Pharmacology Update

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CENTER FOR EVIDENCE-BASED PRACTICES

A partnership between the Mandel School of Applied Social Sciences & Department of Psychiatry at the School of Medicine
Our Mission

The Center for Evidence-Based Practices (CEBP) at Case Western Reserve University is a technical-assistance organization that promotes knowledge development and the implementation of evidence-based practices (EBPs) for the treatment and recovery of people diagnosed with mental illness or co-occurring mental illness and substance use disorders.

Our technical-assistance services include the following:
- Service-systems consultation
- Program consultation
- Clinical consultation
- Training and education
- Program evaluation (fidelity & outcomes)
- Professional peer-networks
- Research
Service innovations for people with mental illness, substance use disorders

- **SAMI**
  - Substance Abuse & Mental Illness
  - Strategies for co-occurring disorders

- **IDDT**
  - Integrated Dual Disorder Treatment
  - The evidence-based practice

- **DDCAT**
  - Dual Diagnosis Capability in Addiction Treatment
  - An organizational assessment & planning tool

- **DDCMHT**
  - Dual Diagnosis Capability in Mental Health Treatment
  - An organizational assessment & planning tool

- **IPBH**
  - Integrated Primary & Behavioral Healthcare

- **SE/IPS**
  - Supported Employment/Individual Placement & Support
  - The evidence-based practice

- **TRAC**
  - Tobacco: Recovery Across the Continuum
  - A stage-based motivational model

- **MI**
  - Motivational Interviewing
  - The evidence-based treatment

**www.centerforebp.case.edu**
Learning Objectives

• 1. List newly-approved medications for the treatment of severe mental illness and substance use disorders.
• 2. Discuss common interactions between psychiatric medications and substances of abuse.
• 3. Identify strategies to increase medication non-adherence and to decrease substance use in patients with dual disorders.
General Guidelines for Psychopharmacology of Dual Disorders

• Determine mental illness and substance abuse diagnosis
  – Avoid treating substance induced symptoms
  – Do not withhold meds in presence of substance abuse

• Use meds with low abuse potential
  – Avoid creating new addictions (benzo & stim)

• Use meds with low lethality
  – High prevalence of overdose in dual disorders
  – Avoid tricyclics, MAO-I, toxic combinations
General Guidelines (continued)

• Consider selecting med that also reduces craving or substance use (SSRI, Clozapine)
• Consider prescribing meds specific for the treatment of addiction (naltrexone, disulfiram)
• Dispense limited amounts
• Monitor closely for response
Psychotropic Medications

- Mechanism of action
- Indications and therapeutic effects
- Adverse effects
- Common side effects
Antidepressants

- SSRIs: Prozac, Zoloft, Celexa, Lexapro, Paxil, Luvox
- SNRIs: Effexor, Cymbalta, Pristiq
- TCAs: amitriptyline, doxepin, desipramine, nortriptyline, imipramine, and several others
- MAOIs: Nardil, Parnate
- Other antidepressants: Wellbutrin, Remeron, Trazodone, Serzone
Antidepressants: Mechanism

• Most work by increasing the amount of neurotransmitters in the brain
• Common neurotransmitters that regulate mood:
  – Serotonin
  – Norepinephrine
  – Dopamine
Antidepressants: Indications

- Major Depression
- Bipolar Disorder, depressed phase
  - Use in combination with mood stabilizer
- Panic Disorder
- Obsessive-Compulsive Disorder
- PTSD
- Social Phobia
- GAD
- Smoking Cessation (Wellbutrin)
- Others: Bulimia, PMDD
Antidepressants: Adverse Effects

• SSRIs: generally very safe; “SSRI withdrawal”
• SNRIs: Effexor may increase diastolic BP
• TCAs: may be lethal in overdose in small amounts, cardiac toxicity, anticholinergic toxicity
• MAOIs: adrenergic crisis when dietary amines ingested, serotonin syndrome when mixed w/ SSRIs
Antidepressants: 
Adverse Effects

• Wellbutrin: ↑ seizure risk in doses over 450mg
• Trazodone: priapism
• Serzone: liver failure
Antidepressants:
Common Side Effects

• SSRIs: nausea, sweating, headache, insomnia, sedation, jitteriness, dizziness, sexual dysfxn.
• SNRIs: nausea, sedation, insomnia, dizziness
• TCAs: dry mouth, blurred vision, constipation, sedation, hypotension, tachycardia, urinary hesitancy
• MAOIs: hypotension, insomnia, agitation, sedation, sexual dysfxn, dry mouth, constipation, peripheral neuropathies
Antidepressants: Common Side Effects

- Wellbutrin: headache, dry mouth, agitation, weight loss, insomnia, constipation, tremor
- Remeron: sedation, weight gain, dry mouth, constipation, hypotension
- Trazodone: sedation, hypotension, headache
- Serzone: sedation, dizziness, dry mouth, nausea, constipation, blurred vision, headache
Conventional Antipsychotics

• Most work by blocking dopamine (D2) receptors

• Indicated for the treatment of psychotic disorders, including
  – schizophrenia
  – schizoaffective disorder
  – bipolar disorder, acute mania or psychosis
  – major depression with psychotic features
Conventional Antipsychotics

- **High Potency:**
  - Haldol
  - Prolixin
  - Stelazine
  - Navane
  - Orap

- **Moderate Potency:**
  - Loxitane
  - Moban
  - Trilafon

- **Low Potency:**
  - Thorazine
  - Mellaril
  - Serentil
Conv. Antipsychotics: Adverse Effects

- **NMS**: neuroleptic malignant syndrome
  - Potentially lethal; includes hyperthermia, autonomic instability, sweating, confusion, elevated CK, rigidity, fluctuating consciousness

- **Tardive dyskinesia**
  - Late-developing involuntary movement disorder, common in mouth, tongue, upper extremities
Conv. Antipsychotics: Adverse Effects

• Dystonia
  – Extremely uncomfortable involuntary muscle spasm; may be life-threatening if it occurs in the larynx

• Hyperprolactinemia
  – Associated with amenorrhea, galactorrhea, and sexual dysfunction
Conv. Antipsychotics: Common Side Effects

• **High Potency meds:**
  - Dystonia
    - Muscle spasms
  - Akathisia
    - Motor restlessness
  - Parkinsonism
    - Rigidity
    - Tremor
    - Bradykinesia

• **Low Potency meds:**
  - Sedation
  - Hypotension
  - Weight gain
  - Anticholinergic s/e
    - Dry mouth
    - Blurred vision
    - Constipation
    - Urinary retention
Novel Antipsychotics

• “SGAs”: second-generation antipsychotics
• Block D2 receptors, but also block serotonin receptors
• Advantages over conventional antipsychotics
  – Decreased EPS and little/no prolactin elevation; may be better for negative symptoms
• Clozapine: only med clearly more effective than all others for psychosis (esp. treatment resistant schizophrenia)
Novel Antipsychotics

- Clozapine = Clozaril
- Risperidone = Risperdal
- Olanzapine = Zyprexa
- Quetiapine = Seroquel
- Ziprasidone = Geodon
- Aripiprazole = Abilify
- Paliperidone = Invega
- Asenapine = Saphris
- Iloperidone = Fanapt
- Lurasidone = Latuda
Clozapine (Clozaril)

• Used for treatment-resistant psychosis
• Adverse effects:
  – Agranulocytosis in 1.6% of patients—must check WBC regularly
  – Dose-related seizures
• Side effects: sedation, tachycardia, weight gain, hypersalivation, dizziness, constipation, nausea, headache, hypotension, diabetes
Risperidone (Risperdal)

- May be more effective for (-) sx vs. conventional meds
- Does cause EPS (>6mg) and ↑ prolactin
- Side effects: dizziness, hypotension, headache, nausea, vomiting, anxiety, rhinitis, coughing, weight gain, QT prolongation
- Injectable form (Q 2 wks) → “Risperdal Consta” (doses: 12.5, 25, 37.5, 50)
Olanzapine (Zyprexa)

• Most closely resembles clozapine
• Also has antimanic and antidepressant effect vs. placebo
• Adverse effects: new-onset diabetes and diabetic ketoacidosis
• Side effects: sedation, weight gain, constipation, dry mouth, dizziness, elevation of SGPT
• Injectable form (Q2-4 weeks) → “Zyprexa Relprevv” (doses: 150, 210, 300, 405)
Quetiapine (Seroquel)

- Blocks dopamine, serotonin, alpha-adrenergic receptors
- Usually requires multiple daily doses
- Adverse effects: cataracts (in beagles); ? Risk in humans
- Side effects: hypotension, sedation, elevated LFTs, decreased T3 and T4, weight gain
Ziprasidone (Geodon)

- Blocks more serotonin than dopamine
- Must be given twice daily with food
- May cause less weight gain vs. others
- Adverse effects: causes QTc increase on EKG; caution in those with cardiac disease, low K or low Mg
- Side effects: nausea, sedation vs. activation, dizziness, hypotension
- Short-acting injection available
Aripiprazole (Abilify)

• Partial agonist at D2 and serotonin 1A receptors; blocks serotonin 2A receptors
• “dopamine-serotonin system stabilizer”
• Side effects: nausea, vomiting, anxiety, headache, sedation, hypotension, tachycardia, insomnia, akathisia, EPS, weight gain
Paliperidone (Invega)

• The primary active metabolite of risperidone
• Usual dose 6mg daily, max dose 12 mg daily
• Potential for GI obstruction
  – Patient may notice tablet-shaped “shell” in stool
• Injectable form: “Invega Sustenna” (Q4 weeks)
• Most common side effects:
  – extrapyramidal symptoms, tachycardia, akathisia, somnolence, dyspepsia, constipation, weight increased, and nasopharyngitis
Asenapine (Saphris)

• Blocks serotonin 2A, dopamine 2, alpha-adrenergic, and histamine receptors
• Fast-dissolving sublingual form (5 & 10 mg)
• Approved for both Schizophrenia and Bipolar I
• Most common side effects:
  – somnolence/sedation/hypersomnia (23%), dizziness (10%), EPS other than akathisia (7%), akathisia (5%) oral hypoesthesia (5%) and weight increased (5%)
Iloperidone (Fanapt)

- Blocks D2, D3, 5HT1a, alpha1 and alpha2c receptors; low affinity for histamine; no affinity for muscarinic receptors
- Approved for schizophrenia—6 to 12mg twice daily, max dose 24mg daily
- Metabolized by CYP2D6 and CYP3A4
- Can increase QTc
- Most common side effects:
  - Dizziness (20%), Somnolence (15%), Tachycardia (12%), Nausea (10%), Dry mouth (10%), Weight gain (9%)
Lurasidone (Latuda)

- Blocks D2, 5HT2a, alpha 2a and 2c; partial agonist at 5HT1a; little affinity for histamine and muscarinic receptors
- Approved for Schizophrenia—usual dose 40mg daily, max dose 80mg daily
- Cannot use with CYP3A4 inducers/inhibitors
- Most common side effects
  - Somnolence (22%), Akathisia (15%), Nausea (12%), Parkinsonism (11%), Vomiting (8%), Insomnia (8%)
Mood Stabilizers

• Before 2002, only 2 FDA-approved drugs for bipolar disorder
• Novel antipsychotics are also approved for Bipolar Disorder
• Many other drugs are used off-label
  – Many (not all) are also anticonvulsants
• Also used to treat sx of schizoaffective disorder, anxiety disorders, aggressive behavior, etc.
Mood Stabilizers

• FDA Approved:
  • Lithium
  • Valproic Acid
  • Lamotrigine

• Not yet approved:
  • Carbamazepine
  • Gabapentin
  • Topiramate
  • Tiagabine
  • Oxcarbazepine
Lithium

- Naturally occurring cation
- Blocks G-proteins and PIP (post-synaptically)
- Aim for blood levels of 0.6-1.2 mEq/L
- Adverse effects: hypothyroidism, renal effects, cardiac effects, teratogenic, lithium toxicity
- Side effects: sedation, decreased cognition or creativity, dry mouth, hand tremor, weight gain, polydipsia/polyuria, nausea, diarrhea
Valproic Acid

• Depakene and Depakote (divalproex sodium)
• Increases brain levels of GABA
• Blood levels of 50-100 mcg/mL are therapeutic in seizures
• Adverse effects: hepatotoxicity, pancreatitis, aplastic anemia, increase in LFTs, teratogenic
• Side effects: n/v/d, sedation, dizziness, tremor, weight gain, alopecia, ataxia, heartburn
Lamotrigine

• Anticonvulsant approved for Bipolar disorder
  – May be helpful during depressed phase
• Blocks glutamate & voltage-gated Na channels
• Adverse effects: severe rash, may lead to Stevens-Johnson syndrome; caution when mixing with valproic acid
• Side effects: benign rash, headache, blurred vision, ataxia, dizziness, nausea, fatigue
Carbamazepine

- Blocks sodium channels
  - Both voltage-gated and pre-synaptic
- Induces its own metabolism: must increase dose after 2-3 weeks
  - Lowers levels of many meds (BCP, antipsychotics)
- Adverse effects: aplastic anemia, hepatitis (both are rare but potentially fatal), teratogenic
- Side effects: dizziness, ataxia, sedation, dysarthria, nausea, rash, low sodium
Anxiolytics

- Many SSRIs treat anxiety disorders
- Other classes of meds include benzodiazepines and buspirone
- Benzodiazepines activate the GABA-A receptor complex
- Buspirone is a partial agonist at the serotonin 1A receptor
Benzodiazepines

• Large class of meds, usually listed by half-life
  – Long: Valium, Klonopin, etc.
  – Moderate: Ativan, Serax, etc.
  – Short: Xanax, Halcion, etc.

• Adverse effects: tolerance, dependence, withdrawal if suddenly stopped, memory impairment, ? Teratogenic

• Side effects: sedation, ataxia, dizziness
Buspirone

- Not effective for panic disorder, used for GAD
- Delayed onset (2-4 wks) vs. benzodiazepines
- Does not cause dependence or withdrawal
- Side effects: dizziness, nausea, headache, nervousness
Hypnotics: The “Z-drugs”

- Non-Benzodiazepine drugs that are used to treat insomnia; they *act like* benzodiazepines
- NOTE: they are still **controlled substances** and have addictive potential
- Zolpidem—Ambien
- Zaleplon—Sonata
- Zopiclone—Imovane (not available in US)
- Eszopiclone--Lunesta
Psychotropic Medications

• Risks and Interactions to consider when prescribing for clients with dual disorders
Potential Risks and Interactions in Clients With Dual Disorders

Antidepressant Medications

• Tricyclic antidepressants
  – Chronic alcohol use may induce metabolism and decrease levels
  – Additive cardiotoxicity with cocaine
Potential Risks and Interactions in Clients With Dual Disorders

Antidepressant Medications (continued)

• MAO Inhibitors
  – Tyramine present in alcoholic beverages may produce elevated blood pressure – hypertensive crisis
  – Potentiation of sympathomimetic effects of stimulants – hypertension/hyperpyrexia
  – Toxic interaction with meperidine (hypertensive crisis)
Potential Risks and Interactions in Clients With Dual Disorders

• SSRIs
  – Possibly lower seizure threshold

• Other antidepressants
  – Alcohol or benzodiazepines increase cognitive and motor side effects of mirtazapine
  – Venlafaxine elevates blood pressure, as does alcohol use and withdrawal
  – Bupropion lowers seizure threshold which could increase risk of seizure with cocaine use or alcohol withdrawal
Potential Risks and Interactions in Clients With Dual Disorders

Antipsychotic Medications

• Conventional
  – Possible increased risk of dystonia, akathisia, and tardive dyskinesia
  – Risk for hyperpyrexia in combination with stimulants
  – Cigarette smoking lowers blood levels
Potential Risks and Interactions in Clients With Dual Disorders

Antipsychotic Medications (continued)

• Novel (Atypical)
  – Risk of respiratory suppression with combination of clozapine and benzodiazepines
  – Alcohol may synergistically increase sedative effects of clozapine
  – Clozapine lowers seizure threshold
Potential Risks and Interactions in Clients With Dual Disorders

Mood Stabilizers

• Lithium
  – Specific interactions not documented

• Valproic acid
  – Potential for liver toxicity

• Carbamazepine
  – Potential for liver toxicity
Potential Risks and Interactions in Clients With Dual Disorders

**Anxiolytics**

- Benzodiazepines
  - Substantial abuse potential
- Buspirone
  - Specific interactions not documented
Potential Risks and Interactions in Clients With Dual Disorders

**Stimulants**
- Possible abuse potential

**Antiparkinsonian Medications**
- Possible abuse potential
Summary

– Use novel antipsychotics and newer antidepressants
  • Safer, reduce negative and cognitive symptoms
  • Enhance rehabilitation efforts
– Avoid benzodiazepines, stimulants, anticholinergics in active substance abusers
– Educate patients and families
  • Benefits of taking meds
  • Risks of substance use in conjunction with meds
– In general: do not withhold psychotropics in patients with substance use disorders
Medications to treat Substance Dependence

• Alcohol dependence
  – Disulfiram, acamprosate, naltrexone, topamax

• Opiate dependence
  – Naltrexone, methadone, buprenorphine

• Nicotine dependence
  – NRT, bupropion, varenicline, etc

• Other drug dependence?
Disulfiram

• Inhibits metabolism of ETOH (Alcohol dehydrogenase)
• Acetaldehyde accumulates and causes “hangover” HA, flush, malaise, nausea, vomiting, increased blood pressure
• Risk for hepatotoxicity
  – Monitor liver enzymes
Disulfiram

- Supervised administration 125-500 mg/day
  - Clinician or family 2-5 days/week
- Decrease alcohol use by deterring impulsive drinking
- May need to raise dose to elevate effect
- Reports of increased psychotic symptoms (rare)
- Educate, informed consent
- Appropriate in action stage treatment with motivated clients
Acamprosate

• A synthetic taurine derivative with a structural resemblance to gamma amino-butyric acid (GABA)
• Re-calibrates the GABA and glutamate neurotransmitter systems
• Recommend abstinence at start of treatment
• May reduce sx of post-acute withdrawal
  – Insomnia, anxiety, restlessness, dysphoria
Acamprosate

- Recommended dose: 666 mg three times a day
- Renal excretion; few drug-drug interactions
- Reduce dose in those with renal impairment
- Well-tolerated with discontinuation rate similar to placebo
  - Diarrhea, dose-related and transient, is most common side effect
- Safe in overdose
- Teratogenic in animals
Acamprosate:
Recent Research

• 2004: European meta-analysis of 17 clinical trials showed 36% continuous abstinence at 6 months (vs. 23% who took placebo)
• 2006: Two large U.S. trials failed to confirm efficacy
• Why the discrepancy?
  – More severe alcohol dependence in European trials
  – European patients had been abstinent longer than patients in U.S. trials
Naltrexone

• Blocks opioid receptors that are involved in the rewarding effects of drinking alcohol and alcohol craving
• Blocks effect of opiates
  – May precipitate opiate withdrawal in abusers
• Risk for hepatotoxicity
  – Monitor for liver enzymes
Naltrexone

- Efficacy highest in patients who can abstain for 4 to 7 days before initiating treatment
- No negative effect with use
- Some clients notice anxiolytic effect
Long-Acting Naltrexone

- Given monthly, 380 mg appears to have increased efficacy versus 190 mg
- May have increased efficacy for men vs. women, and those abstinent when medication is initiated vs. those still drinking
Long- Acting Naltrexone

- Discontinuation rate- 14% in patients on 380 mg a month, 7% in patients on 190 mg a month and placebo. Most common side effects: nausea, injection site reaction, headache.
- LFTs remained stable throughout the medication trial
Naltrexone:
Recent Research

• 2005: Cuts the relapse risk during first 90 days by 36% (28% relapse rate on oral naltrexone vs. 43% relapse rate on placebo)

• 2005: Injectable naltrexone resulted in a 25% reduction in proportion of heavy drinking days vs. placebo

• Overall: helps to curb consumption in patients with multiple “slips” but less effective in maintaining abstinence
Topiramate

• NOTE: unlike acamprosate, disulfiram, and naltrexone, topiramate is not FDA-approved for alcoholism
  – Approved for treatment of seizure disorders
• ↑ GABA and ↓ glutamate transmission
  – Precise mechanism of action is unclear
• Requires slow upward titration
• Efficacy has been established in individuals who were still drinking at the time of starting the medication
Topiramate:  
Recent Research

• 2 Randomized Controlled Trials (RCTs) showed significant increase in proportion of individuals with 28 consecutive days of abstinence (2003, 2007)

• Magnitude of the effect may be larger than that for naltrexone and acamprosate (!)
Other Agents to Reduce Drinking

- **Nalmefene** (opiate antagonist)
  - Reduces alcohol relapses; ↓ liver toxicity vs. naltrexone (no pill form available yet)

- **Ondansetron** (5HT-3 antagonist)
  - Reduced days of drinking for early onset alcoholism
Naltrexone

• **Opiate antagonist** to treat opiate dependence
• All effects of opiates are blocked
  – Must be detoxed and opiate-free or else will cause opiate withdrawal syndrome
• Non-compliance is the main barrier to success
• Most useful for highly motivated patients w/ external circumstances
  – Impaired professionals, parolees, probationers, etc
Methadone

• Opiate agonist to treat opiate dependence
• Well-studied and effective treatment
  – Normalizes function/return to work, decreases crime/violence, reduces HIV exposure
• Doses > 70mg/day generally better than low doses
• Enhanced services = improved outcomes
  – Counseling, medical, social/vocational services, etc
• No contraindication in SMI, though not well studied
Buprenorphine

- **Opioid partial agonist**
  - ↓ risk of overdose and ↓ abuse potential
  - May precipitate opiate withdrawal in dependent individuals

- Approved for treatment of opiate dependence
  - Maintenance dose in the range of 8-16 mg daily

- Sublingual route of administration
  - Subutex = Bup only; Suboxone = Bup + Naloxone
  - Suboxone Sublingual Film (Sept 2010 release)
Buprenorphine

- Approved in U.S. (2002) as office-based treatment vs. ‘methadone clinics’
- Individual doctors may treat up to 30 patients at a time, using an special DEA #
  - After 1 year, may increase to 100 patients
- Must be addiction medicine/addiction psychiatry certified OR complete 8-hr training
Buprenorphine: Recent Research

• The SAMHSA Evaluation of the Impact of the DATA Waiver Program
  – FINAL REPORT in March 2006
• Buprenorphine clinically effective and well accepted by patients.
• Waiver Program has ↑ the availability of medication-assisted treatment for opioid addiction.
• Adverse effects, whether involving diversion or adverse clinical events or public health consequences, have been minimal.
• The 30-patient limit on individual physician practices and cost / reimbursement issues may be decreasing potential access to treatment.
• For more information, see www.buprenorphine.samhsa.gov
Nicotine Replacement Therapy (NRT)- General Issues

• Recent practice guidelines have advised the use of NRT for all patients attempting to stop smoking
• Studies have consistently demonstrated that the addition of NRT to behavioral interventions doubles the quit rates
• Nicotine replacement products: gum (prescription, OTC), patch (prescription, OTC), nasal spray (prescription only), inhaler (prescription only)
NRT- Nicotine Patch

• Number of cigarettes smoked per day can be used to guide patch dosing

<table>
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<th>Cigarettes/day</th>
<th>Patch dose (mg/day)</th>
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<td>22-44</td>
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<tr>
<td>&gt;40</td>
<td>44+</td>
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Non-Nicotine Products for Smoking Cessation

• Bupropion
• Nortriptyline
• Clonidine
• Combination treatments
  NRT + Bupropion
  NRT + Naltrexone
Buproprion

- Marketed as antidepressant (Wellbutrin) and as smoking cessation aid (Zyban)
- Use at 300mg dose to help with smoking cessation
- May be more effective in combination with nicotine replacement
- Common side effects: headache, dry mouth, insomnia, activation, weight loss
Non- Nicotine Products for Smoking Cessation (2)

• **Varenicline** *(partial nicotinic receptor agonist)*
  – May be as efficacious or slightly more efficacious versus bupropion in leading to sustained cessation

• **Rimonabant** *(cannabinoid receptor antagonist)*
  – May promote less weight gain in quitters

- **Vaccine** *(NicVAX)*
Chantix (varenicline)

- Partial agonist at the Alpha-4,Beta-2 neuronal nicotinic acetylcholine receptor
- Start medication 1 week before the quit date
  - Day 1 to 3 → take 0.5mg daily
  - Day 4 to 7 → take 0.5mg twice a day
  - Day 8 to end of tx → take 1mg twice a day
- Take after eating and with 8 oz. of water
- Usually take for 12 weeks, but some make take for an additional 12 weeks
Chantix (varenicline)

- Common side effects: nausea, sleep disturbance, constipation, gas, vomiting
- If on dialysis or have kidney problems, may need to reduce the dose
- Has not been studied in pregnant or breastfeeding women
Chantix: Recent Research

- May 2006: FDA approves Chantix
- November 2007: FDA Early Communication
  - adverse event reports on Chantix related to changes in behavior, agitation, depressed mood, suicidal thoughts, and attempted and completed suicide.
- February 2008: FDA Public Health Advisory
  - Tell your health care provider about any history of psychiatric illness before you start taking Chantix.
  - Immediately tell a doctor if you or someone you care for has any changes in mood and behavior while being treated with Chantix
Cocaine Use Disorders-Pharmacotherapies (1)

• Agents possibly useful in withdrawal phase (None FDA approved)
  –Amantidine- indirect Dopamine (DA) agonist
  –Propranololol- ß- blocker

Cocaine Use Disorders-Pharmacotherapies (2)

Agents possibly useful in relapse prevention (None FDA approved)

– GABAergic Agents
  • Baclofen- GABA- B agonist
  • Topiramate- facilitates GABA neurotransmission, inhibits glutamate neurotransmission
  • Tiagabine- selective blocker of GABA reuptake transporter

– Disulfiram- blocks enzymatic degradation of cocaine and DA
Agents possibly useful in relapse prevention (cont.)

- **Modafanil**- enhances glutamate neurotransmission, reduces cocaine craving and may block cocaine-induced euphoria. NIH/ NIDA clinical trials in progress (Spring 2006)

- **Vaccine (TA-CD)**- human trials promising, need to produce minimum antibody level for efficacy in reducing cocaine self-administration. Human trials have used a series of three vaccinations.
Rimonabant and Marijuana Dependence?

- Rimonabant (Acomplia) available in Europe and S.A.
- Process in US (for Zimulti) has been stalled due to concerns re: severe psychiatric side effects
- CB1 and CB2 are 2 known cannabinoid receptors
  - Rimonabant is a selective CB1-A endocannabinoid receptor antagonist indicated for the treatment of obesity
- ??—Use in marijuana dependence
  - THC and anandamide activate these receptors, increasing appetite (marijuana “munchies”)

Med Non-adherence

• Assess and adjust for adherence
• Monitor dose-taking
• Consider med interactions, alcohol and cigarettes
• Retest for medication blood levels
Med Non-adherence (continued)

• Does the client understand the benefits of taking medication?
• Does the client believe that taking medication will help him or her make progress towards achieving personally desired goals?
• Are there bothersome side effects that need to be addressed?
• Does the client misattribute certain problems or symptoms to the medication that may be due to other causes?
Med Non-adherence (continued)

• Is the client afraid of specific interactions between medication and substances of abuse, leading to non-adherence when using substances?
• Does the client need a helpful prompt to overcome forgetfulness or disorganization?
• Can taking medication regularly be fit into the client’s daily routine?
• Is the medication regimen unnecessarily complicated?
Hope for Recovery

• People with dual disorders often lack experiences of success and have lost hope
• Medications in conjunction with other interventions can increase hope for a better life
  – Via reduction in bothersome symptoms
    • Target clients’ complaints + psychiatric symptoms
  – Via reduced craving for substances
  – Via support for sobriety
Summary

• Prescribing principles guide practice for patients with dual disorders

• All SAMI providers need to be familiar with:
  – Strategies to decrease medication non-adherence
  – Detoxification guidelines
  – Medication side effects and alcohol/drug interactions
  – Medications helpful in treating addiction
Resources

• Mary Brunette, MD of Dartmouth Psychiatric Research Center
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