



Role of Medications in Recovery and the Prevention of Relapse

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Clinical Challenges

- Beliefs
- Adherence
- Integration
- Patient selection
- Side effects
- Coverage

POT-SHOTS — Brilliant Thoughts in 17 words or less

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EST. LISTEN NO. 7824.

MY
ATTEMPTS
TO
ELIMINATE
SOME OF
MY BAD
HABITS

ARE
MEETING
WITH

FANATICAL
RESISTANCE.



Ashleigh Brilliant

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Beliefs

- Limited medical education on addiction
- Physician beliefs about addiction reflect those of society

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POT-SHOTS NO. 281.

AGREE WITH ME NOW:



*Callaghan
Billings*

IT WILL SAVE SO MUCH TIME.

[Integration]

- Combining psychosocial and spiritual practice with evidence-based pharmacological treatments

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[Adherence]

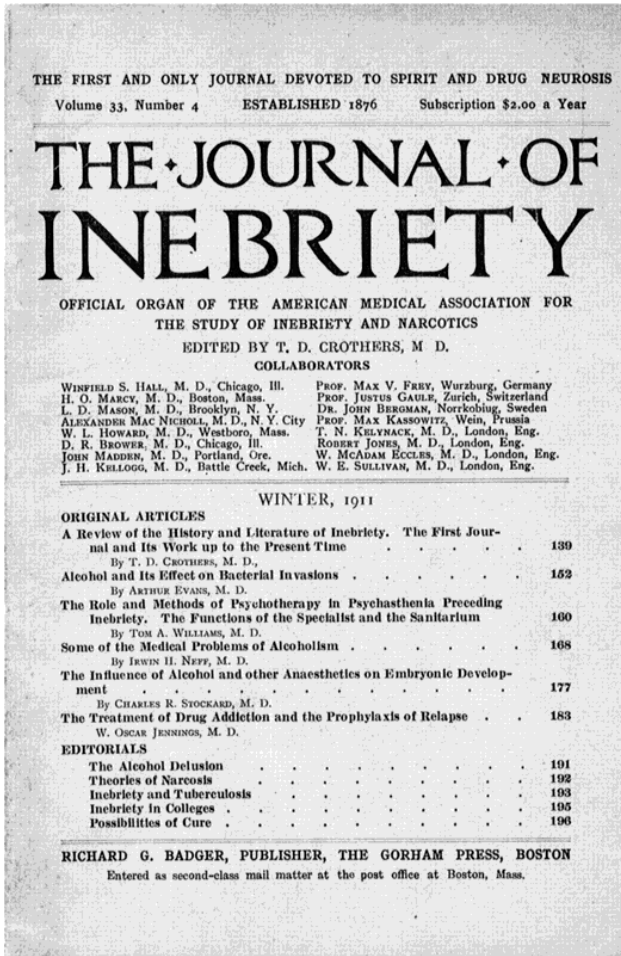
- Need to account for stage of change
- Motivational readiness
- Conviction/confidence



Undertreatment of alcohol use disorders

- 17.6 million Americans meet criteria for an alcohol use disorder (abuse + dependence)
- 7.9 million meet criteria for alcohol dependence
- 2.2 million are seeking treatment
- 100,000 are prescribed at least one of the FDA approved medication

Medications



- Naltrexone
 - Oral
 - Injectable (Vivitrol)
- Acamprosate
- Disulfiram

[Naltrexone]

- Alcohol produces its positive reinforcing effects through the opioid system
- Pure opioid antagonist
- Effective in treatment of alcoholism and opiate addiction
- Blocks cue-triggered craving
- Blocks the 'high' and increases the negatives

Naltrexone

- Naltrexone can decrease:
 - The percentage of days spent drinking
 - The amount of alcohol consumed on a drinking occasion
 - Relapse to excessive and destructive drinking



Naltrexone

- Great majority of studies show significant benefit over placebo
 - Antidepressant studies: under 50% response
- May work best in patients who have early onset drinking, strong craving and strong family history
 - These patients seem to have a gene variant causing increased b-endorphin sensitivity
 - Without naltrexone this group did poorly in studies
- Genomic differences translate into different treatment responses

[Naltrexone]

- Oral (Revia) and injectable (Vivitrol)
- Primary drug-drug interaction: Opioids
- Challenges
 - Side effects (nausea in small percentage)
 - Adherence
 - Physician awareness and knowledge
 - Integration with psychosocial treatment
 - Optimal duration of treatment unknown

[Vivitrol]

- Poor adherence with oral medication translates into worse outcome
 - 10% relapse rate in adherent patients vs
 - 43% relapse rate in non-adherent patients
- Injectable, depot formulation of naltrexone
- Thirty day duration of action

[Vivitrol]

- Depot formulation helps to enhance adherence
- Steady state blood levels after the second month
- Bypasses liver metabolism limits potential for drug-drug interactions

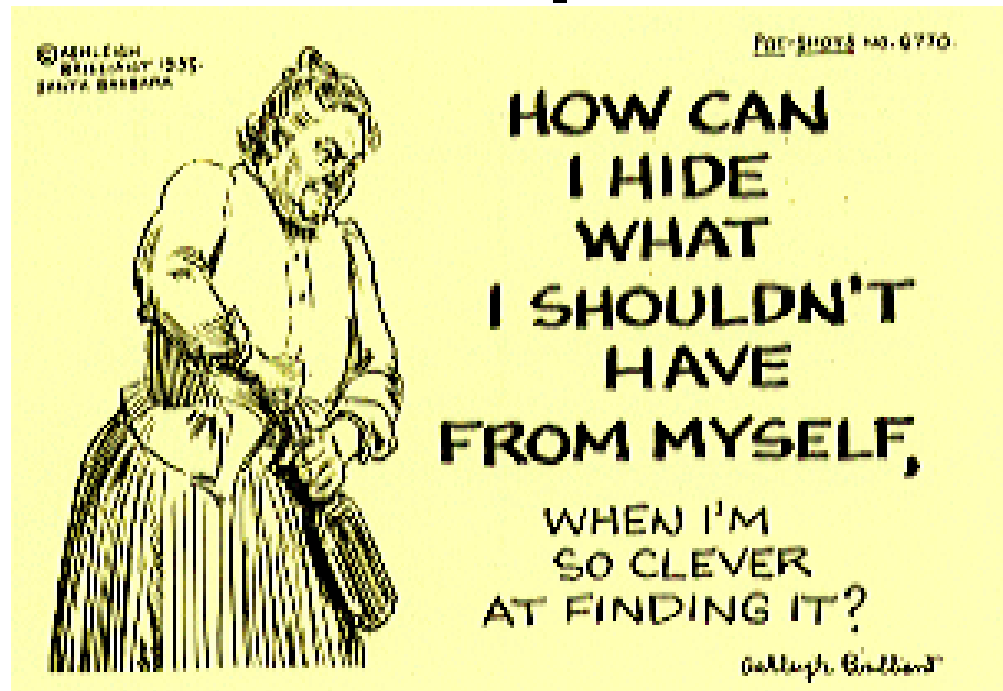
[Vivitrol]

- For patients abstinent for seven days prior to their first injection:
 - 97% reduction in median drinking days per month
 - 92% reduction in median heavy drinking days per month
 - Two to three fold increase in total abstinence

Vivitrol

- Pain treatment issues
- Good overall side effect profile
 - Nausea
 - Injection site reaction

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[Acamprosate (Campral)]

- NMDA receptor antagonist
 - Glutamatergic (excitatory) system
- Blocks craving: particularly context and stress-related cues
- Use in detoxified patients engaged in active psychosocial treatment
- Doubles abstinence rates
- May have additive benefits with naltrexone in some patients

[Acamprosate]

- No liver metabolism or toxicity
- No drug-drug interactions
- Greater rates of complete abstinence
- Longer times to first drink
- May be neuroprotective
- Challenge: three time a day dosing

[Acamprosate]

- Acamprosate worked in patients with high severity (>15 drinks/day, continuous drinking pattern, inpatient detox)
(*Ladewig et al. 1993, Lhuintre et al. 1990, Kiefer et al. 2003, Poldrugo 1997*)
- But not in subjects with moderate pattern (>12 drinks/day, episodic drinking, no need for inpatient detoxification)
(*Chick et al. 2000, Namkoong et al. 2003*)

Craving pathways

- Withdrawal relief craving
 - Alcohol-associated negative mood states
 - Acamprosate: reduces cravings induced by protracted withdrawal cues
 - Littleton 1995, Spanagel and Zieglansberger 1997, Verheul et al 1995
- Reward craving
 - Alcohol associated positive mood states
 - Motivational effects of positive mood and alcohol cues blocked by naltrexone
 - *Monti et al 1999)*

[Hypothesis]

- Naltrexone works better in reward craving by blocking the incentive salience of alcohol cues
- Acamprosate works better in relief craving.
 - Relief craving is associated with a longer duration of addiction, high intake, continuous drinking style, and occurrence of physical withdrawal signs

[Disulfiram (Antabuse)]

- Oldest drug treatment for alcohol dependence
- Blocks the metabolism of alcohol
- Drinking on it causes severely aversive symptoms
- Limited double-blind, placebo controlled studies
- Challenges:
 - Toxicity
 - Adherence

[Conclusions]

- Alcohol dependence is a treatable brain disease
- Research is edifying the biological mechanisms involved



[Conclusions]

- Increased understanding of neurobiology is allowing for the development of effective, targeted pharmacotherapies
- State of the art, evidenced-based treatment must integrate behavioral and medical therapies to produce the best outcomes.