INTERACTIONS BETWEEN PSYCHIATRIC MEDICATIONS AND SUBSTANCES OF ABUSE

Presented by:

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Myths

Treat the underlying problem, concurrent disorder vanishes

Medications are useless and/or dangerous while actively using substances

Truths

Integrative treatment is best practice

Can't wait for abstinence to treat; warn about bad combinations and possible consequences

CLASSES OF DRUGS

- Depressants
- Stimulants
- Hallucinogens
- Psychiatric Medications
- OTC (Over the Counter) Medications

PSYCHIATRIC MEDICATIONS

PURPOSE: to help treat chronic or acute psychiatric symptoms and disorders

- **antidepressants:** depression, anxiety, bulimia, ADHD, impulsivity, OCD
- **mood stabilizers:** bipolar disorder, anger, epilepsy
- **anti-psychotics:** schizophrenia, psychotic depression, agitation, bipolar disorder, severe anxiety, PTSD, refractory depression, borderline personality
- **sedatives**: short term relief for anxiety, insomnia
- **stimulants**: ADHD, refractory depression

OTC (OVER THE COUNTER) MEDICATIONS

- Caffeine – 'Wake-ups", Red Bull, etc.
- Ephedrine/Pseudoephedrine - Sudafed, cough & cold medications
- Dextromethorphan - Robitussin DM
- Dimenhydrinate - Gravol
- Diphenhydramine - Benadryl, Nytol, Sleep Eze D
- Codeine preps – Tylenol #1
- Guarana, energy drinks

WHAT SHOULD YOU BE WORRIED ABOUT?

OVERDOSE RISK

- **DEPRESSANTS**
  - Central Nervous System (CNS) depression, respiratory depression, coma, death
  - **Highest risk** with opioids, barbiturates, alcohol
  - Benzodiazepines in high doses, especially combined with alcohol &/or other depressants
- **STIMULANTS**
  - very unpredictable; some risk due to mix of drug & activity/exertion
  - dehydration, overheating, cardiovascular problems, seizure
  - paranoia, agitation, hallucinations
- **HALLUCINOGENS**
  - Not much direct risk from overdose per se, however psychiatric effects can lead to dangerous situations (e.g. a “bad trip”), or trigger underlying disorder

WITHDRAWAL RISK

- Potentially life-threatening withdrawal (seizures, hallucinations)
  - alcohol
  - barbiturates
  - benzodiazepines (from high doses)
- Generally not life-threatening:
  - opioids
  - stimulants

DRUG INTERACTION THEORY

When two or more substances are taken at or near the same time an interaction may occur, which may create new effects that are different than those from either drug taken alone.

They may:

- **act independently** of each other
- **enhance each other's effects**
  - Potentiation: multiplying the effects of two drugs rather than simply doubling the dose (e.g. 1+1=3)
- **have an antagonistic effect**
  - some drugs decrease or block the effects of others

Drug Interactions may occur when combining prescribed psychotropic medications and:

- other prescribed drugs (including medications prescribed for medical conditions)
- over-the-counter medications
- herbal and natural products
- alcohol
- tobacco
- substances of abuse

Challenges in Anticipating Interactions

- Drug potency, strength, dose
- Drug purity – contaminants, adulterants
- Research studies lacking, inconclusive, unethical
- Drug interaction information based on unproven theory or case reports with incomplete data
- Clients not forthcoming
- Over-the-counter drugs, herbal products and grapefruit juice not often reported by clients

Challenges in Anticipating Interactions….

DEPRESSANTS

- 2 bottles Oxycontin
- 12 Vicodin (hydrocodone + acetaminophen)
- 2 bottles of Nyquil (doxylamine, pseudoephedrine, acetaminophen, DM)
- 18 chlorpheniramine antihistamines
- 10 sleeping pills (benzodiazepines?)
- Vodka

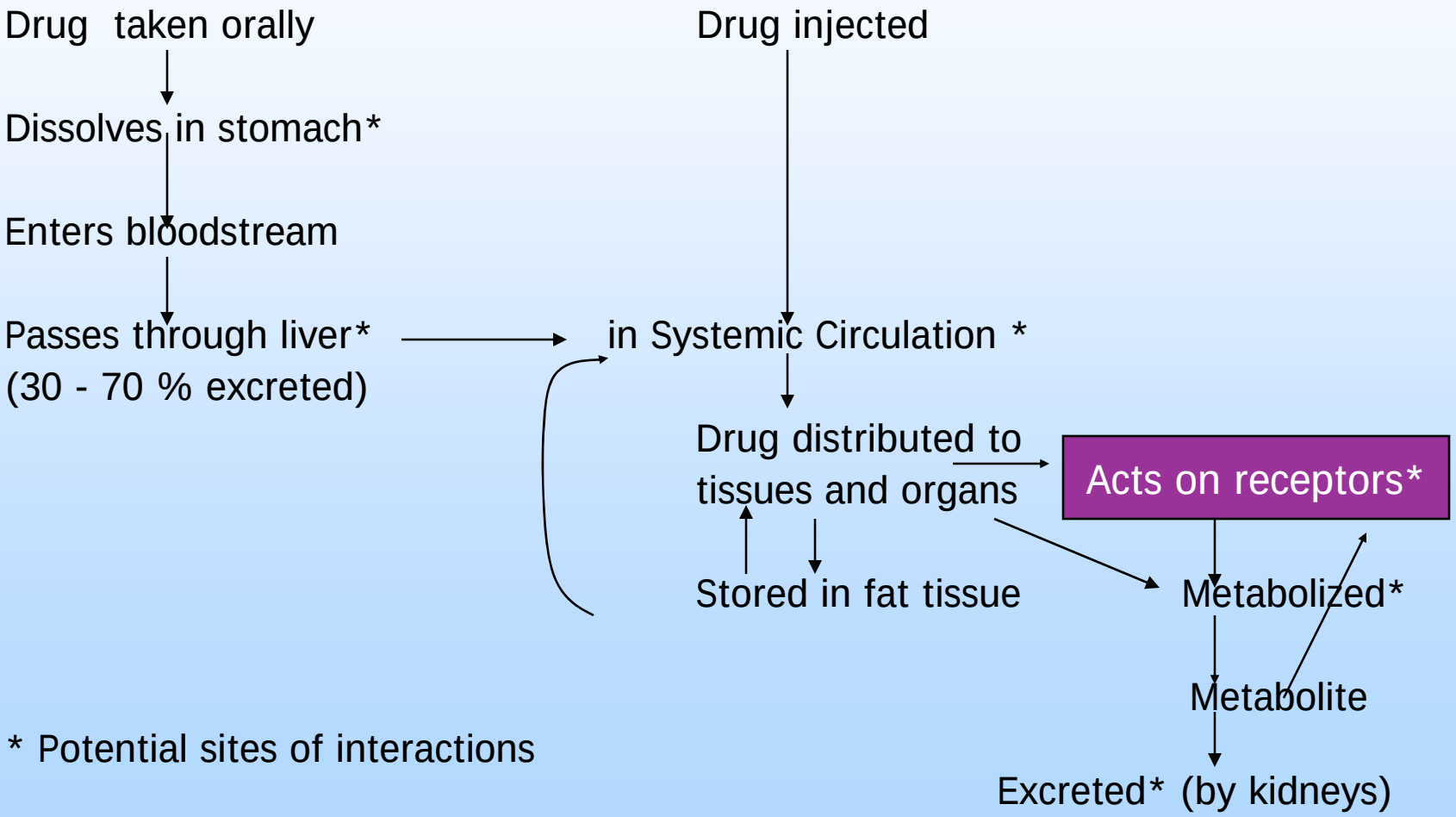
STIMULANTS

- 6 Ritalin (methylphenidate)
- 20 clenbuterol (beta-2-agonist used as diet pill)
- 18 herbal uppers (ephedra?)
- energy drink (caffeine?)

GI MEDS

- 8 antacid reflux tabs
- 1 bottle of stomach upset mixture Pepto Bismol
- 10 Zantac (ranitidine) tablets

Drug Interaction: Drug Effects in the Body



* Potential sites of interactions

Pharmacodynamic Interactions:

Based on the way the drug works on the body

Additive / Synergistic - two drugs with the same effect

- increased drug effects (e.g. euphoria, relaxation)
- increased side effects (e.g. drowsiness, nausea, overdose)

Opposing – two drugs with opposite effects

- do not necessarily 'cancel each other out'

Counterproductive – drug exacerbates underlying condition; more of a disease/drug interaction than true drug interaction

Pharmacokinetic Interactions:

One drug changes how the body handles other drugs, either increasing or decreasing blood levels of one or both drugs

Absorption:

- drug movement from administration site to bloodstream

Distribution

- drug movement from bloodstream to the rest of the body
- psychotropics must cross the *blood brain barrier* to reach their site of action (p-glycoprotein interactions?)

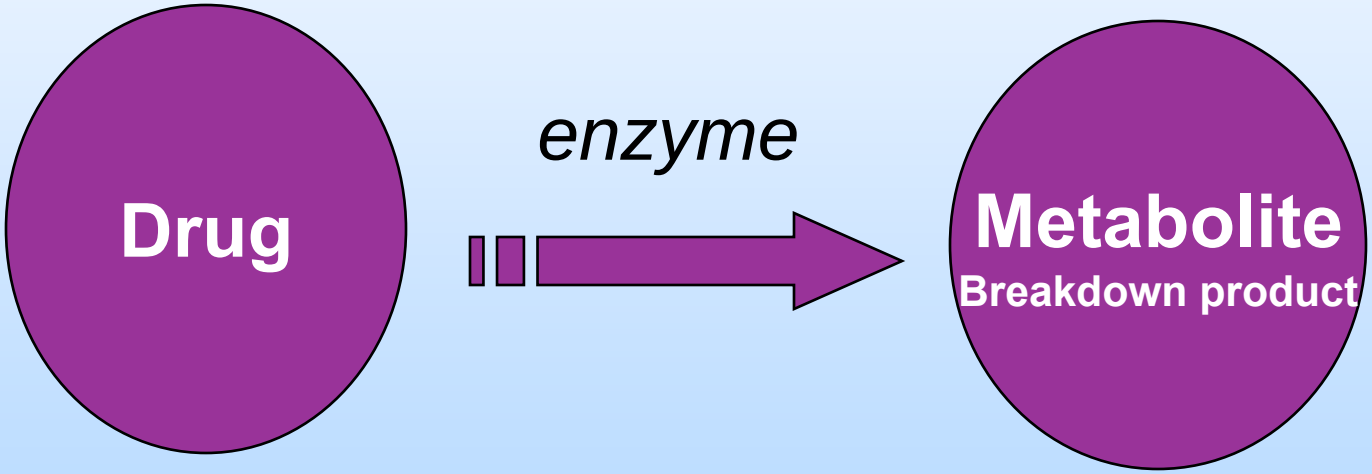
Metabolism

- transformation of drug by chemical processes

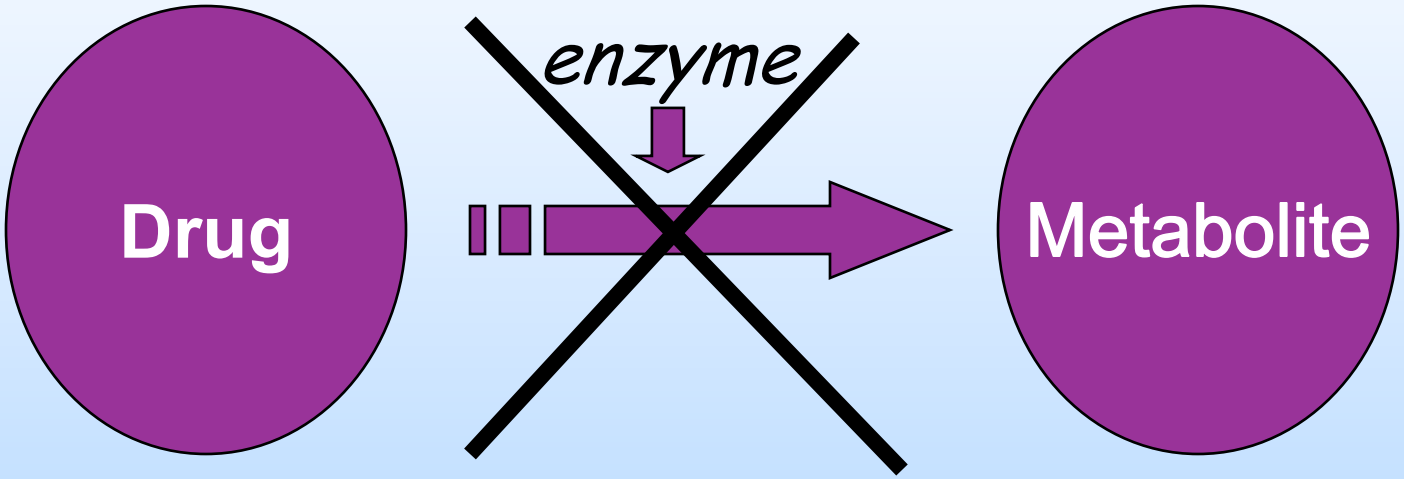
Excretion

- routes of leaving the body for drug and drug metabolites

Metabolism



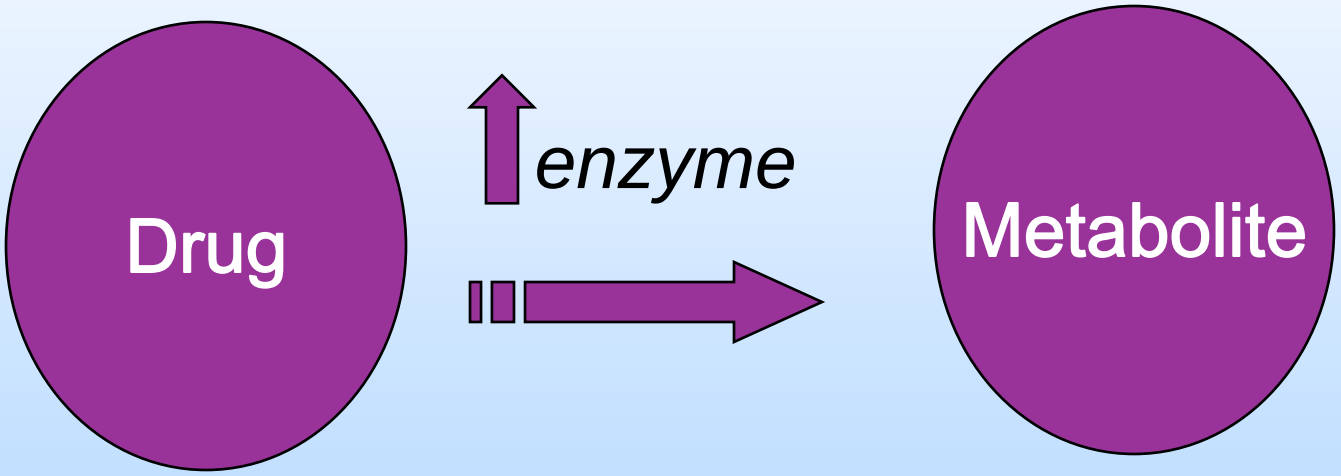
Inhibitor= drug that blocks or slows down the enzyme



Examples of Inhibitors:

- some antidepressants eg. fluoxetine
- some antibiotics eg. clarithromycin
- some antifungals eg. ketoconazole
- grapefruit juice
- acute alcohol use

Inducer = drug that stimulates the enzyme



Examples of Inducers: carbamazepine, phenobarbital
chronic alcohol use
St John's Wort
smoking (combustion products, not the nicotine itself)

Trying to Anticipate Drug Interactions

- Experiences with drugs in same class or with similar effects
- Case reports in the literature
- Identify liver enzymes that metabolize the drug
- Experiments with healthy volunteers
- Look at the pharmacological profile (i.e. what receptors or neurotransmitters are involved)
- Concurrent disorders studies (e.g. study of psychiatric medication to decrease cravings and substance use)
- “Anecdotal” reports from clients (?)

IMPACT OF SUBSTANCE USE ON SYMPTOMS AND DISORDERS

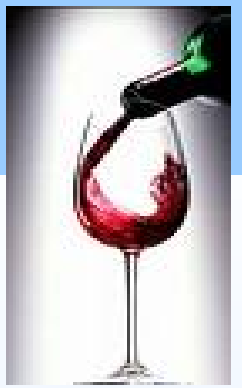
REASONS FOR USING SUBSTANCES

- To help to relieve isolation, loneliness, boredom, despair
- To facilitate peer/social engagement
- To gain a general sense of well-being
- To self-medicate symptoms(?)
- To treat medication side effects (?)

Self Medication Using Substances to Treat Symptoms and Side Effects

- Positive symptoms: alcohol, cannabis used to sedate, numb, attempt to suppress auditory hallucinations
- Negative or dysphoric symptoms: nicotine, alcohol, cannabis, cocaine used to try to increase mood
- Cognitive symptoms: nicotine, alcohol, cannabis, cocaine commonly used to try to increase focus/attention
- Extrapyramidal symptoms (EPS): nicotine, alcohol, cannabis, cocaine commonly used to decrease parkinson-like side effects

Mood Disorders and Depressants



- Can **initially** cause disinhibition, increased mood, 'self-esteem', decrease anxiety, numb unpleasant feelings, create 'escape' from problems and symptoms
- Can make symptoms of depression and anxiety worse
- Can mask manic symptoms
- Can result in mixed episode in bipolar disorder
- Can further impair cognitive symptoms, decision making abilities
- Will also likely lead to increased sedation, confusion and disorientation – especially combined with medications

Mood Disorders and Stimulants

May be used in an attempt to increase mood, self-esteem, alertness, counteract effects of sedating medications

Cocaine & Amphetamine

- worsen the course of bipolar disorder
- may induce mania, mixed episode

Caffeine

- worsens anxiety, agitation, insomnia

*'**Crash'** following stimulant use can make depressive symptoms worse, increase suicidality

Mood Disorders and Ecstasy

- May be an attempt to mask depressive symptoms, BUT
- 1 to 4 days after ecstasy use: depression-like symptoms
  - poor sleep, fatigue, lack of appetite
  - lower concentration, memory problems
  - depressed mood
  - anxiety, irritability, paranoia
  - anhedonia, lower libido
- Scores approaching Clinical Depression Curran & Travil '97
- Case reports: Suicidal ideation / Suicide days after use

Benazzi and Mazzoli, 1991, Cohen 1996

Anxiety Disorders and Stimulants

- excessive caffeine or stimulant use - mimic symptoms of anxiety, counteract sedation and increase insomnia
- increased heart rate, nervousness, flushed face, gastrointestinal disturbances, muscle twitching, palpitations and sweating
- may request higher doses of benzodiazepines to mask both underlying symptoms AND stimulant effects

Schizophrenia and Alcohol

- People with psychosis use alcohol primarily euphoric/relaxing effects
- May increase dementia/ mood disorder, anxiety/sleep disorder/ sexual problems

Schizophrenia and Cannabis

- Hallucinogen - mimics some symptoms of schizophrenia (hallucinations, delusions, anxiety, depersonalization, paranoia)
- impaired motor coordination, confusion, restlessness, and memory loss
- decrease the effectiveness of the antipsychotic drugs by making the psychosis worse and increase relapse

Schizophrenia and cocaine

- reduces negative symptoms & relieves feelings of depression
- may feel that it increases 'focus' or attention
- may cause dystonia and/or dyskinesia
- increases agitation and propensity for violence

Schizophrenia and Smoking

- Smoking rate in general population: 25-30%
- Smoking rate with schizophrenia: 70-90%
- nicotinic receptors in brain are somehow related to both the disorder and to the pharmacology of some antipsychotics
- Reduces sensory gating deficits transiently and may improve attention
- Enhances acetylcholine release; may help memory, EPS
- Smoking decreases sedation and orthostatic hypotension
- EPS & TD rates may be higher in smokers

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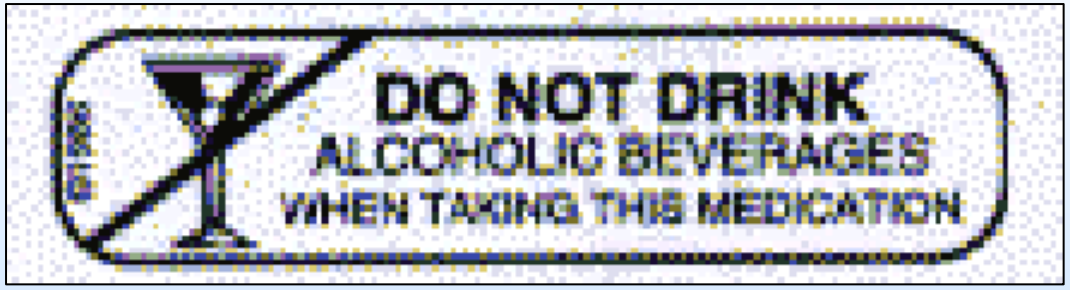
SPECIFIC DRUG INTERACTIONS

Alcohol and Antidepressants?



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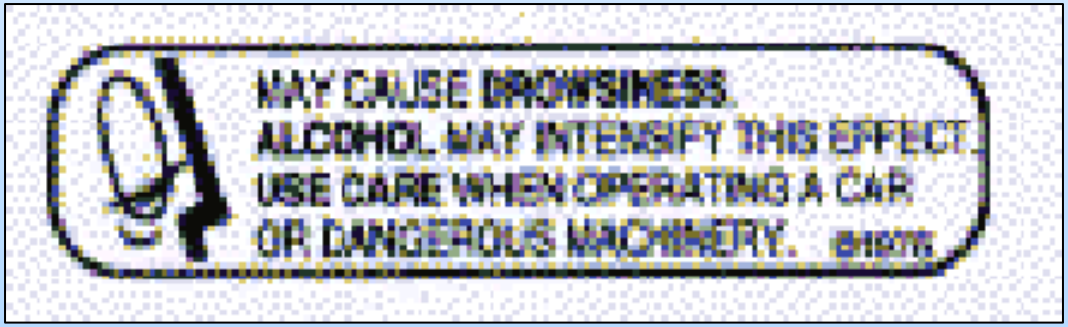

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Alcohol and…

Antidepressants

- may interfere with therapeutic effects

Mood stabilizers

- potentiates intoxicating effect

Benzodiazepines

- potentiates depressant effects
- increased potential for overdose

Antipsychotics

- side effects worsened
- increase the CNS depressant effects
- increase the risk of tardive dyskinesia

Antidepressants and Stimulants

- can increase jitteriness, anxiety
- 'crash' after use can increase depressive symptoms
- increased heart rate in combo with some tricyclic antidepressants (TCAs, eg. desipramine)
- remember that caffeine is a stimulant, and it is in food and beverages other than coffee!
- possible hypertensive reaction if taken with MAOIs (monoamine oxidase inhibitors)

Antidepressants and Ecstasy

- **SSRI + ecstasy → serotonin syndrome?**
  - Both increase serotonin availability in synapses; therefore, can be associated with a risk of serotonin syndrome
  - Pharmacokinetic interactions can also occur
    - Paroxetine & fluoxetine both inhibit metabolism of ecstasy, possibly leading to increased levels
  - SSRIs may be used to in an attempt enhance the effect of ecstasy; raver chat sites also theorize that SSRI can protect against possible neurotoxicity of ecstasy

SSRI's and Ecstasy

- Case reports of fluoxetine (Prozac) pre-treatment
- Typically 20 mg approx 40 mins prior to **Ecstasy** ingestion (125-250 mg)
- "calmer", "less jaw clenching", "improved sleep", "less thirst" McCann & Ricaurte. (1992). J Clin Psychopharm. 13(3): 214-217

- NOT proven to prevent neurotoxicity in humans
- No studies to-date examining use of SSRI pre-treatment and depression

Antidepressants and Ecstasy

SSRI + ecstasy → blunting of ecstasy effects?

- In a controlled experiment, citalopram reduced most of the subjective effects of ecstasy (heightened mood, increased self-confidence, extroversion, intensification of sensory perception).

- Proposed that citalopram, by binding to the pre-synaptic serotonin reuptake pump, blocked ecstasy's ability to release serotonin from neurons.

- Anecdotal reports of SSRIs seem to indicate a blunting the effect of ecstasy, but important for clients to know that the effect of combining SSRIs with ecstasy is unpredictable

Antidepressants and Cannabis

- May use cannabis to try and decrease anxiety or to help sleep, but over time the cannabis can exacerbate depressive symptoms and sometimes cause increased anxiety and sleep disturbance
- Some reports of combination with tricyclic antidepressants causing lightheadedness, rapid heart rate, labile mood and delirium
- May increase anticholinergic side effects (e.g. dry mouth) and risk of orthostatic hypotension

Antipsychotics and Smoking

- Smoking stimulates metabolizing enzyme CYP1A2 resulting in faster clearance of some antipsychotic drugs (e.g. clozapine, olanzapine)
- Can decrease blood level concentrations of some antipsychotics by 20-100%
- Can decrease both the efficacy and side effects
- People who smoke often need higher doses of antipsychotic meds
- Smoking Cessation…. What happens? May have increased side effects, may need to decrease dose

Antipsychotics and Cocaine

- People with symptoms of psychosis may have a relapse of symptoms

- antipsychotics can diminish the pleasurable effects of cocaine and amphetamines by blocking their access to dopamine receptors.

Antipsychotics and Cannabis

- can increase the side-effects of antipsychotic meds
- Cannabis can:
  - lower blood pressure
  - increase CNS depression (e.g., sedation, confusion)
  - increase extrapyramidal side-effects, such as stiffness, tremor and difficulty initiating movement
  - Increase anticholinergic side-effects such as constipation, dry mouth and urinary retention.
- May stimulate drug metabolizing enzymes resulting in faster clearance of antipsychotics from the body (?)

Antipsychotics and caffeine

- Caffeine may inhibit the metabolism of several antipsychotics—most notably clozapine and olanzapine.
- important to tell clients to keep their caffeine intake relatively consistent
- A person taking antipsychotics should not change his or her caffeine intake without consulting physician
- a relapse of symptoms could result if the plasma level of antipsychotic drops low enough.

SUMMARY AND CLINICAL POINTERS

Why Talk about Side Effects?

- try to reassure client that most common side effects will go away after a couple of weeks or can be managed
- be honest so client has real insight as to what to expect and how to deal with side effects
- informed client– more empowered, less risk of relapse
- less reason to self-medicate
- improves compliance
- increase therapeutic alliance

Medication Management in Concurrent Disorders

- Safety issues (withdrawal, overdose, drug interactions)
- Detox with meds in an inpatient setting if possible
- Stabilize severe mental illness
- Treat major mental illness REGARDLESS of ongoing substance use
- Continue medications with provision you are working toward substance control

Medical Management of Concurrent Disorders

- Not an exact science
- Ongoing developments in the relationship and aim for treatment
- Continuous re-evaluation of symptom causes and medication choices
- Think of both disorders when making medication choices
- Consult with experts if you need to

Management of Drug Interactions

- Inform all prescribers about current medications - GP's, psychiatrists, dentist
- When possible take all prescriptions to one pharmacy so there is one computer record
- Ask pharmacist about OTC meds & check ingredient list on combination products (will sometimes change!!)
- Scheduling different dosing times can sometimes minimize interaction (but not always)
- Some interactions cannot be avoided, so close monitoring and dosage adjustment is essential

Management of Drug Interactions

- Some websites have drug interaction programs, but significance of each interaction needs to be assessed and put in proper context by MD or pharmacist
- Some interactions are more theoretical, and may not have clinical significance
- Some drug interactions are good
  - Using a 2nd drug to decrease a "bad" metabolite of the first drug
- Not all combinations can be anticipated or tested, so new drug interactions are being discovered every day!!

What Can You Do?

- Know your clients. They can be your best resource.
- Be aware of abrupt changes in their physical and mental state (document these changes)
- Communicate with other caregivers
- Always ask & educate clients about substance use & abuse, including harm reduction strategies and overdose prevention
- **Know when the situation requires immediate clinical intervention!!**
- Non-urgent inquiries: CAMH - Addiction Clinical Consultation Services (ACCS) (1-800-720-2227)

Websites

www.erowid.org
(especially 'search' and experience vaults)
www.camh.net
www.healthyontario.com
www.mentalhealth.com
www.crazymeds.us
www.nami.org
www.nida.nih.gov
www.bcwomens.ca/info/shop.htm
- C&W bookstore – Youth Health - "Cocktails"