Bridging the Gap: Medical and Mental Health Medications

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Disclosures

I do not have (nor does any immediate family member have) actual or potential conflict of interest, within the last twelve months; a vested interest in or affiliation with any corporate organization offering **financial support or grant monies** for this continuing education activity; or any affiliation with an organization whose philosophy could potentially bias my presentation

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Pharmacist Learning Objectives

- Identify and manage clinically significant drug-drug interactions between medical and psychotropic medications
- Recognize medical medications that may contribute to psychiatric symptoms
- Identify and acknowledge duplications in therapy regarding mental health and medical medications
- Review common laboratory values affected by mental health medications

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Technician Learning Objectives

- Identify psychotropic medications that have a higher potential for drug-drug interactions
- Recognize medical medications that may cause psychiatric symptoms
- Identify classifications of psychotropic and medical medications
- Review common laboratory values affected by psychotropic medications

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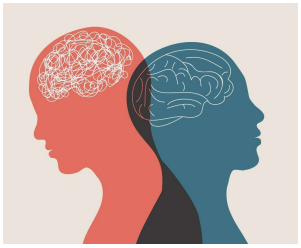
Introduction

Comorbidity

- The simultaneous presence of two or more diseases or medical conditions in a patient



30% of individuals have a co-occurring mental health and chronic physical condition

Why Do We Care?

Mental Health Disorder

Physical Condition

Gentil L, Grenier G, Meng X, Fleury MJ. Impact of Co-occurring Mental Disorders and Chronic Physical Illnesses on Frequency of Emergency Department Use and Hospitalization for Mental Health Reasons. Front Psychiatry. 2021 Nov 22;12:735005

More medications results in greater risk for drug interactions, adverse effects, and duplications in therapy

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Part 1: Clinically Significant Drug-Drug Interactions

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Background

- Drug Interactions
  - Theoretical or Clinically Significant
    - Clinically significant interactions involve narrow therapeutic window drugs
  - Pharmacokinetics or Pharmacodynamics

Cytochrome P450 Family	
Substrate	Drugs that are metabolized by cytochrome enzymes
Inducer	Enhance the activity of the cytochrome enzymes
Inhibitor	Decrease the activity of the cytochrome enzymes

Olanzapine is a substrate of CYP 1A2
Chemicals formed in cigarette smoke is an inducer of CYP 1A2

Clinical Outcome: Patients who start or quit smoking may need a dose adjustment of olanzapine. The chemicals cause olanzapine to be metabolized from the body quicker

Demler TL. Psychiatric Drug-Drug Interactions. US Pharm. 2012;37(11):HS16-HS19

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Case 1: Drug-Drug Interactions

Use the provided information to identify potential drug interactions for this patient

- 41 year old female
  - Presenting Symptoms: fatigued, poor concentration, hopeless mood
  - PMH: Deep Vein Thrombosis, Bipolar Disorder, Breast Cancer in remission
  - Vitals/Labs: BP 142/88 mmHg, 5'2" 145 LBS, CrCl 89 ml/min, LFTs- WNL
  - Current Medications: Tamoxifen 20mg daily, Ibuprofen 800 mg daily PRN pain, Carbamazepine 200mg daily, Warfarin 7.5 mg daily, Paroxetine 10mg daily, Multivitamin daily

What drug interactions are of concern?
How can each of the drug-drug interactions be managed?

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Clinically Significant Drug-Drug Interactions

Anticoagulants, Antiplatelet		
Name	**Indications**	**Drug Interaction Consideration**
Warfarin	Afib, DVT, PE	S enantiomer (potent): substrate of CYP 2C9, 3A4 R enantiomer: substrate CYP 1A2, 2C19, 3A4
Apixaban, Rivaroxaban	Afib, DVT, PE	Substrate of CYP 3A4
Clopidogrel	Cardiovascular events	Metabolized by CYP 2C19 to active metabolite

- Warfarin
  - INR is used to monitor efficacy, Goal 2-3
  - Be aware of inhibitors/inducers of CYP 2C9 and 3A4
- Clopidogrel
  - Metabolized to an active form. Inhibition results in increased risk of stroke
- Antidepressants + Bleeding
  - Serotonin inhibits platelet aggregation
  - Increased risk of bleeding when combined with NSAIDs, anticoagulants, antiplatelets

Look Out For:
Carbamazepine
Phenobarbital
Valproic Acid
Fluvoxamine
Modafinil
Fluoxetine

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Clinically Significant Drug-Drug Interactions

Anticancer Agents		
Name	**Indication**	**Drug Interaction Consideration**
Tamoxifen	Treatment of Breast Cancer	Metabolized by CYP 2D6 to active metabolite

- Tamoxifen
  - Prodrug that must be metabolized to an active form
  - Inhibition results in 1.9 fold increased risk of breast cancer recurrence

Look Out For:
Bupropion
Fluoxetine
Paroxetine

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Clinically Significant Drug-Drug Interactions

Antiretroviral Agents		
Name	**Indication**	**Drug Interaction Consideration**
Protease Inhibitors: Ritonavir	Treatment of HIV	Strong CYP 3A4 Inhibitor

- Protease Inhibitors
  - May increase the concentration of mental health medications
  - Benzodiazepines, Antipsychotics
  - Clinical Recommendation
    - Monitor for increased adverse effects in patients on protease inhibitors and mental health medications
    - Dose adjustment (down) may be necessary

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Clinically Significant Drug-Drug Interactions

Beta Blockers		
Name	**Indication**	**Drug Interaction Consideration**
Metoprolol Nebivolol Propranolol Timolol	Hypertension	Substrate of CYP 2D6

- Beta Blockers
  - Propranolol is used for tremors, nightmares, performance anxiety
  - Increased concentration may result in drops in blood pressure, dizziness, fatigue, syncope
  - Clinical Recommendation
    - Monitor heart rate and blood pressure
    - Counsel patient on: dizziness and fatigue

Look Out For:
Bupropion
Fluoxetine
Paroxetine

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Clinically Significant Drug-Drug Interactions

- Hormone Contraceptives
  - Estrogen is metabolized by CYP3A4
  - Inducers may decrease estrogen component by 50%
    - Increased risk of unintended pregnancy
  - Clinical Recommendation
    - Utilize a backup method of contraception while using and 4+ weeks after discontinuing
    - Progesterone only contraceptive may be appropriate

Look Out For:
Carbamazepine
Phenobarbital
Topiramate
Oxcarbazepine

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Clinically Significant Drug-Drug Interactions

- Lithium
  - Completely renally cleared
  - Cytochrome P450 enzymes, not a concern
  - Other medications may increase the risk of toxicity
    - ACE Inhibitors, ARBs, Diuretics, NSAIDs
  - Clinical Recommendations
    - Monitor lithium levels 12 hours post dose every 6 months, more if indicated
    - Stay well hydrated during summer months
    - Diet should be consistent, report changes

Look Out For:
ACE Inhibitor
ARBs
Diuretics
NSAIDs
Caffeine

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Lithium Toxicity

- Mild Toxicity (1.5-2.0 mEq/L)
  - GI (N/V, loose stools, diarrhea)
  - CNS (lethargy, drowsiness, coarse hand tremor, muscular weakness)
- Moderate Toxicity (2.0 – 2.5 mEq/L)
  - GI (N/V diarrhea)
  - CNS (confusion, nystagmus, ataxia, myoclonic twitches, dysarthria)
  - Cardiac (EKG changes)
- Severe Toxicity (> 2.5 mEq/L)
  - GI (N/V diarrhea)
  - CNS (grossly impaired consciousness, seizures, syncope, coma)
  - Cardiac (EKG changes, death)
  - Kidney (renal insufficiency)

Treatment: Discontinue medication → Gastric Lavage → Supportive Care
Severe Toxicity: Hemodialysis (Goal Serum Concentration 1 mEq/L)

Gitlin, M. Lithium side effects and toxicity: prevalence and management strategies. *Int J Bipolar Disord.* 2016;4(27)

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Case 1: Drug-Drug Interactions

- 41 year old female
  - Current Medications: Tamoxifen 20mg daily, Ibuprofen 800 mg daily PRN pain, Carbamazepine 200mg daily, Warfarin 7.5 mg daily, Paroxetine 10mg daily, Multivitamin daily

What drug interactions are of concern?
- Paroxetine inhibits Tamoxifen's conversion to active form via CYP2D6
- Warfarin + Ibuprofen + Paroxetine results in an increased risk of bleeding
- Carbamazepine increases the clearance of Warfarin which may increase risk of clotting, reflected by a lower INR

How can each of the drug-drug interactions be managed?
- Consider alternative antidepressant: Venlafaxine, Mirtazapine
- Monitor INR more frequently, adjust Warfarin dose as indicated
- Counsel and monitor for easier bleeding, bruising

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Part 1: Take Home Points

- When adding or removing medications – dose adjustments may be warranted
- Enzyme induction takes time to resolve
  - Interaction may occur after drug discontinuation
- Enzyme inhibition is dose dependent and resolves more quickly
- Potential Psychotropics
  - Antipsychotics: Ziprasidone, Paliperidone
  - Antidepressants: Mirtazapine
  - Benzodiazepines: Lorazepam, Oxazepam, Temazepam

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Part 2: Medical Medications and Psychiatric Symptoms

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Case 2: Psychiatric Symptoms

Use the provided information to identify risk factors for this patient

- 78 year old male, diagnosis of depression
  - Presenting Symptoms: auditory hallucinations, paranoid behavior, flat affect
  - PMH: Hyperlipidemia, Smoker 1PPD, Parkinson's disease
  - Vitals/Labs: BP 117/81 mmHg, 6'1" 175 LBS, CrCl 81 ml/min, LFTs - WNL
  - Current Medications: Carbidopa/Ldopa 25/250 QID, Atorvastatin 20mg daily, Vitamin D 50,000 units weekly

Which medications may increase the risk of psychiatric symptoms?
What risk factors does the patient have that may contribute to psychiatric symptoms?

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Background

- Medical medications resulting in psychiatric symptoms
  - The onset is typically spontaneous
  - May occur at normal dose or dose increase, withdrawn
  - The cause is due to pharmacokinetic and pharmacodynamics reason

Definitions	
Pharmacokinetic	The absorption, distribution, metabolism, and excretion of a drug
Pharmacodynamic	The physical affects of a drug

ropinirole - dopamine agonist used for Restless Leg Syndrome

It increases dopamine in the brain, which may result in psychotic symptoms or exacerbation of pre-existing psychotic symptoms

Raju, N. N.; Kumar, K. S. V. R. Naga Pavan; Nihal, Gyan[1]. Management of Medication-Induced Psychiatric Disorders. Indian Journal of Psychiatry 64(Suppl 2):p S281-S291

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Medical Medications Psychiatric Symptoms

Name	Indication	Psychiatric Symptoms
Antiparkinson's Agents	Parkinson's disease	Highest risk, 60% of cases
Digoxin	Heart failure, Atrial Fibrillation	Secondary to toxicity or electrolyte imbalance Dose dependent
Mefloquine	Malaria treatment/prophylaxis	Dose dependent Onset within hours
Chloroquine	Malaria treatment/prophylaxis	Residual symptoms may occur
Isotretinoin	Acne	Conflicting data secondary to age and indication
Interferon Alpha	Viral infection, Hepatitis C	10% of cases Residual symptoms may occur
Corticosteroids	Various	Onset within 1 day Prednisone highest risk > 40mg/day
Anabolic Androgen Steroids	Various	Risk upon withdrawal More common in abuse
Beta Blockers	Hypertension, Various	Lipophilic beta blockers have greatest risk

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Medical Medications Psychiatric Symptoms

- Risk Factors
  - Medication Specific
    - Polypharmacy, high doses, route of administration, fast administration, narrow therapeutic window
  - Patient Specific
    - Past or present mental health disorder, hepatic insufficiency, age, stress, postpartum
- Management
  - Self limiting symptoms, symptoms resolve within a day
  - Lower the dose
  - Utilize antipsychotics
  - Retrial at lower dose may be appropriate

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Case 2: Psychiatric Symptoms

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Which medications may increase the risk of psychiatric symptoms?
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Part 3:
Duplications in Therapy

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Case 3: Duplications in Therapy

- 87 year old male
  - Presenting Symptoms: faint, dizziness upon standing
  - PMH: BPH, Anxiety, Hypertension, Diabetes, PTSD
  - Vitals/Labs: BP 91/43 mmHg, 5'9" 125 LBS, CrCl 67 ml/min, LFTs – slightly elevated
  - Current Medications: Venlafaxine 150mg daily, Prazosin 2mg HS, Propranolol 10mg PRN, Metformin 500mg BID, Tamsulosin 0.4mg daily, Lisinopril 10mg daily

What duplication of therapy is present?

What are the implications of the duplication of therapy?

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Duplication of Therapy

Medications utilized for hypertension have the biggest implication

Name	Mental Health	Medical
Clonidine	ADHD, Withdrawal, Insomnia, Tourette's syndrome	Hypertension
Guanfacine		Hypertension
Prazosin	Nightmares	Hypertension
Propranolol	Anxiety, Tremors, Migraines	Hypertension, Angina

Management

- Be aware of medical implication of mental health medication
- Utilize one medication to treat multiple indications
- Utilize a different medication class for treatment
- Counsel patients on signs and symptoms to be aware of

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Case 3: Duplications in Therapy

Use the provided information to identify potential drug interactions for this patient

- 87 year old male
  - Presenting Symptoms: faint, dizziness upon standing
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  - Current Medications: Venlafaxine 150mg daily, Prazosin 2mg HS, Propranolol 10mg PRN, Metformin 500mg BID, Tamsulosin 0.4mg daily, Lisinopril 10mg daily

What medication concerns are present?
What are the implications of the duplication of therapy?

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Part 4: Laboratory Values Affected by Psychotropic Medications

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Case 4: Laboratory Values

- 48 year old female
  - PMH: Depression, Anxiety, Mood lability, AUD
  - Vitals: BP 140/77 mmHg, 5'4" 192 LBS

Chem7	Lipid panel	CBC	CMP	Misc Labs
Na 134 mEq/L	TC 195 mg/dL	WBC 5.2 x 10^6/L	AST 57 IU/L	Vit D 31.7 ng/mL
K 4.0 mEq/L	HDL 60 mg/dL	Hg 14.2 g/dL	ALT 41 IU/L	A1C 5.4
Cl 101 mEq/L	TG 127 mg/dL	Hct 42.9%	eGFR >60	Folate 7.9 ng/mL
CO2 30 mEq/L	LDL 139 mg/dL	Plt 266 x 10^6/L		TSH 2.79 mIU/L
SCr 1.1 mg/dL		RBC 4.81 x 10^6/mL	Urine Tox	
BUN 15 mg/dL			Amphet Neg	
Glu 99 mg/dL			Barb Neg	
			Opi Neg	
			Marijuana Pos	
			Cocaine Neg	
			EtOH Neg	

Prior to starting a mental health medication, what considerations are made, based on presented lab values?

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Laboratory Values

- Antidepressants
  - Weight Gain: Mirtazapine, MAOIs, TCAs, Paroxetine
    - Monitor at baseline, 3, 6, 12 months, annually
  - Blood Dyscrasias: Mirtazapine, Citalopram, TCAs
    - Not common. Monitor if indicated
  - Electrolytes: SSRIs, SNRIs
    - Monitor sodium in higher risk patients
  - Blood Pressure: SNRIs – Venlafaxine
    - Dose related, monitor routinely

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Laboratory Values

- Antipsychotics
  - Weight Gain: Clozapine, Olanzapine, Quetiapine, Risperidone

American Diabetes Association (ADA) – monitoring protocol for second generation antipsychotics (SGA)							
	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually	Every 5 Years
Personal/ Family History	X					X	
Weight (BMI)	X	X	X	X	X		
Waist Circumference	X					X	
Blood Pressure	X			X		X	
Fasting Plasma Glucose	X			X		X	
Fasting Lipid Profile	X			X			X

  - Prolactin: First generation antipsychotics, Risperidone
    - Monitor in those with positive screening

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Laboratory Values

Mood Stabilizers

Name	Weight	LFTs	Blood Dyscrasias	TSH	Electrolytes	Other
Lithium	X			X		
Valproic Acid	X	X	X			X
Carbamazepine		X	X		X	
Oxcarbazepine		X	X		X	
Lamotrigine	Does not typically require additional lab workup					

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Laboratory Values

- Stimulants
  - Blood pressure, Heart Rate
  - Height, Weight
    - Pediatric patients

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Case 4: Laboratory Values

- 48 year old female
  - PMH: Depression, Anxiety, Mood lability, AUD
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Chem7	Lipid panel	CBC	CMP	Misc Labs
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Glu 99 mg/dL			Barb Neg	
			Opi Neg	
			Marijuana Pos	
			Cocaine Neg	
			EtOH Neg	

Prior to starting a mental health medication, what considerations are made, based on presented lab values?

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Questions

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