Clinical Pearls - Dermatology 2017

Case 1
This 38 year old male patient is of African descent. He has tried multiple creams to get rid of these irritating bumps on his beard area. What is the most effective treatment of these bumps?

a. Topical tretinoin nightly
b. Stop shaving
c. Topical 1% hydrocortisone cream
d. Topical clindamycin solution
e. Oral doxycycline

Correct answer: b  Stop shaving.

Discussion:
Pseudofolliculitis barbae can have several synonyms including: shave bumps, razor bumps, barber’s itch, ingrown hairs, folliculitis, barbae traumatica. It is a chronic disorder occurring most often in the beard area of men who shave. It favors those of African descent with darkly pigmented skin and tightly curled hairs. The ends of tightly curled hair have a greater tendency to curve back into the skin. The sharp cut end of the hair initially causes an invagination of the epidermis. This intrafollicular and transfollicular penetration causes inflammation and microabscesses. Long standing disease can cause hypertrophic, hyperpigmented scars and keloids.
The only way to completely treat the disease is to stop shaving, and either let the beard grow or utilize hair removal techniques such as depilatories or laser.

If patients need to shave, they should do the following to optimize the condition:

a. Use electric clippers that leave stubble 1-2 mm long or a sharp blade that does not cut hair too close.

b. Massaging with gentle soap and a wash-cloth or soft toothbrush may help the “release” of ingrown hairs.

c. Use shaving cream, moderate amount of lather, do not let it dry out

d. Use a sharp blade and shave with grain of hair. Specialized razors that use a guard system to prevent a very close shave (eg, bump fighting razor) may be helpful.

e. Rinse with tap water and apply soothing aftershave. If significant irritation occurs, can use 1% hydrocortisone cream for 1-2 days at a time.

Adjuvant treatments such as topical tretinoin, topical antibiotics or benzoyl peroxide can be helpful (but to a lesser degree than managing the hair growth).

Pearl:
Pseudofolliculitis barbae most often occurs in the beard and is due to curly hairs that ingrow when shaved. The only way to cure the disease is to stop shaving. Shaving techniques can be optimized to improve but not cure the condition.

References:
Case 2
This gentleman has chronic athlete’s foot. It has been difficult for him to adequately treat and so you decide to use a fungicidal agent that will give him the best chance of eradication of his disorder. Which treatment did you prescribe?

a. Topical clotrimazole
b. Oral itraconazole
c. Miconazole powder
d. Nystatin cream
e. Terbinafine cream

Correct answer: e. Terbinafine cream

Discussion:
Fungal infections of the skin in immunocompetent patients are usually caused by either dermatophyte infections or yeast infections.

Dermatophytes cause conditions such as tinea pedis, tinea corporis, onychomycosis, tinea cruris. The most common causes are *Trichophyton rubrum, Trichophyton mentagrophytes* and *Trichophyton tonsurans*. If you are able to perform a KOH under the microscope, you see hyphae because these infections are in mold form in tissue and in culture.

Another common cause of fungus infections in immunocompetent patients is Candida yeast infections. These are commonly seen in wet occluded areas of body such as under the breasts, under a large pannus or in intertriginous areas. Candida infections are caused by various forms of *Candida* species, and you will see spores or very long pseudohyphae on microscopic KOH.
Most of these skin infections will respond to topical agents. Oral agents are needed for extensive infections or infections that have moved down deep in the skin into the hair follicles.

The common topical agents for superficial fungal infections of the skin are:

**Imidazoles:** Clotrimazole, Econazole, Miconazole, Oxiconazole

**Allylamines:** Naftifine, Terbinafine

**Polyenes:** Nystatin

**Others:** Ciclopirox, Undecylenic acid

**Imidazoles** block cell membrane synthesis of fungus via fungal cytochrome p-450 14-alpha-demethylase. They are broad spectrum and will treat yeast and dermatophytes. They are **fungistatic** for dermatophytes.

**Allylamines** block cell membrane synthesis via inhibition of squalene epoxidase. They are best for dermatophytes and are **fungicidal**.

**Polyenes** bind irreversibly to cell membrane sterols. They work best against yeast infections.

Ciclopirox chelates polyvalent cations in fungal cytochromes. It works on yeast and dermatophytes but is not fungicidal for dermatophytes.

**Pearl:**

Allylamines (eg Terbinafine) are fungicidal for dermatophyte infections and treatment of choice for pure tinea pedis, tinea corporis or tinea cruris. Imidazoles will help with dermatophytes but are fungistatic only. Imidazoles are treatment of choice for yeast infections of the skin such as Candida albicans or tinea versicolor.

**References:**


Case 3
This 28 year old female complains of pruritic round spots on her legs. She has tried topical clotrimazole lotion without improvement. What would you recommend next?

a. Topical triamcinolone 0.1% cream  
b. Topical moisturizer  
c. Topical terbinafine  
d. Topical clindamycin lotion  
e. Sunprotection and sunscreen

Correct answer: a. Topical triamcinolone 0.1% cream

Discussion:
The main differential diagnosis for these plaques is nummular dermatitis verses tinea corporis. They are not in the sun exposed areas like lupus. They are not widespread like plaques of pityriasis rosea.

It can be very difficult to clinically differentiate nummular dermatitis (nummular eczema) and tinea corporis. KOH scrapings can be done if you have the equipment available. Also fungal cultures can be helpful. Unfortunately the KOH in this case might be negative due to antifungal use. This is similar to drawing blood cultures after the patient has already had antibiotics. If it
is critical to make a diagnosis, you might have the patient stop the antifungal and return for another scraping 2-3 weeks later.

Adults do not get tinea corporis very often. They often get tinea pedis, onychomycosis, or tinea cruris. When an adult has tinea corporis, there should be an identifiable source of infection. This source can be a pet, a child or most likely self -inoculation from another skin source such as tinea pedis, tinea cruris or onychomycosis. If you have a patient with suspected tinea corporis, you should ask about and look for the source of infection. Look at their feet, toenails, and genital skin.

Nummular dermatitis (nummular eczema) presents as coin-shaped, eczematous lesions. The spots are often very itchy and most often seen on the legs and forearms. The lesions are well demarcated with hyperkeratosis, often of the edge. Generally these patients have a history of dry sensitive skin, aggressive soap use, no moisturizer, or atopic dermatitis. The treatment is topical steroids, moisturizer and limiting trauma and friction.

Pearl:
If a patient has round scaling plaques with a history of sensitive skin and if they do not have any other signs or symptoms of fungus infection elsewhere on body, they are more likely to have nummular eczema than tinea corporis.

References:
Case 4
This patient has tried the home freezing kit, office cryotherapy and Compound W on these multiple stubborn warts. She hopes to avoid scars. She wants a treatment that does not hurt and does not want to do home treatments. What would you consider next for her?

- a. Carbon dioxide laser ablation
- b. Contact sensitization with diphenylcyclopropenone and immunotherapy
- c. Intralesional candida injection
- d. Intralesional bleomycin
- e. Photodynamic therapy

Correct answer: c. Intralesional candida injection

Discussion:
There are many treatments for warts. Cryotherapy and home salicylic acid have about equal cure rates and are the best studied.
Cochrane Database 2006:
- Best evidence for salicylic acid. They compared 5 placebo controlled trials. Cure 73% vs placebo 48%.
- Cryotherapy vs Salicylic acid. No difference in 2 trials.
Efficacy of contact sensitization, 5FU, bleomycin and photodynamic therapy to be determined.

- Carbon dioxide laser emits wavelengths of light in the infrared portion of the spectrum. The chromophore is water. The epidermis and dermis are 80% water so the light emitted destroys 80 % of the tissue that it touches. The procedure is painful and can easily cause scarring.
- Contact sensitization with diphenylcyclopropenone is a painless treatment that upregulates the immune system. Patients are sensitized to the topical medication then apply a very dilute concentration nightly at home.
- Intralesional bleomycin is often used in warts. It easily destroys the virus but is painful, unpredictable and can cause scarring.
- Photodynamic therapy has been used. This consists of an application of photosensitizing agent followed by its photoactivation by light. This creates singlet oxygen which induces necrosis.
- Candida antigen injection can be done monthly in a physician office. If it is effective, one wart can be injected and all of the warts will resolve without scarring. (Candida antigen use for wart treatment is off label.)

Candida antigen for intradermal testing strength can be measured several ways:
1. Weight to volume (w/v)
2. Protein nitrogen units/ml (PNU/ml)
3. Allergy units/ml (AU/ml)
4. Bioequivalent allergy units/ml (BAU/ml)

A common protocol that is utilized in our office uses candida extract of 1000PNU/ml.

If one chooses the extract based on weight to volume, 1:1000 (1 gram of raw material per 1000ml) is advised instead of the 1:10 (which is too concentrated)

Inject 0.3ml into the largest wart based on its surface area.
Inject at base of wart, intradermal, to induce immune reaction. Subcutaneous injection is too deep.
Repeat at 2-4 week intervals for 5 cycles.
Patients must be monitored in office for 30 minutes to watch for hypersensitivity reaction.
We do not inject patients that have uncontrolled asthma, poorly controlled heart disease or patients on beta-blockers due to risk of more dangerous anaphylactic reactions.
You must have EpiPen immediately available.
Post injection management

a. Cool compresses and elevation for swelling
b. Oral antipyretics for pain
c. Use of treated area is as tolerated
d. Return if excessive edema causes cyanosis, numbness of signs of infections with streaking or expanding erythema.

Pearl:
Candida antigen injections induce immune reactions to wart virus and can help resolve warts in patients with intact immune systems. It is a bit painful but requires injection into only 1 lesion every month. It may result in resolution of the non-injected warts.

References:
Phase 1 clinical trial of intralesional injection of Candida antigen for the treatment of warts.

Intralesional immunotherapy of warts with mumps, Candida, and Trichophyton skin test antigens: a single-blinded, randomized, and controlled trial.
Case 5

This 54 year old female has a pruritic area just medial to her left scapula. She is using back scratchers, rubbing against a door, applying moisturizer, topical steroids and nothing helps. What is the most likely diagnosis?

a. Post herpetic neuralgia
b. Trigeminal trophic syndrome
c. Notalgia paresthetica
d. Brachioradial pruritus
e. Meralgia paresthetica

Correct answer: c. Notalgia paresthetica

Discussion:
All of these conditions are forms of neurocutaneous dyesthesias. Dyesthesia is a generic term for cutaneous symptoms such as pruritus, burning, tingling, stinging, crawling, cold or even pain without a primary cutaneous condition. Dyesthesias are possibly caused by nerve trauma, impingement or irritation.

Post herpetic neuralgia is a dyesthetic pain that develops in the dermatome affected by the varicella zoster virus. You may see scarring and dyschromia in the area as well.
Trigeminal trophic syndrome (TTS) presents as crusted ulcers of the central face, nasal alae, and may involve the upper lip and cheek. TTS is caused by self-inflicted trauma triggered by paresthesias and dysesthesia secondary to damage to the sensory portion of the trigeminal nerve. This can occur after ablation of the gasserian ganglion for trigeminal neuralgia or after stroke that affects the trigeminal nerve.

Brachioradial pruritus presents with intermittent pruritus or burning pain of the dorsolateral aspects of the forearms and elbows. Cumulative solar damage and nerve root impingement due to degenerative spine disease may be contributory factors. Meralgia paresthetica involves the lateral or anterolateral upper thigh due to damage to the lateral femoral cutaneous nerve.

Notalgia paresthetica results in focal intense pruritus of the upper back. It is most commonly seen on the medial scapular borders. Often there are no skin changes. There may be hyperpigmented patches due to chronic rubbing. It is caused by a suspected alteration of the cutaneous sensory nerves of the upper back (possibly related to localized impingement from degenerative changes in the corresponding vertebrae). Usually there are no other neurologic defects.

The treatment for notalgia paresthetica involves topical anesthetics such as lidocaine, pramoxine, capsaicin cream. There are counter irritants such as menthol and camphor. Topical steroids are rarely helpful. If the symptoms are severe, then gabapentin, oxcarbazepine, amitriptyline or other medications used to treat neuropathic pain may be tried.

Pearl:
Notalgia paresthetica is a form of cutaneous dysesthesia thought to be caused by alteration of the cutaneous sensory nerves of the upper back. There are usually no other associated neurologic symptoms.

Reference:
Case 6
This patient has been treated twice for scabies with topical permethrin 5% cream. He has typical burrows between the finger webs, around the wrists and itchy bumps on the penis. He will initially get better for several weeks then start itching again. What is the most likely reason for relapse?

- a. Asymptomatic mite carriers in the household
- b. Carpets not shampooed.
- c. The dog is also infected
- d. The mites have developed resistance to the permethrin
- e. The diagnosis is incorrect

Correct answer: a. Asymptomatic mite carriers in the household
Discussion:
The most common reason for scabies relapse is failure to treat the asymptomatic mite carriers in the household. The host’s immune system must become sensitized to the mite. There are often close contacts who are scabies “carriers” and do not develop symptoms. You must treat all family members and close contacts at the same time as the patient. Patients need two topical treatments 1 week apart. The most common treatment is permethrin 5% cream applied overnight to the entire body surface from head to toe. This is repeated in 7 days. Fomites such as clothing, linens, and towels used within the last week must be washed in hot water, dried on high heat or stored in bags for 10 days.

The usual fomites spread through intimate contact. Carpet will not harbor live mites over 24 hours without human contact. Pets cannot harbor human *Sarcoptes scabiei var hominis* and do not need to be treated. Fortunately there is not reported resistance of *Sarcoptes scabiei var hominis* to permethrin.

This clinical photo and the history are great for scabies. The sites of predilection are the wrists, finger webs, axilla, areole, umbilicus, genital skin and buttocks.

Pearl:
The most common cause for scabies relapse is reinfection from close contacts who were asymptomatic untreated carriers of the mite.

References:
Mounsey KE, McCarthy JS. Treatment and control of scabies. Current opinion in infectious diseases.2013 April; 26(2):133-139,
Case 7

This patient thinks she has rosacea. She has tried oral doxycycline, topical metronidazole and topical azelaic acid without improvement. What is next best treatment option for her?

- a. Vascular laser
- b. Oral minocycline
- c. Topical hydrocortisone 1% cream
- d. Oral isotretinoin
- e. Permethrin cream 1%

Correct answer: a. Vascular laser

Discussion:
There are four main types of rosacea. Erythematotelangiectatic, papulopustular, phymatous and ocular.

The photo is of the erythematotelangiectatic form. The prominent clinical features are the persistent centrofacial erythema, flushing, telangiectasias, and skin sensitivity. This form does not respond well to the traditional topical and systemic antibiotics used in rosacea. We rarely recommend topical steroids as they can worsen all forms of rosacea. There is a new topical permethrin cream approved for papulopustular rosacea as it treats the demodex mites that proliferate in rosacea affected skin.

The general recommendations for management of erythematotelangiectatic rosacea include gentle skin care, minimize irritation, sun protection and laser therapy of the prominent blood
vessels. There are 2 new topical products approved to help with the flushing, brimonidine topical gel 0.33% and oxymetazoline hydrochloride cream 1.0%. Both of these give temporary relief only and can cause worsening of rosacea or rebound erythema.

Pearl:
Laser or light based therapies directed at blood vessels are very effective in the erythematotelangiectatic subtype of rosacea.

References:

Case 8
A 16 year old high school student has sweaty palms. It is embarrassing and troublesome to him. He has trouble gripping the basketball when he gets excited. When he takes a standardized test, the paper often gets so wet it crumples and will not feed into the grading machine. What would be the first line treatment for him?

- a. Topical aluminum chloride or aluminum chloride hexahydrate
- b. Iontophoresis
- c. Botulinum toxin A injections
- d. Oral anticholinergic agent
- e. Oral beta-adrenergic agonist

Correct answer: a. Topical aluminum chloride or aluminum chloride hexahydrate

Discussion:
Most over the counter antiperspirants are not strong enough. There is one over the counter 12.5% aluminum chloride (Certain Dri) that will sometimes help. Usually first line is topical 20% aluminum chloride hexahydrate. These solutions must be applied to dry surfaces at night when sweating is diminished. Occlusion with gloves or plastic film enhances penetration. Application is usually three to five nights then as needed. The salt precipitates in the sweat duct and blocks it. The main side effect is irritation.

Tap water iontophoresis is done with a machine where the patient puts their hand or foot into a tray of water, 20 minutes three times weekly. The medical device is used to pass to mild electric current through water in shallow pans. The current passes through the skin surface and blocks the sweat duct. The machine can be bought for home use.
Botulinum toxin A injections are given every 4-6 months. They work wonderfully to prevent release of acetylcholine. The pitfalls are the pain and the expense.

Oral anticholinergic agents (oxybutynin, glycopyrrolate) work nicely but have potential side effects of dry mouth, urinary retention, confusion, palpitations, and blurred vision.

Beta-adrenergic blockers work best in anxiety related hyperhidrosis.

Pearl:
Topical 20% aluminum chloride hexahydrate when used correctly is first line therapy for palmar and plantar hyperhidrosis. The solution must be applied at night to dry surfaces. Once the surface is wet with sweat, the solution will not work.

Reference:
Clinical Pearls – Geriatric Medicine
Ericka E. Tung, M.D.

Case 1

An 82 year old woman with early stage Alzheimer’s disease is currently hospitalized following the surgical treatment of a femoral neck fracture. On post-operative day # 2, the floor nursing staff page you because she is difficult to arouse and intermittently mumbling about a little boy running around her hospital room.

It will be 3 hours before you can get back to the hospital from your clinic, and you wish to confirm your suspicion of delirium.

Which test will you ask the patient’s bedside nurse to perform?

A. Mini-mental Status Examination (MMSE)
B. Confusion Assessment Method (CAM)
C. Glasgow Coma Scale (GCS)
D. 4A Test (4AT)
E. Geriatric Delirium Scale (GDS)

Correct Answer: D

Discussion:
Acute delirium is a serious medical urgency characterized by acute and fluctuating inattention, alteration in level of consciousness, and other cognitive deficits. Delirium is common among older hospitalized adults with a reported incidence as high as 50%. Older adults who develop delirium are at heightened risk for deleterious health outcomes including prolonged length of stay, increased risk of nursing home placement and death. A history of dementia is a strong risk factor for development of delirium, increasing the risk by 2-5 fold.

Despite the common and critical nature of this syndrome, delirium often goes undetected. Healthcare workers miss the diagnosis more than 50% of the time, making it impossible to intervene and treat the syndrome in its earliest stages. Several instruments have been developed to aid clinicians in the detection of delirium at the bedside. The most widely utilized tool, the Confusion Assessment Method (CAM) includes both a questionnaire and a diagnostic algorithm. The questionnaire assesses the presence, severity and fluctuation of 9 delirium features including acuity, inattention, disorganized thinking, altered level of consciousness, disorientation, memory impairment, perceptual disturbances, psychomotor agitation/retardation and altered sleep-wake cycle. The algorithm hones in on the four key elements of the DSM criteria for delirium (acute or fluctuating course, inattention, disorganized thinking, altered level of consciousness.) While the CAM takes only 5 minutes to administer, clinicians must be formally trained for optimum accuracy.
The 4AT is a novel screening tool for the detection of delirium. The assessment test requires 2 minutes to administer and little to no training for the administering clinician. The test is comprised of four domains: level of alertness, 2 brief cognitive screens and acuity/fluctuation. The 4AT has a sensitivity of 89.7% and a specificity of 84.1% for delirium. It is free to use and available online at: www.the4at.com.

Clinical Pearl:
The 4AT is a simple, sensitive and specific method of detecting delirium in the hospitalized older adult.

References:

Case 2
An 87 year old woman residing at a local nursing home has a history of mild vascular dementia, hypertension and DJD of the knees. You are called by her nurse, as she has had 3 difficult nights this week. On these evenings, she was noted to be irritable, unsteady, and refused night-time personal cares. Last night she fell again, but did not injure herself. Her daytime behaviors were unchanged. The patient herself has no concerns. The nursing staff also reports that her urine is cloudy and concentrated in appearance.

Given her behavioral changes and gait instability, the patient’s nurse has collected a dip urine which revealed +leukocyte esterase and + nitrite.

Which one of the following is the best next step?

A. Ciprofloxacin x 3 days
B. Fosfomycin x 1 dose
C. Order urinalysis, culture and sensitivity
D. Initiate cranberry capsules
E. Observe for two days and reassess

Correct Answer: E

Discussion:
Asymptomatic bacteruria (ASB) is a common condition among older adults, especially among institutionalized seniors. In the long term care setting, 25-50% of women and 15-40 % of men have ASB. This clinical finding is defined as greater than 100,000 colony forming units (CFU/ml) of the same uropathogen on two occasions in the patient who is without signs or symptoms of
a urinary tract infection (UTI). ASB represents a colonization state that does not require treatment with antibiotics, as previous studies have shown that treatment neither improves morbidity nor mortality in this demographic group.

Distinguishing ASB from symptomatic UTI can be a challenge in the long term care setting. Nursing home residents often struggle with cognitive impairment making it difficult for them to recall or report their symptoms. Additionally, clinicians are attuned to the fact that infections often present atypically in the frail older adult. Resultantly, older long term care residents are frequently over-treated for ASB. Philips and colleagues found that the most common treatments include fluoroquinolones and nitrofurantoin, for an average duration of 7.6 days. With overtreatment, long term care residents are at heightened risk for adverse drug events, antibiotic resistance and Clostridium difficile infections.

One study sought to identify clinical features associated with bacteriuria plus pyuria in non-catheterized nursing home residents with clinically suspected UTI. This group found that myriad clinical presentations including behavioral changes, falls, malaise, and syncope often prompted clinicians to order urinary studies. However, these symptoms occur as frequently in older adults with negative as with positive urine cultures. Available evidence does not support a clear association between mental status changes and UTI. Similarly, changes in the character of urine such as odor or turbidity are also insufficient, by themselves for a diagnosis of infection.

Consensus criteria for initiation of empiric antimicrobial therapy for presumed UTI in the long term care resident include acute dysuria with or without fever, acute confusion or chills with at least one new or worsening genitourinary symptom.

**Clinical Pearl:**
Changes in the appearance of urine or behavioral symptoms in isolation should not warrant urine studies.

Just say NO to the treatment of bacteriuria in older adults unless specific urinary symptoms or fever are present.

**References:**
Case 3

A 79 year old retired man comes into the office for follow-up of HTN, DM2, and mild cognitive impairment. During the course of your visit, he struggles to tell you how he is taking his medications and you begin to worry about his adherence.

His medications include: glargine, aspart, aspirin, metoprolol, lisinopril, atorvastatin. Physical examination: BP 130/70, HR 66 bpm. Cardiac examination is unremarkable. Mini Mental Status Examination (MMSE) score is 27/30.

As you walk him to the clinic check out desk you notice his worsening gait, instability. He turns to you with a puzzled look as he remarks that he can’t remember where he parked his car.

Which of the following characteristics is most strongly associated with unsafe driving in this patient?

A. Timed Up and Go score of 20 seconds  
B. Mini-Mental Status Examination score of 27  
C. Clinical Dementia Rating Scale level of 2  
D. Self-reported driving mileage reduction  
E. Self-rating of safe driving ability

Correct Answer: C

Discussion:
By 2050, the population of Americans aged 65 and older will reach 89 million and constitute 25% of licensed drivers. With our increasingly mobile society, many older adults will embark upon encore careers, new volunteer activities and higher levels of social connectivity. Unfortunately, the risks for fatal motor vehicle crash (MVC) increases significantly after age 70 and adults aged 85 and older have one of the highest fatality rates per mile driven.

Determination of driver fitness requires clinicians to undertake a holistic approach. Functional status, medications, vision, cognition and motor/sensory capacity must be assessed.

Older adults with dementia are at 2-8x increased risk for motor vehicle crash, however it is important to recognize that cognitive impairment is measured on a spectrum and those with very mild cognitive impairment may still be safe to drive. Thus, clinicians are frequently tasked with determining whether an individual’s cognitive impairment is severe enough to impact driving safety. The Mini Mental Status Examination is one of the most widely utilized mental status tests however; among frequent drivers, the MMSE does not predict risk of motor vehicle crashes. Data correlating MMSE score and on the road driving performance has also been conflicting. Composite batteries of cognitive testing, which assess multiple cognitive and functional domains, more reliably determine driving fitness when compared to single cognitive domain tests. The Clinical Dementia Rating (CDR) has been established as a useful tool that can
help clinicians identify those at high risk for unsafe driving. The CDR encompasses several functional domains including memory, orientation, judgement, problem solving, community affairs, hobbies and personal care. Individuals can be trichotomized into three risk groups. Individuals with a CDR of 0-0.5 are at low risk for unsafe driving, those with a CDR of 0.5-1 should be evaluated with an in-depth assessment. Those with a CDR of 2 should immediately stop driving.

Commonly utilized compensation strategies such as co-piloting and reduction of milage have not been shown to reduce risk for MVC and may be a surrogate for loss of driving capacity. Similarly, a patient’s rating of their own driving fitness is not useful for predicting driving safety.

**Clinical Pearl:**
In patients with dementia, it’s not a matter of “if” but rather a matter of “when” they should stop driving. It is necessary to assess multiple cognitive domains when making the determination of “when.”

**References:**

**Case 4**

A 76 year old man with a history of moderately severe dementia, atrial fibrillation, and stable coronary artery disease currently resides in a local nursing home due to his cognitive impairment. His wife calls your office because of his worsening symptoms. Specifically, he has seemed more frightened during the evening. She tells you that he no longer wants to participate in evening activities and on more than one occasion, he has described a large wolf that sneaks into his room when the staff are not present. During the day, the patient does well, but she notes that he often naps for 3-4 hours after breakfast.

Physical examination of this patient at the nursing home reveals a calm, pleasant, elderly man. He struggles with all cognitive domains but follows one step commands without difficulty. His gait is slow and hesitant. He has no evidence of tremor or rigidity.

**What is the best pharmacologic therapy for this patient’s symptoms?**

A. Donepezil 10 mg once daily  
B. Memantine 20 mg once daily  
C. Quetiapine 12.5 mg every afternoon  
D. Citalopram 20 mg once daily  
E. Risperidone 1 mg every afternoon
Correct Answer: A

Discussion:
Dementia with Lewy Bodies (DLB) is increasingly recognized as one of the most common forms of non-Alzheimer’s Dementia. Individuals with DLB experience a number of troublesome symptoms that are characteristic of the syndrome including fluctuating cognitive impairment, delusions, well-formed visual hallucinations and parkinsonism. The non-cognitive or so called neuropsychiatric symptoms of dementia can be especially distressing to caregivers and loved ones.

Managing neuropsychiatric symptoms of DLB poses a unique challenge for clinicians. Neuroleptic medications, which are commonly utilized for behavioral dyscontrol and hallucinations in other forms of dementia can result in severe and potentially fatal sensitivity with DLB. It has been established that individuals with DLB often have severely depleted cholinergic neurotransmission. Additionally, many have more preserved post-synaptic muscarinic receptors than individuals with Alzheimer’s disease. These pathologic findings suggest that patients with DLB may be more favorably responsive to cholinesterase inhibitor medications.

One randomized study conducted by Mori et al. found Donepezil to be significantly superior to placebo on both behavioral and cognitive measures. Similarly, in another placebo controlled, double blind multicenter study, DLB patients receiving rivastigmine experienced less apathy, anxiety and hallucinations than those randomized to placebo.

Clinical Pearl:
Recognize the signs and symptoms of DLB and understand that DLB patients often respond more favorably to cholinesterase inhibitor therapy than those with other dementia subtypes.

References:

Case 5

A 67 year old teacher is scheduled for a general health maintenance visit. She has well controlled diabetes, hyperlipidemia, and depression. She mentions to you that she may retire earlier than she’d like to because she is bothered by incontinence several times per day. She has had this since her hysterectomy two years ago, but it seems worse now. She states that when she gets an urge to urinate “I’ve got to get to the bathroom fast!” She also reports leakage with coughing and laughing.
Her medications include: atorvastatin, metformin, oral conjugated estrogen, paroxetine, aspirin.


Which of the following would be the most appropriate next step in management of this patient?

A. Start oxybutynin 5 mg po bid
B. Discontinue estrogen therapy
C. Discontinue paroxetine
D. Begin timed voids
E. Start mirabegron

Correct Answer: B

Discussion:
Urinary incontinence is common among women of all ages, but especially prevalent among older women with a prevalence of 45%. Several nonpharmacologic, pharmacologic, and surgical therapies are available for management. However, before starting a new treatment, analysis of current medications that can worsen incontinence should be undertaken. Medications such as alpha-1-blockers, diuretics and caffeine can worsen incontinence.

While topical estrogen preparations have modest positive impact on urinary leakage, the impact of systemic menopausal hormone therapy (MHT) has been less fruitful. A recent large meta-analysis reveals that oral MHT actually has a negative effect on incontinence. In this analysis, post-menopausal women receiving oral MHT were 30% more likely to have worsening of their incontinence when compared to women not receiving MHT. Similarly, in a large multicenter randomized trial of post-menopausal women who were continent at baseline, those treated with MHT were at significant risk of developing new stress and urge incontinence.

The pathophysiology of this finding is elusive, as estrogen is trophic for the lower urinary tract. Estrogen reduces total collagen concentration and decreases cross linking of collagen, and some authors have theorized that decreasing levels of mature collagen and increases in immature cross-linkages could contribute to poor urethral support.

Clinical Pearl:
There are several potentially reversible causes of incontinence, such as medications, and (surprisingly) these include menopausal hormone therapy.
References:

Case 6

68 year old retired journalist presents for his annual wellness visit. You are running 30 minutes behind schedule with three moderately complex patients waiting to be seen. He is feeling well aside from mild knee pain, refractory hypertension and occasional word finding difficulty.

His medications include: naproxen, glucosamine-chondroitin, lisinopril, and metoprolol. His physical examination is normal.

Which of the following tests would help you efficiently detect cognitive impairment in this gentleman?

A. Mini-Mental Status Examination (MMSE)
B. Mini-Cog
C. AD-8
D. Clock Draw Test
E. No testing is indicated, screening for cognitive impairment is not recommended

Correct Answer: B

Discussion:
The role of dementia screening has been a point of much controversy over the past 10 years. In its most recent guideline update, the US Preventive Services Task Force stated that the current data was insufficient (I statement) to assess the balance of benefits and risks for cognitive screening among asymptomatic adults. Similarly, the Canadian Task Force for Preventive Health Care recommended against screening asymptomatic older adults for dementia. Yet, clinicians are urged to detect cognitive impairment during the CMS endorsed Annual Wellness Visit.

In this particular case, the clinician is not making the decision to screen or not to screen. The patient in fact, is symptomatic as he is struggling with word finding difficulty. While screening asymptomatic populations is a controversial topic, case finding or timely evaluation of those seniors with subjective or objective cognitive symptoms is endorsed by the USPSTF, the GSA and the IAGG.

Timely detection and diagnosis of cognitive impairment is associated with a number of important benefits. Clinicians can provide important anticipatory guidance to patients and
their loved ones. Additionally, clinicians can simplify chronic disease treatments to encourage safety and sustainability.

The Mini-Cog test is a 3 item recall, followed by a clock drawing test. The sensitivity of the test ranges from 76-99% and the specificity ranges from 83-93%. While achieving similar diagnostic performance as other commonly utilized tests such as the MMSE and the 7 Minute Screen, the Mini-Cog takes 3 minutes to administer and is less vulnerable to educational and cultural bias. These characteristics make it an ideal tool to utilize during an Annual Wellness Visit or general medical examination. Those patients scoring abnormally on the Mini-Cog require a more in-depth cognitive assessment.

Clinical Pearl:
Utilization of the Mini-Cog is an effective, efficient tool for determining those at high risk for dementia.

References:

Case 7

An 81 year old male with a history of DM (HbA1C = 8), modified hypertension and mild HFPeF visits your office to establish care. He is new to your community and asks you about “screening tests.” His cousin just passed away from metastatic colon cancer and he asks you whether he should undergo colon cancer screening. He has never been screened before. His functional status is good and he continues to volunteer at a local elementary school.

On physical examination, BP 100/58, HR 80/min, BMI is 27. Cardiac examination reveals a late-peaking murmur in the RUSB radiating to the carotids. Lung and abdominal examination are normal.

Which of the following should you recommend?

A. Order a screening colonoscopy
B. Order a CT colonography
C. Advise him against colon cancer screening
D. Recommend stool DNA testing
E. I’m not sure, it depends on his preferences

Correct Answer: C
Discussion:
The heterogeneity among senior adults makes assessment of the risks and benefits of cancer screening a significant challenge. Older adults with multiple comorbidities and a shorter life expectancy have less time to benefit from a screening test and may die from other non-cancer conditions after a positive test. Additionally, older persons are at higher risk for harm from procedural complications. Adding to this clinical challenge, many existing guidelines regarding when to stop screening are ambiguous and fail to inform providers how to calculate the individual patient’s life expectancy. At this time a valid “one size fits all” prognostic index is not available. Clearly, a systematic approach to screening in the elderly is needed.

When deciding whether or not to order a cancer screening test, clinicians must consider estimated remaining life expectancy, comorbid burden, functional status, and the patient’s goals of care and preferences for screening. Remaining life expectancy can be estimated with age and race specific life tables. The benefits of breast and colon cancer screening occur only after a lag time of 5-10 years, accordingly, patients with a life expectancy shorter than this lag time are less likely to benefit from screening. While a recent study found that one time screening for colorectal cancer in older adults who have never been screened is potentially cost effective, this particular patient has other comorbidities that limit his ability to receive benefit from the test. The ABIM and AGS Choosing Wisely initiative recommends against screening for breast, colorectal, or prostate cancer if life expectancy is estimated to be less than 10 years.

Several non-disease specific indices have been developed to predict mortality for older persons. While useful, it can be challenging for the busy clinician to choose the correct index. Eprognosis.org is a free electronic application that provides clinicians and their patients with practical, evidence based information that can aid in shared decision making at the point of care.

Clinical Pearl:
In general screening tests for colon cancer are not recommended for those with a life expectancy of less than ten years. Eprognosis.org helps clinicians and older adult patients make cancer screening decisions.

References:
Case 8

An 80 year old woman with a history of moderately severe Alzheimer’s Dementia and metabolic syndrome is brought to the office by her distraught daughter. Her caregiver daughter expresses concerns regarding her mother’s worsening mood, paranoia and outbursts of anger. It has gotten to the point that she can no longer help her mother bathe or perform personal cares.

Physical examination: BMI 41, BP 130/84, HR 90. Timed up and go: difficulty rising from chair without assistance, 30 seconds. The patient is sitting calmly in the examination room, but becomes more physically agitated as you move to help her onto the examination table.

In addition to performing a thorough physical examination and basic laboratory evaluation, which of the following should you consider if conservative measures are ineffective?

A. Lorazepam 0.5 mg 30 minutes prior to personal cares
B. Quetiapine 25 mg twice daily, 12.5 mg prior to personal cares
C. Memantine 10 mg twice daily
D. Acetaminophen 650 mg twice daily and oxycodone 2.5 mg twice daily
E. Trazodone 25 mg three times daily

Correct Answer: D

Discussion:
The neuropsychological (NPS) or behavioral symptoms associated with dementia are found with all subtypes and stages of cognitive impairment. Manifestations are varied with examples including: physical aggression or agitation, disturbances of mood, wandering, and repetitive vocalizations. Often NPS signify an individual’s attempt to communicate an unmet need in the setting of progressive loss of language skills. In this particular case, the patient is very likely trying to communicate fear or pain at the time of personal cares. Her physical aggression and agitation during bath time and movement onto the table are likely a strong message to caregivers.

In non-emergent settings, nonpharmacologic therapies such as environmental modification, caregiver education, and physical activity should be utilized first. If the symptoms continue to distress the patient, pharmacologic therapies can be considered. To date, a number of pharmacologic therapies have been utilized to treat NPS. Although commonly used, atypical antipsychotic medications and benzodiazepines are associated with risk for adverse events such as stroke and increased fall risk, respectively. One key trial randomized long term care residents with dementia associated agitation to a stepwise protocol for the treatment of pain versus usual care. The intervention utilized acetaminophen, morphine, buprenorphine transdermal patch and pregabalin. Individuals receiving the stepped analgesia intervention experienced a clinically significant decrease in agitation and pain.
Clinical Pearl:
Untreated pain is a very common cause of behavioral dyscontrol. Consider the use of stepped analgesia to treat physical agitation in the patient with dementia and untreated pain.

References:
Case 1

A 75 year old man is admitted from a long term care facility to the hospital because of right lower extremity cellulitis. He has had two identical admissions within the last year. He uses compression stockings on a daily basis for residual right lower extremity edema. On physical examination the temperature is 38.5 degrees Centigrade, pulse 110, BP 130/85. The right lower extremity is warm, erythematous, edematous and tender from mid-calf to the knee; a few red streaks are noted in the distal thigh. There is a well healed saphenous vein harvest site on the right calf from a previous coronary artery bypass. No tinea pedis is noted and there are no breaks in the skin. He has had mild to moderate residual swelling of the right calf since the last episode of cellulitis 3 months ago. He responds well to parenteral cefazolin and is ready for discharge.

Which of the following options will be most effective in preventing further episodes of cellulitis in this patient?

A. Order nasal swab for MRSA; decolonize with nasal mupirocin if positive
B. Initiate Penicillin VK orally, 250 mg twice daily
C. Initiate Trimethoprim-Sulfamethoxazole double strength once daily
D. Initiate ceftriaxone 2 grams IM once monthly
E. Daily skin lubrication and topical antifungal treatment for the interdigital web spaces

Correct answer: B

Discussion:

Recurrent cellulitis is common, most frequently in the setting of chronic venous insufficiency or lymphedema. Residual edema may worsen after each bout of cellulitis. Patients who have had saphenous vein harvest in the setting of coronary artery revascularization surgery, as in this case, are at increased risk for recurrent cellulitis because of residual swelling in the affected leg. Non purulent cellulitis is typically caused by hemolytic streptococci and not by Staphylococcus aureus. Although this patient resides in a long term care facility, determining and eliminating MRSA nasal carrier state is not indicated. Trimethoprim-sulfamethoxazole, though active against MRSA, has less activity against streptococci and would therefore not be a rational choice for the prevention of cellulitis even in the setting of nasal colonization. Ceftriaxone, though active against streptococci does not have a half-life long enough to provide measurable serum concentration to last a month and is therefore not an ideal choice. Tinea pedis is frequently a portal of entry for bacteria but there is no evidence that preemptive treatment with topical anti—fungal therapy is helpful. A double-blind randomized, controlled trial involving patients with two or more episodes of lower extremity cellulitis found that daily administration of oral Penicillin VK 250 mg twice daily resulted in a significantly reduced recurrence rate(22%) compared to 37% in the placebo. In this case, the only evidence-based intervention for prevention of recurrent cellulitis is daily oral penicillin.
Clinical Pearl:

An evidence based option for reducing the frequency of recurrent lower extremity cellulitis is the daily use of oral Penicillin VK, 250 mg twice daily.

References:


Raff AB, Kroshinsky D. Cellulitis: A Review. JAMA 2016; 316(3):325-337

Case 2

A 36 year old woman removed a small tick from her posterior knee after a one day trip to a state park in Westchester, New York. The trip occurred in May and during the trip she wore shorts, hiked with her husband and recalls no other insect bites. The tick, described as the size of a poppy seed was flushed down the toilet. She is concerned about Lyme disease and asks for your advice. She has read that Westchester County is heavily endemic for Lyme.

Which one of the following interventions would be most appropriate?

A. Amoxicillin 500 mg three times daily for a week
B. Doxycycline 200 mg once
C. Doxycycline 100 mg twice daily for 10 days
D. Baseline Lyme serology; if negative, repeat in 6 weeks and treat if positive
E. Discuss tick precautions; no further treatment or evaluations indicated

Answer: E

Discussion:

Although Lyme disease is a common tick-borne illness in the United States, even in Lyme-endemic regions, only 1 to 3% of patients who have a tick bite will develop Lyme disease. Several measures may be taken for the prevention of Lyme and other tick-borne infections, including daily body checks for ticks, minimizing skin exposure to ticks by wearing long pants and the consistent use of DEET-containing repellants. A published study demonstrated that a single 200 mg dose of doxycycline was 87% effective in preventing erythema migrans; however, a third of the patients who took the large, single dose of doxycycline developed significant gastrointestinal side effects. This option is only suggested when a documented Ixodes tick has been attached for 36 hours or longer and when the drug can be started within 72 hours. In this illustrative case, the tick was neither attached for 36 hours nor engorged, obviating the need for antimicrobial therapy. There is no data supporting the use of amoxicillin and a ten day course of doxycycline would only be indicated for documented early Lyme disease. Lyme serology should not be ordered in asymptomatic individuals, since false positive tests may result in unnecessary antibiotic treatment.
Clinical Pearl:

Prevention of Lyme Disease with 200 mg of oral doxycycline following a tick bite may be used under highly specific circumstances: an identified deer tick that is engorged and attached for ≥ 36 hours in regions of the country that are heavily endemic for Lyme disease; patients who meet these criteria need to be warned about GI side effects.

References:


Sanchez E, Vannier E, Wormser GP and Hu, LT. Diagnosis, Treatment and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis and Babesiosis: A Review. JAMA; 315(16):1767-1777

Case 3

A 65 year old man is hospitalized with community acquired pneumonia and treated with parenteral ceftriaxone, followed by levofloxacin with resolution of fever and cough; his illness began three days after returning home from a vacation to the Dominican Republic. Two weeks later he reports six to eight watery stools per day accompanied by fever, cramping abdominal pain. On physical examination, the temperature is 38.8°C, pulse 100, blood pressure 110/80. There is moderate abdominal tenderness but no other abnormal findings. WBC 12,000, Creatinine 1.3 mg/dL. A stool specimen is positive for C. difficile toxin and the patient is discharged from the hospital on oral metronidazole for ten days with resolution of symptoms. One week later, he develops cramping abdominal discomfort and bloating with two to three loose stools per day, especially after meals. The abdominal discomfort is somewhat relieved after defecation. No fever is reported

Which one of the following would be the most appropriate next step in the management of this patient?

A. Test stool for C difficile toxin; treat with metronidazole if positive
B. Test stool for C difficile toxin; treat with vancomycin if positive
C. Treat presumptively with metronidazole for probable recurrence
D. Increase soluble fiber, reassurance
E. Check stool for leukocytes

Answer: D

Discussion:

Diarrhea due to Clostridium difficile is a formidable nosocomial infection, accounting for 453,000 cases and 29,000 deaths annually in the United States. Although treatment with either metronidazole (for mild to moderate cases) or vancomycin (for severe disease) is effective in alleviating symptoms, the recurrence rate is ≥ 20%. Risk factors for recurrence includes older age, concomitant antibiotic use, worse initial disease severity and concomitant use of proton pump inhibitors. Since prolonged C difficile shedding in stool can persist even after appropriate treatment, a test of cure is not recommended. In
this case, the post treatment symptoms are quite mild and also suggestive of irritable bowel syndrome (IBS), given the post prandial loose stools and relief of abdominal discomfort after defecation. Post infectious irritable bowel syndrome is a well-recognized sequela of infectious gastroenteritis, including diarrhea cause by C difficile. Because of the mild nature of these symptoms it would be reasonable to withhold additional antimicrobial treatment and to offer conservative treatment, including soluble fiber and reassurance. The presence of fecal leukocytes suggests a mucosally-invasive etiology which would be unlikely in the absence of fever, systemic symptoms or leukocytosis, all of which are absent in this case; the test also suffers from low sensitivity.

Clinical Pearl:

The diagnosis of post infectious IBS should be considered in patients who develop mild diarrhea and abdominal discomfort following antimicrobial treatment for CDI; because of prolonged excretion of toxin after treatment, repeat CDI testing should not be done.

References:

Gupta A, Khanna S. Repeat Clostridium difficile Testing. JAMA 2016; 316(22)2422-2423


Case 4

A 50 year old male presents with a one year history of intermittent epigastric distress in the absence of weight loss, dysphagia or gastrointestinal bleeding. He has tried over the counter antacids with little relief. Physical examination is normal except for mild upper abdominal tenderness. A complete blood count is normal and stool testing for Helicobacter antigen is positive. The patient declines endoscopic evaluation but has read about the role of Helicobacter in dyspepsia and would like to be treated.

Which one of the following treatment regimens would be most effective?

A. Proton pump inhibitor(PPI) + Clarithromycin+ Amoxicillin for 7 days
B. PPI + Clarithromycin+ Amoxicillin for 14 days
C. PPI + Bismuth + metronidazole + tetracycline for 14 days
D. PPI + Levofloxacin + Amoxicillin for 14 days
E. PPI + Amoxicillin for 5 days followed by PPI + clarithromycin + metronidazole for 5 days

Answer: C

Discussion:

H. pylori is the most common chronic bacterial infection and can cause nonspecific dyspepsia; a test and treat strategy has been suggested for patients who are less than 55 years of age who have no “alarm symptoms.” Because of widespread antimicrobial resistance, standard eradication regimens are
increasingly ineffective and triple regimens are no longer recommended. The recently published Toronto Consensus strongly recommends that all H. pylori eradication regimens consist of quadruple therapy administered for 14 days. Levofloxacin should only be included in the antimicrobial regimen in patients who have previously failed eradication attempts and should not be part of the initial regimen. Sequential therapy is no longer recommended.

Clinical Pearl:

The initial treatment of Helicobacter pylori should consist of quadruple therapy, given for 14 days; shorter regimens are no longer recommended.

References:


Case 5

A 26 year old woman with a prior history of recurrent urinary tract infection, presents to the office with a five day history of dysuria, frequency and urgency in the absence of fever or flank pain. Because the symptoms began during the weekend, she initiated treatment with levofloxacin (left over from a previous prescription) and pyridium. Two days ago, she noted that her lips were intermittently blue and presents for further evaluation; she denies shortness of breath. Several members of her family have had deep venous thrombosis and pulmonary emboli. She is sexually active and smokes half a pack of cigarettes daily. Medications include oral contraceptive, levofloxacin, high doses of vitamin C and pyridium. Physical examination: afebrile, pulse 100, BP 135/88, pulse oximetry 88% on room air; appears anxious. Blue-tinged lips, mild suprapubic tenderness. Heart and lung examination are normal. No calf swelling or tenderness. Arterial blood gases are normal

What is the most appropriate next step in the management of this patient?

A. Pulmonary CT Angiography
B. Echocardiogram with “bubble” study
C. Stop levofloxacin
D. Stop pyridium
E. Stop ascorbic acid

Answer: D

Discussion:

The most likely cause of the apparent cyanosis is methemoglobinemia caused by Pyridium (phenazopyridine), a known cause of this disorder and an over the counter drug that is frequently used for the symptomatic treatment of cystitis; since she is minimally symptomatic, stopping the drug will be sufficient. Ascorbic acid and levofloxacin have not been associated with acquired methemoglobinemia. There is no role for echocardiography particularly in the absence of dyspnea or chest pain. Despite the family history of thromboembolic disease, pulmonary embolism in the absence of dyspnea would be an
unlikely cause of her lip discoloration; a CT of the chest would therefore not be indicated. Methemoglobinemia should be suspected in the setting of decreased oxygen saturation in the setting of a normal paO2, as in this patient. Acquired methemoglobinemia can be caused by a variety of drugs, aniline dyes and local anesthetics. It is caused by the oxidative conversion of the ferrous to the ferric version of iron which poorly binds oxygen.

Clinical Pearl:

Acquired methemoglobinemia can be caused by a long list of both prescription and nonprescription medications, including phenazopyridine(AZO™), which should be stopped immediately when this complication occurs.

References:


Case 6

A healthy 60 year old woman presents to your office for advice regarding the prevention of recurrent urinary tract infections. She has a remote history of Stage I breast cancer at age 50 which was successfully treated with lumpectomy and radiation therapy. For the last three years she reports 3 to 4 episodes of cystitis each year; each episode consists of dysuria, urgency and frequency without fever, chills or flank pain. She has been successfully treated with short courses of antibiotics including nitrofurantoin, trimethoprim-sulfa and fosfomycin with prompt resolution of symptoms. She is sexually active but reports that none of these episodes have been associated with intercourse. She is not interested in taking prophylactic suppressive antibiotics.

Which one of the following interventions is most likely to be successful in preventing these infections?

A. Cranberry capsules
B. Vaginal estrogen
C. Probiotics
D. Urine acidification with high doses of ascorbic acid
E. Boric acid vaginal suppositories for acidification

Correct answer: B

Discussion: Daily use of cranberry products has been suggested to prevent urinary tract infections for over fifty years, based on the supposition that urinary tract infection can be prevented by acidification. Certain lectins in cranberries have also previously been reported to prevent bacterial adherence to
uroepithelial cells. A Cochrane review published in 2012 showed no benefit of cranberry products for the prevention of UTI’s and several additional well-designed studies confirmed their non-utility. There is little published evidence to support the use of boric acid or ascorbic acid to prevent UTI’s and no convincing evidence in favor of probiotics. However, there are several studies supporting the successful use of vaginal estrogen for UTI prevention; vaginal estradiol may be used in lieu of topical estrogen cream. Although this patient has a remote history of breast cancer, she is at low risk of recurrence and the serum concentrations of estrogen achieved by vaginal estrogen are very low. Topical estrogen reduces the ability of bacteria to adhere to the uroepithelial mucosa and may also lower the pH of the vagina.

Clinical Pearl:

Topical estrogen has been shown to reduce the frequency of urinary tract infection in postmenopausal women and may be used when patients or physicians prefer to avoid antimicrobial prophylaxis.

References:


Case 7

A 20 year old female presents with pain, swelling and purulent discharge from the helix of her left ear 10 days after receiving a piercing of the left helical rim at a local shopping mall. Three days ago the pain and swelling increased and did not improve with removal of the earring and topical neomycin. There is no fever or systemic symptoms. Physical examination is normal except for redness, edema and exquisite tenderness involving the helical rim; no fluctuance is noted.

Which one of the following interventions is most appropriate?

A. Cephalexin  
B. Clindamycin  
C. Ciprofloxacin  
D. Trimethoprim-sulfamethoxazole  
E. Hydrocortisone cream for suspected neomycin hypersensitivity

Correct answer: C

Discussion:

Ear and body piercing have enjoyed widespread popularity with ear piercing being the most common. Minor infections can occur after the ear lobe is pierced but more serious infections, caused by Pseudomonas aeruginosa, can complicate cartilaginous, helical piercings. The cartilaginous portion of the ear is avascular and more prone to deep seated, possibly disfiguring infections which may require surgical debridement and drainage. Pseudomonas is estimated to cause 95% of infections following
piercing procedures of the cartilage. Ciprofloxacin is the only antibiotic in the list of choices that has activity against this organism. Cephalexin, clindamycin and trimethoprim sulfamethoxazole are active against streptococci and staphylococci and against MRSA (trimethoprim-sulfamethoxazole, clindamycin). Although contact dermatitis from neomycin is quite common, it would not be associated with such severe symptoms and edema.

Clinical Pearl:

Infections following transcartilaginous piercing of the ear (peri-chondritis) are typically caused by *Pseudomonas aeruginosa* and should be treated with antimicrobial agents which have activity against this organism.

References:

Keene WE, Markum AC and Samadour M. Outbreak of *Pseudomonas aeruginosa* infections caused by commercial piercing of upper ear cartilage. JAMA 2004; 291(8):981-985


Case 8

A 35 yr old woman develops severe abdominal pain, profuse diarrhea, fever, and chills two days before returning home from a trip to Thailand. While in Thailand, she went to the beach and ate food (chicken and oysters) from street vendors. She started ciprofloxacin with only minimal relief of symptoms and seeks further advice. Physical examination discloses an ill appearing young woman with a temperature of 38° Centigrade, blood pressure 110/70 and pulse 100. She has diffuse abdominal tenderness and increased bowel sounds.

What is the most likely cause of her illness?

A. *Salmonella enteritidis*
B. *Vibrio parahemolyticus*
C. *Campylobacter jejuni*
D. *Shigela sonnei*
E. *Shiga-toxin producing E. coli*(STEC)

Correct answer: C
Discussion:

Diarrhea is the most common travel-related disorder when visiting low-income parts of the world. E. coli is the most common cause of traveler's diarrhea in most parts of the developing world except Southeast Asia (Cambodia, Thailand) where Campylobacter is the predominant etiologic agent, as in this case. Although fluoroquinolones like ciprofloxacin are typically the preferred treatment of choice for the majority of destinations where E. coli is predominant, azithromycin is the empiric antibiotic of choice for travelers to South or Southeast Asia because of the high prevalence of fluoroquinolone-resistant Campylobacter species. Shigellosis causes bloody diarrhea and tenesmus, which are not seen in this patient and the other choices would likely have responded quickly to ciprofloxacin. Understanding the epidemiology and distribution of pathogens causing travelers’ diarrhea is essential in developing a treatment plan.

Clinical Pearl:

Campylobacter is the most common cause of travelers’ diarrhea in Southeast Asia and should be treated with azithromycin rather than ciprofloxacin because of widespread fluoroquinolone resistance.

References:

Palliative Medicine Clinical Pearls
Molly Feely MD, FACP, FAAHPM

Case #1
You are called by the hospice nurse about a patient of yours on home hospice. He is a 46 y.o. man with end-stage non-small cell lung cancer with a life expectancy of only several weeks. Based on the nurse’s description of his sense of hopelessness, helplessness, anhedonia and guilt you diagnose him with major depression. He has no prior history of depression. His current medications include: Extended release morphine 60mg po tid, immediate release morphine 20mg po q4h prn, gabapentin 600mg po tid, senna 2 tablets po bid.

Which of the following is the best option to manage his depression?

   A. No intervention as these symptoms are normal at the end-of-life
   B. Initiate mirtazapine 15mg po qhs increasing to 30mg qhs in one week
   C. Initiate duloxetine 60mg po qhs increasing to 60mg po bid in one week
   D. Initiate ketamine 10mg sublingual qid
   E. Initiate methylphenidate 5mg po bid increasing to 10mg po bid in three days

Correct answer: E Initiate methylphenidate 5mg po bid increasing to 10mg po bid in three days

Discussion:
Psychological distress is common in terminally ill patients nearing the end of their life and is a source of suffering. Grief is a normal, adaptive reaction to loss or impending loss and a separate entity from depression. While grief is normal and adaptive, depression is not normal even at the end-of-life. Depression can be challenging to differentiate from normal grief. Usual screening tools are less helpful at the end-of-life as the vegetative symptoms usually associated with depression (alterations in sleep, appetite, energy, etc.) are common physical symptoms frequently present in those with end-stage disease. Thus we often look to alternative symptoms such as helplessness, hopelessness, anhedonia, guilt, and persistent suicidality to suggest a diagnosis of depression. Fortunately, depression at the end-of-life is just as responsive to usual treatment as depression in otherwise healthy individuals. However, one does have to take into account the patient’s life expectancy when choosing an antidepressant medication. Most antidepressants take weeks to achieve effect. In a patient with a short life expectancy, methylphenidate is the best studied option for depression management. There is good evidence for effectiveness and patient response is measured in a day or two making this the ideal drug for depression in those with a short life expectancy. While ketamine is also associated with immediate onset of effect, there are only a few case series describing benefit of ketamine for mood and, therefore, it would be second line therapy if he fails the methylphenidate.

Clinical Pearl: Consider methylphenidate for depressed patients with a life expectancy of days to weeks.
Reference:

Case #2
A 76 y.o. woman with severe long standing joint destructive rheumatoid arthritis presents to your clinic for follow up of her chronic constipation. She continues to report ongoing symptomatic constipation unrelieved by her current regimen requiring enemas several times a week. Medical work-up of her constipation has been unrevealing. Her pain is currently well controlled on her current opioid regimen and improved pain control has allowed her to achieve independence in her ADLs. Current medications include:
- Prednisone 10mg daily
- Extended-release morphine 60mg bid
- Senna 4 tablets bid
- Polyethylene glycol 17gm in 8oz liquid bid
- Bisacodyl 3 tab tid

Which of the following interventions would be the next best step in managing her constipation?

- A. Switch her from oral morphine to a fentanyl patch
- B. Add methylnaltrexone 12mg subQ injection daily to the current laxative regimen
- C. Add lactulose 30mL po qid prn
- D. Stop laxative regimen and begin naloxegol 25mg po daily
- E. Discontinue opioid pain medications

**Correct answer:** D Stop laxative regimen and begin naloxegol 25mg po daily

Discussion:
Opioid induced constipation is nearly universal in patients on scheduled opioid pain relievers and tolerance does NOT develop to constipation over time. Opioid induced constipation occurs with all opioids and there is no evidence that one opioid is less constipating than another. When an aggressive laxative regimen fails to adequately manage opioid induced constipation, a peripherally acting mu-opioid receptor antagonist (PAMORA) should be considered. PAMORAs are mu receptor antagonists that do not cross the blood-brain barrier and therefore only act peripherally. As such, PAMORAs block the mu receptors in the gut thereby relieving opioid induced constipation without adversely affecting pain control. They are highly effective. All laxatives should be stopped upon initiation of PAMORA therapy. Laxative can be added back after 3 days if laxation response to PAMORA alone is inadequate. Bowel obstruction is an absolute contraindication to PAMORAs.

Two PAMORAs are currently FDA approved for opioid induced constipation. Methylnaltrexone is approved for chronic non-cancer pain (studied up to 52 weeks) and for palliative patients, including patients with cancer (studied up to 4 months). Methylnaltrexone comes as a
subcutaneous injection daily or a newly available oral tablet. Naloxegol is a derivative of naloxone that has been pegylated to prevent transmission across the blood-brain barrier. Naloxegol is only oral and is FDA approved for chronic non-cancer pain only (studied up to 52 weeks). The existence of now two oral PAMORAs has simplified the management of outpatients with opioid induced constipation considerably over the older subcutaneous route. Naloxegol is metabolized via CYP3A4 and has the potential for numerous, significant drug interactions.

**Clinical Pearl:** Consider oral peripheral acting mu-opioid receptor antagonists (PAMORAs) in outpatients with opioid induced constipation who have failed aggressive laxative regimen.

References:


Case #3

A mildly anxious, never married, 79 y.o. woman is on your clinic schedule as a hospital follow up after her 4th hospitalization in the last 9 months. She has multiple medical co-morbidities and has been clinically and functionally declining over the last year. You recognize her life expectancy at less than 1 year and further recognize the need to do some advance care planning but worry about how this patient might respond to a conversation about what the future may hold for her.

Which of the following statements about advance care planning for this patient with a serious illness is true?

A. Advance care planning does not worsen anxiety, depression or hopelessness  
B. Patients with serious illness will bring up advance care planning topics themselves when they are ready to discuss them.  
C. Advance care planning is ideally done when there is a therapeutic decision that needs to be made.  
D. While it decreases non-beneficial care at the end-of-life, it has no impact on patient quality-of-life or family bereavement.  
E. Physician Order for Life Sustaining Treatment (POLST) form is synonymous with advance care planning.

**Correct Answer:** A. Advance care planning does not worsen anxiety, depression or hopelessness
Discussion:
Advance care planning is a process of communication or conversation between health care providers and patients and families in which patients’ preferences, goals and values are identified and from which the rationale for future care is derived. When advance care planning occurs in patients with serious, life-threatening illness (defined as a life expectancy of roughly less than a year), such conversations are sometimes called serious illness conversations to differentiate them from advance care planning done in well adults. Serious illness conversations are considered high value care by the American College of Physicians and recommended for all patients with serious illness. Studies show that patients expect their physicians to initiate the conversation and patients will rarely bring up this topic on their own even when they desire further discussion. Ideally, these conversations occur at times of relatively stability early in the course of disease rather than at times of crisis. Numerous studies show improved patient/family outcomes in patients who have engaged in serious illness conversations including:

- less non-beneficial care at the end-of-life
- care congruent with wishes
- improved quality of life for the patient
- improved family bereavement
- reduced overall cost of care

Furthermore, extensive evidence shows that these conversations are NOT associated with any loss of hope nor are they associated with any increase in depression or anxiety. In fact, several studies suggest that anxiety and depression may actually be improved following these conversations.

Accurate and retrievable documentation of serious illness conversations is important so that all providers can access the patient’s wishes and so that the evolution of these wishes can be followed iteratively. Physician Orders for Life Sustaining Treatment (POLST) forms are transferable physician order sets regarding specific interventions the patient does or doesn’t want performed. It presumes a serious illness conversation has taken place in order to elucidate the patient’s wishes but there is no place on the form to document the patient’s rationale for their decision making. Therefore, a POLST form in isolation is nothing more than a physician order. Ideally every POLST form should be traceable back to appropriate documentation of the serious illness conversation that occurred which subsequently led to a POLST form being filled out.

**Clinical Pearl:** Serious illness conversations/advance care planning does not worsen anxiety

Reference:
Case #4
A 38 y.o. woman with metastatic breast cancer is admitted to your hospital service with dehydration secondary to nausea and vomiting for the last 36 hours. The onset of her nausea coincides with the initiation of morphine for cancer related pain. There have been no other recent medication changes and she has tolerated her stable chemotherapy regimen without nausea. She had a normal BM this morning.

Which intervention is most appropriate to manage her opioid induced nausea?

A. Switch opioids from morphine to fentanyl for pain
B. Continue morphine and add scheduled prochlorperazine for 5 days
C. Stop morphine and start a lidocaine patch
D. Continue morphine and add ondansetron as needed
E. Switch from morphine to tramadol pain

Correct answer: B. Continue morphine and add scheduled prochlorperazine for 5-7 days

Discussion:
Nausea is a common side effect of opioid pain medication, occurring in 10-40% of patients. Fortunately, tolerance to the nausea develops over 5-7 days in over 90% of patients who develop opioid induced nausea. The risk of nausea is similar for all opioids; no one opioid is less likely to cause nausea as another (this includes tramadol). As such, early opioid rotation in the first 5-7 days prior to the development of tolerance may simply reset the clock back to day zero. Additionally, patients may view the nausea as medication intolerance rather than an expected but temporary side effect. Therefore most experts recommend trying to treat through the nausea for the first several days before considering opioid rotation.

Opioid pain medication can induce nausea via multiple different mechanisms. Opioids can stimulate the vestibular system inducing a vestibular nausea. Opioids decrease GI motility and the resultant gut inertia or frank constipation can induce nausea. However the most common mechanism by which opioids induce nausea is via stimulation of the chemoreceptor trigger zone through dopaminergic pathways. Therefore, antiemetics with anti-dopaminergic activity are considered first line therapy for opioid induced nausea/vomiting. Scheduling the anti-dopaminergic antiemetic is preferable to prn dosing in the setting of scheduled opioids.

Clinical Pearl: Anti-dopaminergic antiemetics are first line therapy for opioid induced nausea.

References:

http://prc.coh.org/pdf/Nausea-FF%203-10.pdf accessed 01/29/2017
Case #5
A 48 y.o. woman presents to your office for routine follow up her primary biliary cirrhosis. She complains of relentless, severe pruritus that prevents her from sleeping. She is desperate for relief. She has failed prior trials of all topical agents, as well as diphenhydramine, doxepin, loratadine and hydroxyzine. She is already taking high dose cholestyramine.

Her PMH is significant for a remote history of IV heroin use now on methadone maintenance therapy. She is HIV positive with an undetectable viral load, well managed on HAART. 

MEDS: cholestyramine 4gm bid, methadone 20mg daily, Atazanavir 300 mg/ritonavir 100 daily
She has widespread excoriations on exam.

Which of the following interventions is most appropriate to manage her cholestatic pruritus?

A. Naltrexone 12.5mg po bid
B. Rifampin 150mg po tid
C. Sertraline 100mg po daily
D. Dronabinol 10mg po tid
E. Gabapentin 600mg po tid

Correct answer: C. Sertraline 100mg po daily

Discussion:
Pruritus is a complex sensation of multiple etiologies. There is evolving evidence that the sensation of pruritus may be neurologically mediated and may involve opioid ligands. Increasingly, it is becoming apparent that pruritus is commonly a centrally mediated process rather than a histamine related phenomenon. These theories have opened novel therapeutic options for pruritus, including cholestatic and uremic pruritus.

Cholestyramine is first line therapy for cholestatic pruritus despite a lack of robust evidence. Opioid antagonists naloxone and naltrexone are effective for the management of both cholestatic and uremic pruritus. However, both agents reverse the effect of opioid pain relievers inducing acute opioid withdrawal in patients using opioids and therefore should be avoided in patients on concomitant opioid pain relievers.

Sertraline, along with other serotonergic blocking agents including mirtazapine and ondansetron, has also been reported to relieve pruritus in patients with opioid induced pruritus, uremia, polycythemia vera, malignancy and cholestasis. Sertraline has the best evidence supported by a small randomized, placebo-controlled trial.

Two clinical studies support the efficacy of rifampin for liver induced pruritus. However, rifampin interacts with multiple medications (including HIV medications and methadone) and thus is only appropriate for selected patients. It is hypothesized that rifampin’s enzyme inducing capacity may be key to its effectiveness in pruritus. Additionally, rifampin use is associated with hepatotoxicity and patients utilizing this drug should be carefully monitored.
Isolated case series have reported benefit in pruritus of dronabinol, s-adenosylmethionine and grapefruit juice. Dronabinol, a synthetic cannabinoid, would be a poor choice in a patient with a history of chemical dependancy. Gabapentin and pregabalin have been shown to be effective for uremic pruritus but have not been studied in cholestatic pruritus.

**Clinical Pearl:** Naloxone/Naltrexone, Sertraline and Rifampin are effective agents for cholestatic pruritus.

**References:**


Case #6
A 57 y.o. Amish man with a history of longstanding dyspepsia managed with sodium bicarbonate slurry is admitted to your hospital service with persistent hiccups for the last 48 hours to the point of being unable to maintain sleep or hydration. EGD reveals only evidence of GERD. In addition to antireflux therapy, you start him on chlorpromazine 25mg IV q6h escalating the dose to 50mg IV q6h without benefit to his hiccups.

Which of the following is a reasonable second line therapy for the management of this patient’s hiccups?

A. Amlodipine
B. Baclofen
C. Lorazepam
D. Phrenic nerve ablation
E. Dexamethasone

**Correct answer:** B. Baclofen

**Discussion:**
Persistent or intractable hiccups are an uncommon but miserable symptom to have. Persistent hiccups persist for 48 hours and intractable hiccups occur longer than 2 months. The treatment of hiccups has been written about for more than a century. Chlorpromazine is the only medication with FDA approval for the management of hiccups although the evidence for its efficacy is sparse, consisting of only small case controlled trials. The lack of robust evidence is a theme in the management of hiccups. Metoclopramide probably has the best evidence for efficacy in hiccup management with a randomized, placebo controlled trial of 36 patients. Baclofen had efficacy in a prospective cohort study. Gabapentin has been shown to be beneficial in a few case series. Phrenic nerve ablation has shown promise but would be
considered as a last resort. Dexamethasone is a described cause of hiccups that often responds to rotation to an alternative steroid agent.

**Clinical Pearl:** Metoclopramide and baclofen are considered second line agents in the treatment of hiccups.

References:


Case #7
A 61 y.o. woman undergoing CHOP-R chemotherapy for large B cell lymphoma is admitted to your hospital service with dehydration secondary to intractable nausea/vomiting for several weeks. Nausea is worse after chemotherapy and worse at the sight of food but present continuously. Her nausea does not worsen after taking opioid pain medication nor does it worsen when riding in the car. Imaging shows no evidence of constipation or bowel obstruction.

Medications include:

- fentanyl patch 25mcg q3days,
- hydromorphone 2mg po q4h prn pain
- ondansetron RDT 8mg sublingual qid
- prochlorperazine 25mg per rectum bid
- dexamethasone 4mg po bid
- lorazepam 1mg po q4h prn nausea

Which of the following is most likely to improve her nausea?

A. Stop all opioids  
B. Add promethazine 10mg IV qid  
C. Add scopolamine patch 1.5mg q3day  
D. Start olanzapine RDT 10mg sublingual qhs  
E. Add dronabinol 10mg po tid

**Correct answer:** D. Start olanzapine RDT 10mg sublingual qhs
Discussion:
Nausea in patients with advanced cancer is an extremely troubling symptom. Most patients rate intractable nausea worse than intractable pain. In patients with cancer, nausea can stem from multiple potential etiologies. Elucidating the correct etiology helps to target antiemetic therapy increasing the likelihood of successful treatment. In our patient there is no exacerbation of her nausea after taking opioids making opioid induced nausea less likely. As such, stopping opioids is unlikely to be beneficial and highly likely to worsen her cancer related pain. Additionally her nausea does not worsen riding in the car suggesting that there is not a vestibular component to her nausea. Scopolamine is a muscarinic receptor blocker effective primarily for vestibular nausea. While promethazine has a small amount of dopaminergic blockade, it too is primarily a muscarinic receptor blocker most effective for vestibular nausea which our patient does not seem to have.
Our patient’s nausea worsens after chemotherapy suggesting a chemotherapy induced nausea component as well as an anticipatory nausea component evidenced by the worsening nausea at the sight of food.
The management of chemotherapy induced nausea and vomiting has been dramatically improved with protocol driven guidelines for prophylactic management at the time of emetogenic chemotherapy. Most patients are well managed but not all.
Olanzapine has been used for nausea in palliative medicine circles for more than a decade. In the last 3 years multiple randomized controlled trials have demonstrated the efficacy of olanzapine as prophylaxis as well as breakthrough treatment for chemotherapy induced nausea/vomiting. Olanzapine is a unique antipsychotic medication that blocks multiple neurotransmitters including 5-HT, dopamine, histamine, alpha-adrenergic and muscarinic receptors thereby covering most bases for nausea management in one drug. Its effectiveness in chemotherapy induced nausea/vomiting has been demonstrated in multiple randomized controlled trials and it is now an option for management in the NCCN guidelines for management of chemotherapy induced nausea/vomiting.
Dronabinol is a weakly effective anti-emetic for chemotherapy induced nausea vomiting. The studies showing benefit of dronabinol in chemotherapy induced nausea vomiting largely predated the development of effective 5-HT receptor blockers and it has a minimal role in modern day management of patients with this condition.

**Clinical Pearl:** Consider olanzapine for the management of refractory chemotherapy induced nausea/vomiting.

References:

Wood GJ, Shega JW, et al. Management of intractable nausea and vomiting at the end-of-life: “I was feeling nauseous all the time…nothing was working.” *JAMA*. 2007;298(10):1196-1207 (doi:10.1001/jama.298.10.1196)
Case #8
A 74 y.o. woman is admitted to your hospital service with severe GOLD stage IV COPD and dyspnea. She is on maximal medical management for her COPD. Her oxygen saturation is 94% on 2L nasal cannula at rest and with activity. Her main symptom is severe breathlessness with minimal exertion. She is functionally independent in all her ADLs. Her goal is to maximize her quality of life. She reports intolerances to multiple oral medications (including delirium from multiple opioids) and strongly desires to avoid oral medications if at all possible.

Which of the following interventions is most likely to improve her dyspnea?

A. Morphine 2.5mg nebulized qid  
B. Use a fan for as needed for dyspnea relief  
C. Prescribe a gait aid such as a walker to help relieve her dyspnea  
D. Increase her oxygen to 4L nasal cannula  
E. Prescribe ABH (Ativan-Benadryl-Haldol) gel massaged into the inner wrist three times a day for dyspnea

Correct answer: C. Prescribe a gait aid such as a walker to help relieve her dyspnea.

Discussion:
Dyspnea is a common and distressing symptom in many patients with serious illness. After maximal medical management of the underlying disease and non-pharmacologic interventions, systemic opioids are first line pharmacologic therapy for severe, chronic dyspnea. The evidence for the effectiveness of systemic benzodiazepines for dyspnea relief is mixed and they are considered second line. This patient wished to avoid oral medications for her dyspnea. ABH gel is an old preparation widely used in hospice in the past for nausea. The gel, which contains a combination of lorazepam, diphenhydramine and haloperidol, was rubbed together between the inner wrists. A definitive study several years ago showed that none of these medications is systemically absorbed through intact skin and this medication is no longer used therapeutically. Nebulized opioids continue to garner interest due to their extreme tolerability and the presence of mu-opioid receptors in the bronchial tree. Numerous low quality studies of nebulized opioids have shown mixed results. Two older systematic reviews showed no benefit to nebulized opioids over nebulized saline. A more recent systematic review done utilizing Cochrane methodology showed a modest benefit to nebulized opioids. However, on further investigation this was primarily due to a single outlier study. When the outlier was removed the results again showed no significant benefit to nebulized opioids over nebulized saline. Oxygen is not effective for breathlessness in patients without hypoxemia. Several non-pharmacologic interventions are effective for relief of dyspnea. While widely used due to their simplicity and safety, hand-held fans for dyspnea actually have minimal evidence to support their use. A Cochrane systematic review concluded that there was not enough evidence for or against fans for dyspnea management. Gait aids and breathing training both had moderate evidence supporting their use in the relief of dyspnea and chest wall vibration.

and neuromuscular stimulation both had strong evidence supporting their effectiveness in the relief of dyspnea. The majority of patients in all of these studies had COPD; there was a paucity of patients with heart failure, neuromuscular disease or cancer.

**Clinical Pearl:** Gait aids are simple, widely available and effective for dyspnea management in patients with COPD.

References:
Ekström M, Abernethy AA, Currow DC. The management of chronic breathlessness in patients with advanced and terminal illness. *BMJ* 2015;349:g7617

Clinical Pearls in Pulmonary Medicine
Craig Daniels, MD

Case 1
Question:
A 53 year old man with a history of asthma and multiple emergency room visits returns to your office after a recent hospitalization for asthma, which required intubation and mechanical ventilation. He recovered acutely and was discharged 36 hours after presentation and has just completed 5 days of 40mg/day of prednisone. His inhaler technique is good and he is using his short-acting β2 agonist, his long-acting β2 agonist and a moderate dose inhaled corticosteroid as prescribed. He is a reliable historian and works as computer programmer.

He complains of chronic cough and sudden onset of coughing paroxysms and shortness of breath triggered by smoke, perfume and other noxious odors, which do not improve with use of albuterol. During these episodes, he is witnessed to have cough and loud wheeze during inspiration. In between episodes, he is troubled by cough, but denies dyspnea and is physically active.

Examination is normal. Lungs are clear. Heart is regular without murmur. Spirometry and Chest X-ray are normal.

Which of the following is the next best management step?
A. CT Neck and Chest
B. Allergy testing
C. Step up inhaled corticosteroid and taper oral prednisone
D. Laryngoscopy

Correct Answer: D

Discussion:
Completion of laryngoscopy is the most appropriate test to diagnose vocal cord dysfunction in this patient with episodic cough and stridor triggered by noxious stimuli and failure to improve despite appropriate therapy for asthma.

Vocal Cord Dysfunction (VCD) is characterized by involuntary adduction of the vocal cords during inspiration. It overlaps with a diagnosis of asthma in over 20% of patients and is a “mimic” of asthma, particularly in patients who do not respond to appropriate asthma therapy. VCD is associated with airflow limitation, dyspnea, and stridor (inspiratory wheeze). The diagnosis is made by laryngoscopy with visualization of inspiratory vocal cord adduction. The sensitivity of laryngoscopy to detect sporadic VCD can be improved by provocation with noxious stimuli or exercise. Our understanding of VCD has changed over the past decade. While initially thought to be “psychogenic” or “functional” in etiology, we now recognize a separate category of irritant-associated VCD. These patients experience an enhanced glottis closure reflex triggered by various irritants (noxious inhalants and odors, laryngeal/pharyngeal
acid reflux, and rhinitis). Patients with irritant-associated VCD will complain of irritant sensitivity/triggers, often have a chronic cough, and are frequently initially diagnosed as asthma. Treatment of associated conditions which contribute to laryngeal/pharyngeal irritation (OSA, GERD, rhinitis) and avoidance of known triggers coupled with referral to speech pathology for biofeedback and teaching of laryngeal control techniques are recommended.

CT scan of the neck and chest would not diagnose VCD. The presence of stridor could prompt one to consider an extra-thoracic airway lesion. However, this patient has resolution of his symptoms between episodes and a normal activity level, which makes airflow obstruction unlikely.

While frequently confused with allergy and asthma, irritant associated VCD does not respond to asthma therapy or corticosteroids and should be considered in patients with triggered inspiratory wheeze and dyspnea who fail asthma therapy.

**Clinical Pearl:** Vocal Cord Dysfunction is characterized by sudden onset upper airway stridor or noisy breathing, mimics asthma, and may be caused by glottic sensitivity to irritant triggers.

**References:**

**Case 2**
**Question:**
A 37 year old woman diagnosed with asthma at age 20 is evaluated for difficult to control asthma. Over the past 3 years, she has had 7 ED visits and 3 hospitalizations for asthma. She has severe seasonal allergies and has tested positive to animal dander and pollen. She adheres to allergen avoidance strategies, and is compliant with her medications. She does not smoke. She has been on oral glucocorticoid therapy for 8 months and flares when tapered below 20mg daily. In addition, her asthma therapy includes as needed short-acting β2 agonist, long-acting β2 agonist, anticholinergic, and high-dose inhaled corticosteroid.

Examination shows scattered wheezes. Heart is regular without murmur. There is no rash. Spirometry shows moderate obstruction and Chest X-ray shows mild hyperinflation. CBC demonstrates 5% eosinophils and IgE is elevated at 562 U/mL.

**Which of the following is the next best management step?**
A. Allergen desensitization
B. Omalizumab
C. Prednisone 20mg daily without taper
D. Home environmental testing

**Correct Answer:** B
Discussion:
Severe asthma is defined as the need for continuous high-dose inhaled corticosteroids or oral steroids (> 50% of the year) to prevent exacerbation. Severe asthmatics account for 10% of all patients diagnosed with asthma and suffer from frequent exacerbations, high healthcare utilization, and frequent ED visits. Patients who are dependent on oral corticosteroids have a high likelihood of negative side-effects for skin, bone, and metabolic health. Omalizumab is a monoclonal anti-IgE antibody, approved by FDA for treatment of severe allergic asthma in patients with IgE elevation and inadequate asthma control despite high-dose inhaled corticosteroids. Recently, several monoclonal antibodies have been approved for treatment of severe asthma. Of these, two anti-Interleukin 5 monoclonal antibodies, mepolizumab and reslizumab, have demonstrated efficacy similar to omalizumab in treatment of severe asthma with eosinophil elevation and/or elevation in IgE. Head to head trials of these medications are not available to guide clinicians in deciding which therapy is more beneficial for selected patients with asthma. These approved therapies are injectable, expensive, and carry risks for anaphylaxis, helminthic infections, and the potential to unmask eosinophilic diseases such as Churg-Strauss vasculitis. Despite the expense of these medications, the decrease in medication use and healthcare utilization makes them cost effective for selected patients. With the advent of monoclonal therapy to treat severe asthma, clinicians should be aware of the eosinophilic phenotype, test for IgE levels, and guide patients with steroid dependence towards consideration of appropriate monoclonal therapies.

Allergy desensitization is an accepted therapy for patients with mild to moderate asthma and known allergic triggers. However, in patients with severe asthma there is an unacceptable risk for antigen desensitization to cause acute systemic allergic reaction and acute bronchospasm, especially in those with recent oral steroid use or reduced FEV1. High risk patients should be first considered for anti IgE therapy prior to desensitization therapy.

Continued oral prednisone therapy is associated with development of Cushingoid complications including long-term skin and bone disease. Patients with oral steroid dependence to treat asthma should be considered for monoclonal antibody therapy.

Environmental testing is expensive and does not add value over allergy testing to identify potential allergic triggers.

Clinical Pearl: Monoclonal antibody therapies are efficacious and potentially cost effective in treatment of patients with severe asthma with eosinophilic phenotype and/or elevated IgE who are not controlled with high-dose inhaled corticosteroids.

References:

Case 3  
Question:  
A 72 year old woman with COPD and increasing dyspnea and productive cough presents to the ED. After appropriate evaluation, she is diagnosed with COPD exacerbation and admitted for management. She has a history of osteoporosis and 3 prior admissions this year for COPD exacerbation. Her outpatient COPD medications include inhaled short and long-acting $\beta_2$ agonists, inhaled long-acting anticholinergic, and low-dose inhaled corticosteroid. She is supported with oxygen, short acting bronchodilators, given a single dose of methylprednisolone 125mg IV, and admitted to a medical floor.

**Which of the following is the best management choice for continued corticosteroid therapy?**

A. IV methylprednisolone, 125 mg bid until clinical improvement  
B. Oral prednisone starting at 80 mg/day to taper to off over 21 days  
C. Oral Prednisone 40mg daily for 5 days without taper  
D. Inhaled high-dose corticosteroid until 1 month after discharge

**Correct Answer: D**  

Discussion:  
For patients presenting to the ED with COPD exacerbation, oral prednisone, 40mg daily for 5 days duration, has similar clinical outcomes as higher dose, longer duration strategies with less total steroid exposure. Exacerbations are a common cause of morbidity and mortality in patients with COPD. In these patients, systemic glucocorticoid therapy has been known to improve clinical outcomes. To prevent adverse effects, it is desirable to decrease the total dose and duration of systemic corticosteroids. Previously, the dose and duration of therapy had not been established, leading to wide practice variation. However, a recent randomized clinical trial has now demonstrated equivalent risk for re-exacerbation in patients treated with 40mg oral prednisone for 5 days versus 14 days.

In patients able to take oral medications, prednisone is nearly 100% bioavailable by the oral route. A recent Cochrane analysis showed high-dose IV corticosteroids increase total steroid exposure and steroid-induced complications, but do not improve clinical outcomes in patients with COPD exacerbation when compared to low-dose oral regimens.

International guidelines recommend short duration (7 – 14 days) of oral therapy for COPD exacerbation. New evidence from the REDUCE trial supports reduced duration of steroid use (5 days) without clinical impact when compared to 14 days. While selected patients may benefit from 14 days of corticosteroids, current data no longer support prolonged duration steroids with tapers over 21 days or longer.

Several randomized clinical trials show benefit for systemic corticosteroids in patients hospitalized with COPD exacerbation. The use of inhaled corticosteroids to further reduce exposure to systemic corticosteroids in patients with COPD exacerbation is not known to be a
safe treatment strategy. At this time, consensus guidelines recommend short duration, low-dose systemic corticosteroids for patients hospitalized with COPD exacerbation.

**Clinical Pearl:** In patients presenting to the ED with COPD exacerbation, oral prednisone, 40mg daily for 5 days duration, has similar clinical outcomes to higher dose, longer duration strategies, with less total steroid exposure and fewer side-effects.

**References:**


**Case 4 Question:**
You are evaluating a 66 year old woman in clinic 4-weeks after a recent hospitalization for COPD exacerbation. She was hospitalized for 3 days, received empiric antibiotics, 5 days of prednisone 40mg, and was initiated on oxygen by NC.

Currently, she is functional in her own home, continues to drive, and gets intermittent assistance for large household tasks. She is comfortable at rest, but continues to have exertional dyspnea. She is using 2L oxygen per NC at rest and with activity. She remains on inhaled short β₂ agonist, inhaled long-acting β₂ agonist, inhaled long-acting anticholinergic, and inhaled moderate-dose corticosteroid.

Her office spirometry shows FEV1 of 46% predicted. Her BP is 138/80, pulse is 70, RR is 20 with oxygen saturation 92% on 2L NC.

**Which of the following is the next best management choice?**
- A. Pulmonary Rehabilitation
- B. Prednisone 40mg daily for 5 days
- C. CT Chest
- D. Sputum Culture

**Correct Answer: A**
Discussion:
In patients recovering after hospitalization from acute exacerbation of COPD, pulmonary rehabilitation has been shown to improve exercise tolerance, respiratory symptoms, and quality of life. Clinical guidelines recommend these patients be considered for referral to pulmonary rehabilitation, ideally within 3 weeks of hospitalization. Pulmonary rehabilitation is likely an underutilized treatment. It is indicated for patients with COPD who have persistent symptoms despite optimal therapy or moderate to severe disease by spirometry (FEV1 < 50%). While not known to improve lung function, pulmonary rehabilitation is associated with numerous positive clinical outcomes including improved exercise capacity and reductions in symptomatic dyspnea, anxiety, depression, and healthcare utilization.

While beneficial for treatment of COPD exacerbations, there is no known benefit for oral prednisone in patients with chronic dyspnea due to COPD. Since steroids carry adverse risk when given repeatedly or for prolonged duration, they should be avoided in this population.

This patient is debilitated from COPD and recent hospitalization and there is no role for CT scan of the chest during follow up. This patient does not have evidence for acute infection and does not have known bronchiectasis. The role of routine culture in follow up of COPD exacerbation is not established.

Clinical Pearl: In patients recovering after hospitalization for acute exacerbation of COPD, pulmonary rehabilitation has been shown to improve exercise tolerance, respiratory symptoms, and quality of life. Clinical guidelines recommend these patients be considered for referral to pulmonary rehabilitation, ideally within 3 weeks of hospitalization.

References:

Case 5
Question:
A 50 year old man with a BMI of 36 comes to your office for general medical visit. His primary complaint is daytime fatigue which has worsened in the past 6 months. Three years ago, he was diagnosed with mild OSA by home-overnight polysomnography. He was prescribed CPAP at 5cm pressure through a nasal interface, which he didn’t tolerate and does not use.

Eight months ago he slipped on the stairs and developed mechanical low back pain which has evolved into chronic pain requiring scheduled oxycodone, acetaminophen, and gabapentin. In addition he has anxiety and depression treated with paroxetine and nighttime insomnia treated with zolpidem QHS. Since initiating these medications, his spouse has observed an increase in both loud snoring and apneas. His daytime sleepiness has made it difficult for him to stay awake at his sedentary desk job and he has been warned he may be fired.
He declines your recommendation to reinitiate CPAP due to past history of intolerance.

Which of the following is the next best management step?

A. Discontinue gabapentin  
B. Discontinue oxycodone  
C. Discontinue paroxetine  
D. Discontinue zolpidem

Correct Answer: B

Discussion:

Opioid use is associated with risk of acute worsening of sleep disordered breathing when added to patients with untreated OSA and is a known cause of central and obstructive sleep apnea. Polypharmacy and OSA with non-compliance are common clinical challenges. Medications with the potential to worsen sleep-disordered breathing and increase daytime sleepiness are commonly prescribed for the treatment of anxiety, depression, and pain. Clinicians should be aware of the increased risk for prescription narcotics to worsen unrecognized or untreated OSA in both outpatient and hospital settings.

Gabapentin is not known to worsen sleep disordered breathing and is commonly used to treat restless legs syndrome. It has the potential to cause drowsiness and may contribute to daytime sleepiness in this patient. It would be reasonable to consider cessation of gabapentin if this patient remains fatigued after discontinuation of narcotics and assessment for persistent OSA.

Paroxetine and other SSRIs are not known to worsen sleep disordered breathing/OSA and should be continued to treat underlying anxiety and depression when present.

Zolpidem and other non-benzodiazepine sedating medications are commonly used in conjunction with CPAP to improve tolerance and induce sleep. They are considered safe in patients with sleep disordered breathing.

Clinical Pearl: Opioid use is associated with risk of acute worsening of sleep disordered breathing when added to patients with untreated OSA and in addition, is a known cause of central and obstructive sleep apnea.

References:


Case 6  
Question:  
A 79 y.o. man with persistent pleuritic chest pain sees you in your office 6 weeks after admission for pneumonia. While in hospital he had a thoracentesis for a right pleural effusion
which was culture negative, cytology negative, and showed pH 7.3, LDH 800 and Protein 5.4. He was treated for community acquired pneumonia with azithromycin and discharged to home.

Examination shows diminished BS and dullness over right base. Heart is regular without murmur. Serum LDH is 266 and serum total protein is 6.0.

You order repeat thoracentesis which returns with similar fluid characteristics, including negative culture and cytology.

Which of the following is the next best management step?

A. Observation
B. Levofoxacin 750mg for 14 days
C. Bronchoscopy
D. CT chest

Correct Answer: D

Discussion:
This patient has persistent pleuritic chest pain and an unresolved exudative pleural effusion of uncertain etiology. Despite prior negative cytology, cancer is the most likely diagnosis to explain his presentation. Continued aggressive evaluation, beginning with CT chest is the next best management choice. Evaluation of pleural effusion is a common diagnostic problem. In the United States, most pleural effusions are caused by heart failure, infections (pneumonia), and cancer. Thoracentesis should be completed to further evaluate all pleural effusions in which diagnostic uncertainty is present. It is useful to categorize effusions as transudative (non-inflammatory) and exudative (inflammatory). This patient has an exudative pleural effusion by Light’s criteria (pleural effusion LDH/serum LDH > 0.6 and/or pleural effusion protein/serum protein > 0.5). As many as 1/3rd of pleural effusions remain “undiagnosed” despite an appropriate initial evaluation. While it is occasionally reasonable to observe a
transudative pleural effusion of uncertain cause, undiagnosed exudative pleural effusions can be associated with sinister diagnoses including PE, Cancer, and Tuberculosis. Continued evaluation and referral for expert consultation should be considered. Observation is not recommended. Pleural effusion cytology is certainly useful when it returns positive and should be completed on all pleural effusions in which cancer is considered a possible diagnosis. However, cytology has a poor sensitivity to detect cancer involving the pleural space. Repeating cytology on large volume thoracenteses improves diagnostic yield to as high as 60% in patients with pleural effusion caused by cancer. Occasionally, exudative pleural effusions require referral for assessment of surgical pleural biopsy to diagnose or exclude cancer.

Bronchoscopy is not effective in the initial assessment of pleural disease. Bronchoscopy is useful in assessing pulmonary processes which may cause pleural effusion, such as a lung mass. In this patient with pleuritic chest pain and an unresolved exudative effusion, mesothelioma and bronchogenic carcinoma should be considered. CT chest is the next best diagnostic step to further define the lung parenchyma and pleural space for mass or infiltrate.

Pneumonia can cause parapneumonic exudative pleural effusion and empyema. These patients characteristically have signs and symptoms of respiratory infection. Untreated infections of the pleural space typically worsen acutely (days, not weeks) and are readily diagnosed by culture of pleural fluid. This patient is not likely to benefit from empiric antibiotic such as levofloxacin.

**Clinical Pearl:** Exudative pleural effusions often remain undiagnosed despite initial appropriate evaluation and are commonly caused by cancer and other sinister diagnoses. Continued aggressive evaluation, including CT chest and, when appropriate, referral for expert consultation are recommended.

**References:**

**Case 7**
**Question:**
You are called to evaluate a 52 y.o. inpatient with new onset confusion. He was admitted to the hospital rehabilitation unit 3 days ago with debility resulting from treatment of recurrent lymphoma. When you arrive, his wife is concerned stating “he’s just not right”. He had local I&D of a furuncle on his chin 2 hours earlier. He has been neutropenic for 1 week.

He is currently being treated with levofloxacin, acyclovir, and fluconazole. Labs show WBC of 0.8 (ANC 280). Current vital signs are; BP – 95/50, Pulse – 85, RR – 18, (96% on RA) Temp – 37.5 Pertinent Exam shows this patient is thin, in no distress. There is gauze/tape over chin incision. He has a normal – CV/Resp/Abd exam. Neurologic exam is consistent with confusion.

You immediately order blood cultures, IV cefepime and vancomycin, and 2.5 liters of lactated ringers.
Which of the following is the next best management choice?

A. Order serum lactate
B. Obtain CT Chest with IV contrast
C. Obtain central line
D. Add IV amphotericin

Correct Answer: A

Discussion:
This patient is hospitalized for infection and now has an elevated respiratory rate and change in mental status. These findings meet the criteria for the new consensus definition of sepsis by qSOFA criteria. From the time of sepsis recognition, clinicians have 3-hours to order blood cultures, initiate IV antibiotics, administer a 30cc/kg body weight volume challenge, and measure serum lactate. Since the early 1990’s sepsis has been diagnosed by identifying 2 of 4 SIRS criteria (WBC; > 12k or < 4k, Temperature; > 38.0 or < 36.0 C, Respiratory rate; > 20, Pulse; > 90) in the presence of confirmed or suspected infection. Severe sepsis required evidence of end organ injury due to hypoperfusion and septic shock required persistent hypoperfusion after volume challenge. Sepsis diagnosis by SIRS criteria has been criticized for its complexity as well as its poor sensitivity and specificity. This patient does not meet criteria for sepsis by SIRS criteria, as he has low WBC with normal RR, Temp, and pulse.

In 2016, new international consensus criteria defined sepsis as hypoperfusion due to infection and established criteria to diagnose sepsis as patients with confirmed or suspected infection with 2 of 3 qSOFA criteria (RR ≥ 22, Systolic BP ≤ 100mmHg, any alteration in mental status). The nomenclature of “severe sepsis” was removed. Septic shock is similarly diagnosed when hypoperfusion persists as a cause for end-organ injury despite volume expansion (30cc/kg body weight).

High-quality care of patients with sepsis includes achievement of 3 and 6 hour care goals. Recent clinical trials support prior studies which show early antibiotics and resuscitation (volume expansion) are life-saving measures and prevent the escalation of hypoperfusion into multiorgan failure. It is imperative that all clinicians who practice in a hospital setting be aware of the new diagnostic criteria for sepsis as well as the 3-hour sepsis bundled care components. This patient meets criteria for sepsis, has had blood cultures, antibiotics, and volume expansion. Lactate should be measured to complete the bundle.

CT scan of the chest would not be indicated as the initial action in resuscitation of a patient with sepsis, which is likely due to blood stream infection from skin incision.

A central line may be required to support blood pressure via vasopressors if hypoperfusion persists after, or during, volume challenge. However, the initial action in this setting would be to complete the 3-hour bundle elements immediately with a plan to place central line depending on the patient’s response.
Neutropenic patients are at risk for fungal infections and antifungal therapy may be considered as appropriate empiric therapy in the right clinical setting (TPN or bowel source in a neutropenic patient). However, this patient’s recent skin incision makes gram positive bacteria such as MRSA the likely source of infection; appropriate antibiotic coverage for skin pathogens was ordered.

**Clinical Pearl:** Sepsis is defined as hypoperfusion due to infection and current criteria to diagnose sepsis are defined as - patients with confirmed or suspected infection and with 2 of 3 qSOFA criteria (RR ≥ 22, Systolic BP ≤ 100mmHg, any alteration in mental status). From the time of sepsis recognition, clinicians have 3-hours to order blood cultures, initiate IV antibiotics, administer a 30cc/kg body weight volume challenge, and measure serum lactate.

**References:**

**Case 8**
**Question:**
You are asked to see a 73 year old man hospitalized for recurrent bouts of CHF. His ejection fraction is noted to be 30%. He has been appropriately treated with a diuretic, ACE inhibitor, and a beta blocker in appropriate doses. He has also been recently diagnosed with central sleep apnea by sleep study.

In this patient with reduced ejection fraction heart failure, treatment of **central sleep apnea** with positive airway pressure strategies is associated with which of the following outcomes?

A. Improved quality of life  
B. Reduced hospitalization  
C. Reduced risk for mortality  
D. Reduced sleep-related desaturation events

**Correct Answer: D**

**Discussion:**
In patients with reduced ejection fraction heart failure, obstructive sleep apnea (OSA) and central sleep apnea (CSA) are independently associated with poor prognosis and death. For those patients with CSA, positive airway pressure, delivered continuously or via a targeted volume strategy (Adaptive Servo Ventilation; ASV) has been shown to reduce the number of desaturation events during polysomnography, but has not been shown to improve quality of life, reduce hospitalizations, or reduce mortality.

Obstructive sleep apnea (OSA) and/or CSA are present in ½ of patients with low ejection fraction heart failure. When present, they are associated with poor quality of life, higher likelihood of hospitalization, and poor prognosis. In patients with OSA, CPAP therapy is recommended and effective while the treatment of CSA remains uncertain. Two high-quality
Clinical trials have been completed to assess the role of nocturnal ventilation in systolic heart failure patients with CSA. The CANPAP trial did not show a survival advantage or reduced hospitalization rate for CHF patients with CSA treated with CPAP. Recently, the Serve-HF trial assessed ASV in CHF patients with CSA and found an increased risk of mortality without improvement in quality of life or hospitalizations. Mortality was increased despite effective control of central sleep apnea during ASV therapy.

Reduced ejection fraction heart failure is one of the most common clinical problems facing internal medicine physicians. Because ½ of these patients have OSA and/or CSA, it is imperative clinicians appreciate and apply current evidence. When present, CHF patients with OSA should be treated with CPAP. At this time, the safest strategy for management of CHF patients with CSA should be optimization of medical therapy with use of nocturnal oxygen to prevent severe desaturations. While further trials are needed, there is no evidence to support the routine use of PAP strategies for treatment of CSA in CHF patients.

**Clinical Pearl:** CHF patients with OSA should be treated with CPAP. In CHF patients with CSA, there is insufficient evidence to support the routine use of PAP and use of ASV may increase mortality.

**References:**

CASE 1
A 53-year-old woman with last menstrual period occurring 3 years ago presents to you with complaints of a 6 pound weight gain over the last three years. She indicates that she hasn’t changed anything about her diet or exercise routine. She’s extremely distressed by this, feels it has corresponded to the onset of menopause and wants to know if you would recommend menopausal hormone therapy to help her lose weight.

Physical exam reveals a BMI of 26.4.

Question
All of the following statements regarding weight changes in this woman’s situation are true except?
A. Aging, more than menopause, is associated with weight gain in midlife women
B. Declining estradiol levels at menopause are associated with more central fat distribution
C. Decreased lean body mass is associated with weight gain in midlife women
D. Menopausal hormone therapy is associated with weight loss
E. Decreased physical activity is associated with weight gain in midlife women

Correct Answer: D

Discussion
Weight gain is a common concern among midlife women, in whom the average weight gain is 1.5 pounds per year. Although this disturbing trend coincides temporally with the menopause transition, current data suggest that aging, as opposed to menopause itself, is the primary factor responsible for weight gain in midlife women. There are several changes that occur with aging that contribute to weight gain, including a decline in lean body mass and subsequent reduction in the resting metabolic rate. In addition, aging is associated with decreased physical activity, further exacerbating the age-related decline in lean body mass and resulting in decreased energy expenditure with exercise as well as at rest. Thus, if women do not intentionally reduce caloric intake and/or increase physical activity in midlife, weight gain is likely to result from a positive net energy balance.

Menopause is associated with more central fat distribution, but not specifically with weight gain. In addition, sleep disturbances, e.g., night sweats, insomnia, obstructive sleep apnea, are common in midlife women and are associated with daytime fatigue and reduced physical activity, and consequently, with weight gain. Mood disturbances occur in up to ¼ of peri- and postmenopausal women, and can interfere with healthy lifestyle choices, e.g., regular physical activity and healthy dietary choices.

Menopausal hormone therapy is used for management of bothersome menopausal symptoms in recently menopausal women without contraindications, and while it is associated with favorable changes in fat distribution, it is not associated with weight changes.

Not only is obesity associated with more frequent or severe vasomotor symptoms (hot flashes and night sweats) in midlife women, obese women have a significantly increased risk for cardiovascular disease, certain cancers, and overall mortality compared to age-matched controls. Primary care providers are in a position to identify women experiencing weight gain in midlife, validate their concerns, and provide counseling and recommendations for weight management.
Clinical Pearl
Aging rather than menopause is the primary contributor to weight gain in midlife women.

References:

CASE 2
A 36-year-old woman presents with no menses for the last 8 months. She is a gravida 0 and reports mild vasomotor symptoms.

Past medical history is remarkable for hypothyroidism for which she takes levothyroxine.

Laboratory investigations revealed an FSH of 86 mIU/ml, estradiol of <10 pg/mL 6 weeks ago under the care of another clinician. You repeat these tests and note an FSH of 75 mIU/ml, estradiol of 15 pg/mL. A urine pregnancy test is negative.

Question
Which of the following is true?

A. She has a <2% chance of spontaneous remission and pregnancy
B. She should undergo additional evaluation to include TSH, prolactin, FMR1 premutation, karyotype and 11-hydroxylase antibody testing
C. Ovarian biopsy will be useful to confirm the diagnosis
D. Progestin withdrawal testing will be useful to confirm the diagnosis
E. Ovarian antibody testing will be useful to confirm the diagnosis

Correct Answer: B

Discussion
Primary ovarian insufficiency (POI), formerly known as premature ovarian failure, has a prevalence of 1% and is defined by the depletion or dysfunction of ovarian follicles with cessation of menses in a woman under the age of 40 years. Causes include genetic abnormalities, autoimmune disease, iatrogenic e.g., radiation or chemotherapy, infections, among others. The term premature ovarian failure has been abandoned as ovarian function may wax and wane, and spontaneous remission and pregnancy occur in about 5-10% of women.

POI may present with abrupt cessation of menses (spontaneously, following pregnancy or after discontinuation of oral contraceptive pills), but also may begin with oligomenorrhea or abnormal uterine bleeding. Primary amenorrhea occurs in about 10% of women with POI. Although 10-15% of affected women will have a family history in a first degree relative, the majority of cases are sporadic.

In addition to a complete history and physical examination, laboratory evaluation is suggested for any woman under the age of 40 years who has missed 3 or more consecutive menstrual cycles and has had a negative pregnancy test. Initial testing includes an FSH, estradiol, TSH and prolactin. If the initial FSH is elevated
(typically >20 mIU/ml), the FSH should be repeated with an estradiol level in one month. Other recommended laboratory tests include adrenal antibodies (21-hydroxylase antibody-positive in 4% of women), with evaluation of adrenal reserve if positive (50% of those with adrenal autoimmunity will develop adrenal insufficiency), karyotype and fragile X mental retardation 1 (FMR1) premutation testing.

A progestin withdrawal test is not helpful and may delay diagnosis as 50% of women with POI will experience a withdrawal bleed. Ovarian biopsy lacks specificity and is not helpful.

Clinical Pearl
A woman under the age of 40 years who has experienced 3 or more consecutive months of amenorrhea and a negative pregnancy test should be evaluated for primary ovarian insufficiency with initial testing consisting of an FSH, estradiol, TSH and prolactin level.

References:

CASE 3
You have confirmed a diagnosis of primary ovarian insufficiency in this woman. She reports some vaginal dryness, but only mild vasomotor symptoms. She would welcome a pregnancy if it were to occur, but understands it is unlikely.

Question
Which treatment(s) would you recommend for her?

A. Estradiol patch 0.1 mg plus a progestogen
B. Estradiol patch 0.05 mg plus a progestogen
C. Low dose vaginal estrogen
D. Venlafaxine
E. Oral contraceptive pill

Correct Answer: A

Discussion
Although no studies have directly assessed optimal hormone doses or serum levels for treatment of women with POI, many experts recommend using the equivalent of a 100 mcg transdermal estradiol patch, which provides serum estradiol levels approximating those in premenopausal women (about 100 pg/mL). A progestogen is required for endometrial protection if a woman has a uterus. Existing clinical trial data regarding the risks and benefits of hormone therapy do not pertain to women with POI, and multiple medical societies suggest continuing with hormone therapy at least until the average age of menopause (age 51 years in the United States) to prevent potential adverse long term health consequences, including increased risk of cardiovascular disease, cognitive impairment and osteoporosis.

While the term “hormone replacement therapy” has fallen out of favor when referring to use in postmenopausal women who have experienced menopause at an average age, the term is appropriate for women with POI who have experienced premature estrogen deficiency, as the goal truly is to “replace” what
normally would have been present. Thus, even in the absence of significant vasomotor symptoms, systemic hormone therapy is still needed.

Although low dose vaginal estrogen may be needed in addition to systemic MHT to address symptoms of vaginal dryness, in women with POI it would not be sufficient for prevention of adverse long-term health outcomes related to the early loss of estrogen.

Oral contraceptives provide supraphysiologic doses of estradiol, and are not recommended as first line treatment unless the patient also desires contraception. Anecdotal reports of pregnancy while on an oral contraceptive exist and may relate to failure of suppression of the very high FSH levels associated with POI, and backup contraception could be considered in women who do not desire pregnancy.

In addition to provision of adequate hormone replacement, attention to psychological health is important. Women with POI experience unexpected infertility and many report severe emotional distress. Review of alternate family planning options should be provided in addition to emotional support with referral to a mental health professional as indicated. Counseling regarding cardiovascular risk reduction, osteoporosis prevention and fracture risk reduction is also recommended.

**Clinical Pearl**

Unless a strong contraindication exists, hormone “replacement” therapy is indicated for women with POI and should be continued at least until the average age of menopause to prevent potential long term adverse cardiovascular, neuro-cognitive and bone effects.

**References:**


**CASE 4**

A 52 year old woman has recently completed treatment for invasive breast cancer. She is now on tamoxifen and presents to you with moderate to severe vasomotor symptoms. She wants to know what her options are for management.

**Question**

There is evidence suggesting efficacy for all except which one of the following nonhormonal options for management of her vasomotor symptoms?

A. Cognitive behavioral therapy  
B. Hypnosis  
C. SSRI/SNRI  
D. Gabapentinoids  
E. Exercise

**Correct Answer: E**

**Discussion**

While the majority of women (75% or greater) will experience vasomotor symptoms (VMS) during the menopausal transition, most will use nonhormonal therapies for treatment of symptoms, either because of personal preference, concerns about potential risks associated with menopausal hormone therapy (MHT), or because of contraindications to MHT (e.g., hormonally sensitive cancers). Nonhormonal therapies for
treatment of VMS are myriad, but effectiveness has been demonstrated in few. Determining whether a nonhormonal treatment for VMS is effective is thwarted by a high placebo response rate of 20%-60%, with more anxious women demonstrating a higher placebo response. Recent comprehensive reviews of the literature on nonhormonal therapies for VMS by the North American Menopause Society and the Endocrine Society provide some guidance.

While the use of cooling techniques (e.g. dressing in layers, using a fan) and avoidance of triggers (e.g., alcohol, tobacco, caffeine, spicy foods) seems intuitive, there is a lack of clinical trial data demonstrating efficacy, and the reality is that most women have already tried these lifestyle modifications before seeking treatment for bothersome menopausal symptoms with their health care provider. Clinical trial data do not support using exercise to manage VMS, although there are certainly many other benefits of a regular exercise program for midlife women. Similarly, over-the-counter supplements, herbal therapies, acupuncture, paced respirations, yoga, chiropractic therapies and relaxation have not demonstrated consistent benefit for VMS management, and recommending their use for VMS management is likely to delay more effective treatment.

In contrast to exercise, there are clinical trial data suggesting a beneficial effect of weight loss on VMS. Clinical hypnosis for relief of VMS has been studied in two clinical trials, both revealing significant reductions in VMS. Cognitive behavioral therapy (CBT) has shown benefit for VMS symptom bother without a change in VMS frequency in two randomized, double-blind controlled trials. Barriers to the use of clinical hypnosis and CBT include time commitment and access to qualified providers.

S-equivalent derivatives of soy isoflavones and mindfulness-based stress reduction hold some promise, but additional study is needed. The same is true of stellate ganglion blockade.

Nonhormonal prescription therapies that have demonstrated efficacy for VMS treatment include SSRIs/SNRIs, gabapentinoids (gabapentin and pregabalin) and clonidine, though the last is seldom used due to adverse effects. The only nonhormonal FDA-approved medication for VMS is low dose paroxetine salt 7.5 mg.

Recommended daily doses of citalopram or escitalopram are 10-20 mg daily; paroxetine 10-20 mg or low dose paroxetine salt 7.5 mg; venlafaxine 37.5-75 mg; desvenlafaxine 100-150 mg; gabapentin 900 mg; pregabalin 150-300 mg. Paroxetine and fluoxetine should be avoided in women on tamoxifen due to potent inhibition of CYP-2D6, the enzyme that converts tamoxifen to its active metabolite, endoxifen. Venlafaxine, desvenlafaxine, citalopram and escitalopram are less potent inhibitors of CYP-2D6 and are safer options for tamoxifen users.

**Clinical Pearl**
Many behavioral and nonhormonal treatments are available for management of vasomotor symptoms in women who are unwilling or unable to use systemic menopausal hormone therapy.

**References:**

**CASE 5**
A 56 year old woman with last menstrual period occurring four years ago presents to your office with concerns about vaginal dryness and dyspareunia. She has tried vaginal lubricants and moisturizers without relief of
symptoms. She also reports an occasional mild hot flash and difficulty with urinary frequency, urgency and some occasional urge incontinence.

Her past medical history is unremarkable.

Her physical examination reveals pale, thin vulvar and vaginal tissues. Laboratory testing reveals a normal urinalysis.

**Question**

You should suggest which of the following to her?

- A. Observation as no effective treatment strategies are available
- B. She should continue to have penetrative sexual activity (use it or lose it)
- C. Low dose vaginal estrogen therapy
- D. Systemic estrogen therapy
- E. Continuing with vaginal lubricants and moisturizers as this condition is likely to improve with time

**Correct Answer: C**

**Discussion**

Genitourinary syndrome of menopause (GSM), formerly known as vulvovaginal atrophy, commonly affects postmenopausal women. It is estimated that about 50% of postmenopausal women will experience symptoms such as vaginal itching, burning, soreness, dyspareunia, urinary frequency, urgency and urge incontinence as a result of the loss of ovarian estrogen production after menopause. Further, unlike vasomotor symptoms, it is a chronic and progressive condition and unlikely to improve over time.

In a the recent REVIVE (REal Women’s Views of Treatment Options for Menopausal Vaginal ChangEs) Survey, only 24% of over 3000 women responding identified menopause as a cause of their symptoms. Consistent with other survey studies, only 50% of women reported discussing their symptoms with their health care provider (HCP), and only 10% of symptomatic women received a diagnosis. In addition, the majority of HCPs didn’t bring up the topic with their patients, underscoring the importance of patient-clinician communication regarding this issue.

Over-the-counter lubricants may help reduce friction and increase pleasure during sexual activity. While not as effective as hormonal treatments, moisturizers used every few days to help maintain moisture may effectively reduce or resolve symptoms for some women. In terms of hormonal therapies, systemic and low dose vaginal estrogen remain the gold standard, although low dose vaginal estrogen (available as vaginal cream, ring or tablet) is preferred over systemic estrogen if genitourinary symptoms are the only concern. Although long-term safety data beyond 52 weeks are lacking, expert opinion suggests that treatment with low dose vaginal estrogen be continued for as long as women are distressed by their symptoms. Concomitant use of a progestogen is generally not indicated or recommended, but any unscheduled vaginal bleeding should be evaluated in a woman using low dose vaginal estrogen.

Ospemifene is an oral SERM that is FDA-approved for the treatment of moderate to severe dyspareunia. The CO2 vaginal laser has demonstrated promising results in 12 week efficacy studies, but sham-controlled studies and long-term safety data are lacking.

Women should be counseled to avoid painful penetrative sexual activity as continuing to have painful sex may contribute to or worsen pelvic floor muscle dysfunction, anxiety, and fear of penetration. If dyspareunia
persists after 8-12 weeks of hormonal treatment of GSM, re-evaluation is indicated as persistent symptoms may be the result of a vulvar dermatosis or dermatitis, pelvic floor muscle dysfunction or vaginismus, or vulvodynia, and treatment may need to be redirected as indicated.

GSM symptoms are common in breast cancer survivors, especially those on aromatase inhibitors (AIs). However, the safety of low dose vaginal estrogen therapies in women with a history of breast cancer is unknown. Because the goal of AI treatment is to block estrogen synthesis, even the small increases in serum estradiol levels (still well below the premenopausal range) seen with the use of the low dose vaginal estrogen ring or tablet may be significant. Tamoxifen is generally less of a problem for postmenopausal women as it may even have a weak estrogenic effect on the vagina. As GSM can be a significant quality of life issue, low dose vaginal estrogen therapy is sometimes considered for women who do not respond to over-the-counter nonhormonal treatments after a review of potential risks versus benefits with the patient and her oncologist. The use of topical lidocaine a few minutes prior to sexual activity may relieve superficial pain associated with penetration in women with a history of breast cancer. Pelvic floor physical therapy may be useful for women with associated pelvic floor muscle dysfunction.

**Clinical Pearl**
Genitourinary syndrome of menopause is a common, under-recognized and under-treated chronic and progressive problem for which there are many effective therapies.

**References:**


**CASE 6**
A 49 year old white woman presents to you with concerns about her mood. She is a gravida 3, para 2 with last menstrual period occurring 15 months ago. She reports a six month history of significant mood lability, difficulty with low mood and tearfulness, and progressive withdrawal from her normal social activities. She also reports hot flashes that are occurring every 1-2 hours during the day, and at least one night sweat awakening her each night.

She has a history of premenstrual mood issues which did not require treatment with an antidepressant. She has a history of a single depressive episode associated with a difficult divorce several years ago which was treated with citalopram for one year.

She has a high school education, is a single mother, and is experiencing financial stress with the recent loss of her job.

**Question**
Which of the following is true regarding depression in this midlife woman?

A. Reproductive-related depressive episodes (e.g., premenstrual syndrome, postpartum depression) are unlikely to be associated with mood changes during the menopause transition
B. A history of a prior depressive episode is a strong predictor of midlife depression
C. Risk factors for midlife depression include a college education, being white, employment and the lack of vasomotor symptoms
D. First line treatment for depression in midlife women with vasomotor symptoms is estrogen-based hormone therapy
E. Antidepressants are less likely to be effective during the menopause transition than at other times in a woman’s life

Correct Answer: B

Discussion
Depression is more common in women than in men and is a leading cause of disability in women. Certain reproductive time frames are associated with a greater vulnerability in terms of mood for women. These reproductive “windows of vulnerability” include the premenstrual time frame, postpartum and the menopause transition and may relate to an increased sensitivity to hormonal fluctuations. Cross-sectional and longitudinal studies have demonstrated an increased risk for depressive symptoms and major depressive disorder in perimenopause and early postmenopause. A strong predictor for midlife depression is a prior history of depression (hormonally related or not), but even women without a history of depression appear to be at greater risk during the menopause transition. Demographic, psychosocial, socioeconomic and health-related risk factors or moderators for depression include unemployment, low education, being black or Hispanic, having multiple life stressors and low social support, and having poor health, vasomotor or sleep symptoms.

Prospective studies have examined the trajectories of depressive symptoms in midlife. The presence of sleep problems and recent distressing life events were associated with more persistent or recurrent symptoms in the Study of Women Across the Nation (SWAN), while the Australian Longitudinal Study on Women’s Health noted that factors associated with stable high or increasing depressive symptoms were a history of depression, socioeconomic and health-related issues (unemployment, obesity, being a smoker, having night sweats), experiencing a prolonged perimenopause or having had a hysterectomy plus oophorectomy.

First line treatment of depression in midlife women remains antidepressant therapy. In those with recurrent depression, past response to treatment should guide the selection of an antidepressant. Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are a good choice for those who have not received treatment previously. The choice of antidepressant is based not only on efficacy, but also takes into consideration side effect profile (sexual side effects, weight gain, medication interactions) and additional potential benefits (management of vasomotor symptoms, pain, sleep).

Estrogen therapy is not considered first line treatment for depression, but it may have a favorable effect on neurotransmitters impacting mood. A recent randomized controlled trial, the KEEPS-Cognitive and Affective Study, showed a mood benefit with oral conjugated equine estrogens but not with transdermal estradiol in recently menopausal women without depression. Women experiencing menopause often report multiple symptoms, including vasomotor, sleep and mood symptoms. When estrogen therapy is used for treatment for menopausal symptoms, it may also augment or potentially minimize the need for antidepressant treatment in midlife women with depression. It should be noted that discontinuing estrogen therapy is associated with mood disturbance, and may trigger recurrent depression in women with a prior history.

While a postmenopausal estrogen-based hormone therapy regimen can be used for women who are menopausal and appropriate candidates for the use of hormone therapy, perimenopausal women benefit
from estrogen paired with an adequate dose of progestin to suppress ovulation, (e.g., a low dose oral contraceptive if no contraindications or formulations with lower estrogen doses combined with progestin).

Clinical Pearl
The menopause transition may be a window of vulnerability in terms of risk for depression in midlife women. While antidepressant therapy remains first-line treatment for depression in women during the menopause transition, estrogen-based therapy may be leveraged for mood enhancing effects as well as for management of vasomotor symptoms and sleep disturbance.

References:

CASE 7
A 65 year old woman presents to your office with concerns about a letter she received from her insurance company denying coverage for her menopausal hormone therapy. She is a gravida 2, para 2 with last menstrual period at the age of 52. She has been on menopausal hormone therapy since then, most recently with an estradiol patch 0.05 mg changed twice weekly and micronized progesterone 100 mg nightly. She is asymptomatic on her current regimen, but has vasomotor symptoms if she forgets to replace the patch as scheduled. She would very much like to continue with hormone therapy as she states she feels better on it and believes that it contributes to her quality of life. She asks your opinion regarding continuing on menopausal hormone therapy.

Her past medical history is remarkable for hypothyroidism which is treated. Breast cancer screening is current. She has exited cervical cancer screening with adequate prior screening.

Physical examination reveals a blood pressure of 126/74. Her BMI is 23.7.

Question
How do you advise her?
A. Discontinue estrogen and progesterone as she has reached the age of 65 years
B. Switch to low dose vaginal estrogen cream
C. Switch to an SSRI/SNRI
D. Attempt reduction in the estradiol dose, providing the option of returning to the last effective dose if bothersome symptoms recur
E. Discontinue progesterone

Correct Answer: D
Discussion

Systemic menopausal hormone therapy (MHT) is most commonly initiated to manage bothersome vasomotor symptoms, and it remains the most effective treatment. While short term use of MHT was advocated for several years, recent studies have shown that the mean duration of vasomotor symptoms is longer than first assumed, and many women suffer from bothersome symptoms for a decade or longer. In addition to being used for vasomotor symptom management, MHT is also used in some women at high risk for fracture in whom other therapies are not appropriate or are associated with unacceptable adverse effects.

Safety concerns are a primary consideration for discontinuation of MHT. The Women’s Health Initiative demonstrated differing safety profiles for women with a uterus who took the combination of oral conjugated equine estrogens (CEE) and medroxyprogesterone acetate (MPA) versus women without a uterus who took oral CEE alone. In women on CEE plus MPA, the risk of breast cancer was modestly increased after a mean duration of 5.6 years of use, as was the risk of stroke. In women on CEE alone, there was no increased risk of breast cancer after a median of 7.2 years of use. The risk of coronary heart disease (CHD) was not increased in women who initiated CEE plus MPA or CEE alone in their 50s, but the risk of CHD was increased in women initiating MHT in their 70s. There are also differences in risk between routes of administration, with oral estrogen being associated with increased risk of venous thromboembolism and stroke, whereas transdermal estrogen does not appear to carry this same risk in observational studies, though randomized controlled clinical trial data are lacking. Age is a risk factor for both venous thromboembolism and stroke, so there may be safety advantages to the use of transdermal estrogen over oral estrogen, particularly for women considering long term use.

A key point is that there are no existing clinical trial data on the balance of risks and benefits for women who initiate MHT around the time of menopause and continue long term. Despite lack of guidance from clinical trials, clinicians caring for menopausal women commonly encounter questions about the long term use of MHT in practice. Women with a uterus require a progestogen with estrogen for endometrial protection (as long as they remain on systemic estrogen), and should be counseled regarding the increased risk of breast cancer associated with CEE plus MPA. The benefit to risk ratio is more favorable for women without a uterus who are able to use estrogen alone.

Further complicating the matter, estrogen is included on a list of potentially inappropriate medications for adults over the age of 65, and patients and clinicians may receive letters from insurance companies regarding potential risks of MHT in this population and potentially denying coverage. Two medical societies, the North American Menopause Society and the American College of Obstetricians and Gynecologists, have provided statements recommending against the arbitrary discontinuation at the age of 65. Rather, shared decision making, taking into account patient preferences and an individualized assessment of the benefit to risk balance is recommended.

Regardless of the method of discontinuation of MHT (slow taper versus abrupt discontinuation), approximately 50% of women will experience recurrent symptoms. A reasonable approach based on expert opinion is to consider a trial of tapering the dose and discontinuation after several years of use, providing reassurance to the patient that the last effective dose can be resumed without a follow up visit if bothersome symptoms recur. If a woman remains asymptomatic on the lowest dose, discontinuation may be attempted. Some women may benefit from extended duration use of MHT for symptom management, perceived improvement in quality of life, and for prevention of osteoporosis. A transdermal route of administration may provide safety advantages over oral.
Low dose vaginal estrogen therapy will not treat vasomotor symptoms, but may be needed for management of the symptoms of genitourinary syndrome of menopause (vaginal dryness, dyspareunia, urinary frequency, urgency and urinary tract infections), especially as the systemic dose of estrogen is tapered and potentially discontinued. Vaginal estrogen therapy can be continued long term as indicated, and although concomitant use of a progestogen is not indicated with low dose vaginal estrogen therapy, any vaginal bleeding in a postmenopausal woman should be evaluated.

Estrogen is more effective for management of menopausal symptoms than an SSRI/SNRI. A taper of the estrogen dose should be attempted before consideration of the use of an SSRI/SNRI for symptom control. In addition, this class of medications is also on the list of potentially inappropriate medications for adults over the age of 65 years.

**Clinical Pearl**
MHT should not be discontinued on the basis of age alone. MHT use is individualized, and long-term use can be considered after a review of symptoms, the benefit to risk balance, treatment goals and patient preferences. Transdermal estrogen may have safety advantages over oral for women considering long-term use.

**References:**

**CASE 8**

**Practice Gap**
Approximately 45% of all pregnancies are unintended, and the U.S. Department of Health and Human Services’ Healthy People 2020 campaign aims to increase the proportion of pregnancies that are intended by 10% between 2010 and 2020.

**Reference**

A 48 year old woman presents to you for routine care. She is a gravida 3, para 3 with last menstrual period occurring last month. Her menses are regular, occurring every 28-30 days and lasting about 5 days. She reports the flow is moderate to heavy on the first two days of her cycle and light for the last three days. She asks you whether she needs contraception at her age (she does not desire pregnancy), and if so, what her options are. She reports some occasional moderate night sweats just before and during her menstrual cycle.

Her past medical history is unremarkable. She used an oral contraceptive pill in her 20s and 30s without difficulty.

She was divorced a couple of years ago and recently started dating again.
Her physical exam reveals normal blood pressure and a BMI of 24.5.

Question
All except which one of the following are correct regarding contraception in this midlife woman?

A. Non-contraceptive benefits of an oral contraceptive pill include management of vasomotor symptoms, regulation of menses, reduction of heavy menstrual bleeding and treatment of acne
B. Age alone is not a contraindication to any contraceptive method
C. She no longer requires contraception as unintended pregnancy rates are very low for women in their 40s
D. The five year levonorgestrel intrauterine system (LNG-IUS) is a good option for perimenopausal women requiring contraception and can be used later for endometrial protection as the progestogen component of menopausal hormone therapy
E. A woman who is amenorrheic for greater than 12 months on a hormonal contraceptive cannot be considered menopausal and may still be ovulating

Correct answer: C

Discussion
While fecundity is significantly decreased for women in their 40s, unintended pregnancy rates are still high, around 40% (similar to that of women in their teens and 20s). The risks (to the mother and the fetus) associated with pregnancy in older women are greater and include gestational diabetes, gestational hypertension and pre-eclampsia as well as an increased risk of fetal aneuploidy, fetal chromosomal abnormalities and spontaneous fetal loss. Perimenopausal women who are sexually active are at risk for unintended pregnancy, and effective contraception is required if pregnancy is not desired.

Age alone is not a contraindication to any contraceptive method, and selection of a contraceptive method factors in patient preferences, efficacy, and potential risks and benefits. Sterilization is permanent, and options include tubal ligation, hysteroscopic tubal occlusion or partner vasectomy. Barrier methods (male and female condoms, cervical cap and diaphragm) are non-hormonal, are widely available, reduce transmission of sexually transmitted infections, and can be used in combination with spermicides. Failure rates are high with typical use, however, and range from 12% for cervical cap/diaphragm to 18-21% for male and female condoms respectively. The copper intrauterine device (IUD) has a low failure rate of about 1%, and can be used long term and as emergency contraception if inserted up to 5 days after unprotected sex. Barrier and other nonhormonal methods of contraception will not provide symptom relief for perimenopausal women experiencing vasomotor symptoms, and the copper IUD may exacerbate heavy menstrual bleeding.

Hormonal contraceptive methods include progestin-only methods and combined estrogen and progestin options (combined hormonal contraception-CHC). Utilizing a progestin-only method avoids some of the potential adverse effects associated with estrogen-containing options, but they are unlikely to alleviate vasomotor symptoms, and some are associated with irregular bleeding. The levonorgestrel-releasing intrauterine system (LNG-IUS) is approved for contraception for up to 5 years, but there is evidence that it may provide endometrial protection for as long as 7 years (off-label indication in the US). It is highly effective, with a failure rate of well under 1%. Advantages of this method of contraception in perimenopause include reduction in menstrual bleeding, with about 30% of women experiencing amenorrhea after one year, and the ability to add in postmenopausal estrogen therapy as indicated for management of menopausal symptoms. Other progestin-only options include pills, implants and injections.
CHC have a failure rate of about 9% with typical use. Non-contraceptive benefits of CHC include reduction in vasomotor symptoms, heavy menstrual bleeding, dysmenorrhea, and pain with endometriosis; improvement in acne and menstrual migraine; regulation of menses; bone protection; and reduced risk of endometrial and ovarian cancers with prolonged use. In terms of risk, CHC are associated with 2-4 fold increased risk of venous thromboembolism (VTE) or ischemic stroke. These events are uncommon in young women, so the relative risk is low. However, the baseline risk of these adverse events increases with age independent of CHC use, and thus would be expected to be higher in older reproductive aged women on CHC than in younger women on CHC. It is also important to note that the risk of ischemic stroke and VTE associated with pregnancy and postpartum is increased roughly 4-10 fold.

Studies regarding the risk of breast cancer associated with CHC have been mixed, with speculation that there may be variations in risk depending on dose or the particular formulation of CHC. Overall, there is not a strong signal for CHC and breast cancer risk, but additional study is needed. The risks and benefits of CHC must be considered for each woman, taking into account her medical history and personal preferences. CHC remains an option for healthy perimenopausal women.

Menopause is defined as amenorrhea for 12 months, which is a valid means of assessing women who are not on hormonal contraception. Amenorrhea in a woman on CHC or a progestin-only method does not necessarily equate to cessation of ovulation. Similarly, a woman may experience monthly withdrawal bleeds on CHC when she is no longer ovulating. Deciding when to transition from contraception to a postmenopausal hormone therapy regimen for management of menopausal symptoms can be challenging, but about 90% of women are menopausal by age 55 and about 95% by age 56.

Discontinuing hormonal contraception periodically for 2-3 months to evaluate for amenorrhea is disruptive, requires backup contraception and may result in symptoms related to estrogen withdrawal. Monitoring FSH or estradiol levels is not useful as levels can be highly variable during perimenopause. There are also some women who utilize hormonal contraception for symptom management (control of bleeding, menstrual migraine, treatment of vasomotor symptoms) and who are not concerned about contraception (not sexually active, prior tubal ligation or partner with vasectomy). When a woman is menopausal and no longer able to conceive, it is desirable for safety reasons to switch from CHC to a postmenopausal hormone therapy regimen if indicated for symptom management as CHCs contain a much higher dose of estrogen (approximately 4 times the dose of estrogen contained in postmenopausal hormone therapy).

Clinical Pearl:
For women wishing to avoid pregnancy, effective contraception is required until menopause. Hormonal contraception may be considered for use in healthy, sexually-active perimenopausal women for prevention of pregnancy and for symptom management after appropriate counseling.

References: