POLYPHARMACY

Pre-test Questions

Easy

1. Which is the best example of polypharmacy?
   a. Your patient is filling her medications at more than 1 drugstore.
   b. Your patient is taking more than 2 medications.
   c. Your patient is taking more than 9 medications.
   d. Your patient is taking a potentially inappropriate combination of medicines.

2. Why are older adults more at risk of problems with polypharmacy?
   a. Older adults like taking lots of medicines.
   b. Older adults are less likely to see a physician.
   c. Older adults are more likely to have comorbidities requiring pharmacologic intervention.
   d. None of the above

3. True or False: Older adults account for a large proportion of ambulatory visits in the US.
   a. True
   b. False

Medium Difficulty

1. Which is the most effective method of managing polypharmacy?
   a. Use a “brown-bag review” of medications at each office visit, to ensure an accurate med list.
   b. Limit your patients’ medication list to no more than 4 medicines.
   c. Regularly assess patient adherence to the medication regimen.
   d. (a) and (c)

2. An 84-year-old man with COPD and chronic atrial fibrillation has been on a stable dose of warfarin for over a year, with INR values being between 2.0 and 2.8. Recently he was admitted to the hospital with a severe UTI, then was discharged for home health PT and OT for functional disability. His urinary symptoms have resolved, and his therapies have started well; however, he has asked you to see him for follow-up. His main complaint is bleeding gums. His current medications are warfarin (same dose as pre-hospitalization), trimethoprim/sulfamethoxazole (to complete his UTI treatment), terazosin (for bladder outlet symptoms), theophylline (for COPD), low-dose aspirin, and over-the-counter ginkgo balboa (to help with his memory). Blood tests show that his INR is now 6.8.

Which of the following medications is LEAST LIKELY to be contributing to your patient’s gum bleeding?
   a. Trimethoprim/sulfamethoxazole
   b. Terazosin
   c. Theophylline
   d. Aspirin
   e. Ginkgo balboa
3. An 82-year-old woman with a history of left-sided CVA 12 months ago presents to your office complaining of decreased appetite due to low-grade nausea for the past month. She has no complaint of abdominal pain, constipation, diarrhea, fever, lower urinary tract symptoms, dysphagia, or heartburn. Her past medical history includes the CVA 12 months ago, CHF due to systolic dysfunction, GERD, dyslipidemia, HTN, and DM type 2 (diagnosed 11 months ago). Her home fingerstick readings have been between 80 and 180 over the past month. Her medications include esomeprazole, digoxin, clopidogrel, glyburide, simvastatin, and lisinopril. Her vital signs include BP 135/85 without orthostatic changes; HR 72 and regular; unremarkable cardiovascular, pulmonary, and abdominal exams; negative Hemoccult of stool; and Brunnstrom stage 5 right-sided hemiparesis that is unchanged since discharge from acute rehab.

Which of the following actions would MOST LIKELY lead to a diagnosis and treatment of the patient’s nausea and anorexia?

a. Check hemoglobin, hematocrit, iron, and total iron-binding capacity, and increase esomeprazole dose to BID
b. Add metoclopramide and order a gastric motility study
c. Hold her simvastatin and order a liver panel and creatine phosphokinase
d. Hold her digoxin and order a serum digoxin level
e. Check her electrolytes, BUN, and creatinine, and order a renal ultrasound

4. What is/are potential risk(s) in treating elderly patients with proton-pump inhibitor (PPI) therapy?

a. Increased risk of hospital-acquired pneumonia
b. Increased risk of fractures
c. Increased risk of community-acquired Clostridium difficile diarrhea
d. (a) and (b)
e. (a), (b), and (c)
Which one of these medications is the LEAST likely to be contributing to her increased confusion?
   a. Trazodone  
   b. Phenytoin  
   c. Diltiazem  
   d. Naproxen

3. Which of the following proposed drug interactions is/are accurate?
   a. Calcium carbonate + ciprofloxacin: Calcium may decrease oral absorption of quinolones  
   b. Vitamin D + digoxin: Vitamin C may decrease oral absorption of digoxin  
   c. Lisinopril + ibuprofen: May decrease antihypertensive effect, increase risk of renal toxicity  
   d. (a) and (c)

4. Your 82-year-old patient arrives for her appointment concerned that she needs a vitamin B₁₂ shot like her sister is used to getting from her physician. Which of your patient’s medications is associated with lower vitamin B₁₂ levels?
   a. Esomeprazole  
   b. Probenecid  
   c. Chloral hydrate  
   d. Esmolol
Vignette

Mrs. Z is a 79-year-old woman admitted last night to your acute inpatient rehabilitation unit after hospitalization for a right-sided CVA. Her past medical history includes the CVA, HTN, insomnia, hypercholesterolemia, congestive heart failure, mild dementia, osteoarthritis, back pain, depression, and post-herpetic neuralgia. This morning at the therapy gym, you found the patient asleep in the standing frame walker.

Her medications include:

- Aspirin 81 mg PO daily
- Valsartan 160 mg PO daily
- Atenolol 50 mg PO daily
- Simvastatin 20 mg PO QHS
- Celecoxib 200 mg PO daily
- Benazepril 20 mg PO daily
- Diphenhydramine 25 mg PO Q6h PRN itching
- Pregabalin 75 mg PO BID
- Citalopram 40 mg PO daily
- Amitriptyline 10 mg PO QHS
- Duloxetine 20 mg PO daily
- Morphine sulfate 1 mg IV Q2h PRN pain
- Cyclobenzaprine 5 mg PO daily PRN spasms


Further questioning in the presence of the patient’s daughter reveals that the patient has had 3 falls over the past month, each occurring in the morning. The patient’s daughter reports that she is confused at times, usually after waking up in the morning.

Tasks

1. Review this Web-based module on polypharmacy in the elderly:
   http://northwestahec.wfubmc.edu/learn/protect/courseware/index.cfm?session_pk=63108&person_id=sample0000&module_pk=634


3. Rank this patient’s medications from the least inappropriate to the most inappropriate.

4. Identify significant drug-drug interactions.

5. Identify significant drug-disease interactions.
Commentary — Polypharmacy
Gerald Bilsky, MD

Polypharmacy is a problem encountered by every health care practitioner, and it is possible that any given clinician may have contributed to the problem. This situation transcends medical specialty, patient age, and situation. As a practicing physiatrist focusing on patients suffering from traumatic brain injury and spinal cord injury, I have encountered polypharmacy on a daily basis over the last 20 years of practice. Inherently, providers want to help their patients and address problems as they present. Many patient complaints seem relatively minor and are encountered multiple times every day. “My back hurts.” “My feet are swollen.” “I am not holding my urine as well recently.” Each of these in isolation may be manageable with a simple intervention. Unfortunately, rarely do these clinical entities exist in isolation.

Most older patients or patients with chronic disabilities already have underlying medical problems and chronic medication regimens. They may also see multiple providers with specific areas of expertise. Thus, the potential to prescribe medications that may have synergistic, antagonistic, or adverse interactions is a reality, and unintended adverse outcomes are more likely to occur. Analgesics, in particular the opioid-class agents, can lead to cognitive changes with short-term challenges and perhaps even longer-term issues. Impaired decision-making while under the influence of prescription medications can have physical and financial repercussions. There are dangers with basic household navigation, let alone driving. Dangerous side effects, such as constipation and possible obstipation (which can lead to intestinal obstruction), may also develop.

Diuretics are frequently prescribed for lower-extremity edema. Though often effective in the short run, they are often not a good long-term solution. Diuretics may mask underlying causes that require a physician’s attention, such as deep venous thrombosis or heart failure, and result in the clinician overlooking the more serious condition. If not followed closely with routine blood chemistry, diuretic use can cause dehydration, renal failure, and even death due to metabolic abnormalities (hypokalemia). Often, diuretic use can result in volume depletion, leading to orthostatic hypotension that can precipitate falls and their life-threatening sequelae.

Heavily advertised agents used in the treatment of urinary incontinence are not innocuous and carry significant side effects. Primarily anticholinergic in function, these medications can cause cognitive impairment, orthostasis, urinary retention, and constipation, and they often have little clinical effectiveness. Recent studies have shown that proper bladder rehabilitation (pelvic muscle rehabilitation) is often as effective as these risky drugs.

The theme is apparent. Providers need to be diligent in obtaining a complete medication record before prescribing new drugs. Furthermore, it is always prudent to make suggestions to the patient’s primary care physician, rather than actually prescribing a medication, if there is concern about the veracity of the medication profile. By following the principles of good geriatric medicine, one will be providing high-quality patient care.
**Pain Management and Medications**  
Jose Garcia-Corrada, MD

While pain is not an inevitable consequence of aging, it is certainly more common as we advance in age. Degenerative conditions, insufficiency fractures, post-herpetic neuralgia, certain malignancies, and other painful syndromes are more prevalent in older persons.

It is important to recognize the burden of pain in the most frail and to address the fact that pain is often under-recognized and undertreated in the geriatric population. The American Geriatric Society has published guidelines to aid in this purpose: The management of persistent pain in older persons. *J Am Geriatr Soc.* 1998 May;46(5):635-651. With awareness of the geriatric syndromes, we can recognize that pain assessment and management can be mutually challenging for patient and clinicians for a variety of reasons:

- Lack of report for fear of being a burden to caregivers or family
- Fear of undesired work-up or physician visits
- Patient and health care provider misconceptions about opioid medications
- Not wanting to be seen as an “old person”
- Lack of social support and access to care due to transportation or mobility problems
- Cognitive and memory dysfunction
- Cost concerns about treatment, including physical therapy and medicines
- Frailty and high risk of treatment complications
- Multiple comorbidities

While working in a geriatric hospital for several years as a physiatrist with a subspecialty in pain medicine, I have experienced first-hand the limitations and challenges in treating some of the most frail geriatric patients. Some of these experiences can be quite humbling to physicians as to how limited we really are in finding a “cure” for some chronic conditions. That being said, there are even more numerous successful clinical encounters that yield mutually satisfactory outcomes. The lessons learned serve as a common denominator to most of my successful encounters. Not surprisingly, one might consider these “common sense” and applicable to good general medical principles. I will attempt to summarize some of these below:

1. Confirm that the appropriate diagnosis has been made, especially in persistently painful conditions or those that require diagnosis by exclusion.

2. Establish mutual and realistic functional goals of therapy. This is crucial for success. Pain score alone is a poor measure of outcome and sometimes unattainable.
   a. This requires listening to the patient and clarifying any misconceptions early on.
   b. Set goals for both pharmacological and non-pharmacological management.
   c. Enlist caregivers in giving histories and monitoring the functional effects of therapy. This is especially important when treating patients with cognitive dysfunction.

3. Do not exceed your clinical level of comfort. Refer to a specialist when indicated.
   a. Consider multidisciplinary involvement in patients with any one of the following: persistent pain; significant emotional component; or dementia.
      i. A collaborative team includes physiatry, psychology, psychiatry, pain medicine, PT, OT, and others.
b. Often the warning signs of early dementia are not evident until a significant stressor such as new onset of pain (or flare-up of a familiar painful condition) causes a disruption in the physical and psychosocial homeostasis. Patients may be more forgetful and/or present with dysfunction in basic and instrumental activities of daily living not previously seen. The alert clinician should then consider prompt referral and/or appropriate work-up.

4. Consider rapid and multisystemic effects of deconditioning in the elderly, i.e., treat pain promptly and promote early mobility and rehabilitation as indicated.
   a. Physical and occupational physical therapy, aquatic exercise, wellness centers, etc.

5. When pharmacologic treatment is indicated:
   a. Avoid contraindicated medications for the elderly such as:
      i. Propoxyphene
      ii. Diphenhydramine
      iii. Amitriptyline
      iv. Alprazolam, diazepam — see the link for the Beers criteria: http://archinte.ama-assn.org/cgi/content/full/163/22/2716
   b. The agent must correlate with the degree of pain and dysfunction.
      i. Scheduled medications may be appropriate in some patients with cognitive impairment.
         1. Recruit family or caregivers, when appropriate, for monitoring compliance and side effects.
         2. If the patient is admitted to an assisted living facility or nursing home, review the medication profile and write clear orders to ensure compliance.
      ii. Short-acting opioid medication vs. long-acting (avoid if opioid-naïve)
      iii. Adjuvants
         1. Muscle relaxants should be short-term agents only, used for acute spasms (most are CNS depressants).
            a. Gabapentin, pregabalin, etc. (also sedating and may increase fall risk)
   c. Monitor closely for compliance, complications, drug interactions, or side effects of therapy.
      i. Recognize and educate on the implicit need for trial and error in some therapies. It is sometimes helpful to start with a subtherapeutic dose to monitor tolerance alone.
      ii. Often, the patient’s fear of constipation with opioids is a barrier to appropriate pain control. This should never be overlooked, since constipation can be anticipated and effectively treated with laxatives.
   d. Time dosing of medications close to anticipated painful activity, social function, or activities of daily living.
   e. Start low and go slow on dosing of any medication.
   f. Be mindful of polypharmacy and its impact on geriatric syndromes when choosing medication or treatment.

6. Consider consultation for interventional pain management if the systemic side effects of medications outweigh the benefits.
Delirium Post-test Questions

Easy

1. Which is the best example of polypharmacy?
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   d. None of the above

3. True or False: Older adults account for a large proportion of ambulatory visits in the US.
   a. True
   b. False

Medium Difficulty

1. Which is the most effective method of managing polypharmacy?
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   b. Limit your patients’ medication list to no more than 4 medicines.
   c. Regularly assess patient adherence to the medication regimen.
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2. An 84-year-old man with COPD and chronic atrial fibrillation has been on a stable dose of warfarin for over a year, with INR values being between 2.0 and 2.8. Recently he was admitted to the hospital with a severe UTI, then was discharged for home health PT and OT for functional disability. His urinary symptoms have resolved, and his therapies have started well; however, he has asked you to see him for follow-up. His main complaint is bleeding gums. His current medications are warfarin (same dose as pre-hospitalization), trimethoprim/sulfamethoxazole (to complete his UTI treatment), terazosin (for bladder outlet symptoms), theophylline (for COPD), low-dose aspirin, and over-the-counter ginkgo balboa (to help with his memory). Blood tests show that his INR is now 6.8.

Which of the following medications is LEAST LIKELY to be contributing to your patient’s gum bleeding?
   a. Trimethoprim/sulfamethoxazole
   b. Terazosin
   c. Theophylline
   d. Aspirin
   e. Ginkgo balboa
3. An 82-year-old woman with a history of left-sided CVA 12 months ago presents to your office complaining of decreased appetite due to low-grade nausea for the past month. She has no complaint of abdominal pain, constipation, diarrhea, fever, lower urinary tract symptoms, dysphagia, or heartburn. Her past medical history includes the CVA 12 months ago, CHF due to systolic dysfunction, GERD, dyslipidemia, HTN, and DM type 2 (diagnosed 11 months ago). Her home fingerstick readings have been between 80 and 180 over the past month. Her medications include esomeprazole, digoxin, clopidogrel, glyburide, simvastatin, and lisinopril. Her vital signs include BP 135/85 without orthostatic changes; HR 72 and regular; unremarkable cardiovascular, pulmonary, and abdominal exams; negative Hemoccult of stool; and Brunnstrom stage 5 right-sided hemiparesis that is unchanged since discharge from acute rehab.

Which of the following actions would MOST LIKELY lead to a diagnosis and treatment of the patient’s nausea and anorexia?

- a. Check hemoglobin, hematocrit, iron, and total iron-binding capacity, and increase esomeprazole dose to BID
- b. Add metoclopramide and order a gastric motility study
- c. Hold her simvastatin and order a liver panel and creatine phosphokinase
- d. Hold her digoxin and order a serum digoxin level
- e. Check her electrolytes, BUN, and creatinine, and order a renal ultrasound

4. What is/are potential risk(s) in treating elderly patients with proton-pump inhibitor (PPI) therapy?

- a. Increased risk of hospital-acquired pneumonia
- b. Increased risk of fractures
- c. Increased risk of community-acquired *Clostridium difficile* diarrhea
- d. (a) and (b)
- e. (a), (b), and (c)

Difficult

1. You are seeing a 76-year-old woman with a history of osteoarthritis, hypertension, type 2 diabetes, and coronary artery disease. Lately she has found her hip pain limiting her usual activities of daily living and has come to the office to seek your advice. Her medications include lisinopril, metformin, multivitamins, and atenolol. Which medication should you recommend at this time?

- a. Acetaminophen 650 mg PO Q6h PRN pain
- b. Ibuprofen 400 mg PO Q6h PRN pain
- c. Acetaminophen/propoxyphene 650/100 mg PO Q4h PRN pain
- d. Celecoxib 200 mg PO daily

2. A 90-year-old woman in a subacute rehab facility has been acting more confused over the past several days. Vital signs are normal and the patient has no signs or symptoms suggesting an infection, acute coronary syndrome, or dehydration. The possibility of her medications causing the increased confusion is raised. None of her medications is new and there have been no dosage changes within the past week. Her medications include trazodone, phenytoin, clonazepam, diltiazem, and naproxen.
Which one of these medications is the LEAST likely to be contributing to her increased confusion?
   a. Trazodone
   b. Phenytoin
   c. Diltiazem
   d. Naproxen

3. Which of the following proposed drug interactions is/are accurate?
   a. Calcium carbonate + ciprofloxacin: Calcium may decrease oral absorption of quinolones
   b. Vitamin D + digoxin: Vitamin C may decrease oral absorption of digoxin
   c. Lisinopril + ibuprofen: May decrease antihypertensive effect, increase risk of renal toxicity
   d. (a) and (c)

4. Your 82-year-old patient arrives for her appointment concerned that she needs a vitamin B₁₂ shot like her sister is used to getting from her physician. Which of your patient’s medications is associated with lower vitamin B₁₂ levels?
   a. Esomeprazole
   b. Probenecid
   c. Chloral hydrate
   d. Esmolol
Answer Key — Questions

Easy

1. (d) Polypharmacy refers to a potentially inappropriate combination of medications. While it is true that a higher number of medications puts patients at risk of polypharmacy, it is not in and of itself indicative of polypharmacy.

2. (c) With the increasing age of the US population comes an increased incidence of comorbid conditions. Consequently, the risk of polypharmacy is prominent in care of the elderly.


Medium Difficulty

1. (d) Two keys to managing medication use in the elderly are accurate medication listing and assessment of compliance. A “brown-bag review” of medications, where the patient takes all of his or her medicines to the doctor’s office, can be an effective way of not only gauging the true list of medications but also detecting any problematic medications. Just as important is assessing patient adherence to the medication regimen.

2. (b) Terazosin. Many medications and over-the-counter phytotherapies can prolong the anticoagulation effects of warfarin. This can be due to the effects on protein binding (theophylline) or drug metabolism (trimethoprim/sulfamethoxazole or ginkgo balboa). In addition, although low-dose aspirin is not contraindicated in patients on warfarin, in the setting of a high INR, its use can exacerbate bleeding. Terazosin has no known effects on the metabolism, bioactivity, or action of warfarin.

3. (d) Hold the digoxin and order serum digoxin level. Digoxin toxicity in the elderly often presents differently than in younger adults. Anorexia, nausea, and/or confusion are much more common manifestations of digoxin toxicity in the elderly than bradycardia or arrhythmias. Lack of symptoms, negative abdominal exam, and negative stool occult blood make worsening GERD, peptic ulcer disease, or gastritis less likely as a cause for the nausea. History is not consistent with diabetic gastroparesis, as diabetes is a new diagnosis and the nausea does not occur just with eating. Likewise, there is nothing from history or physical exam to suggest HMG-CoA reductase inhibitor toxicity or renal failure.

4. (a) Elderly patients on long-term PPI treatment are at increased risk of fractures, community-acquired pneumonia, and hospital-acquired Clostridium difficile–associated diarrhea.

Difficult

1. (a) Acetaminophen is the best initial choice for this patient. Ibuprofen and the patient’s lisinopril may precipitate renal failure and decrease the antihypertensive efficacy of the lisinopril. Propoxyphene is on the Beers criteria list for potentially inappropriate medication use in the elderly. Celecoxib, while a selective COX-2 inhibitor that runs a lower theoretical risk of GI side effects, is not the best initial choice; given the patient’s stated history of cardiovascular disease, and Celebrex’s potential for increased stroke and MI risk, its
initiation warrants a discussion with the patient. It would be better to start with acetaminophen and work from there.

2. (c) Diltiazem. Even though medications and dosages have not recently changed, toxicity in the elderly can still occur, due to subtle changes in drug metabolism or clearance over time, or other interacting medical conditions. Trazodone, an antidepressant, and clonazepam, a benzodiazepine, are both CNS-active agents that can cause confusion. All NSAIDs, including naproxen, have been associated with confusion in the elderly. Phenytoin, especially when at serum levels above the therapeutic range, also is associated with confusion. Diltiazem is the one medication listed that is not associated with increased confusion in the elderly.

3. (d) Ciprofloxacin should be given 2 hours before calcium, or 6 hours after, due to potential interference with oral absorption. Vitamin D has no known effect on oral absorption of digoxin. Lisinopril and ibuprofen may combine to precipitate renal failure, and in combination they may decrease the antihypertensive effect of lisinopril.

4. (a) Any patient on long-term PPI treatment, not just the elderly, is at increased risk of lower Vitamin B12 levels. Also reported are lower levels of vitamin C in patients taking PPIs.

Answer Key — Vignette Tasks

Rank this patient’s medications from the least inappropriate to the most inappropriate. Aspirin (stroke secondary prophylaxis), atenolol/valsartan/benazepril (CHF and HTN), simvastatin (hypercholesterolemia), celecoxib (osteoarthritis), pregabalin (neuropathic pain), morphine sulfate (breakthrough pain), citalopram (antidepressant), duloxetine (antidepressant/anti-neuropathy agent), diphenhydramine (anticholinergic agent), amitriptyline (tricyclic antidepressant), cyclobenzaprine (muscle relaxant). Note that the following medications are listed in the Beers criteria article as potentially inappropriate: diphenhydramine (sedation), amitriptyline (strong anticholinergic effects and sedation), cyclobenzaprine (anticholinergic adverse effects, sedation, and weakness).

Identify significant drug-drug interactions. Benazepril and valsartan (an ACE inhibitor with an angiotensin II receptor blocker may precipitate hypotension and worsen renal function); celecoxib and atenolol (combination may cause sodium/water retention, worsening patient’s CHF and HTN); aspirin with celecoxib (may increase risk of GI bleeding); citalopram with amitriptyline, duloxetine, pregabalin, and cyclobenzaprine (may precipitate serotonin syndrome, neuroleptic malignant syndrome, and/or tricyclic antidepressant toxicity); cyclobenzaprine with diphenhydramine and/or amitriptyline (may increase risk of CNS depression); morphine sulfate with cyclobenzaprine and/or diphenhydramine and/or amitriptyline (anticholinergic effects increased, may precipitate severe constipation or worsen CNS depression).

Identify significant drug-disease interactions. In this patient with cognitive impairment (MMSE 20/30) and a history of falls, using any of the centrally acting agents might be problematic, especially in combination (amitriptyline, cyclobenzaprine, duloxetine, pregabalin, citalopram, diphenhydramine, morphine sulfate). The patient appears flushed, suggesting the possibility of serotonergic overactivity, perhaps due to medications (citalopram, amitriptyline, duloxetine, pregabalin, cyclobenzaprine); also the patient appears to be orthostatic, suggesting the possibility of too much BP medication “on board” (atenolol, valsartan, benazepril).