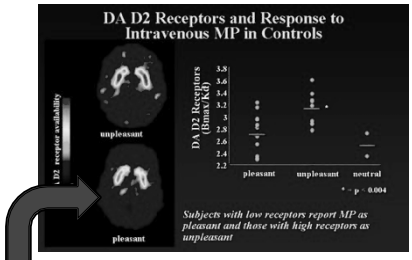


Physiology of Addiction 27

Abnormal response to Ritalin (methylphenidate) is due to abnormal brain chemistry



Abnormal response to Ritalin (methylphenidate) is due to abnormal brain chemistry



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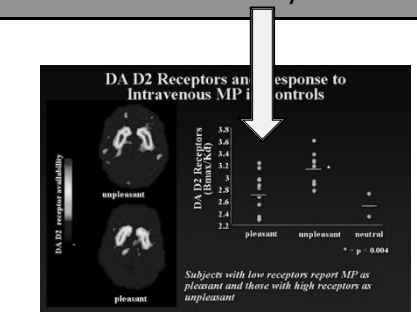
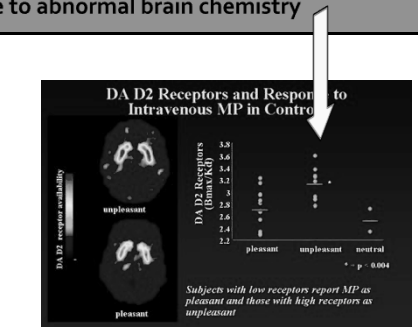


Abnormal response to Ritalin (methylphenidate) is due to abnormal brain chemistry



Predisposed to addiction?

- Those who "enjoyed" methylphenidate (amphetamine) had LOWER levels of dopamine.
- Those who found it "unpleasant" had NORMAL levels of dopamine
- Conclusion?
  - -addiction is an abnormal response to reward

Predisposed to addiction?

- Women who have an abnormal receptor (brain protein) for dopamine had brain scans
- Those who had the abnormal receptor enjoyed a milkshake LESS
- **Were more likely to gain weight!**
- Conclusion?
  - -addiction is an DECREASED response to NORMAL reward
  - If you don't like something as much, you need to compensate!

"I feel like I don't belong in my own skin...."

anonymous alcoholic

- Decreased Dopamine receptors =decreased Dopamine =
- **Decreased Hedonic Tone**
- **Salsitz 2006**

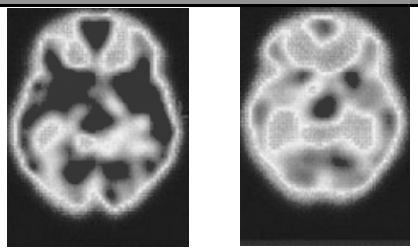
Can you find the (alleged) future alcoholic?

Decreased "hedonic tone"

Why Can't They Stop?????

- Alcoholics/addicts who finish treatment will often relapse when they re-enter society.
- They will almost ALWAYS relapse if they undergo quick detox and re-enter society.
- But: their withdrawal is gone.
- SO: why do they relapse?????

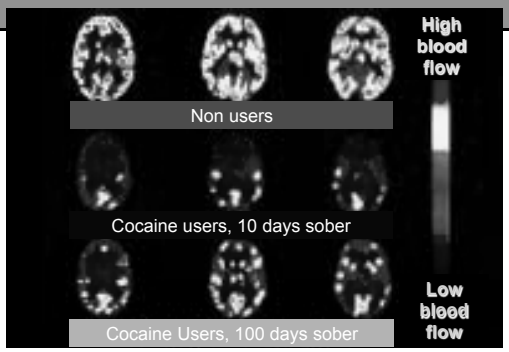
Stimulants & Blood Flow



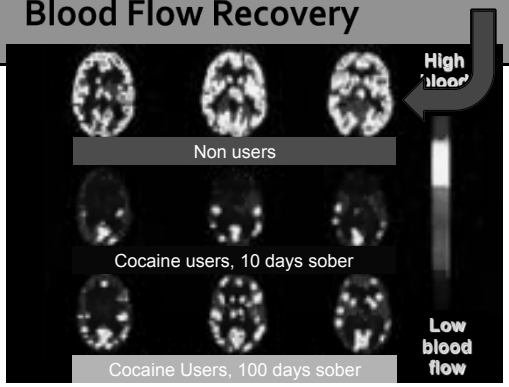
Healthy Control **Cocaine-dependent**

Gottschalk, 2001, Am J Psychiatry

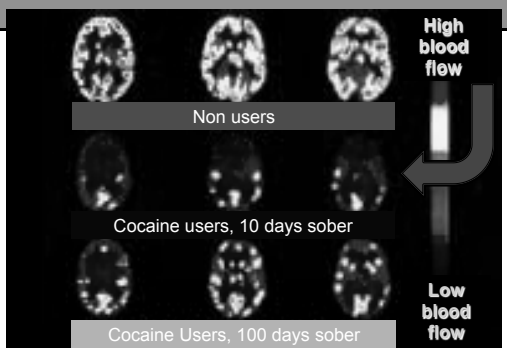
Blood Flow Recovery



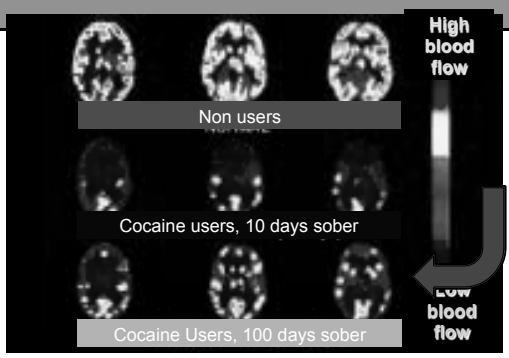
Blood Flow Recovery



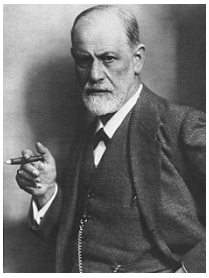
Blood Flow Recovery



Blood Flow Recovery



Doctor, am I an addict?



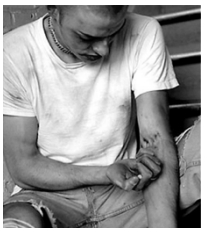
How to Recognize Addiction: DSM IV definition

- Tolerance
- Withdrawal
- Take more/take longer than intended
- Can't cut down or control use
- Great deal of time spent in obtaining/ using /recovering
- Important activities given up 2º to use
- Use despite physical/ psych problem

How to recognize addiction: working definition

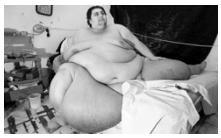
- A chronic progressive disease characterized by the following physical and psychological symptoms (the four (five) C's):
- **Craving**
- **Compulsion**
- Loss of **Control**
- Continued use despite **consequences,** and
- **Chronic** use

Chemical Dependence

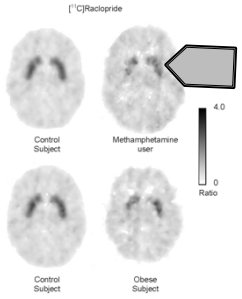


Chemical Dependence ?

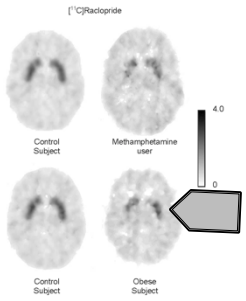
Behavioral Dependence



methamphetamine addicts have decreased DA



Obese subjects have decreased DA: just like methamphetamine addicts!!!



"Hi…I'm Joe. I'm cross addicted"

Addiction Transfer

- People who recover from alcoholism may:
  - Gain weight
  - Increase their smoking
  - Start gambling
  - Become involved in sexual addiction, internet addiction

Addiction Transfer

- People who undergo **gastric bypass surgery** may:
  - Become alcoholics
  - Develop chronic pain-→opiate dependence
  - Gain weight!

Abuse vs. dependence

- You are worried about your best friend.
- She has a 20 year history of heavy drinking and has just been diagnosed with hypertension and hyperlipidemia (high cholesterol).
- You advise her to quit.

Abuse vs. dependence

- You went to the Dawn Farm lecture on addiction and you know it is a "disease".
- To your surprise, she does so, without any treatment.
- You vow never to waste your time going to any more Dawn Farm lectures.
- ***How did she do it?????***

Is it abuse…or is it dependence?

- Failure to fulfill work/school/social obligations
- Continued use is risky situations (ie, drunk driving)
- Recurrent legal problems (DUI)*
- Continued use despite social or interpersonal problems (MOR)
- Never fit the criteria for dependence

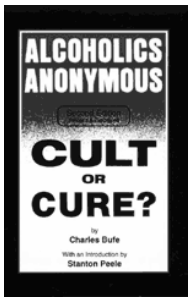
Abuse vs. dependence

- The majority of patients you see with drug/ alcohol problems do NOT have addiction
- Most people with drug/alcohol problems <u>will be able to stop on their own.</u> (William White)
- The 4Cs helps you to determine which ones have addiction!

Is addiction a myth?

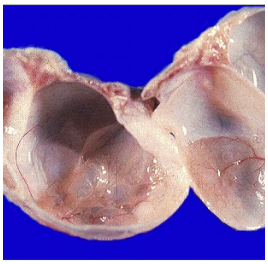
http://www.peele.net/

- Most people who have a problem with alcohol or drugs will stop on their own
- The majority of people who stop do so without treatment.
- Even many heroin "addicts" will "quit" and resume normal lives.



Which patient has cancer?

A 45 YEAR OLD WITH AN OVARIAN TUMOR.



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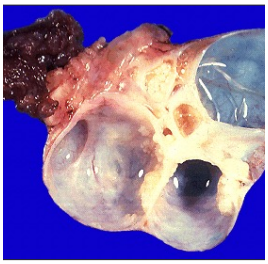
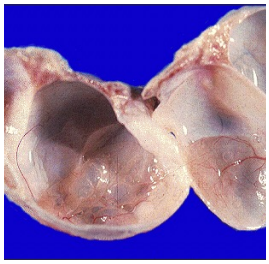
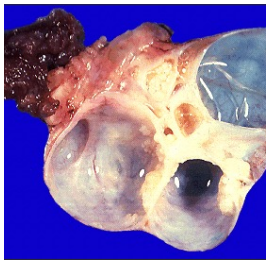


Which patient has cancer?

NO FAMILY HISTORY

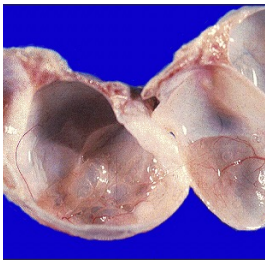


FAMILY HISTORY OF BREAST CANCER

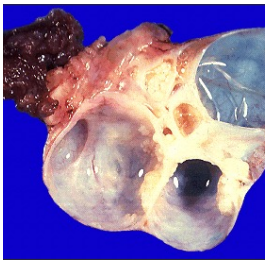


Which patient has cancer?

NO GENETIC PREDISPOSITION



HAS THE BREAST CA/ OVARIAN CA GENE "BRCA"



Is addiction a myth?

- "Abuse is a BEHAVIOR….
- Addiction is a DISEASE!!"

  - Mark Minestrina, MD
    - Brighton Hospital

RELAPSE: the problem with addiction

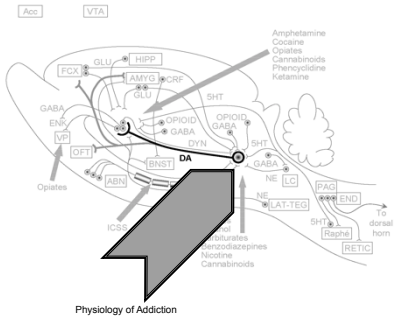
- "anyone can quit drinking……"
- "Just walk up and hit a cop!"

  - Herb Malinoff, MD

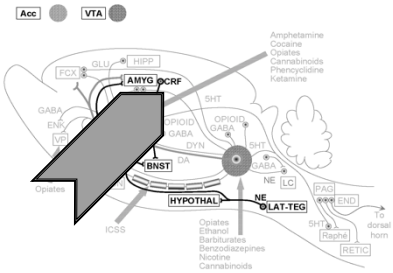
RELAPSE: the problem with addiction

- **Drug** triggered: "I thought I could (eat/ smoke/drink) just one…."
- **Stress** triggered: "I' m going through too much right now. Gimme that!"
- **Cue** triggered: "Wet faces and wet places"

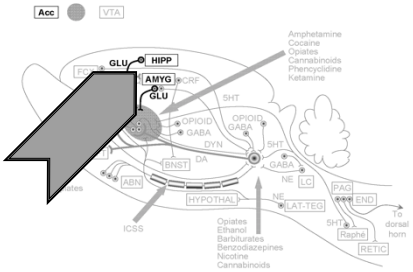
Drug Triggered Relapse: Gardner 2006



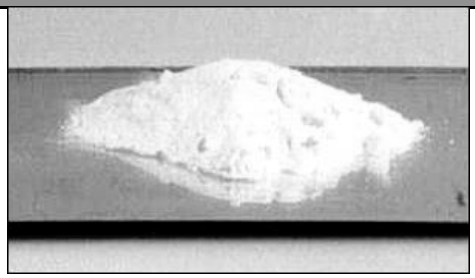
Stress Triggered Relapse: Gardner 2006



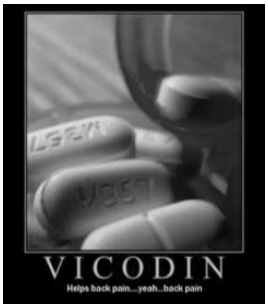
Cue Triggered Relapse: Gardner 2006



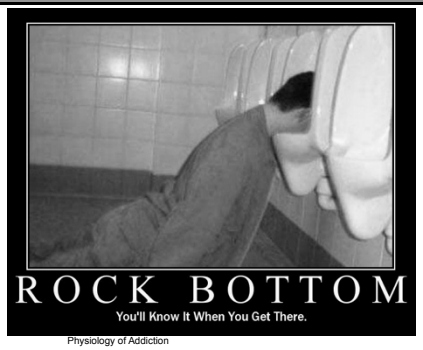
Which of these cues do you respond to?



Dynamic Duo



Consequences of addiction



Consequences: Alcohol

- Hypertension: the most common cause of "essential" (unexplained) hypertension is alcohol.
- Diabetes: damage to the pancreas (temporary or permanent)
- Cholesterol: LDL (bad cholesterol) goes up, triglycerides (fat) goes up.

Consequences? The Liver

- Fatty liver: from drinking; body uses alcohol rather than fat. Fat accumulates.
- Alcoholic Hepatitis: inflammation of the liver; fever, jaundice, pain, nausea and vomiting.
- Viral Hepatitis: usually hepatitis C, from sharing needles, straws (cocaine), sex.
- Cirrhosis: scarring of the liver

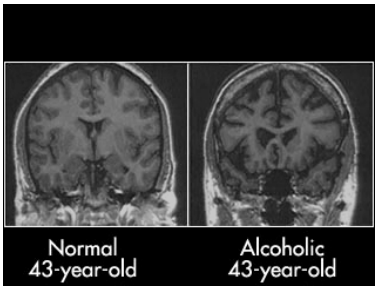
The (keen) Alcoholic Mind

- *Your friend is an alcoholic. His family left him.*
- *When you see him today, he denies that he has a problem, but says that he needs to "take a break". His wife left him, he says, because of his mother in law.*
- As you discuss his situation, you are amazed by his ability to:
  - Minimalize -Rationalize
  - Deny -Deflect

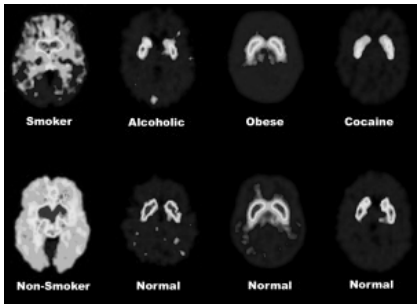
Cognition (thinking) and Addiction

- Recovering addicts make bad decisions
- Ex: 3 weeks into recovery, a man decides to make a trip to.....
- Amsterdam?
- Q: what does an alcoholic bring on a 2nd date?
- A: a U haul.

Cognition and Addiction



Reward pathway in alcoholism & more….



Consequences: brain

- *You are asked to see him in the hospital several years later.*
- *He says he knows you, but cannot remember your name. You become alarmed.*
- *You ask him who the president is, he replies "Who cares? They're all crooks".*
- *He walks with a shuffling broad-based gait and has to hold his hand on the wall to keep his balance.*

Wernike-Korsakoff Syndrome

- Immediately after stopping drinking: **Wernike's encephalopathy** (brain disease)
- Caused by thiamine (B1) deficiency
  - Eye muscles are paralyzed
  - Ataxia (can't walk straight)
  - Encephalopathy: confusion, agitation, restlessness

Korsakoff's psychosis

- Confabulation: make things up
- Retrograde amnesia: can't remember what happened in the past
- Antegrade amnesia: can't remember info you are given (remember these 3 objects…)
- Polyneuropathy: peripherhal nerve damage

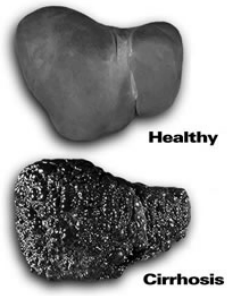
Consequences: liver

- *You see him one more time, several years later. He has been readmitted for vomiting blood, jaundice, and encephalopathy.*
- *He is given multiple transfusions. He has esophageal varices from his cirrhosis.*
- *He is jaundiced. He says that he is asking his sister to pay for a liver transplant. She died 5 years ago….*
- *When he are speaking to him, his hands will occasionally flap.*

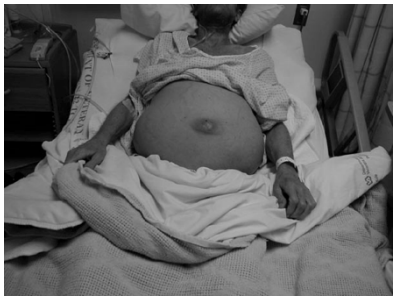
Alcoholic Cirrhosis

- Hardening of the liver (scar tissue)
- Causes blood to back up in the veins feeding the liver:
  - Esophageal varices: vomit blood
  - Hemorrhoids: rectal bleeding
- Can't metabolize toxins: encephalopathy
- Can't make proteins:
  - bleeding (coagulopathy)
  - Can't hold fluids: ascites

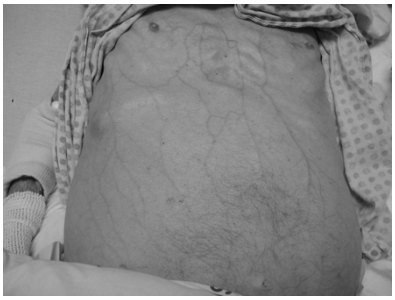
Cirrhosis



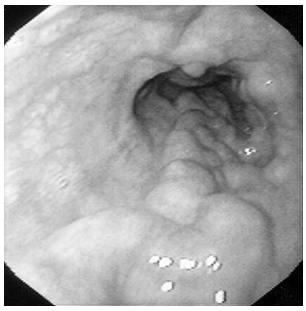
Ascites/Jaundice



"Caput Medusae"

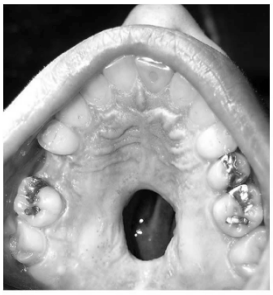


Esophageal Varices

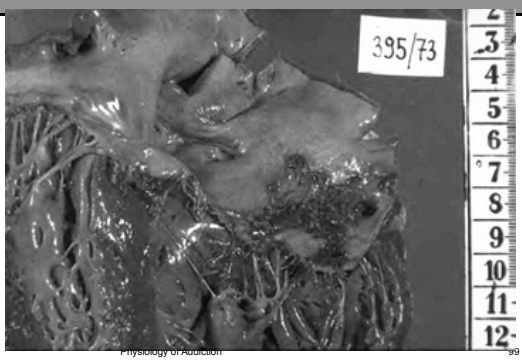


- *He dies several weeks later of liver failure.*
- "Jails, institutions, and death"
  - Narcotics Anonymous

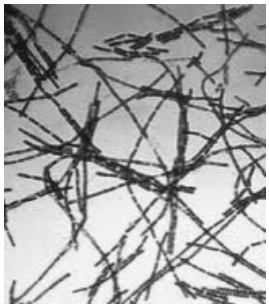
COCAINE

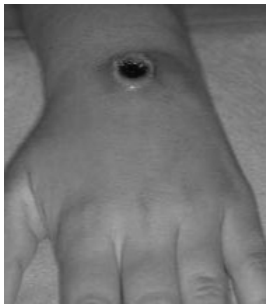


Opiates: endocarditis

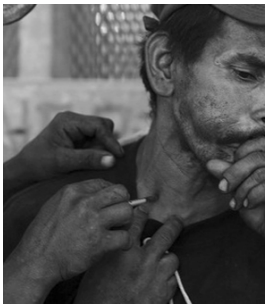


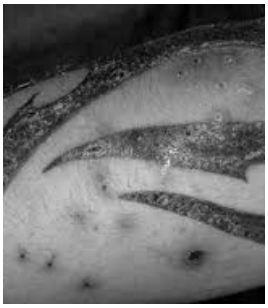
Anthrax!



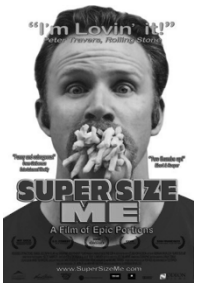


Intravenous Drug Use (IVDU)





FOOD: Supersize Me



Step Two: Overeater's Anonymous

- "We have driven miles in the dead of night to satisfy a craving for food. We have eaten food that was frozen, burnt, stale, or even dangerously spoiled. We have eaten food off of other people's plates, off the floor, off the ground. We have dug food out of the garbage and eaten it."

THE SOLUTION?

TREATMENT OF ADDICTION

TREATMENT OF ADDICTION

- Medical
- Behavioral
- Spiritual
- Surgical

TREATMENT OF ADDICTION: Medical

- Agonists: similar to the "drug"
  - Suboxone for opiate dependence
  - Methadone for opiate dependence
  - Nictotine patches for tobacco dependence
  - THC for marijuana dependence
  - Dilaudid for heroin dependence! (Canada)

TREATMENT OF ADDICTION: Medical

- Antagonists: opposite effect of the drug
  - Naltrexone for opiate dependence
    - Oral: Rivea
    - Injectable: Vivitrol
  - Naltrexone for alcohol dependence: Vivitrol
  - Disulfiram (Antabuse) for alcohol dependence
  - Rimonabant for obesity

BOTTOM LINE:

- In both controlled and retrospective studies, the success rate for most medications is between 40 and 60% (one to two years).
- When patients come off the medication, they relapse.
- Relapse may be associated with an increased chance of overdose and death.

BOTTOM LINE:

- In both controlled and retrospective studies, the success rate for most medications is between 40 and 60% (one to two years).
- When patients come off the medication, they relapse.
- Relapse may be associated with an increased chance of overdose and death.
- ***Why would you expect otherwise?***

Doc, when can I get off this sh*t (medication)?

Detoxing During Pregnancy? Luty 2003

- 101 women underwent detox during pregnancy
- 40 successfully detoxed.
- No adverse fetal effects documented
  - Luty et al, J Sub Abuse Treat 24 (2003); 363 - 367

Detoxing During Pregnancy? Luty 2003

- 101 women underwent detox during pregnancy
- 40 successfully detoxed.
- No adverse fetal effects documented
- But: only **1/101** patients documented to be abstinent at time of delivery!
  - Luty et al, J Sub Abuse Treat 24 (2003); 363 - 367

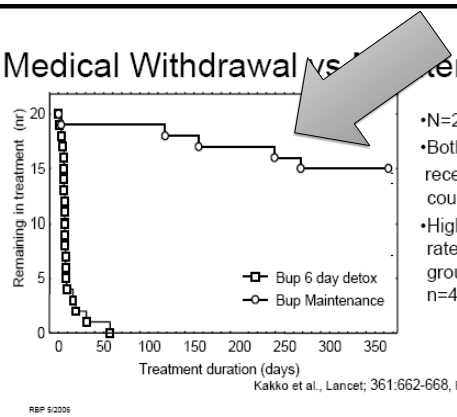
Detoxing During Pregnancy? Luty 2003

- "Nevertheless, very few women who successfully completed detoxification remained abstinent through to delivery"
  - Luty et al, J Sub Abuse Treat 24 (2003); 363 - 367

Maintenance vs. Detox?

- 40 heroin addicts were started on Suboxone.
- 20 were "detoxed" off and offered counseling.
- 20 were kept on Suboxone and offered counseling.
- A year later.....

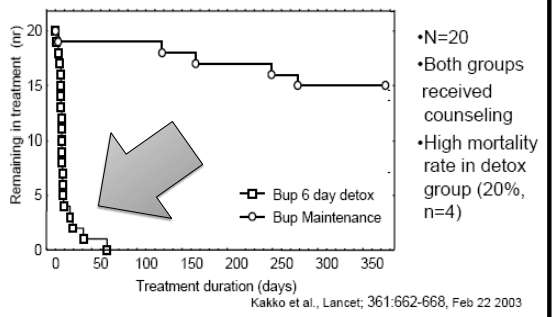
Medical Withdrawal vs. Maintenance



- N=20
- Both groups received counseling
- High mortality rate in detox group (20%, n=4)

Kakko et al., Lancet; 361:662-668, Feb 22 2003

Medical Withdrawal vs Maintenance



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- High mortality rate in detox group (20%, n=4)

Kakko et al., Lancet; 361:662-668, Feb 22 2003

RBP 5/2006

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Short term and long term treatment with buprenorphine in prescription opioid dependent patients

ONLINE FIRST

Adjunctive Counseling During Brief and Extended Buprenorphine-Naloxone Treatment for Prescription Opioid Dependence

A 2-Phase Randomized Controlled Trial

Roger D. Weiss, MD; Jennifer Sharpe Potter, PhD; David A. Fiellin, MD; Marilyn Byrne, MSW; Hilary S. Connery, MD, PhD; William Dickinson, DO; John Gardin, PhD; Margaret L. Griffin, PhD; Marc N. Gourevitch, MD, MPH; Deborah L. Haller, PhD; Albert L. Hasson, MSW; Zhen Huang, MS; Petra Jacobs, MD; Andrzej S. Kosinski, PhD; Robert Lindblad, MD; Elinore F. McCance-Katz, MD; Scott E. Provost, MSW; Jeffrey Selzer, MD; Eugene C. Somoza, MD, PhD; Susan C. Sonne, PharmD; Walter Ling, MD

ORT: yes or no???

126

Phase 1

654 pts → 2 weeks BUP → Taper 3 to 4 weeks, f/u 5 to 12 weeks

ORT: yes or no???

127

Outcome Phase 1

- Only 43 of 653 patients remained abstinent (6.6%)
- All other relapsed!!
- Next step: Phase 2

ORT: yes or no???

128

Phase 2

360 pts → 12 weeks BUP → Taper 1 to 2 weeks, f/u 5 to 12 weeks

ORT: yes or no???

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Outcomes Phase 2

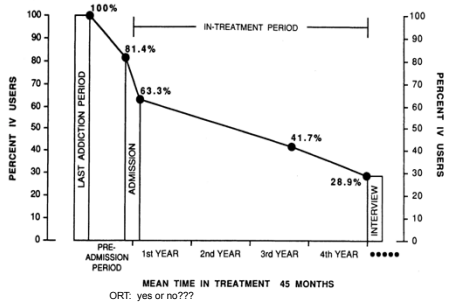
- 49% stayed abstinent when they went back on buprenorphine!
- But when they were taken off buprenorphine again, only 8.6% remained abstinent!

ORT: yes or no???

130

Ball 1988: reduction in IVDU

FIGURE 1. Effect of Methadone Maintenance Treatment on IV Use for 388 Male Methadone Patients in Six Programs

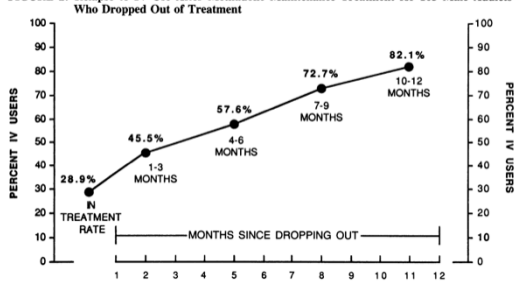


ORT: yes or no???

132

Ball 1988: resumption of IVDU!

FIGURE 2. Relapse to IV Use After Methadone Maintenance Treatment for 105 Male Addicts Who Dropped Out of Treatment



ORT: yes or no???

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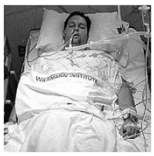
Ultra Rapid Detox?

'Rapid detox' a quick fix for opiate addiction?

By Robert Davis, USA TODAY

Andy Sachs is not the stereotypical opiate junkie. He gets his drugs from a pharmacy, not a street dealer. He began taking his medicine for severe pain, not for the high. And the drug he's hooked on is more widely used than heroin. Six million people a year take OxyContin.



OxyContin addict Andy Sachs undergoes treatment at the Waismann Institute.

By Bob Riha Jr., USA TODAY

Physiology of Addiction

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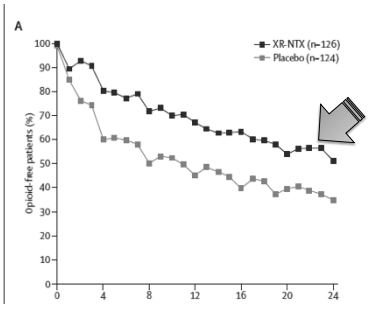
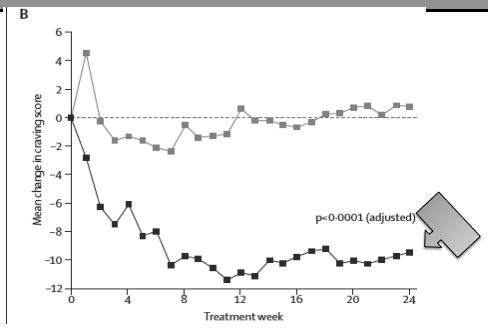
Vivitrol® (injectable naltrexone) for opioid dependence

Vivitrol: abstinence



Vivitrol: craving



Vivitrol: concerns

- As with methadone and buprenorphine, when the medication is stopped, relapse may lead to death due to lack of tolerance.
- It is difficult to treat acute pain while on Vivitrol.

Do You HAVE to Use Meds?

- Docs, Nurses & Pharmacists: HPRP
- Lawyers & Judges: LJAP
- Pilots: HIMS

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Do You HAVE to Use Meds?

- Continuous monitoring
- Treatment / 12 step
- Rapid consequences
- Graded response

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Do You HAVE to Use Meds?

- Hawaii's Opportunity Probation with Enforcement (HOPE)
  - Continuous monitoring
  - Treatment / 12 step
  - Rapid consequences
  - Graded response

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Cognitive Behavioral Therapy (CBT)

- Behavior (drinking) is due to false beliefs (I can't stop)
- Change the false beliefs, change the behavior.
- Apologies to therapists everywhere……

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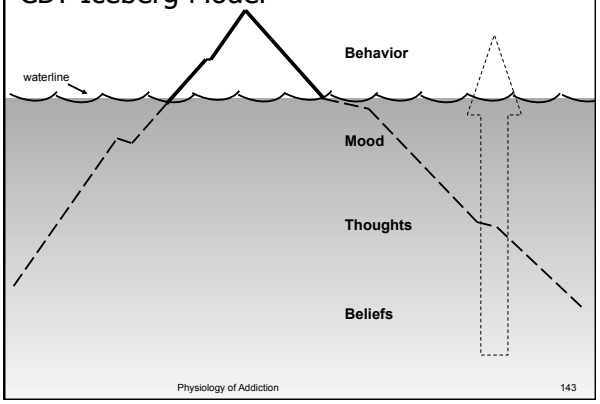
CBT Iceberg Model



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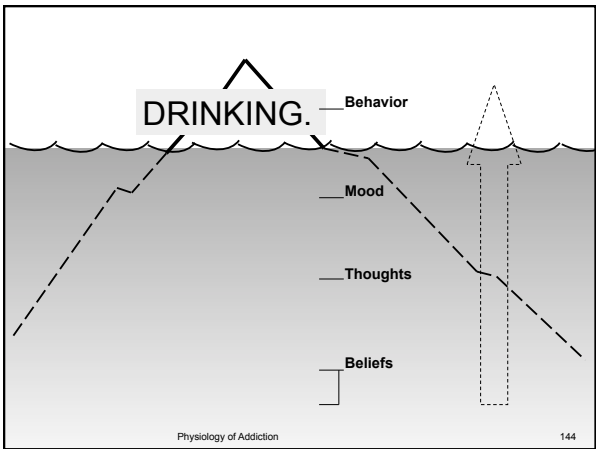

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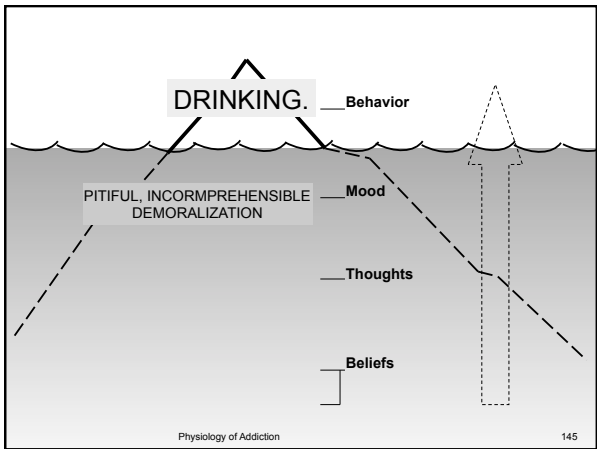

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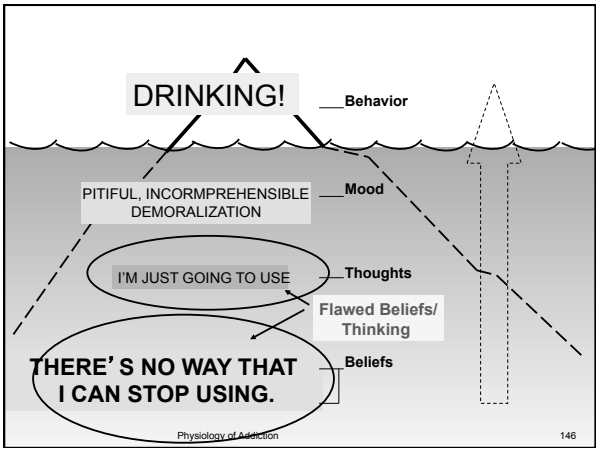

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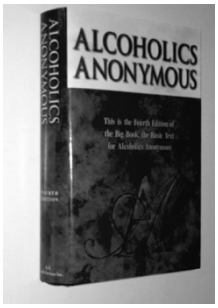
Spiritual solution?



- Alcoholics Anonymous: 734 482 5700 www.aa-semi.org

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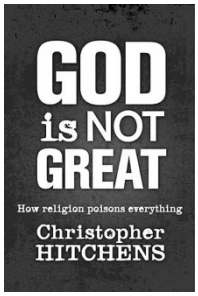
Spiritual Solution? Peele.net



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Spirituality ≠ Religion

?

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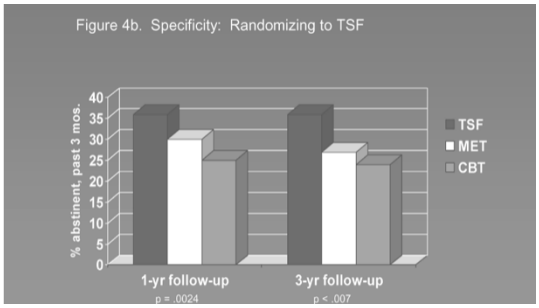
Twelve Step Programs

Food Addicts in Recovery Anonymous

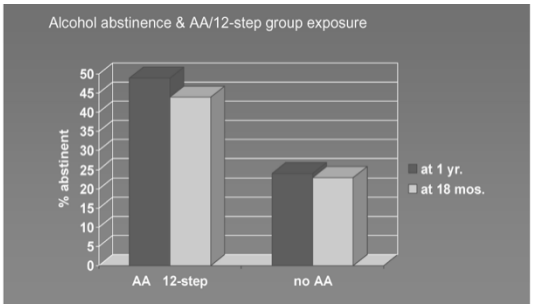
OVEREATERS ANONYMOUS

Physiology of Addiction 152

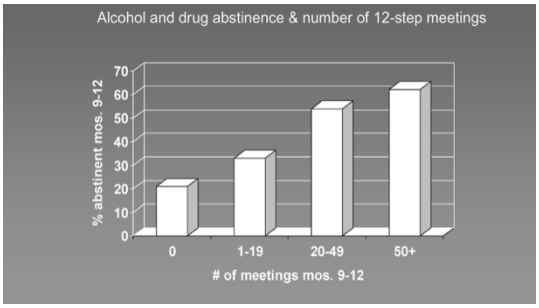
Abstinence by treatment group: Project MATCH



AA involvement in Veterans 1987, 1988



"Dose Response Curve"



TREATMENT OF ADDICTION: Surgical

- Gastric Bypass for eating disorders
- Liver transplant for cirrhosis
  - ETOH and Hepatitis C: most common indication
- Brain surgery for addiction?
  - Destroy the nucleus accumbens (China, Russia)
  - Accidental injury to the insula: quit smoking!

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WHY BOTHER TO TREAT ADDICTION?

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Why Treat Addiction?

Drug Dependence, a Chronic Medical Illness: Implications for Treatment, Insurance, and Outcomes Evaluation

A. Thomas McLellan; David C. Lewis; Charles P. O'Brien; et al.

JAMA. 2000;284(13):1689-1695 (doi:10.1001/jama.284.13.1689)

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Drug Dependence, a Chronic Medical Illness: McLellan 2000

- Only about 40% of patients will be abstinent at one year after treatment.
- Failure rates may be due to lack of aftercare, often due to insurance difficulties
- Low economic status, psych comorbidity and lack of family/social supports also predict relapse.
- Relapse is often viewed as "inevitable" and drug dependence as "hopeless"*

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Drug Dependence, a Chronic Medical Illness: McLellan 2000

- ONLY 60% OF TYPE I DIABETICS ADHERE TO MEDICATION SCHEDULE
- LESS THAN 40% OF ASTHMATICS ADHERE TO TREATMENT REGIMEN
- LESS THAN 40% OF HYPERTENSIVES ADHERE TO THEIR TREATMENT REGIMEN
- DRUG DEPENDENCE =40 TO 60% ADHERENCE

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Addiction: a chronic illness

- If you were to stop taking your insulin, and you wound up in a coma in the ICU, your doctor would say:
- "you need to go back on insulin! You could have died!"
- If you were to stop your Suboxone/methadone/12 step treatment, and wind up in the ICU, your doctor would say:
- "You're an addict. You're hopeless!!!!!"

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Benefits of Opioid Maintenance Therapy (OMT)

- Decreased HIV infection rates
- Decreased incarceration
- Decreased drug use
- Decreased mortality

- McLellan, 2000

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Drug Dependence, a Chronic Medical Illness: McLellan 2000

- "There is little evidence of effectiveness from detoxification or short-term stabilization alone without maintenance or monitoring such as in (opioid) maintenance or AA."

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Chronic, Treatable but Incurable Diseases

- Obesity
- Hypertension
- Diabetes
- Asthma
- Addiction

Which one is an addict?

Contact info: Carl Christensen

- ccmdphd@mac.com
- http://christensenrecovery.com
- Voice mail: 734 448 0226
- Fax: 313 447 2244
- Christensen Recovery Solutions (A2): 734 434 6600