Board of Pharmacy Specialties Examination Process: *Tips for Preparing*

Terry L. Seaton, Pharm.D., FCCP, BCPS
St. Louis College of Pharmacy
St. Louis, Missouri

Presentation Overview

- BPS relationship to ACCP and the Preparatory Courses
- Brief overview of the roles of BPS and ACCP
- General information about the BPS Exam Process
- Some helpful hints for BPS exam takers

Mission of BPS

To *improve patient care* through recognition and promotion of specialized training, knowledge and skills in pharmacy and board certification of pharmacists

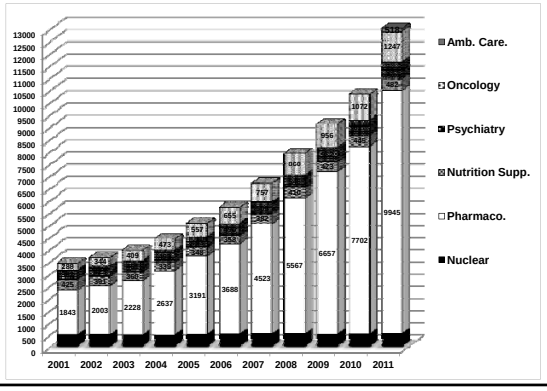
Purposes of BPS

- Recognize specialty practice areas
- Define standards for recognized specialties
- Evaluate the knowledge and skills of individual pharmacy specialists
- Communicate the importance of specialization in pharmacy

Benefits of Specialty Certification

- Self-satisfaction
- Peer recognition
- Professional advancement and opportunities
- Compensation

Board Certified Specialists



Next Exam: October 6, 2012

- Application deadline: *August 1*
- Alternate site or disability accommodation Deadline: *July 1*
- Site change/withdrawal deadline: *September 1*
- Online, mail or fax applications accepted
- Adhere to eligibility criteria

Examination Day

- Review site location
- Be on time!
- Minimize carry-in items
- AM and PM sessions with lunch break
- Keep track of your time
- Provide feedback to BPS

Scoring and Reporting

- Scores are *reported* within 60 days after the exam
- Scores are confidential
- Scoring process is described on the BPS website
- *Certificates* mailed within 60 days after scores are reported

BPS Recertification

- Required every seven (7) years
- Documents a specialist's *current* knowledge and skills
- 100-question recertification examination
- Continuing education options available

Contact BPS

- *Address:* 2215 Constitution Avenue NW Washington, DC 20037
- *Phone:* 202-429-7591
- *FAX:* 202-429-6304
- *E-mail:* bps@aphanet.org
- *Website:* www.bpsweb.org

Preparing for BPS Exams

Important Resources

- BPS *website*
  - BPS Candidate's Guide (available in volume 2 of your Ambulatory Care Preparatory Review and Recertification Course Workbook)
  - BPS examination Content Outlines
- Other certified colleagues
- Preparatory course materials

BCPS Examination Content*

- Domain 1 (50%), Direct Patient Care
- Domain 2 (20%), Practice Management
- Domain 3 (5%), Public Health
- Domain 4 (15%), Retrieval, Generation, Interpretation and Dissemination of Knowledge
- Domain 5 (10%), Patient Advocacy

**See latest Content Outline at www.bpsweb.org*

Self-Assessment

- Area(s) of practice
  - Shadow if needed
- Identify therapeutic areas to review
  - BPS Ambulatory Care Content Outline
- Regulatory issues in ambulatory care
- Literature evaluation skills
  - Statistics and study design

Study Habits

- Group versus individual
- Pace yourself
- Incorporate clinical experiences
  - Case presentations
  - Journal clubs
  - Application of guidelines
  - Regulatory

Utilizing the Preparatory Course

- Gain recent knowledge throughout sessions
  - Guidelines, landmark trials
- Identify strengths and weaknesses
- Complete the self-assessment questions for each section
  - Focus on the best answer
- Ask questions

Other Resources

- ACCP FAQs
  http://www.accp.com/careers/boardFAQ.aspx
- Last chance webinar series
- Professional meetings
- CE programs
- Review articles
- Textbooks
- Guidelines

American College of Clinical Pharmacy

Updates in Therapeutics® 2012:
Ambulatory Care Pharmacy Preparatory Review and Recertification Course

Psychiatric Disorders

Carol A. Ott, Pharm.D., BCPP
Clinical Associate Professor
Purdue University College of Pharmacy

Conflict of Interest Disclosures

- Nothing to disclose

Learning Objectives

1. Describe the DSM-IV, TR (*Diagnostic and Statistical Manual of Mental Disorders,* Text Revision) 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.
2. Relate common drug and nondrug therapy for the psychiatric disorders, including drug, dose, frequency, adverse effects, drug interactions, and monitoring parameters.

Learning Objectives

3. Recommend appropriate initial and maintenance treatment for psychiatric disorders, including duration of therapy.
4. 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.

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.

5

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.

6

Anxiety Disorders Case Questions

- 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?

7

Anxiety Disorders Overview

- Anxiety disorders are the most commonly diagnosed psychiatric disorders, with a 1-year prevalence rate of ~ 15%.
- 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.

Handout Pages 1- 4 – 1-5 8

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.

Handout Pages 1-4 – 1-6 9

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 commonly used, several weeks are needed for onset of action.
- Propranolol or lorazepam may be used as needed for specific situations or events.

Handout Pages 1-4 – 1-7 10

Obsessive-Compulsive Disorder

- 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.

Handout Pages 1-4 – 1-8 11

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.
- Psychotherapy or immersion therapy (subjecting the patient to fearful situations) may be useful to reduce symptoms and improve functionality.

Handout Pages 1-4 – 1-8 12

Post-Traumatic Stress Disorder

- Current focus of the VA system – returning combat veterans.
- May be combat-related or civilian.
- Civilian trauma is easier to treat – likely one-time event versus recurrent.
- Triad of symptoms – reexperiencing, hyper-arousal, avoidance
- SSRIs are first-line therapy, mirtazapine, topiramate, and atypical antipsychotics have been studied as augmenting agents.
- 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 – reexperiencing, hyperarousal, prominent psychosis
  - Adrenergic antagonist (prazosin) – nightmares associated with reexperiencing

Handout Pages 1-4 – 1-8 13

Anxiety Case Question

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.

Handout Page 1-5 14

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

Handout Pages 1-4 – 1-8 15

Sleep Disorders Case

- JJ is a 56 year old man who states that he has not ever slept very well, but complains of worsening of symptoms for the past 4 weeks. He has difficulty falling asleep and wakes up several times per night. His other medical conditions include asthma and hypertension. His current medications are lisinopril 10 mg orally once a day, atenolol 100 mg orally once a day, and an albuterol inhaler, 2 puffs every 6 hours as needed for shortness of breath (added to drug regimen one month ago). JJ weighs 275 pounds and is 6'0" tall. His BMI is 37. He has smoked 1 PPD cigarettes for 25 years. He occasionally drinks alcohol, but has begun to have a drink before bed to "help him sleep".

16

Sleep Disorder Case Questions

- What questions should be asked of JJ?
- What other testing should be done?
- What questions should be asked regarding JJ's medication regimen?
- What sleep medication is the best choice for JJ, if appropriate?

17

Sleep Disorders

- 30% of adults complain of sleep difficulties, 10% suffer from insomnia.
- Weight, medical conditions, medications, and substance use can contribute to disordered sleep.
- Evaluation of conditions, such as sleep apnea or restless leg syndrome, should be performed, if appropriate.
- Drug therapy includes benzodiazepines, non-benzodiazepine hypnotics, and novel sleep medications.
- Use of medications for sleep should be used for short periods of time (10 – 14 days), but is used much longer clinically.
- Cognitive behavioral therapy in combination with short-term medication use has been shown to be more effective long-term than use of medications alone.

Handout Pages 1-9 – 1-14 18

Sleep Disorders – Non-Drug Therapy

- Patients should be counseled on stimulus control and sleep hygiene:
  - Stimulus control – go to bed and wake up at the same time every day, avoid daytime naps, use the bedroom for sleep and intimacy only, schedule "worry time".
  - Sleep hygiene – exercise routinely, avoid caffeine, nicotine, and alcohol prior to bedtime, reduce the use of these if possible, have a comfortable sleeping environment, relaxation therapy

Handout Page 1-10 19

Sleep Apnea

- Obstructive sleep apnea is most common.
- Obesity is a common cause of OSA.
- Treatment of sleep apnea can significantly improve symptoms, including:
  - Weight loss
  - Surgical correction of obstruction
  - Continuous positive airway pressure (CPAP)
- Avoid use of sedative/hypnotic agents in patients with sleep apnea.

Handout Page 1-13 20

Restless Leg Syndrome

- RLS is defined as undesirable sensations in the legs before sleep and the urge to move with resolution of symptoms upon moving.
- Iron deficiency can contribute to RLS – evaluation of the CBC, serum iron, and serum ferritin is suggested.
- Dopamine agonists are considered first-line therapy.
- Other agents used include opiates, clonazepam, and anticonvulsants (carbamazepine).

Handout Pages 1-13 – 1-14 21

Shift Work Sleep Disorder

- SWSD is considered a circadian rhythm disorder that occurs in people who work the night shift or a frequently changing work shift.
- Functional impairment is caused by insomnia during the major sleep period or excessive sleepiness during the major awake period.
- Environmental factors similar to those for insomnia should be evaluated.
- Short-acting benzodiazepines or Z-hypnotics can be considered to improve sleep time.
- Modafinil and armodafinil are FDA-approved to treat the daytime sleepiness associated with SWSD.
- Dosing of these agents is once daily with the dose taken 1 hour before starting shift work.

Handout Page 1-14 22

Sleep Disorders Case Question

What sleep medication is the best choice for JJ, if appropriate?

- A. Diphenhydramine 50mg
- B. Zolpidem 10mg
- C. Temazepam 15mg
- D. Mirtazapine 30mg

Handout Pages 1-10 – 1-12 23

Sleep Disorders Case Answer

- What questions should be asked of JJ?
  - How close to bedtime do you have a drink or smoke a cigarette? What is your bedtime ritual? Has anything changed in the past few weeks?
- What other testing should be done?
  - Epworth Sleepiness Scale, polysomnography for sleep apnea
- What questions should be asked regarding JJ's medication regimen?
  - At what time of day do you take your medications or use your inhaler?
- What sleep medication is the best choice for JJ, if appropriate?
  - If JJ does not have sleep apnea and you are not concerned for alcohol use at bedtime, short-term use of a Z-hypnotic may be considered. A novel sleep agent, such as ramelteon or trazodone, may be used.

Handout Pages 1-9 – 1-13 24

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.

25

Major Depression Case Questions

- 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?

26

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.

Handout Pages 1-15 – 1-16

27

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.

Handout Page 1-17

28

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.
- That said, for some patients, a reduction in symptoms will be the maximal response.

Handout Pages 1-17; 1-24 – 1-25

29

Dose and Duration of Antidepressant Therapy

- Dose and duration are two important factors in treatment success.
- 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

Handout Pages 1-18 – 1-19

30

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

Handout Pages 1-18 – 1-25 31

What to monitor for antidepressants

- 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

Handout Pages 1-18 – 1-27 32

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.

Handout Pages 1-17; `-25 33

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.

Handout Pages 1-17 – 1-24 34

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?
  - While these are hard questions to ask, they are appropriate and not generally offensive to a person with depression. The clinician should ascertain the safety of the patient and the need for referral to psychiatric services.

Handout Pages 1-16 – 1-17 35

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. She states that she has only been sleeping 3 hours per night, but is not fatigued. She exhibits no other symptoms. No other laboratory monitoring has been done for the past year.

36

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?

37

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 10 years.
- Careful questioning is necessary to ascertain a past experience of mania or hypomania.
- Suicide attempts may occur in either mood pole.

Handout Pages 1-27 – 1-28

38

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.

Handout Pages 1-29 – 1-33

39

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.

Handout Pages 1-27 – 1-33

40

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.

Handout Pages 1-27 – 1-33

41

Bipolar Disorder – Treatment Considerations

- Take into account the type of bipolar disorder that is diagnosed.
- Pregnancy
  - Most mood stabilizers are Category D.
  - 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”

Handout Pages 1-33 – 1-34

42

Bipolar Disorder Case Question

What is the most appropriate drug therapy intervention for KW?

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

Handout Pages 1-29 – 1-33

43

Bipolar Case Answer

- 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.

Handout Pages 1-28 – 1-33

44

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.

45

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?

46

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.

Handout Page 1-35

47

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.

Handout Pages 1-35 – 1-37

48

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 payor source for the patient.
- Risperidone is currently the only generic atypical antipsychotic and is commonly used first-line.
- 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.

Handout Pages 1-37 – 1-45 49

Monitoring of 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
  - Evaluation for akathisia requires the clinician to ask the patient if they feel restless or the need to constantly move.
- 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.

Handout Pages 1-41 – 1-43 50

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.

Handout Page 1-46 51

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.

Handout Pages 1-37 – 1-46 52

Schizophrenia Case Answer

- 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.

Handout Pages 1-35 – 1-43 53

Attention Deficit 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 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 is having difficulty falling asleep and 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.

54

Attention Deficit 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?

55

Attention Deficit Disorder Overview

- The prevalence of ADD is thought to be ~6%.
- Many children diagnosed with ADD will continue symptoms into adulthood.
- Risk factors for the development of ADD include family history of ADD 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 ADD with stimulant medications does not increase the risk of substance use, may actually protect against this.

Handout Pages 1-47 – 1-48 56

Principles of Stimulant Use in ADD

- The goal of treatment is to reduce or eliminate symptoms of ADD so that the patient is able to engage and be functional in all environments.
- Hyperactive symptoms are predominant in childhood, inattention in adults.
- ADD 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 ADD.
- Stimulant monotherapy is preferred, may have to use long-acting and short-acting doses of the same agent.

Handout Pages 1-48 – 1-54 57

Which stimulant to choose?

- Methylphenidate, dextroamphetamine, and mixed amphetamine salts are 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.
- Generally, initial therapy is with an immediate release dosage form to find the appropriate dose, then a switch to a longer-acting dosage form is made.

Handout Pages 1-49 – 1-52 58

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.

Handout Pages 1-51 – 1-52 59

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 ADD, may also be useful for insomnia secondary to stimulant use.

Handout Pages 1-52 – 1-54 60

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. Switch to methylphenidate CD long-acting 20mg and evaluate sleep hygiene

Handout Pages 1-49 – 1-54 61

Attention Deficit Disorder Case Answers

- What baseline information should be obtained prior to initiating stimulant therapy?
  - Family history of cardiovascular disease is important to have, 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.
- 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.

Handout Pages 1-48 – 1-54 62

Substance Dependence Case

DF is a 35 year old man who presents to the psychiatric emergency room with belligerent behavior and acute psychosis, including visual and auditory hallucinations. He has a past psychiatric history of schizophrenia and alcohol, nicotine, and cocaine abuse. DF has a history of delirium tremens during past alcohol detoxifications, but has not had seizures associated with this. His current medications include naltrexone 380 mg intramuscularly every 4 weeks, paliperidone palmitate 117 mg intramuscularly every 4 weeks, and sodium valproate ER 1500 mg orally at bedtime. Adherence to IM injections is confirmed, he has not refilled sodium valproate at the pharmacy for 3 months. He has NKDA and smokes 1 PPD cigarettes. The urine toxicology screen is positive for cocaine, BAL is 0.25. DF is admitted to the inpatient psychiatric unit with PRN orders for lorazepam 2mg PO/IM every 2 hours as needed for agitation/withdrawal and haloperidol 5mg PO/IM every 4 hours as needed for agitation, in addition to his usual routine medications. Routine CIWA rating scale performance is ordered per nursing staff.

Substance Dependence Case Questions

- What is the timeframe for the onset of DTs or seizures for DF?
- What oral supplement should be given to DF? Why?
- What are the advantages and disadvantages of routine versus PRN dosing of benzodiazepines for DF?

Tobacco Dependence

- Patients with mental health disorders are considered to smoke tobacco at a greater rate than the general population, with more use associated with a more chronic disease.
- These patients are as likely to stop smoking as those with other medical conditions.
- Nicotine replacement therapy, bupropion, and varenicline, as well as substance abuse psychotherapy, is used successfully in this population.
- Treatment of tobacco dependence in psychiatric disorders is similar to the strategy used in the primary care setting, although patients may be more successful if not asked to set a quit date and are able to use these treatment for a longer period of time than the usual 3 to 6 month window.

Handout Page 1-56 65

Alcohol Dependence

- Patients with a positive blood alcohol level (BAL) upon presentation to the emergency department should be assessed for the risk of delirium tremens (DTs) during alcohol withdrawal.
- Those with a past history of DTs or several past withdrawals should be considered at higher risk and monitored closely using the Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-Ar) routinely.
- Treatment for withdrawal should be either as-needed or routine dosing of a benzodiazepine.
- Thiamine is an important supplement to be given to patients in alcohol withdrawal to avoid the risk of Wernice's encephalopathy.
- FDA-approved treatments for alcohol dependence include disulfiram, naltrexone, and acamprosate.
- Successful treatment of alcohol dependence should include group and/or individual therapy in a substance dependence treatment setting.

Handout Pages 1-57 - 1-58 66

Opiate Dependence

- Prescription drug dependence has become a national epidemic, with many states enacting legislation and prescription monitoring programs to combat this. Use of illicit substances, including heroin, continue to be problematic.
- Opiate withdrawal is not generally a life-threatening condition, but symptomatic treatment is available and includes the use of clonidine, loperamide, NSAIDs, antiemetics, and dicyclomine as-needed.
- The Clinical Opiate Withdrawal Scale (COWS) is commonly used to evaluate the severity of withdrawal symptoms.
- Methadone, buprenorphine, and naltrexone are FDA-approved for the treatment of opiate dependence and can be used in the outpatient setting.
- Methadone maintenance treatment is available in structured, federally-regulated treatment settings and includes psychosocial treatment, as well as drug therapy.
- Buprenorphine may be prescribed by physicians in outpatient settings as set out by the Drug Abuse Treatment Act of 2000 (DATA 2000)

Handout Pages 1-58 - 1-60 67

Cocaine/Stimulant and Marijuana Dependence

- Symptoms of cocaine and stimulant withdrawal are similar, including craving, dysphoria, depression, somnolence, and agitation.
- Significant depression, requiring a consideration for antidepressant treatment, may result and last for several months.
- There are no FDA-approved medications for the treatment of cocaine or stimulant dependence, other than symptomatic treatment of withdrawal.
- Urine toxicology screens in for patients with mental health disorders are commonly found to contain marijuana.
- Acute affects of cannibis abuse can include psychosis and hallucinations, the continued use of marijuana is a risk factor for earlier onset of schizophrenia in at-risk individuals.
- There are no FDA-approved treatments for marijuana dependence, although clinical trials include the use of dronabinol, fluoxetine, lithium, and rimonabant.

Handout Pages 1-60 - 1-61 68

K2/Spice and Bath Salts

- K2 and Spice are synthetic cannabinoids with effects similar to marijuana with the addition of psychosis, aggression, and electrolyte imbalances, specifically hypokalemia.
- Federal and state legislation has recently focused on these “designer drugs” in an attempt to decrease use, although with difficulty in assigning illegality to specific substances and including similar new chemical versions.
- Treatment of K2/Spice abuse acutely includes supportive care, antipsychotics have not been shown to be effective in the acute setting.
- Bath salts are structurally similar to amphetamines and the naturally-occurring substance cathinone.
- The use of bath salts has reached epidemic proportions in some areas of the country, legislation to counter use of K2/Spice has often included bath salt chemicals.
- The acute effects of bath salts include cardiac and CNS adverse events, as well as psychosis and violent behavior.

Handout Pages 1-61 - 1-62 69

Substance Dependence Case Question: What is the most appropriate outpatient medication intervention for DF?

- A. Switch to disulfiram 250 mg orally once daily.
- B. Continue naltrexone IM 380 mg every 4 weeks.
- C. Continue naltrexone IM 380 mg every 4 weeks and ensure psychosocial counseling.
- D. Add acamprosate 666 mg orally three times daily

Handout Pages 1-443 - 1-448 70

Substance Dependence Case Answers

- What is the timeframe for the onset of DTs or seizures for DF?
  - Delirium tremens and/or seizures onset is generally within 96 hours after the discontinuation of alcohol ingestion. Patients may seem fine prior to this with sudden onset of symptoms, requiring diligence in monitoring.
- What oral supplement should be given to DF? Why?
  - Oral thiamine supplementation should be given during the hospitalization to correct thiamine deficiency and decrease the risk of Wernicke’s encephalopathy, especially if there is consideration for IV fluids containing dextrose.
- What are the advantages and disadvantages of routine versus PRN use of benzodiazepines during the withdrawal period?
  - Routine dosing of the benzodiazepine can ensure a reduced risk of withdrawal symptoms, but often causes an increased overall dosing of the drug. PRN dosing based on the CIWA-Ar scale score can more appropriately symptoms and lower the overall dosing burden.

Questions?

72

accp
American College of Clinical Pharmacy

Updates in Therapeutics® 2012:
Ambulatory Care Pharmacy Preparatory Review and Recertification Course

Oncology

Sally Yowell Barbour, PharmD, BCOP, CPP
Duke Cancer Institute at Duke University Hospital

Conflict of Interest Disclosures

- No conflicts of interest

Learning Objectives

- Outline appropriate screening and prevention strategies for lung, prostate, and breast cancers.
- Describe the most common treatment modalities for lung, prostate, and breast cancers.
- Explain the expected outcomes in survival and toxicity with respect to the above cancers.
- Devise and communicate prevention and treatment strategies for common toxicities seen with oral therapies used for treatment, including rash, hypertension, and drug interactions.
- Identify, assess, and recommend appropriate pharmacotherapy for managing the common complications of cancer chemotherapy, including myelosuppression, nausea and vomiting, and anemia.

LUNG CANCER

Patient Case (1-74)

- JH is a 67 year old male who has been admitted for an upper respiratory infection/pneumonia.
- Weight: 150 lbs
- HPI: persistent cough and been treated with several courses of antibiotics with minimal relief of his symptoms. For several days prior to his admission, he complained of worsening cough, increasing shortness of breath, back, weight loss (usually weighs 170 lbs) and occasional blood tinged sputum.
- PMH: Chronic obstructive pulmonary disease (COPD) × 2 years
- FH/SH: Has smoked 2 packs a day for 40 years. Occasional social alcohol use.
- General: Pleasant male in mild distress. Slight breathing difficulties
- Neck: Supple, slight axillary adenopathy
- Lung: Decreased breath sounds, bilateral wheezes
- Extremities: Clubbing of fingers bilaterally
- Labs-see handout
- Workup done during admission reveals:
  - L peripheral mass, enlarged hilar lymph nodes on CXR. 3 × 5 cm mass in upper lobe on CT scan.
  - Biopsy positive for small cell lung cancer.
  - Bone scan positive.
  - Brain CT negative.

Patient Case #1

Which one of the following statements regarding lung cancer is true?

A. It is the second most common cause of cancer-related death.
B. Smoking cessation reduces the risk of developing lung cancer to that of a never smoke after 5 years.
C. Common signs of lung cancer include cough, weight loss, and hemoptysis..
D. Pancoast tumors are characterized by ipsilateral ptosis, miosis, and anhidrosis

Workbook Page 1-74; Answer: Page 1-77

Incidence

- Second most common malignancy in the United States
  - 221,130 new cases in 2011
- Most common cause of cancer-related death
  - 156,940 deaths in 2011
- Peak incidence between 50-70 years
- 5-year survival for all stages is 16%

Etiology/Pathogenesis

- Molecular abnormalities
- K-ras and epidermal growth factor receptor (EGFR)
  - K-ras mutations in adenocarcinoma exclusive to smokers
  - EGFR mutation frequency in non-small cell lung cancer ~13%
  - Mutually exclusive

Risk Factors

- Tobacco abuse
  - Related to 85% of all cases
  - Dose-response relationship
  - Smoking cessation reduces risk
  - Gender differences
- Occupational/environmental exposure
- Asbestos
- Radon
- Other chemicals
- Diet
- Genetic predisposition
- Coexisting lung disease

Prevention/Screening

- Prevention
  - No effective chemoprevention
  - Smoking cessation
- Screening
  - No methods shown to improve survival
  - National guidelines do not recommend routine use of CT for screening for low or moderate-risk individuals
  - Ongoing trials to help with currently conflicting data

Screening cont.

- National Lung Screening Trial
  - 53,000 current or former heavy smokers with at least a 30-pack year smoking history, no signs, symptoms or history of lung cancer, age 55-74
  - Randomized to low-dose helical CT or standard chest x-ray
  - 20% fewer lung cancer deaths in those screened with low-dose CT
- High-risk patients
  - High-risk patients should enroll in clinical trials
  - NCCN does recommend baseline low-dose helical CT for high-risk patients

Lung Cancer

- Small Cell Lung Cancer (SCLC)
  - Accounts for ~16% of all lung cancers
  - Clear relationship to tobacco abuse
  - Most aggressive pulmonary tumors
- Non-Small Cell Lung Cancer (NSCLC)
  - Accounts for ~80-85% of all lung cancers
  - Less aggressive, slower growing
  - Adenocarcinoma is most common
  - Other subtypes: large cell, mesothelioma, squamous

Signs/Symptoms

- Cough
- Hemoptysis
- Dyspnea
- Wheezing
- Hoarseness
- Dysphagia
- Pleural effusions
- Anorexia
- Weight loss
- Fatigue
- Superior vena cava syndrome

Paraneoplastic Syndromes

- Hypercalcemia
- SIADH
- Cushing syndrome
- Eaton-Lambert syndrome
- Pulmonary hypertropic osteoarthopathy
- Clubbing
- Anemia
- Dermatomyositis
- Horner syndrome
- Pancoast syndrome

Patient Case #1 cont.

Workup done during admission reveals L peripheral mass, enlarged hilar lymph nodes on CXR, and 3- × 5-cm mass in upper lobe on CT scan. Biopsy positive for SCLC. Bone scan positive. Brain CT negative. Which one of the stages of disease best represents JH's stage?

- A. Limited stage small cell lung cancer
- B. Extensive stage small cell lung cancer
- C. Stage I small cell lung cancer
- D. Need more information to stage

Workbook Page 1-82; Answer: Page 1-79-83

Patient Case #1 cont.

Which of the following is the most appropriate treatment for JH?

- A. Radiation
- B. Cisplatin/etoposide/radiation
- C. Cisplatin/etoposide
- D. Supportive care

Workbook Page 1-82; Answer: Page 1-82-3

Diagnosis/Staging

- Chest XRT/CT
- Tissue
- PFTs
- Metastatic work-up for SCLC
- SCLC
  - Limited stage
  - Extensive stage
- NSCLC: TNM

Treatment: SCLC

- General
  - Very sensitive to chemotherapy and radiation
  - Overall 5-year survival 5%
- Limited Stage
  - Curative intent-median survival 16-22 months
  - Concurrent chemoradiotherapy followed by PCI
- Extensive Stage
  - Rarely curable-median survival with treatment 9-11 months
    - 2-year survival less than 5%
  - Combination chemotherapy +/- PCI depending on presence of brain metastases and response

Patient Case #2 (1-84)

- NH is a 52 year old female with complaints of dyspnea, hoarseness and cough.
  - HPI: persistent cough and been treated with antibiotics by her primary care physician.
  - FH/SH: Never smoked.
- General: Pleasant, anxious female with mild breathing difficulties
- Lung: Decreased breath sounds on right
- Labs-see handout
- Patient workup: R peripheral mass and pleural effusion on CXR. Mass 3 × 6 cm on CT scan, also mass on R adrenal gland. Pleural fluid + for adenocarcinoma.

Patient Case #2

The most appropriate treatment for NH is?

- A. Best supportive care
- B. Erlotinob
- C. Carboplatin/paclitaxel/bevacizumab
- D. Topotecan

Workbook Page 1-84; Answer: Page 1-85

Treatment: NSCLC

- Resectable Disease (Stages I, II And IIIA)
  - Surgery
  - Chemotherapy for resected Stages II and IIIA
  - Neoadjuvant chemotherapy/radiation option for IIIA
- Stage IIIB
  - Platinum-based chemotherapy with radiation
- Stage IV
  - Chemotherapy improved survival vs. best supportive care
  - No standard chemotherapy regimen (platinum-based preferred)
  - First line therapy based on histology, mutations and performance status

Treatment: NSCLC Cont.

- Treatment based on performance status
  - PS 0-1: Platinum-based doublet
  - PS 2: Single agent or Platinum-based doublet
  - PS 3-4: No benefit for standard cytotoxic chemo
- Role of Mutations
  - Erlotinib for EGFR-positive patients (first line or when discovered)
  - Crizotinib for ALK-positive patients (first line)
- Maintenance chemo for those with response or stable disease (agent depends on histology)
  - Continuation: bevacizumab, cetuximab, pemetrexed or gemcitabine
  - Switch: erlotinib, pemetrexed, docetaxel
- Recurrent disease
  - Docetaxel, pemetrexed, erlotinib
  - Clinical trials

BREAST CANCER

Patient Case #3 (1-86)

- JK is a 56 year old post menopausal Caucasian female who is seen by her primary care physician for her annual visit. She is interested in her options for risk reduction for breast cancer. She is in good heath. She has a significant family history: mother diagnosed at 55, sister diagnosed at 44, maternal aunt diagnosed at 60 and another maternal aunt diagnosed with ovarian cancer at 62. She had menarche at age 12, she had 3 children- the first at age 34, underwent surgical menopause at age 45 with an abdominal hysterectomy (ovaries were spared). She did not take hormone replacement therapy. She did take birth control pills × 10 years and has had normal mammograms since the age of 40.

Patient Case #3 (1-86)

Which of the following is the least significant risk factor for her developing breast cancer?

- A. Family history
- B. Age of first menarche
- C. Age of first pregnancy
- D. Birth control pills

Workbook Page 1-84; Answer: Page 1-87-88

Incidence

- Most common cancer in females in US
  - 232,620 cases (2140 of these in males)
- Second most common cause of cancer-related death in women
- Incidence decreased ~2% per year from 1999-2006
- Mortality decreased steadily since 1990
- Lifetime risk for developing is 1 in 8

Etiology

- Genetics
- Familial breast cancers account for ~ 10% of all breast cancer
- Tumor suppressor genes
  - BRCA 1 and BRCA 2
  - p53
- Tumor progression genes
  - *Her2/neu*
- Others: *c-myc*, cyclin D1

Risk Factors

- Age
- Family history
- Estrogen exposure
- Benign breast disease
- Breast density
- Obesity and BMI
- Physical activity
- Alcohol
- Radiation exposure

No identifiable risk factors other than gender and age in more than 60% of women

Gail Model

- Risk assessment tool:
  - Does the woman have a medical history of any breast cancer or of DCIS or LCIS? — No
  - What is the woman's age? — 56
  - What was the woman's age at the time of her first menstrual period? — 12 to 13
  - What was the woman's age at the time of her first live birth of a child? — >/=30
  - How many of the woman's first-degree relatives - mother, sisters, and/or daughters - have had breast cancer? — > 1
  - Has the woman ever had a breast biopsy? — No
  - What is the woman's race/ethnicity? — White

5 Year Risk: 3.6%
Average woman (age 56): 1.5%

Screening: Average Risk

Intervention	ACS	NCCN
BSE	Age >/= 20; breast awareness; prompt report of changes	Age >/= 20; breast awareness
CBE	Every 1-3 years Annual (40+)	Every 1-3 years (20-39) Annual (40+)
Mammogram	Annual (40+)	Annual (40+)

Prevention

- Surgical
  - Prophylactic mastectomy
  - Bilateral oopherectomy
- Pharmacologic
  - Tamoxifen
  - Raloxifene

Prevention: NSABP Breast Cancer Prevention Trial

- 13,388 high risk women
- Tamoxifen 20mg PO daily vs. placebo x 5 years
- Benefits:
  - Risk of invasive breast cancer ↓ 49% and noninvasive ↓ 50%
  - Reduced risk of ER+ tumors 69%
  - Insignificant reduction in skeletal fractures
- Risks:
  - Risk of early stage endometrial cancer, stroke, pulmonary embolism, deep vein thrombosis (significant in women 50 and older), vaginal discharge and cataracts all increased

Prevention: STAR trial

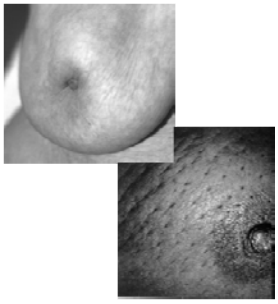
- 19,747 postmenopausal women
- Tamoxifen 20mg PO daily vs. raloxifene 60 mg PO daily
- Benefits:
  - Reduction in incidence of invasive breast cancer, other cancers, stroke, ischemic heart disease and fractures
- Risks:
  - More endometrial hyperplasia, venous thromboembolism and cataracts with tamoxifen

Prevention: Summary-NCCN Guidelines

- Women with history of atypical hyperplasia or lobular carcinoma in situ, 5-year Gail model risk of 1.7% or more, more than 20% lifetime risk and life expectancy greater than 20 years and women who desire risk reduction
- Options
  - Bilateral total mastectomy
  - Bilateral salpingo-oopherectomy
  - Premenopausal: Clinical trial or tamoxifen
  - Postmenopausal: Clinical trial or tamoxifen or raloxifene

Natural History/Presentation

- Unilateral, usually painless, firm, slow-growing mass
- Nipple retraction, dimpled skin, ulceration
- Spreads to lymph nodes, lung, live, bone and brain



Diagnosis/Staging/Prognosis

- History and physical exam (including CBE)
- Diagnostic mammogram and ultrasound
- Biopsy
- Blood counts, LFTs
- ER/PR status, *Her2* status
- Genetic counseling
- Optional: bone scan, PET
- Size
- Stage at diagnosis
- ER/PR status
- *Her2* amplification
- Response to therapy
- Lymph nodes
- Tools
  - Adjuvant! Online
  - Oncotype DX
  - MammaPrint

Treatment: LCIS and DCIS

- Lobular Carcinoma in situ (LCIS)
  - Observation
  - Risk reduction-tamoxifen or raloxifene
  - Bilateral mastectomy
- Ductal Carcinoma in site (DCIS)
  - Lumpectomy without LN surgery plus radiation
  - Total mastectomy
  - Lumpectomy without radiation
  - Consider tamoxifen for 5 years for certain women

Treatment: Early Stage

- Goal: CURE
- Locoregional therapy-surgery with or without radiation
- Neoadjuvant chemotherapy
- Systemic adjuvant therapy for stages IA, IB, IIA and IIB
  - Endocrine therapy
  - Chemotherapy
  - Biologic therapy

Treatment: Locally Advanced

- Stages IIIA, IIIB and IIIC
- Primary systemic chemotherapy
  - Anthracycline-containing regimen with/without taxane
- Followed by local therapy (surgery, LN dissection and radiation)
- Adjuvant therapy after surgery
- Trastuzumab included if *Her2* positive

Treatment: Metastatic/Recurrent

- Goal: palliation, quality of life and prolongation of life
- Median survival 3 years
- Treatment options
  - Chemotherapy (anthracyclines, taxanes, capecitabine)
  - Biologic therapy (trastuzumab, lapatinib, bevacizumab)
  - Endocrine therapy (aromatase inhibitors, antiestrogens, progestins, LHRH agonists, androgens)

PROSTATE CANCER

Patient Case (1-96)

- LB is a 43 yo male who presents to the clinic for his annual visit. He is generally in good health. His wife's father was just diagnosed with prostate cancer and he asks about screening.

Patient Case #3 (1-96)

Which one of the following is the best recommendation for this patient?

- A. Tell him that he is not a candidate for screening since he is younger than 50
- B. Discuss the risks of screening and expected benefits and that in his case the risks likely outweigh the benefits
- C. Discuss the risks of screening and expected benefits and that in his case the benefits likely outweigh the risks
- D. Recommend starting finasteride to prevent prostate cancer.

Workbook Page 1-96; Answer: Page 1-99

Incidence

- Most common malignancy diagnosed in men
  - 240,890 new cases in 2011
  - 1 in 6 lifetime chance of diagnosis
- Second most common cause of cancer-related death in men
  - 33,720 deaths in 2011

Risk Factors

- Age
  - Most important
  - Incidence increase with each decade
  - Median age of diagnosis is 68; rare under 40
- Race
  - More common in African Americans
- Family history
- Socioeconomics
- Genetics
- Diet
- Occupation
- Vasectomy

Prevention

- Finasteride: Prostate Cancer Prevention Trial (PCRT)
  - 18,881 men 55 years and older with low risk of prostate cancer
  - Finasteride 5mg PO Daily vs. placebo
  - 24.8% reduction in prostate cancer prevalence during 7-year period
  - Higher Gleason scores in those who did develop prostate cancer
- Dutasteride: REDUCE
  - 23% lower risk of developing prostate cancer in treatment arm

Prevention Guidelines

- American Society of Clinical Oncology and American Urologic Association
  - Asymptomatic men with PSA </= 3ng/mL who undergo regular screening may benefit from a discussion regarding use of finasteride or dutasteride
  - Men taking these agents for BPH or other urinary symptoms may also benefit from discussion
  - Does NOT recommend use for chemoprevention
- Neither agent FDA approved for chemoprevention

Screening

- Digital Rectal Exam (DRE)
- Prostate-specific antigen (PSA)
  - Specific to prostate not to cancer
  - Most commonly used cutoff is 4ng/mL
- Biopsies
  - Recommended for PSA > 4ng/mL

Screening

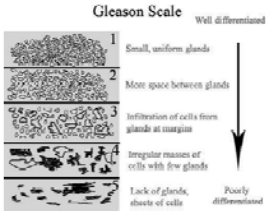
	ACS	NCCN
Intervention	Average Risk: PSA (+/- DRE) starting at age 50 High Risk: PSA (+/- DRE) starting at age 45	All men: PSA and DRE starting at age 50 AA or family history: PSA and DRE at 40-45
Frequency	Every 2 years if PSA <2.5ng/mL Yearly if 2.5ng/mL or higher	If initial PSA <1ng/mL, screen again at age 45 Yearly if initial PSA 1ng/mL or greater

Signs/Symptoms

- Early disease is asymptomatic
- Advanced disease
  - Impotence
  - Alterations in urination
  - Lower extremity edema
  - Anemia
  - Weight loss
- Metastasizes to bone, liver and lung

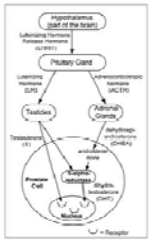
Diagnosis/Staging

- Physical exam, PSA, TRUS, chemistries, bone scan, CT/MRI
- Biopsy
- Gleason grading
- Staging: TNM



Treatment

- Active surveillance
- Radical Prostatectomy
- Radiation
- Androgen deprivation therapy
- Secondary hormonal therapy
- Chemotherapy
- Immunotherapy



Treatment: Clinically localized

- Depends on expected survival, risk of recurrence, Gleason score
  - Active surveillance
  - Radiation therapy
  - Radical prostatectomy with or without LN dissection
  - Androgen deprivation therapy

Treatment: Locally Advanced

- Radiation therapy plus ADT
- Radiation therapy plus brachytherapy with/without ADT
- Radical prostatectomy plus LN dissection
- ADT

Treatment: Metastatic Disease

- Initial
  - ADT
  - Radiation therapy plus long-term ADT
- Recurrent Disease
  - Radiation
  - Observation
  - ADT
  - Surgery

Treatment: Castrate-Resistant Disease

- No metastases
  - Clinical trial
  - Observation
  - Antiandrogen withdrawal
  - Secondary hormone therapy (ketoconazole, steroids)
- Metastases
  - Chemotherapy
  - Clinical trial
  - Palliative radiation
- Asymptomatic
  - Sipuleucel-T

Supportive Care in Prostate Cancer

- Osteoporosis
- Diabetes and cardiovascular disease
- Bone metastases

SUPPORTIVE CARE

Patient Case #7 (1-109)

- DH is a 60 year old female with a recent diagnosis of non-small cell lung cancer. She is scheduled to begin treatment with cisplatin and vinorelbine.

Patient Case #7 (1-109)

All of the following are risk factors for chemotherapy induced nausea and vomiting in DH except?

- A. Gender
- B. Chemotherapy
- C. Anxiety
- D. Disease

Workbook Page 1-109; Answer: Page 1-111-112

Patient Case #8 (1-109)

Which of the following is the most appropriate chemotherapy regimen for DH on day 1?

- A. Palonosetron × 1 dose and dexamethasone × 1 dose
- B. Ondansetron × 1 dose and lorazepam × 1 dose
- C. Palonosetron × 1 dose and fosaprepitant × 1 dose and dexamethasone × 1 dose
- D. Ondansetron × 1 dose and fosaprepitant × 1 dose and lorazepam × 1 dose

Workbook Page 1-109; Answer: Page 1-113

Chemotherapy Induced Nausea and Vomiting

Rank	1983[1]	1993[2]	1995[3]	1999[4]	2004[5]
1	Vomiting	Nausea	Nausea	Nausea	Fatigue
2	Nausea	Constantly tired	Loss of hair	Loss of hair	Nausea
3	Loss of hair	Loss of hair	Vomiting	Constantly tired	Sleep disturbances
4	Thought of coming for treatment	Effect on family	Constantly tired	Vomiting	Weight Loss
5	Length of time treatment takes	Vomiting	Having to have an injection	Changes in the way things taste	Hair Loss

1. Coates A, et al. *Eur J Cancer Clin Oncol.* 1983;19:203-208; 2. Griffin AM, et al. *Ann Oncol.* 1996;7:189-195; 3. De Boer-Dennert M, et al. *Br J Cancer.* 1997;76:1055-1061; 4. Lindley C, et al. *Cancer Pract.* 1999;7:59-65; 5. Hofman M et al. *Cancer.* 2004;101:851-857.

Chemotherapy Induced Nausea and Vomiting

- Acute CINV
  - Nausea and vomiting occurring within the first 24 hours after chemotherapy administration
- Delayed CINV
  - Nausea and vomiting occurring 24 hours or more after chemotherapy administration
- Anticipatory CINV
  - Occurs as a learned response due to poorly controlled CINV
  - Triggered by tastes, odors, sights, thoughts, anxiety
- Breakthrough CINV
  - Nausea and/or vomiting despite recommended antiemetic prophylaxis
- Refractory CINV
  - CINV that persists despite prophylactic and breakthrough medications

CINV: Risk Factors

- Chemotherapy-specific
  - Regimen/agents-dose, combination, emetogenicity
  - Infusion time
  - Repetition
- Patient-specific
  - Younger age (<50 years)
  - Female gender
  - Low alcohol consumption (≤ 1 drink/day)
  - History of nausea with stress
  - History of motion sickness or hyperemesis of pregnancy
  - Patient's initial expectations
  - Previous experience with chemotherapy

CINV: Classes of Antiemetics

Drug	Pathway	Role in CINV	Side Effects
Ondansetron/granisetron/ dolasetron, Palonosetron	Serotonin	Acute	Headache, constipation, asthenia, diarrhea, sedation, QTc effects
Aprepitant/Fosaprepitant	Substance P	Delayed	Injection site/infusion reactions, drug interactions
Dexamethasone	Unknown	Delayed Breakthrough	Transient elevations in glucose, insomnia, anxiety, and gastric upset, psychosis
Prochlorperazine	Dopamine	Breakthrough	Akathisias, sedation, dizziness
Metoclopramide	Dopamine	Delayed	Akathisias, sedation, diarrhea
Haloperidol Olanzapine	Dopamine	Delayed Breakthrough	Akathisias, dystonia, prolong QT, urinary retention, dizziness, hyperglycemia, myelosuppression
Lorazepam	Unknown	Anticipatory Breakthrough	Sedation
Dronabinol/Nabilone	Cannabinoid	Breakthrough Refractory	Sedation, dizziness, dysphoria, euphoria, hallucinations

Key Principles of Antiemetic Control

- Administer antiemetics prophylactically
- Schedule agents to cover the duration of risk of CINV
- Oral and IV antiemetics have equivalent efficacy
- Consider toxicity of antiemetic agent
- Match antiemetic potency to emetogenic potential of chemotherapy
- Combine agents with differing mechanisms
- Individualize regimens
- Antiemetic choice depends on:
  - Emetic risk of therapy
  - Prior experience with antiemetics
  - Patient risk factors
- Consider other non-chemo causes

Patient Case #9 (1-116)

- DH returns to clinic for cycle #2 of her chemotherapy. She tolerated her first cycle of chemotherapy well. Her ANC and platelets are adequate for her to receive her scheduled treatment however her hemoglobin is 9g/dL.

Patient Case #9 (1-116)

Which one of the following would you recommend for this patient?

- A. Complete APPRISE form and initiate epoetin or darbepoetin
- B. Transfuse with packed red blood cells (RBCs)
- C. Delay chemotherapy treatment until hemoglobin recovers
- D. Reduce chemotherapy doses to prevent further decreases in hemoglobin

Workbook Page 1-116; Answer: Page 1-117

Chemotherapy Induced Anemia

- Anemia a common side effect in cancer patients
  - Fatigue affects 60-80% of cancer patients
- Erythropoietic stimulating agents (ESAs)
  - Approved for chemotherapy induced anemia
  - Goal is a reduction in red blood cell transfusions
- Risk Evaluation and Mitigation Strategy (APPRISE)
  - Goal to support informed decisions and ensure risk/benefit education

Patient Case #10 and Audience Response Question

- DH comes into clinic on day 7 of her cycle for an unscheduled visit. She reports a fever of 102°F. Her ANC is 300. She is slightly hypotensive. How should her febrile neutropenia be managed?
  - A. Admit to the hospital for intravenous antibiotic drugs
  - B. Treat as an outpatient with antibiotic drugs
  - C. Initiate a colony-stimulating factor (CSF)
  - D. Discontinue chemotherapy

Workbook Page 1-118; Answer: Page 1-119-121

Neutropenia/Febrile Neutropenia

- Bone marrow suppression is the most common dose-limiting toxicity of cytotoxic chemotherapy
  - Normal range for white blood cell (WBC) count is 4.8–10.8 × 103 cells/mm3
- Absolute neutrophil count (ANC) = WBC × % granulocytes or neutrophils (segmented plus bands)
- Neutropenia is defined as an ANC of 500/mm3 or less or a count of less than 1000/mm3 with a predicted decrease to less than 500/mm3 during the next 48 hours.
- Febrile neutropenia is defined as neutropenia and a single oral temperature of 101°F or more or an oral temperature of 100.4°F or more for at least 1 hour.
  - Decreases in WBC (neutropenia, leucopenia, granulocytopenia) increase the risk of life threatening infections
  - Risk increases with ANC less than 500/mm3, and the most significant risk is when ANC is less than 100/mm3

Neutropenia/Febrile Neutropenia

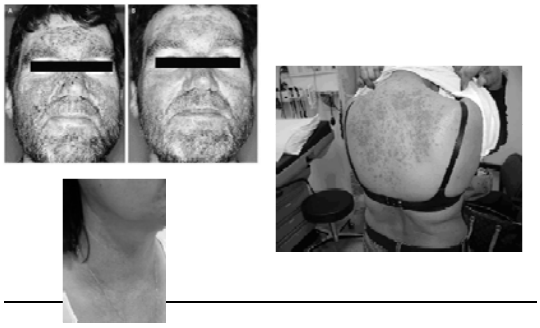
- Prevention
  - Colony stimulating factors
    - Primary vs. secondary prophylaxis
  - Antibiotics
- Treatment
  - Colony stimulating factors
  - Antibiotics
    - Initial assessment of patients with febrile neutropenia includes a risk assessment for complications/severe infection
    - High risk vs. low risk
  - Febrile neutropenia that is considered high risk should receive intravenous antibiotics in the hospital setting.
  - Outpatient an option for low risk

COMPLICATIONS WITH ORAL AGENTS

Skin Toxicities with Epidermal Growth Factor Inhibitors

- Rash is a major complication of EGFR therapy
- Significant pain and pruritis as well as anxiety related to cosmetic appearance can negatively affect QOL
- Over 70% of physicians report holding EGFR therapy due to rash
- Approximately 30% of physicians report discontinuing EGFR therapy due to rash
- Proactive strategies to prevent or alleviate EGFR-associated rash may help to optimize therapy

EGFR Skin Toxicity

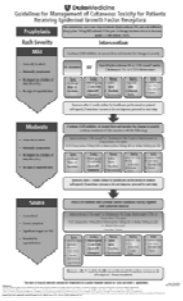


EGFR Skin Toxicity Management

- Class effect
- Usually mild-moderate
  - Incidence 50-100%
  - 8-17% patients require dose mods or disruptions
- Most common areas: face, scalp, neck shoulders & trunk
- Characteristics
  - Often accompanied by pruritis
  - May be dose dependent
  - Waxes and wanes; may spontaneously resolve
  - Rash usually disappears a few weeks after drug discontinuation but may leave a residual hyperpigmentation and xerosis
- EGFR expressed in keratinocytes which make up 90-95% of epidermis

EGFR Skin Toxicity Management

- No standard of care
- Clinical Practice Guidelines
  - Prophylaxis
    - Hydrocortisone 1% cream with moisturizer
    - Sunscreen
    - Minocycline or doxycycline
  - Treatment
    - Alclometasone 0.05% cream or fluocinonide 0.05% cream or clindamycin 1%
    - Minocycline or doxycycline



Hypertension with Angiogenesis Inhibitors

- Commonly seen adverse effect with vascular endoethelial growth factor receptor (VEGF) inhibitors
- Incidence

Agent	Overall Incidence (%)	Grade 3 or 4 Incidence (%)
Sunitinib	15 (Gist) 30 (renal)	4 (Gist) 8-12 (renal)
Sorafenib	10 (hepatocellular) 17 (renal)	4 (hepatocellular) <1-3 (renal)
Pazopanib	47	4 (only grade 3)

Mechanisms of Hypertension

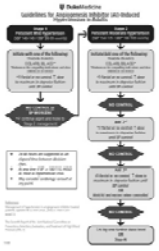
- Effects of VEGF
  - Angiogenic growth factor administration reduces blood pressure
  - Stimulates construction of new capillaries and recruitment of endothelial progenitor cells, leading to decrease vascular resistance
- VEGF blockade
  - Impairs angiogenesis
  - Decreases nitric oxide production and prostaglandin I2 → vasoconstriction

General Management Recommendations

- Identify risk factors
  - Preexisting hypertension
  - Drug dose and duration of therapy
  - Development of proteinuria
- Do not start in patients with uncontrolled HTN
- Monitor BP during treatment
  - Weekly during first cycle, then every 2-3 weeks
  - Continue monitoring post therapy
- Target BP: <140/90mmHg
- Hold or discontinue

Pharmacologic Management

- No preferred treatment
- Follow JNC7 recommendations
- Choice may be guided by
  - Compelling indications
  - Drug interactions
  - Adverse effects profile
- Special considerations
  - Non-dihydropyrimidine CCB and nifedipine-may induce VEGF secretion
  - Drug interactions-diltiazem and verapamil



Drug /Food Interactions

Drug	Interaction
Abiraterone	Do not take with food
Crizotinib	With or without food Inhibitor and Substrate of Pgp; Moderate inhibitor of CYP3A4
Dasatinib	With or without food No H2 blockers or PPIs Metabolized by CYP3A4
Erlotinib	Empty stomach No H2 blockers or PPIs; May consider antacids separated from dose by 2 hours Metabolized by CYP3A4
Everolimus	With or without food Substrate of CYP3A4 and Pgp
Imatinib	Take with food; metabolized by CYP3A4
Lapatinib	Empty stomach Metabolized by CYP3A4
Nilotinib	Empty stomach, metabolized by CYP3A4
Pazopanib	Empty stomach, metabolized by CYP3A4
Sorafenib	Empty stomach
Sunitinib	With or without food

Summary

- Lung, breast and prostate cancer the most common malignancies overall and in men and women
- Advances in treatment are leading to more long term survivors
- Newer agents have different side effect profile than traditional cytotoxic chemotherapy
- Increase in oral agents introduces new challenges to managing these patients