Updates in Therapeutics®2015:
Ambulatory Care Pharmacy Preparatory Review and Recertification Course

Psychiatric Disorders

William A. Kehoe, Pharm.D., MA, FCCP, BCPS
Professor of Pharmacy Practice
University of the Pacific

Conflict of Interest & Disclosures

- Nothing to disclose
- Note: Dr. Kehoe is not an item writer for any of the BPS exams.

Learning Objectives

- Describe the DSM-5 (*Diagnostic and Statistical Manual of Mental Disorders*) criteria, etiology, risk factors, and disease course for the anxiety disorders, sleep disorders, major depression, bipolar disorder, attention-deficit /hyperactivity disorder, schizophrenia, and substance use disorders.

- Relate common drug and nondrug therapy for the psychiatric disorders, including drug, dose, frequency, adverse effects, drug interactions, and monitoring parameters.

Learning Objectives

- Recommend appropriate initial and maintenance treatment for psychiatric disorders, including duration of therapy.

- Assess treatment regimens for significant drug interactions and appropriateness of therapy, including use of polytherapy.

Discussion topics will include a review of therapeutic principles for the above disorders. These learning objectives and a more thorough discussion can be found in the Ambulatory Care Preparatory Review Course Psychiatric Disorders chapter.

Here's how we'll approach this topic….

TODAY

- Review some of the more complex problems (anxiety, depression, bipolar, schizophrenia, ADHD)
- Practice some related questions
- Insights for how to evaluate case scenarios

AT HOME

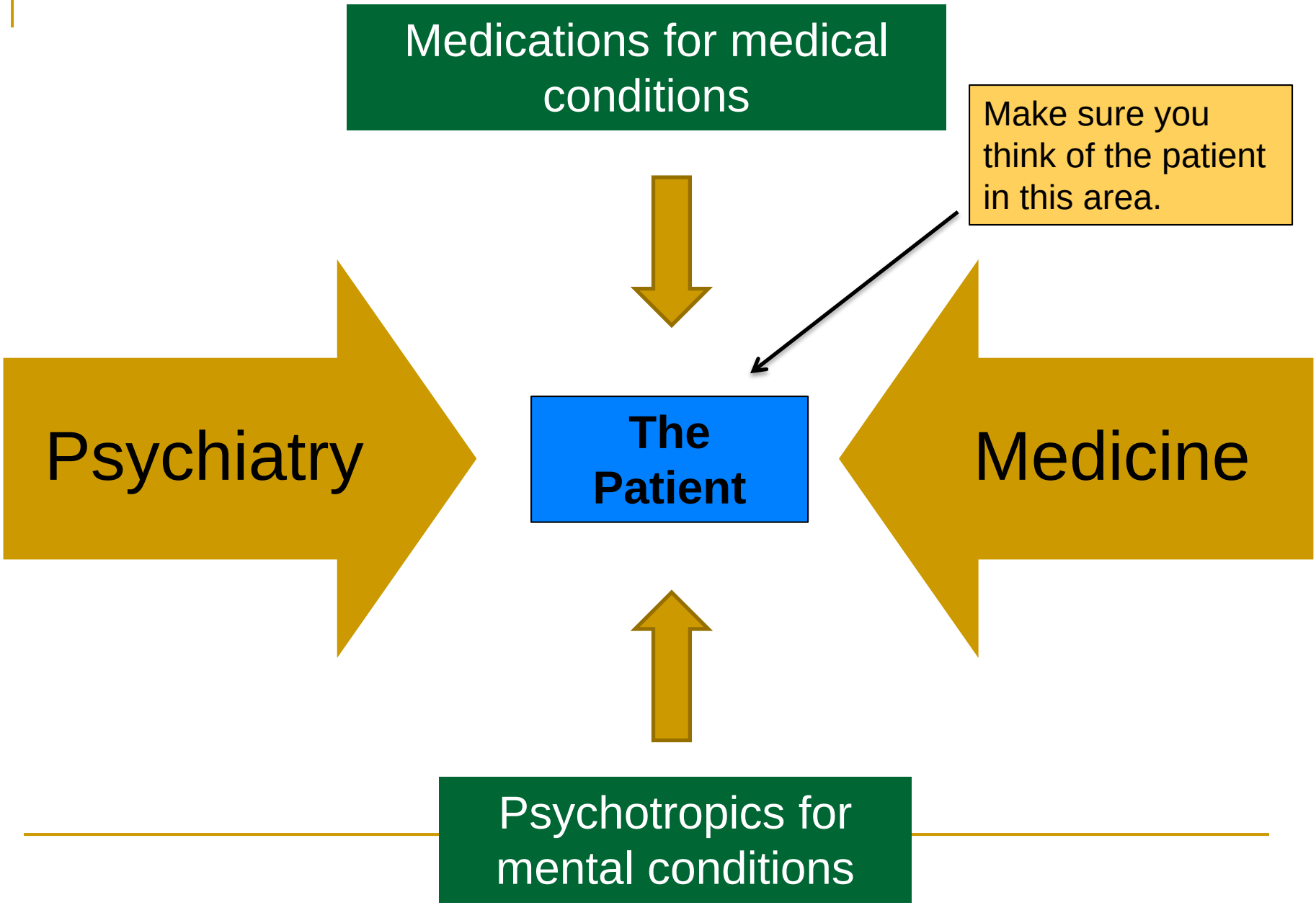
- Some problems are more straight-forward and can be reviewed in the chapter (sleep, substance abuse).
- Feel free to email me if you need help.

What are we going to do today?

- Review most common disorders
- Practice questions
- Group think – “How would I assess a scenario and anticipate questions?”

Rules for “Group Think”

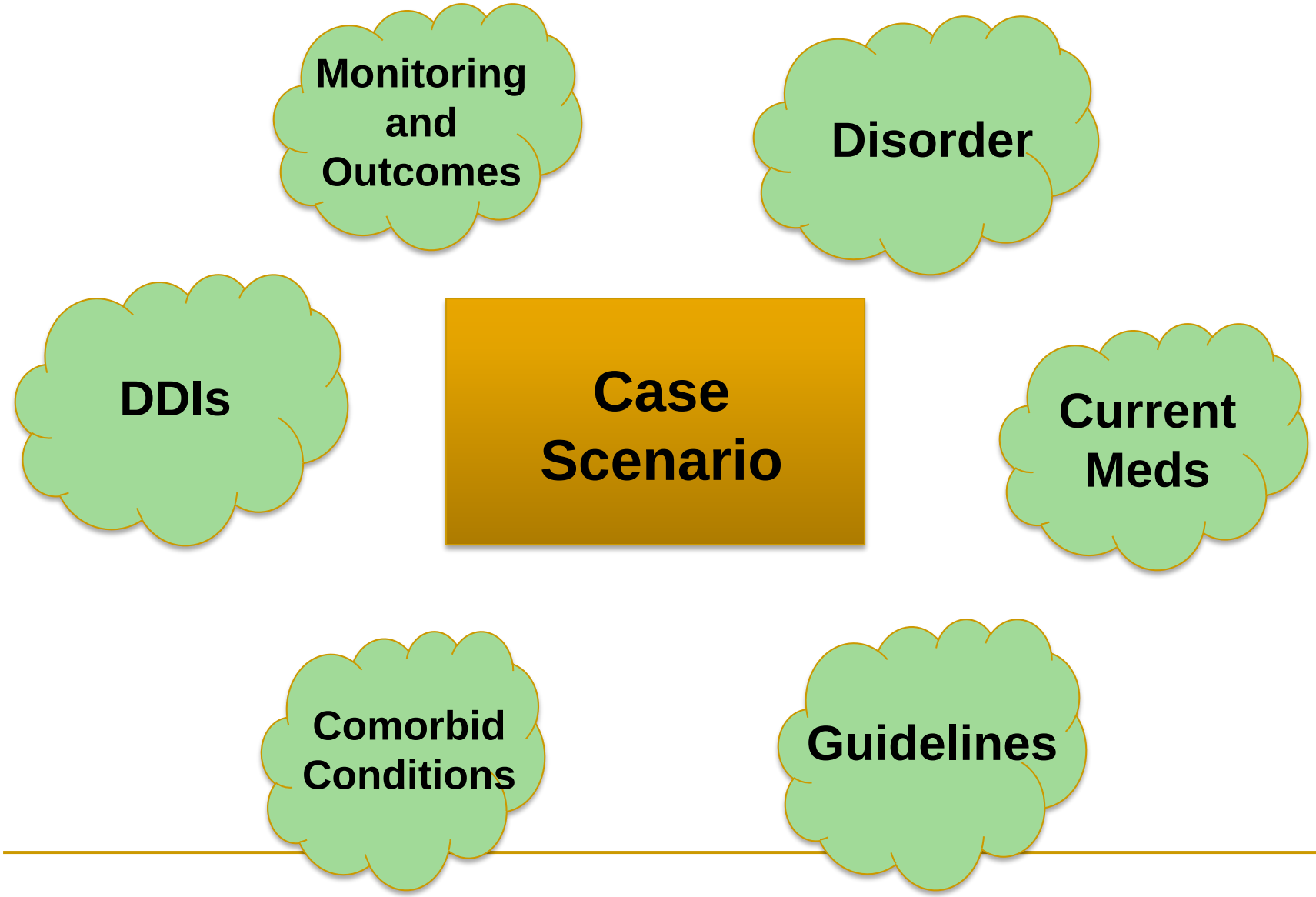
- You’ll see a new scenario.
- You’ll have 2 minutes to talk about this scenario with your neighbors.
- You will be asked to identify important observations in the scenario that will impact your choice of drug therapy.
- We’ll then review how I would think about those observations.


Medications for medical conditions
Make sure you think of the patient in this area.
Psychiatry
The Patient
Medicine
Psychotropics for mental conditions

So how would I approach learning to use and monitor these drugs?

- Know the general principles of evidence-based treatment guidelines for selection.
- Agents within a class often don't differ all that much in efficacy for an indication. We often select based on other drug-related factors.
- I would really know this stuff…
  - For which conditions the classes of meds are used.
  - Side effect profiles, how they differ, and how to manage them.
  - How these drugs impact comorbid psychiatric and medical conditions.

Case scenarios and pharmacotherapy



Principles of Psychiatric Drug Therapy

- Drugs used to treat psychiatric disorders may be used for several different conditions.
- Treatment is often symptom-driven, no drug therapy is “curative” for mental illnesses.
- Adverse effects are common and can be significant reasons for medication non-adherence.
- Never assume that you know what the drug is being used for – always question the patient about their disease states.

Anxiety Disorders Case

MP is a 39 year old woman with a 10 year history of GAD, who presents to clinic with worsening symptoms over the past 2 weeks, including difficulty concentrating at work, insomnia related to worry, and increasing restlessness. Her 19 year old daughter told her 3 weeks ago that she is having problems at school, and is considering dropping out. MP's current medications include paroxetine 40 mg orally at bedtime (taken for 2 years) and lorazepam 0.5 mg orally three times daily as needed for anxiety symptoms. She has not generally used the lorazepam, but has been taking two to three doses daily for the past 7 days. Laboratory results are within normal limits, but MP has gained 40 pounds since initiating paroxetine therapy. She is concerned about this, as well as increasing symptoms although she has been adherent to her medication regimen. She smokes cigarettes ½ PPD, does not use alcohol or other drugs.

Anxiety disorders start on page 1-178

What changes, if any, should be made in MP's routine anxiolytic drug therapy?

- A. Continue paroxetine.
- B. Directly switch to sertraline.
- C. Cross-taper paroxetine to sertraline.
- D. Decrease paroxetine dose.

What should we consider when evaluating MP's anxiety?

- What is the most likely reason for MP's exacerbation of symptoms?
- What changes, if any, should be made in MP's routine anxiolytic drug therapy?
- How do you respond to MP's increasing use of PRN lorazepam?
- What other therapies are available for MP?

Anxiety Disorders Overview

- Anxiety disorders are the most commonly diagnosed psychiatric disorders, with a 1-year prevalence rate of ~ 15%.
- DSM 5 no longer groups OCD and PTSD with the anxiety disorders.
- Diagnosis of anxiety disorders often comes after the patient has suffered symptoms for a long period.
- Drug therapy often includes a serotonergic drug, combined with "bridge" therapy with a benzodiazepine.
- Expectations of treatment include a significant reduction in symptoms, not necessarily complete resolution.
- Serotonergic drugs should be initiated at low doses and increased slowly to minimize the irritability and agitation that are common side effects of these drugs.
  - Paroxetine 10 mg orally at bedtime.
  - Fluoxetine 5 mg or 10 mg orally once a day.

Principles of pharmacotherapy of anxiety disorders

- There are basically three classes of drugs used for a majority of disorders.
  - Benzodiazepines
  - Antidepressants
  - Buspirone
  - Miscellaneous agents (hydroxyzine, beta-blockers, others)
- The key is to know…
  - Which drugs work for which disorders
  - How severe the disorder is and how quickly you need to see a response.

See pages 1-180 through 1-182

Benzodiazepines

- Differentiated by their half-lives and potency.
- Work quicker than the other meds.
- Tolerance and dependence are issues to consider. However, without a history of substance abuse people usually do ok.
- With history of substance abuse, or with other issues (e.g., dementia) consider other classes of drugs.
- Work for GAD, PD, and for some aspects of PTSD (not first-line).

Antidepressants

- Don't work as quickly as BZDPs.
- May see initial worsening due to activating quality of SSRIs. Start with low dose and work up.
- Work for GAD, PD, and an SSRI is considered first choice for PTSD.
- SSRIs work for OCD.

Buspirone

- Affects different neurotransmitter system than BZDPs.
- Relieves anxiety and worry, but does not sedate the patient, cause psychomotor slowing, muscle relaxation, or tolerance/dependence.
- Also does not work as quickly…2-4 weeks.
- Good when substance abuse is an issue, or in the elderly where BZDPs might have cognitive effects or cause falls.
- Does not work well for PD or OCD

Generalized Anxiety Disorder

- Excessive and uncontrolled worrying often for months, about nearly all events in the patient's life.
- Difficulty with concentration, sleep, and functional level, as well as restlessness and irritability.
- Benzodiazepine anxiolytics are very effective as initial therapy, SSRI or SNRI medications are useful long-term treatment.
- The onset of action for SSRI/SNRIs is ~4 weeks.
- Increased use of PRN benzodiazepines can signal increasing symptoms, often related to a recent life event.
- For all anxiety disorders – psychotherapy is a common and often necessary component of treatment.

Table 1 on 1-178

What changes, if any, should be made in MP's routine anxiolytic drug therapy?

- A. Continue paroxetine.
- B. Directly switch to sertraline.
- C. Cross-taper paroxetine to sertraline.
- D. Decrease paroxetine dose.

Anxiety Case Answers

- *What is the most likely reason for MP's exacerbation of symptoms?*
  - The recent information received from patient's daughter, increased worry about outcome of that situation.
- *What changes, if any, should be made in MP's routine anxiolytic drug therapy?*
  - MP is complaining of weight gain since initiation of paroxetine. Can consider switch to another SSRI medication that would not exacerbate weight gain. Must plan for discontinuation of paroxetine (anticholinergic rebound). Antidepressant withdrawal will be minimal if cross-titrate medications.
- *How do you respond to MP's increasing use of PRN lorazepam?*
  - Discuss use with MP, if use is not outside prescribed dosing, continue lorazepam and monitor. Ensure that 0.5 mg dose is adequate for symptoms experienced by MP. Will likely need to continue if switching MP's long-term treatment.
- *What other therapies are available for MP?*
  - Psychotherapy

SA is a 25 year old woman who comes to clinic with complaints of fear, anxiety, sweating, and feeling like she's being watched in group settings. Counseling has not helped. She is able to function with her daily responsibilities. Which option below is best for chronic therapy?

- A. bupropion
- B. buspirone
- C. lorazepam
- D. sertraline

Social Anxiety Disorder

- Many people suffer “stage fright” when confronted with situations like public speaking
- Social anxiety disorder reaches the level of fear in most situations of being humiliated by others or fear of interactions with others.
- Symptoms are physical in nature, including sweating, tachycardia, GI upset.
- SSRI medications are most commonly used, several weeks are needed for onset of action.
- BZDs may be used as “bridging” therapy.
- Propranolol or lorazepam may be used as needed for specific situations or events.

Table 1 on 1-178

SA is a 25 year old woman who comes to clinic with complaints of fear, anxiety, sweating, and feeling like she's being watched in group settings. Counseling has not helped. She is able to function with her daily responsibilities. Which option below is best for chronic therapy?

- A. bupropion
- B. buspirone
- C. lorazepam
- D. sertraline

Obsessive-Compulsive Disorder

- Now included in its own chapter in DSM 5.
- Recurrent thoughts or impulses that lead to behaviors that reduce anxiety.
- Compulsive behaviors may or may not coincide with the recurrent thoughts.
- SSRIs or clomipramine (TCA) are used for long-term treatment.
- Treatment results in ~ 50% resolution of symptoms for most patients.
- Cognitive behavioral therapy targeted at reducing time spent in behaviors or diverting the patient to more useful behaviors may further reduce symptoms.

Table 1 on 1-178

Panic Disorder

- A single panic attack does not indicate panic disorder.
- Panic disorder is defined by recurrent panic attacks that limit functionality.
- Physical symptoms of chest pain, shortness of breath, and sweating commonly accompany psychological symptoms such as fear of losing control or dying.
- SSRIs are used for long-term therapy, benzodiazepines may be used PRN to minimize specific attack symptoms. They may also be used as “bridging” therapy if needed.
- Psychotherapy or immersion therapy (subjecting the patient to fearful situations) may be useful to reduce symptoms and improve functionality.

Table 1 on 1-178

Post-Traumatic Stress Disorder

- May be combat-related or civilian.
- Civilian trauma is easier to treat – likely one-time event versus recurrent.
- Triad of symptoms – re-experiencing, hyper-arousal, avoidance
- SSRIs are first-line therapy, mirtazapine, topiramate, and atypical antipsychotics have been studied as augmenting agents.
- New guidelines (Harvard Psychopharmacology Algorithm Project) see sleep problems as core and suggest treating them first.
- Use of benzodiazepines should be avoided where possible, due to the increased risk of abuse of these agents.
- Combination drug therapy is common with an SSRI agent as the building block – symptomatic treatment follows:
  - Atypical antipsychotic – re-experiencing, hyperarousal, prominent psychosis
  - Adrenergic antagonist (prazosin) – nightmares associated with re-experiencing

Group Think – Anxiety Disorders

SN is a 42 year old man who comes to clinical today with complaints of increasing anxiety over the last few months. He relates it to increased stress at work that is nearly intolerable. His symptoms include restlessness, irritability, constant worry about projects, and insomnia. It's to the point where he is missing days at work, which may cost him his job. He has poorly controlled HTN for which he takes lisinopril and HCTZ and migraines for which he takes sumatriptan as needed. He has no history of drug abuse and drinks only socially 1-2 times per month. His PCP has asked you to recommend treatment.

Major Depression Case

ED is a 31 year old woman with a 5 year history of major depression, with 2 previous episodes. She presents to clinic today with symptoms of fatigue, irritability, and difficulty sleeping. She is in otherwise good health. When questioned, ED endorses feeling hopeless about her life, she is unemployed and is having difficulty finding a job because she is staying in bed most of the day. Her current medication is citalopram 20 mg orally once daily, which she has taken for 2 years. You ask her to fill out a PHQ-9 questionnaire, her score is 17.

Major Depression Case Question

What is the most appropriate drug therapy intervention for ED?

- A. Switch to fluoxetine 20mg.
- B. Increase to citalopram 40mg.
- C. Add mirtazapine 15mg.
- D. Add thyroid supplementation.

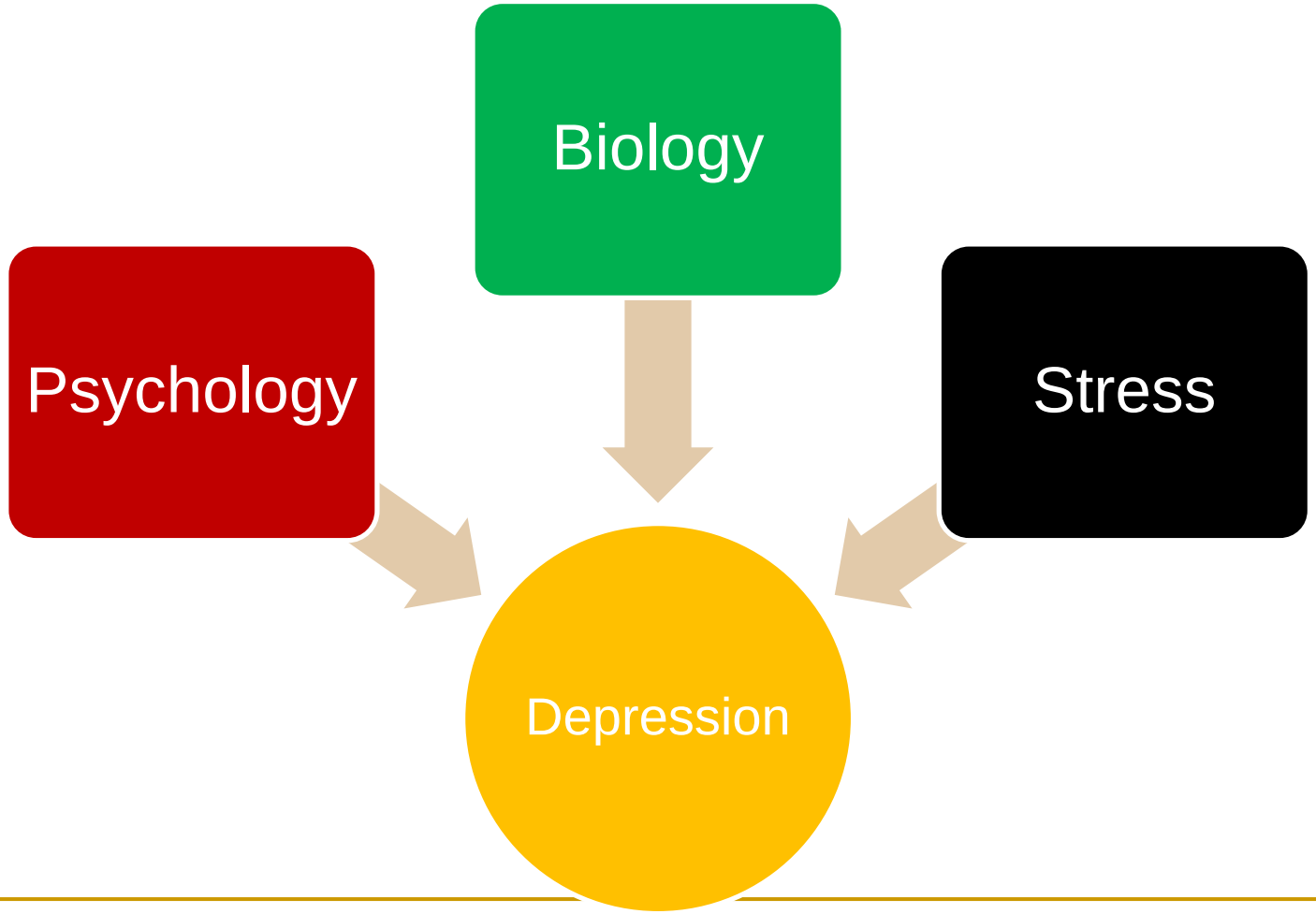
What questions should we ask when evaluating ED's depression?

- How long have you been experiencing these symptoms, are they similar to your previous episodes?
- Have you taken any other antidepressant medications?
- Are you experiencing any pain?
- Do you have thoughts of suicide?

Major Depression Overview

- It is estimated that only 30% of people with depression seek treatment, of those only 30% are adequately treated.
- The lifetime prevalence is ~16%.
- Individuals with depression often present to primary care providers with non-specific symptoms of fatigue and pain.
- Risk factors include being female, middle-aged, life stresses, chronic medical conditions, being widowed or divorced, and having a lower income.
- Some patients have concomitant substance use.

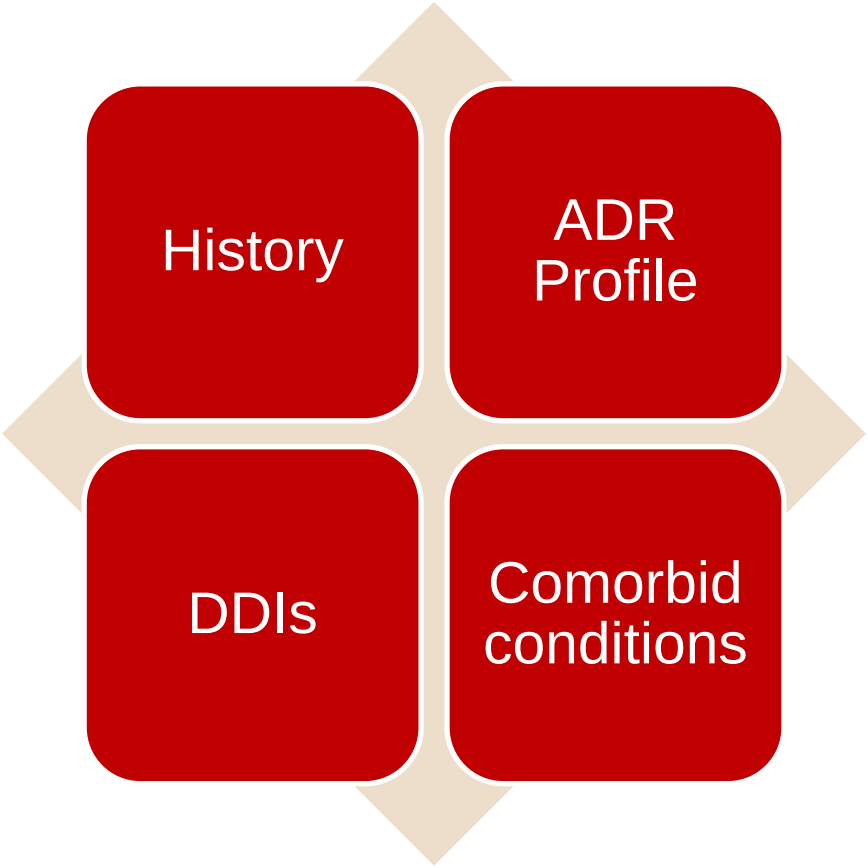
Lots of things contribute to depression



Major Depression Treatment Principles

- The effectiveness of individual antidepressants is similar in clinical trials.
- Drug therapy should be chosen based on adverse effect profiles, doses per day, cost, and patient choice.
- Ascertaining history of antidepressant use may also guide choice of therapy, including history of use in family members.
- Patient counseling regarding onset of effect and duration of treatment will improve adherence.

How would you choose an antidepressant?



Most patients will be started on an SSRI.

Major Depression Pharmacotherapy

- The STAR*D trials are effectiveness trials that focused on the progression of treatment.
- Results suggested that many patients will require several treatment trials and possibly combination medication therapy.
- The goal of treatment with antidepressants should focus on remission of symptoms, not simply response. This often requires > 1 drug.
- That said, for some patients, a reduction in symptoms will be the maximal response.

1-201 and 1-202 and reference 12 in Depression

Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study

Level	Treatment
1	Initial treatment with citalopram
2	Switch: bupropion, sertraline, venlafaxine or CBT OR Augment: citalopram + bupropion, busprione, CBT
2a	Switch CBT to bupropion or venlafaxine
3	Switch: mirtazapine or nortriptyline OR Augment: lithium, T3,bupropion, sertraline, venlafaxine
4	Switch: tranylcypromine OR mirtazapine + venlafaxine

Dose and Duration of Antidepressant Therapy

- Dose and duration are two important factors in treatment success. **Make sure you give the drug a chance to work.**
- Initial onset of action may be within the first 2 weeks, maximal improvement for a specific dose may take 4 to 6 weeks.
- The dose should be increased based on response and tolerability of side effects.
- Moderate doses may be required.
  - Fluoxetine 40 mg orally once daily
  - Citalopram 40 mg orally once daily (max dose)
  - Sertraline 200 mg orally once daily

Major Depression Case Question

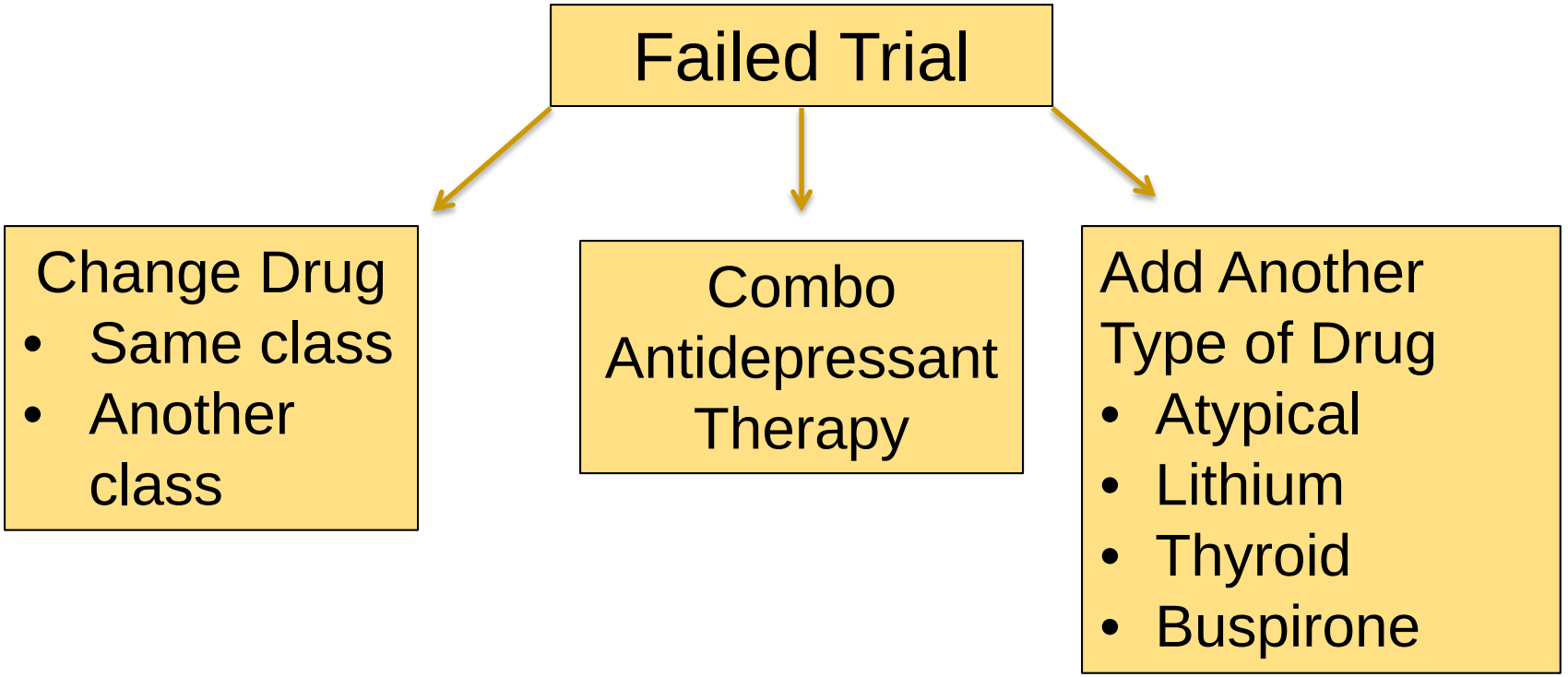
What is the most appropriate drug therapy intervention for ED?

- A. Switch to fluoxetine 20mg.
- B. Increase to citalopram 40mg.
- C. Add mirtazapine 15mg.
- D. Add thyroid supplementation.

If the first trial fails…..

- A switch to a 2nd SSRI is reasonable if the patient tolerated the first one, but didn't respond to therapy.
- SNRIs can be chosen if the patient is complaining of pain.
- TCAs and MAO inhibitors are generally reserved for prior treatment failures.
- Novel antidepressants can be used as first-line therapy or for subsequent therapy
- Recent trials have suggested that combination therapy that accounts for mechanism of action may have a greater remission rate, even with initial treatment.
- May consider augmentation therapy – atypical antipsychotics, thyroid supplementation, lithium

So if my first drug fails after optimal dose and duration…



When might you consider a non-SSRI as initial therapy?

- Bupropion – maybe if there is also ADHD, a history of sexual dysfunction on ADs, smoker who wishes to quit
- Duloxetine – maybe if there is DPN, fibromyalgia, chronic back pain
- TCAs – maybe if there is a history of migraines, DPN
- Paroxetine or venlafaxine – maybe if vasomotor symptoms in post-menopausal women.

HT is a 32 year-old woman with symptoms of a major depressive episode. She has been this way for 8 weeks. Her Ham-D score is 21, and she is not suicidal. Her other medical problems include poorly controlled fibromyalgia and asthma. Which option is most appropriate for her MDE?

- A. bupropion
- B. duloxetine
- C. amitriptyline
- D. fluoxetine

Monitoring antidepressant therapy

- Response – patient report and the PHQ-9
- Suicidal thinking – all antidepressants have a boxed warning for patients younger than 24 years for new onset or worsening suicidal thinking – this should be monitored closely in the first few months of treatment.
- Adverse effects – especially those the patient may not talk about, but may cause lack of adherence.
  - Sexual dysfunction – serotonergic
  - Gastrointestinal side effects
- Antidepressant withdrawal syndrome may present as increased symptoms, including irritability, but will also likely include GI effects.
- Serotonin syndrome
- Pregnancy

Review individual drugs on pages 1-194 through 1-200 for specific parameters. See also page 1-202

Major Depression in Primary Care

- Ambulatory care settings are a primary place for identifying depression.
- Consider this in a differential diagnosis for patients who present with non-specific symptoms.
- Obtain thyroid function tests for any patient with mood symptoms.
- If combination therapy is considered, ensure that there are not overlapping MOAs.

Major Depression Case Question

What is the most appropriate drug therapy intervention for ED?

- A. Switch to fluoxetine 20mg.
- B. Increase to citalopram 40mg.
- C. Add mirtazapine 15mg.
- D. Add thyroid supplementation.

Major Depression Case Answers

- How long have you been experiencing these symptoms, are they similar to your previous episodes?
  - Patients with previous episodes can often express whether the symptoms are similar, leading you to a differential diagnosis of a recurrent episode.
- Have you taken any other antidepressant medications?
  - This will aid in deciding on the need for drug therapy change, including medications that should not be considered. A family history of antidepressant use and response will be useful in guiding drug therapy, as there is some evidence that there is a familial response to treatment.
- Are you experiencing any pain?
  - If the patient is having pain, you may consider using a SNRI as treatment, as the SNRIs are FDA-approved for pain conditions, including fibromyalgia (duloxetine, milnacipran)
- Do you have thoughts of suicide?

Group Think - Depression

LM is a 34 year-old woman who comes to clinic today with complaints of depressed mood, fatigue, lack of interest or motivation in her usual activities, and insomnia. These symptoms have been present for 6 months. Her score on the Beck Depression Inventory suggests mild-moderate depression, which is about a 50% improvement. She currently takes sertraline 200 mg/day and tolerates it well. Her PMH includes epilepsy since age 10 treated with carbamazepine and lamotrigine, obesity treated diet/lifestyle modifications, and HTN treated with HCTZ. She denies EtOH use but does smoke 1 PPD. What would be an appropriate modification to make to her antidepressant regimen?

Bipolar Disorder Case

KW is a 24 year old woman who presents to clinic for follow up and refill of medications used for bipolar disorder. She has a 3 year history of treatment and has had 2 previous hospitalizations, but has been followed successfully by primary care for 1 year. Her current medications are lithium 600 mg orally twice daily and aripiprazole 30mg orally once a day. Her most recent lithium level was 0.8 mEq/L, which was done 3 months ago. She states that she has only been sleeping 3 hours per night, but is not fatigued. She also says that she's been irritable and feels "wound up" and energetic. She exhibits no other symptoms. No other laboratory monitoring has been done for the past year.

Starts on age 1-205

Bipolar Disorder Case Question

What is the most appropriate drug therapy intervention for KW?

- A. Increase to lithium 600mg three times daily.
- B. Maintain lithium and aripiprazole and repeat lithium level to ascertain adherence.
- C. Switch to divalproex and maintain aripiprazole.
- D. Add zolpidem 10mg.

Bipolar Disorder Case Questions

- What symptoms were experienced in previous episodes?
- What laboratory monitoring is needed?
- What adverse effects of atypical antipsychotics should be monitored?
- At what point should a referral be made to psychiatric services?

Bipolar Disorder Overview

- The estimated prevalence of bipolar disorder is ~ 1%.
- The average age at onset is 21 years.
- Patients with bipolar disorder spend more of their life in the depressive pole than in the manic or hypomanic pole.
- Misdiagnosis of bipolar disorder is common, many patients will present with depressive symptoms that are considered to be unipolar depression – the delay in diagnosis has been estimated to be an average of 10 years for some patients.
- Careful questioning is necessary to ascertain a past experience of mania or hypomania.
- Suicide attempts may occur in either mood pole.

Bipolar I Disorder

- In bipolar I disorder, manic or mixed episodes are intermingled with depressive episodes.
- Lithium and valproic acid have shown efficacy as initial monotherapy in bipolar I disorder.
- If the patient is in a manic episode, any antidepressant therapy should be discontinued.
- Combination therapy with lithium and valproic acid or either of those with an atypical antipsychotic is common.

Bipolar II Disorder

- In bipolar II disorder, depressive episodes are intermingled with hypomanic episodes.
- This is commonly thought of as bipolar depression.
- Lithium and lamotrigine are good first-line choices for treatment, with the atypical antipsychotic quetiapine.
- Lamotrigine dosing should follow a slow dose titration and take into account drug interactions to minimize the risk of Stevens-Johnson syndrome.
- Antidepressant treatment is common, it is controversial whether or not this treatment is effective, as well as the risk of a “switch” into a manic episode.

How can bipolar I patients present?

Manic

- Usual manic symptoms
- +/- psychosis

Depressed

- Usual symptoms of major depressive episode
- Tricky part is to know if unipolar or bipolar

Mixed

- Manic features
- Depressive features

Steps in Treatment: Mania

- Give something that will work quickly.
- Initiate mood stabilizer (lithium, anticonvulsant, or atypical) and begin a rapid-acting agent (atypical if not already started or BZDP) if symptoms warrant. Severe symptoms are treated with combinations. Current guidelines consider atypicals as first-line options in acute phase. Also use them in maintenance.
- Assess response and make sure to get Cp into therapeutic range for Li, VPA, or CBZ
- Length of long-term therapy depends on risk/frequency of episodes. More than 1-2 past episodes = very long-term therapy
- Monitor for ADRs and recurrent episodes. May need to continue adjuncts or add an antidepressant

Approach to bipolar disorder

Pure Mania

- May prefer lithium
- VPA is an alternative
- Can add SGA if needed
- Taper/DC antidepressants

Mixed

- May prefer quetiapine or another SGA
- Consider adding VPA
- Lithium is also effective

Depression

- Optimize current mood stabilizer
- If not on mood stabilizer may prefer lithium
- SGAs like quetiapine or VPA can also be used
- Antidepressants are further down and should be used with mood stabilizers

Bipolar Disorder – Mood Stabilizers

- Mood stabilizer drug therapy is considered to be the maintenance treatment in bipolar disorder.
- Lithium and valproic acid are generally first-line treatment.
- Many atypical antipsychotics are FDA-approved for the treatment of bipolar disorder, either as monotherapy or in combination with another mood stabilizer.

How Quick Will Drugs Work for Acute Mania?

- Lithium/Anticonvulsants: Slow onset (several days). Should start, but will usually need something else initially.
- Antipsychotics: Atypicals rapidly effective, good esp. for psychotic or aggressive patients.
- Benzodiazepines: Lorazepam common. Calms patient, may help with sleep

Lithium is a tricky drug to use!

- Monitor Cp closely, it's a tight range
- Watch fluid and electrolyte status
  - Dehydration can increase levels
  - Sodium: hyponatremia can increase levels
- Look for DDIs
  - NSAIDs (e.g. ibuprofen)
  - Diuretics (e.g. hydrochlorothiazide)
  - ACE inhibitors (e.g. lisinopril)
- Use pharmacokinetic interventions to treat or prevent concentration-related ADRs.

Bipolar Disorder – Treatment Considerations

- Pregnancy
  - Most mood stabilizers are Category D.
  - Most atypical antipsychotics are Category C.
  - Recent studies of anticonvulsant mood stabilizers has suggested that valproic acid not only has a risk of neural tube defects, but also negative effects on the IQ of the offspring.
- Lithium is useful for reducing suicidal thinking in bipolar disorder, but can be fatal in overdose.
- Antidepressant treatment is controversial
  - Most time is spent in depression
  - Antidepressants may not be effective
  - Antidepressants may cause a manic “switch”

Bipolar Disorder Case Question

What is the most appropriate drug therapy intervention for KW?

- A. Increase to lithium 600mg three times daily.
- B. Maintain lithium and aripiprazole and repeat lithium level to ascertain adherence.
- C. Switch to divalproex and maintain aripiprazole.
- D. Add zolpidem 10mg.

Bipolar Case Answers

- What symptoms were experienced in previous episodes?
  - Knowledge of previous symptoms helps the clinician ascertain the level of concern for current symptoms. The patient says that she is only sleeping 3 hours per night and is not fatigued, which could be a sign that she is beginning a manic episode.
- What laboratory monitoring is needed?
  - Laboratory monitoring for lithium includes lithium serum concentrations, electrolytes, renal function, and thyroid function testing. For aripiprazole, the patient should have routine monitoring of the total lipid profile and either fasting blood glucose or a HgbA1c.
- What adverse effects of atypical antipsychotics should be monitored?
  - Movement side effects should be evaluated, including drug-induced Parkinson's and akathisia. Specific to aripiprazole, akathisia is a common side effect. The Barnes Akathisia Scale can monitor this side effect.
- At what point should a referral be made to psychiatric services?
  - If the clinician is concerned about the lack of need for sleep and a manic episode.

Group Think – Bipolar disorder

NR is a 36 year-old man with a long history of bipolar disorder treated at the county clinic. He was admitted to their inpatient unit on a 72-hour involuntary hold after police found him wandering the neighborhood ranting about aliens who have taken over his body. He is disheveled, has pressured speech, agitated, and appears hostile to staff. Neighbors told the police this had been going on for several days but is worse today. On admission he has no symptoms of depression. His medications include olanzapine 10 mg daily plus lithium 600 mg twice daily. He has type 2 DM treated with metformin and glyburide. His admission data include: wt 92 kg, ht 68”, BP 156/92. What would be the most appropriate pharmacotherapeutic recommendations to make upon admission? What labs would you order?

Schizophrenia Case

MC is a 24 year old man with a 2 year history of schizophrenia. He presents to the clinic today for medication follow up. He is with his mother, who reports that MC hasn't eaten much in the past 3 weeks, hasn't been showering, and is focused on "spirituality" more lately. He is repetitive in his speech, repeating his answers to your questions three times. His current medications are quetiapine XR 600 mg orally once daily and lorazepam 0.5 mg orally three times daily as needed. MC has been otherwise well since beginning at the primary care clinic 1 year ago. He has a history of 2 hospitalizations, but none in the past year. He smokes 1 PPD of cigarettes, but claims no use of alcohol or other substances. His past psychiatric medication history includes paliperidone, risperidone, olanzapine, and haloperidol, with either no effect or significant side effects. He has had no recent laboratory monitoring.

Schizophrenia Case Question

What is the most appropriate drug therapy intervention for MC?

- A. Increase to quetiapine XR 900mg.
- B. Add paliperidone 6mg.
- C. Evaluate adherence to quetiapine XR.
- D. Switch lorazepam to routine dosing.

Schizophrenia Case Questions

- Is the patient taking his medication?
- What are MC's previous symptoms that led to hospitalization?
- At what point should MC be referred to psychiatric services?
- What monitoring should be done for MC?

Schizophrenia Overview

- The incidence of schizophrenia is ~1%.
- The lifespan of people with severe mental illness is on average 25 years shorter than the general population.
- The average age at onset is the late teens to early 20s for men and ~ a decade later for women.
- Tobacco smoking, poor lifestyle habits, and social isolation likely contribute to this.
- Antipsychotic agents used to treat this condition have significant side effects that exacerbate or cause chronic medical conditions.
- People with severe mental illnesses are often portrayed to have consistent violent tendencies. The reality is that fewer than 1% of people with schizophrenia are ever violent, with most of that violence being self-injurious.

Principles of pharmacotherapy in schizophrenia

- Antipsychotics are the mainstay of treatment.
- These agents represent symptomatic control, not a “cure”.
- Antipsychotics are more effective for the “positive” symptoms.
- Clinical trials suggest that all antipsychotics are similarly effective (with the exception of clozapine).
- Choice of antipsychotic is driven by side effect profile, cost, and patient choice.
- While polytherapy is common, clinical trials suggest that this is no more effective than monotherapy with an increased side effect burden.
- Finding an effective antipsychotic is often a matter of trial and error.
- Adherence to medications can be problematic, this can be improved by consistent and thorough patient counseling.

How to choose an initial antipsychotic?

- The goal of treatment is full remission of symptoms and a return of the patient to their previous functional level.
- First-line therapy consists of an atypical or a typical antipsychotic.
- Doses per day and side effect profile should be considered, as well as the payer source for the patient.
- Typical antipsychotics generally cause more EPS than atypical antipsychotics.
- Atypical antipsychotics are associated with more weight gain and metabolic syndrome and less EPS.
- While clozapine is generally reserved for patients who fail several trials of antipsychotic medications, it has been shown in clinical trials to be the most effective antipsychotic.

Approach to treatment for schizophrenia

Stage 1: 1st episode any SGA* (or FGA), relapse try prior effective agent or switch

Stage 2: Any other SGA (or FGA)* or may consider clozapine if significant suicidality

Stage 3: Clozapine monotherapy if failed two other agents

Stage 4: Limited evidence but some try alternate monotherapy, augmentation, or dual therapy

*Except clozapine at this stage

Monitoring antipsychotic therapy

- The response to treatment is a primary monitoring parameter.
  - The clinician often sees “response” as a reduction in positive symptoms of hallucinations or delusions.
  - The patient may feel that “response” is related to daily life activities, such as improving ability to concentrate allows the return to previous activities.
- EPS – Movement side effects occur commonly.
  - Drug-induced Parkinson’s is easier to evaluate – tremors. Treat with anticholinergics.
  - Evaluation for akathisia requires the clinician to ask the patient if they feel restless or the need to constantly move. Treat with a beta-blocker.
- Metabolic side effects – Hyperglycemia, hypertension, and hyperlipidemia have been associated with the antipsychotics, especially the atypicals.
  - Monitor weight and blood pressure at each visit, if possible.
  - Obtain labs, including fasting blood glucose or HgbA1c and total lipid profile routinely.

Metabolic Side Effects Antipsychotics

Problem	Comments
Weight gain	Clozapine~olanzapine>Risperidone~quetiapine> ziprasidone~aripiprazole. Watch BMI. Encourage diet and exercise. Change drug if needed. Children may be more prone.
Hyperglycemia or diabetes	Clozapine~olanzapine>Risperidone~quetiapine> ziprasidone~aripiprazole. May be related to weight gain. Watch FBG and A1c.
Lipid abnormalities	Clozapine~olanzapine>Risperidone~quetiapine> ziprasidone~aripiprazole. Can see ↑TC, LDL and TG ↓HDL. Encourage diet and exercise. Monitor lipid panels.

Engaging the patient in treatment

- Patients who are referred from psychiatry to primary care for follow-up are generally more stable in their illness.
- Engaging the patient by providing consistent and thorough patient counseling regarding their medications, expectations of treatment, and side effects is the best way to ensure adherence to treatment.
- Clinicians often feel (or are taught) that patients with schizophrenia can't understand patient counseling or will feel overwhelmed by it.
  - Most patients with schizophrenia understand what their condition is and are willing to tolerate significant side effects if the drug therapy will minimize their symptoms.

Schizophrenia Case Question

What is the most appropriate drug therapy intervention for MC?

- A. Increase to quetiapine XR 900mg.
- B. Add paliperidone 6mg.
- C. Evaluate adherence to quetiapine XR.
- D. Switch lorazepam to routine dosing.

Schizophrenia Case Answers

- Is the patient taking his medication?
  - This is important to ascertain, as this will inform drug therapy changes. If the patient is not taking their medications, an increase in dose could exacerbate side effects. Nonadherence to medication could signal the reason for symptom increase, as well as a lack of tolerability to side effects.
- What are MC's previous symptoms that led to hospitalization?
  - The patient in this case is clearly experiencing an exacerbation in symptoms of schizophrenia. It is important for the clinician to understand what the patient's baseline symptoms are and how severe this exacerbation is.
- At what point should MC be referred to psychiatric services?
  - Since MC is clearly symptomatic, a communication to his psychiatrist should be done at this point, with an appointment scheduled as early as possible or the direction of the psychiatrist followed.
- What monitoring should be done for MC?
  - Metabolic monitoring, EPS rating scales.

Group Think - Schizophrenia

RW is a 63 year-old man with long-standing schizophrenia. He has not complied with his quetiapine for several weeks because "I don't like the way it makes me feel." Today he has been brought in by family because he reports hearing voices commanding him to do things. His hygiene has deteriorated and he is increasingly isolative. He has CAD (s/p stent 1 year ago) for which he takes NTG, metoprolol, and clopidogrel. His cardiac status is stable. He has COPD for which he uses fluticasone/salmeterol and tiotropium inhalers. On his last exam his BP = 135/62, HR 78, ECG = NSR with occasional PVCs and QTc = 498. Last week he developed a URI for which he is now receiving levofloxacin. What are your concerns when deciding recommending antipsychotic therapy?

Attention Deficit Hyperactivity Disorder Case

DL is a 7 year old boy who returns to the primary care clinic with his mother for follow up of attention deficit hyperactivity disorder. He was diagnosed 3 months ago after his teacher and parents noticed that he was not completing his work and was acting out in class. DL is currently taking methylphenidate 10 mg orally two times daily in the morning and afternoon (after school). He is able to complete his work in the morning at school, but continues to struggle in the afternoon. He has lost 2 pounds in 12 weeks. DL is currently exhibiting no other adverse effects. His current weight is 50 pounds and he is 74 inches tall. He has no chronic medical conditions and takes no other medications. He has a family history of heart disease and tic disorders. Blood pressure, heart rate, height, and weight were normal prior to initiating methylphenidate therapy.

ADHD Case Question

What is the most appropriate drug therapy intervention for DL?

- A. Switch to methylphenidate OROS long-acting 36mg.
- B. Switch to methylphenidate CD long-acting 20mg.
- C. Add clonidine 0.05mg and evaluate appetite.
- D. Increase methylphenidate to 10 mg orally three times daily.

Attention Deficit Hyperactivity Disorder Case Questions

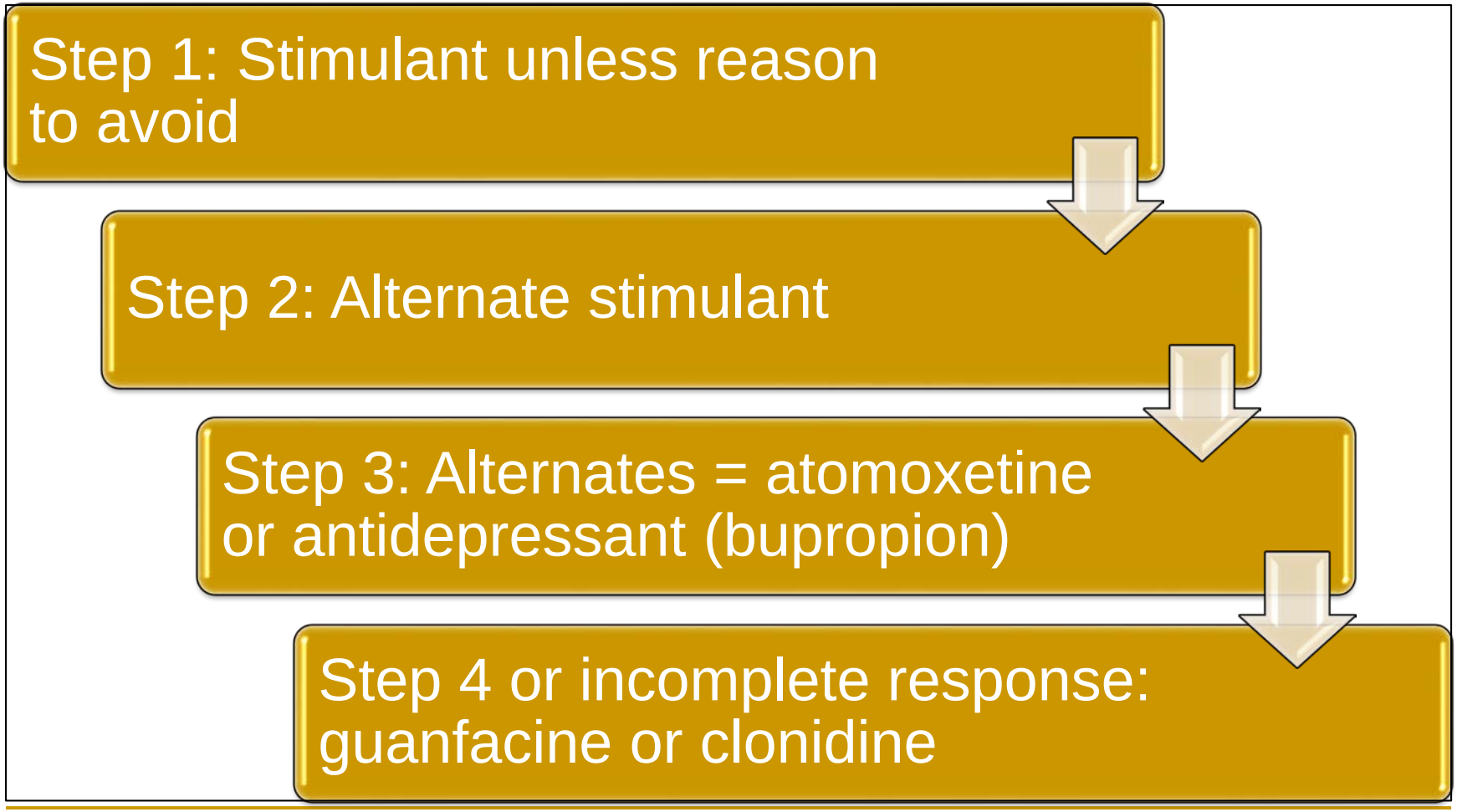
- What baseline information should be obtained prior to initiating stimulant therapy?
- Do you consider methylphenidate to be effective for the patient in this case?
- What medication changes might be considered?
- What is your concern regarding DL's family history of tic disorders?

Attention Deficit Hyperactivity Disorder Overview

- The prevalence of ADHD is thought to be ~6%.
- Many children diagnosed with ADHD will continue symptoms into adulthood.
- Risk factors for the development of ADHD include family history of ADHD or bipolar disorder, low birth weight, maternal smoking, and perinatal stress.
- Modified diets and dietary supplementation have not been shown to be effective.
- Other psychiatric disorders are common comorbidities, including conduct disorders, mood disorders, anxiety, and Tourette's syndrome.
- Treatment of ADHD with stimulant medications does not increase the risk of substance use, may actually protect against this.

1-226 and 1-227

General approach to ADHD



Principles of Stimulant Use in ADHD

- The goal of treatment is to reduce or eliminate symptoms of ADHD so that the patient is able to engage and be functional in all environments.
- Hyperactive symptoms are predominant in childhood, inattention in adults.
- ADHD should be considered a chronic condition that may persist into adulthood.
- The effectiveness of stimulant medication in the treatment of inattention is not “diagnostic” for ADHD.
- Stimulant monotherapy is preferred, may have to use long-acting and short-acting doses of the same agent.

Which stimulant to choose?

- Any of the stimulants can be considered first-line therapy.
- Provider choice is the primary factor in which drug is used first.
- If the first stimulant is not effective, it is reasonable to switch to another, which may result in adequate effect.
- Onset of action is within 30 minutes of an immediate release dose, drug therapy can be re-evaluated every few weeks.
- Clinically, initial stimulant dosing begins with a sustained release dosage form, immediate release formulations may be added to improve efficacy at specific times.

Stimulant Adverse Effect Management

- Baseline information should include the family history of heart disease and the child's history of cardiac structural defect, as well as the family history of psychiatric disorders, including psychotic and tic disorders.
  - If family history of cardiac disease or concern for structural abnormality, the patient should have an EKG, with consideration for reading by a pediatric cardiologist.
  - If family history of psychotic disorder – monitor patient closely for psychotic side effects – hallucinations.
  - If family history of tic disorders – monitor for onset of motor/vocal tics
- Common side effects include insomnia, weight loss, decreased appetite, increased BP/HR, and growth suppression.
  - Insomnia – give last dose by 4pm or switch to long-acting agent.
  - Growth suppression – drug holiday, if possible.
  - Decreased appetite/weight loss – give after a meal, if possible.
  - Increased BP/HR – monitor closely, may require discontinuation.

Use of Alternative Treatments

- Atomoxetine may be useful in patients with a concern for substance use or history of non-adherence.
  - Onset of action is 2 to 4 weeks, must monitor LFTs and suicidal thinking.
- Adrenergic antagonists
  - Clonidine and guanfacine commonly used for the impulsivity associated with ADHD, may also be useful for insomnia secondary to stimulant use.

ADHD Case Question

What is the most appropriate drug therapy intervention for DL?

- A. Switch to methylphenidate OROS long-acting 36mg.
- B. Switch to methylphenidate CD long-acting 20mg.
- C. Add clonidine 0.05mg and evaluate appetite.
- D. Increase methylphenidate to 10 mg orally three times daily.

Attention Deficit Disorder Case Answers

- What baseline information should be obtained prior to initiating stimulant therapy?
  - Family history of cardiovascular disease is important to know, as there is a boxed warning for sudden cardiac death if stimulants are used in children with a cardiac structural defect. History of psychosis or tic disorders may help to ascertain the risk of those side effects.
- Do you consider methylphenidate to be effective for the patient in this case?
  - Yes, DL has symptom improvement in the morning during school after his morning dose, which wears off by the afternoon. This can generally be handled by using a long-acting preparation.
  - We need to continue to monitor his weight and linear growth. Appetite should be monitored and provide nutritious food when he's hungry.
- What medication changes might be considered?
  - Consider adding an immediate release dose after lunch or a switch to a longer-acting methylphenidate dosage form to cover the afternoon school period. May be able to discontinue afternoon immediate release dose.
- What is your concern regarding DL's family history of tic disorders?
  - Stimulant agents may exacerbate an existing tic disorder or promote the emergence of tics in the patient. Those with a family history may be at greater risk of this side effect.

Questions?