



Primary Care RAP April 2020 Written Summary

Editor-in-Chief: Neda Frayha MD

Associate Editor: Kenji Taylor MD, MSc

INTRO: MORE LISTENER LOVE

Neda Frayha MD, Paul Simmons MD

Pearls:

- Temporomandibular joint disorders (TMJ) affect about 15% of the population and are treated with a combination of both supportive measures and education.
- The New Nordic diet is a predominantly fish, berries, whole grain diet with some evidence it is protective against chronic disease such as diabetes and heart disease.
- The key to diagnosis of hypopigmentation is the Woods lamp.
- Firefighters have increased risk of heart disease and cancers due to occupational exposures with guidelines for testing coming from a non-medical organization, NFPA 1582, that recommend additional disease surveillance beyond what is recommended for the general population.

- Reader question: Review temporomandibular joint disorders (TMJ)
 - Anatomy:
 - For a great graphic see link to [AFP article](#)
 - Mandibular condyle inserts into the mandibular fossa of the temporal bone. Between that insertion point is an articular disc. Surrounding it is the muscles of mastication that move the entire complex.
 - Muscles of mastication - temporalis, the masseter, and the medial and lateral pterygoids
 - TMJ disorders (TMD) are thought to be subtype of secondary headache disorder
 - Affects 15% of population
 - Peak between 20-40 years of age
 - Symptoms:
 - Jaw pain and dysfunction
 - Ear ache
 - Headache
 - Related disorders:
 - Chronic headache
 - Fibromyalgia

- Autoimmune disorders
 - Sleep disorders
 - Mental illness
 - Maybe smoking
 - MSK disorders
- Differential:
 - Dry tooth socket
 - Broken teeth
 - Caries
 - Migraine
 - Trigeminal neuralgia
 - Sinusitis
 - Parotitis
 - Giant cell arteritis
- Diagnosis: Clinical
 - History - facial and jaw problems when opening/closing mouth
 - Pearl: TMJ pain will hurt with jaw use right off the bat while GCA pain is more delayed
 - Physical
 - Can they open mouth normally?
 - Signs of bruxism
 - Neck/shoulder muscles spasm, tenderness
 - If displaced, you will hear a single click when opening (displacement of disc) and doubleclick when closing (replacement of disc back into position)
 - Cranial nerves should all be normal
 - Imaging - not recommended unless unclear of the source
 - X-ray (transcranial and transmaxillary views), MRI, CT, ultrasound have all been used
- Treatment:
 - 40% get better on their own
 - Supportive measures and education: jaw rest, stretches, a soft diet, warm compresses, and stress management, relaxation techniques. Avoid clenching teeth, chewing ice, biting objects such as chewing on pencils or pens as a habit
 - Physical therapy
 - Acupuncture
 - Biofeedback
 - DO NOT immobilize the jaw
 - Pharmaceuticals may actually do more harm than good
 - Consider treating depression/anxiety
 - Referral to dentist or OMFS
- **Reader question: The New Nordic diet**

- Similar to the Mediterranean diet with a heavy emphasis on fish. Also includes berries, apples, pears, legumes, cruciferous vegetables like cabbage, rye breads and similar kinds of whole grain. Emphasizes canola oil instead of olive oil.
- Showed a possible benefit on risk of MI in overall population and stroke in men → not statistically significant. Other studies have shown benefit with LDL levels and blood pressure
- **Bottomline:** Diet rich in fish, berries, cabbage, whole grain can be good for you
- **Reader question: Hypopigmentation**
 - Differential:
 - 1. Pityriasis alba - mainly affects children, atopic-type condition
 - 2. Pityriasis versicolor - affects young adults, malassezia furfur (fungus)
 - 3. Vitiligo - generally starts to affect adults over 30, autoimmune system where melanocytes are destroyed
 - Physical:
 - Woods lamp is key!
 - Do in dark room with lamp 4-5 inches away from skin
 - Vitiligo - bright white under light and clearly demarcated
 - Hypopigmentation due to loss of blood vessels - skin may appear pale (not white), accentuated by UV light
 - Fungi - each may cause different colors
 - Treatment:
 - 1. Pityriasis alba → self-limited, emollients, hydrocortisone 1% or topical calcineurin inhibitors if severe
 - 2. Pityriasis versicolor → topical antifungals like ketoconazole or terbinafine, selenium sulfide or zinc pyrithione
 - Hypopigmentation can last for months even after treatment
 - 3. Vitiligo → topical steroids or calcineurin inhibitors, photochemotherapy, dermatology referral
 - Be on the lookout for other autoimmune disorders (hypothyroidism, celiac, DM1)
- **Reader question: Do firefighters need different screening given their exposures from fighting fires?**
 - 1.3 million firefighters in the US and Canada
 - Workers are exposed to carcinogens from combustion products
 - Other occupational risks include: cardiovascular disease, musculoskeletal injuries, depression, and suicidality, and different kinds of cancers
 - Heart disease is the number one risk
 - Sudden death from heart event is the most common cause of death
 - 44% of on-duty death was due to sudden cardiac death
 - Studies in 2006, 2013 showed elevated risk of multiple myeloma, non-Hodgkin's lymphoma, mesothelioma, prostate and testicular cancer
 - Increased risk of occupational hearing loss
 - Trauma from losing friends and working under threat of death

- Guidelines:
 - National Fire Protection Association (NFPA) puts out guidance called NFPA 1582. Consists of firefighters, administrators who review the medical literature and consult medical professionals. This is not endorsed by other medical societies and does not have a lengthy explanation of their development process.
 - OSHA does not have guidance about medical screening but enforces the NFPA1582 standard
 - Recommendations:
 - Annual history and physical
 - Blood work every 3 years if < 40 that includes complete blood count, complete metabolic panel, lipid panel, urinalysis, and analysis for any chemical exposures as indicated. Vision screening and audiogram.
 - PFT's annually
 - CXR baseline and then every 5 years
 - ECG baseline and annually if > 40 or as clinically indicated
 - Some sources suggest echo and stress test beginning at 40
 - Cancer screening
 - Colonoscopy at age 40 or 50
 - Routine breast, cervical, prostate
 - CT scan annually for lung cancer if >55 and any kind of smoking history or current smoking or recently quit
 - Bladder cancer screening with urinalysis
 - Screening for sleep disorders
 - Screening for depression and anxiety disorders

REFERENCES:

1. Gauer RL, Semidey MJ. Diagnosis and treatment of temporomandibular disorders. *Am Fam Physician* 2015; 91(6):378-386.
2. Scrivani SJ, Keith DA, Kaban LB. Temporomandibular disorders. *N Engl J Med* 2008; 359(25):2693–2705.
3. Cooper BC, Kleinberg I. Examination of a large patient population for the presence of symptoms and signs of temporomandibular disorders. *Cranio* 2007; 25(2):114–126.
4. Aggarwal VR, Lovell K, Peters S, et al. Psychosocial interventions for the management of chronic orofacial pain. *Cochrane Database Syst Rev* 2011;(11):CD008456.
5. Mujakperuo HR, Watson M, Morrison R, et al. Pharmacological interventions for pain in patients with temporomandibular disorders. *Cochrane Database Syst Rev* 2010; (10):CD004715.

Transgender Care

Elizabeth Lamos MD, Neda Frayha MD

Pearls:

- The goals of hormone therapy are two-fold: suppress endogenous sex hormones and maintain the sex hormones within the normal range for the person's affirmed gender.
- Give hormone therapy a year to have full physical effect before considering surgical options.
- The ideal approach to transgender care is multidisciplinary with a team that includes a primary care doctor, endocrinologist, mental health provider and surgical team.

- **Background:**
 - 1.4 million Americans currently identify as transgender
 - Gender identify = internal sense of being male, female, or for some, something indeterminate
 - Gender expression = outward manner in which a person expresses or displays their gender
 - Transgender individual = individual whose gender identity or the gender in which they wish to live and be accepted as is different from the one that they were assigned at birth
 - Transgender male = assigned female at birth, identifies as male
 - Transgender female = assigned male at birth, identifies as female
 - Gender non-conforming = person who doesn't fit anyone's stereotype or how they should look or act based on the sex that they were assigned at birth
 - Gender dysphoria = the distress and the unease experienced by an individual if their gender identity or designated gender are not completely congruent
- **How to determine who may be appropriate?**
 - Affirmed in their gender decision
 - Important to have gender therapists to help people go through process of understanding if they are transgender
 - Informed consent (capacity to make decision, appropriate age)
 - Mental health stability
- **Hormone therapy:**
 - Overall goals -
 - 1. Suppress endogenous sex hormone production
 - 2. Maintain the sex hormone levels within the normal range of the individual's affirmed gender
 - Not all individuals will want the same things out of therapy so that will have to be a conversation with them
 - Transgender females
 - Spironolactone suppresses testosterone
 - Goal of testosterone 50ng/dL
 - Estradiol (patch, injection, pill) to feminize

- Pearl: avoid synthetic estrogens like ethinyl estradiol because they can't be measured
 - Goal of estradiol 100-200 pg/mL
 - Not enough evidence to recommend use of progesterone
 - Transgender males:
 - Testosterone as a patch, gel or injection
 - Goal of total testosterone 300-700 ng/dL
 - See patients every 3 months for the first year and then space out to once or twice a year afterwards
- **Risk of therapy:**
 - Transgender males
 - Erythrocytosis
 - Increase LFTs
 - Increase risk of coronary disease, stroke, high blood pressure, and a signal for breast and uterine cancer
 - Transgender females
 - Thromboembolic risk increase
 - Counsel to stop smoking
 - Increase risk of prolactin, breast cancer, coronary artery disease, stroke, gallstones and high triglycerides
- **What to expect after starting therapy?**
 - Transgender male:
 - 6-12 months expect facial and body hair growth, scalp hair loss, increased muscle mass or strength, and a deepening of their voice. Also oily skin, fat redistribution and cessation of menses
 - Transgender female:
 - 3-6 months expect redistribution of fat, decrease in muscle mass and strength, softening of the skin, breast growth and decreased testicular volume.
 - Pearl: You will NOT see a voice change
 - Option for voice coaching and vocal surgeries
- **Fertility options prior to initiation of therapy?**
 - Transgender female:
 - Sperm banking
 - Some evidence that if you stop estrogen you can recover function of the testes
 - Transgender male:
 - Embryo freezing
 - May stop hormone therapy and pursue pregnancy
 - Contraception is important depending on if individual maintains organ of assigned gender
- **GU Exam:**

- Important to have a trans-competent GYN or urologist or yourself available and to discuss this with the patient
- **Surgical management:**
 - Usually give a year for the hormones to have their full effect on the physical appearance before any augmentation therapy
 - Transgender male: chest surgery, genital surgery, hysterectomy, ovariectomy, phalloplasty, vaginectomy
 - Transgender female: chest surgery with breast augmentation, genital surgeries, voice surgery, facial feminization, tracheal shaves
- **Team Structure:**
 - Ideally multidisciplinary - primary care provider, mental health provider, endocrinologist, surgeon team

REFERENCES:

1. Hembree, WC, Cohen-Kettenis PT, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. JCEM 2017; 102 (11): 3869-3903
2. Standards of Care, The World Professional Association for Transgender Health. <https://www.wpath.org/publications/soc>.

Diabetic Neuropathy

Harpreet Tsui DO, Neda Frayha MD

Pearls:

- **Prevention through good glycemic control and regular screening for diabetic neuropathy is key.**
- **First-line treatment is pregabalin and duloxetine.**
- **Background:**
 - Types of diabetic neuropathy:
 - 1. Cardiovascular autonomic neuropathy
 - 2. Individual mononeuropathies
 - 3. Chronic inflammatory demyelinating polyneuropathy
 - 4. Distal symmetric polyneuropathy (DSPN, 75% of neuropathies)
 - 20% of those with type 1 diabetes will develop after 20 years
 - 50% of those with type 2 diabetes will develop after 10 years
 - Can lead to diabetic foot ulcers and Charcot's foot
- **Diagnosis: clinical**
 - History - burning, paresthesias that are worse at night, hyperalgesia, allodynia, numbness/tingling
 - Exam -
 - Small fiber - pinprick and test for temperature sensation

- Large fiber - monofilament testing
- Ankle reflexes
- Check out AFP 2014 article for a 3-minute comprehensive exam
- Studies -
 - No need for referral to neurology for EMG unless asymmetry, motor > sensory function loss, rapid progression
 - Rule out vitamin B issues and thyroid issues
- **Screening:**
 - 50% of patients don't have symptoms, which means routine screening (foot exam) is important
 - American Diabetes Association 2017 recommendations:
 - Screen five years after diagnosis of DM1 and at the diagnosis of DM2
 - Consider screening those with prediabetes who have any symptoms
- **Treatment:**
 - First-line: pregabalin (per AAN)
 - In order patients, careful with side effects like dizziness, somnolence, peripheral edema
 - Dosing starts low at 25mg daily all the way up to 300mg max daily dosage
 - First-line: duloxetine (SNRI)
 - Side effects include somnolence, dizziness, constipation and decreased appetite
 - Max dose 60mg daily
 - Venlafaxine (SNRI)
 - Can lower seizure threshold
 - Gradual tapering is recommended
 - Dose 150-225mg daily
 - Cochrane Review 2015 showed not better than placebo but an option that may work for some patients
 - Gabapentin
 - Not great evidence on efficacy but available as a generic
 - Needs to be renally dosed
 - Effective in ranges of 1800-3600mg per day
 - Amitriptyline (TCA)
 - Not FDA-approved but small trials show improvement in pain
 - Desipramine and nortriptyline with similar efficacy
 - Increased risk of arrhythmia and myocardial infarction
 - Topical capsaicin
 - Some data showing efficacy
 - Common complaint of burning at site of application
 - Lidocaine
 - Limited data but worth a try
 - Alpha lipoic acid

- Potent antioxidant thought to counteract the oxidative stress of diabetes on the nerves
 - Randomized control trial (SYDNEY 2) showed improvement in pain with 600mg daily
- Opioids
 - NOT indicated

REFERENCES:

1. Pop-Busui R, Boulton AJM, Feldman EL, et al. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. *Diabetes Care*. 2016;40(1):136-154. doi:10.2337/dc16-2042
2. Miller J, Carter E, Shih J, Giovinco N. How to do a 3-minute diabetic foot exam. *J Fam Pract*. 2014;63(11). <https://www.mdedge.com/familymedicine/article/88218/diabetes/how-do-3-minute-diabetic-foot-exam>. Accessed January 13, 2020.
3. Gallagher HC, Gallagher RM, Butler M, Buggy DJ, Henman MC. Venlafaxine for neuropathic pain in adults. *Cochrane Database Syst Rev*. 2015;8. doi:10.1002/14651858.cd011091.pub2
4. Ziegler D, Ametov A, Barinov A, et al. Oral Treatment With α -Lipoic Acid Improves Symptomatic Diabetic Polyneuropathy: The SYDNEY 2 trial. *Diabetes Care*. 2006;29(11):2365-2370. doi:10.2337/dc06-1216
5. Bril V, England J, Franklin GM, et al. Evidence-based guideline: Treatment of painful diabetic neuropathy: Report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. *Neurology*. 2011;76(20):1758-1765. doi:10.1212/wnl.0b013e3182166ebe
6. Bansal V. Diabetic neuropathy. *Postgrad Med J*. 2006;82(964):95-100. doi:10.1136/pgmj.2005.036137
7. Kasznicki J. State of the art papers Advances in the diagnosis and management of diabetic distal symmetric polyneuropathy. *Arch Med Sci*. 2014;10(2):345-354. doi:10.5114/aoms.2014.42588
8. Feldman, E. Management of diabetic neuropathy. In: Eichler A (Ed). *UpToDate*. <https://www.uptodate.com/contents/management-of-diabetic-neuropathy>

Food Allergies, Parts 1&2

Torie Grant, MD, MHS, Neda Frayha MD

Pearls:

- If you do send a large panel of allergy testing, do not take out food from the child's diet if they are tolerating that food. That can actually end up sensitizing them to the food and lead to a new food allergy.
- Fatality is rare with food allergies but is most often associated with a delay in administration of epinephrine. If you are concerned, give epinephrine because antihistamines and steroids alone will not cut it.
- Emerging treatments include a peanut patch and oral immunotherapy. These are NOT cures but designed to help with small amounts of exposure from cross-contamination.
- **Background:**
 - Definitions:
 - Allergy - involves mast cells that release histamine, leukotriene and other types of allergy mediators that lead to symptoms if the allergen is consumed AND is often confirmed with skin prick testing or blood IgE testing.
 - Pearl!: negative predictive value of allergy testing is 97% while the positive predictive value is only 50% (meaning, people may test positive for it but not actually have an allergic reaction)
 - Affects 1 in 6 children in the western hemisphere, 6 million children in the US
 - Allergies are on the rise for hypothesized reasons:
 - Improvement in hygiene so we have fewer exposure to microbes/bacteria
 - We are feeding babies less of the food adults eat
 - Specific allergies on the rise: milk, egg, peanut, tree nuts (almonds, cashews, pistachios, hazelnuts, pecans, walnuts, pine nuts, macademia nuts), wheat, fish, shellfish and soy
 - Pearl!: Toughest allergies to outgrow are nut allergies, fish and shellfish. Half of kids will outgrow milk, egg and wheat allergy by about age 5.
- **History:**
 - What exactly did you eat?
 - When was the onset of symptoms?
 - What were the symptoms?
 - Hives, flushing, lip swelling, trouble breathing, sheezing, runny nose, congestion, dizziness, lightheadedness
 - Is this the first time you ate the food?
 - Do you ever NOT have symptoms when you eat this food?
 - A difference between food sensitivity or intolerance and allergy is that you have the reaction every time with a true allergy
- **Allergy testing:**

- Allergy testing can lead to harm. For example, if a child who may have a propensity for an egg allergy (but is not allergic and eats eggs without issue) gets tested. The test comes back weakly positive so they are told to stop eating eggs. Three months pass until they see the allergist who retests and finds their numbers have shot up. By removing the eggs from the diet, that child can be pushed into developing an egg allergy. Had they continued to eat eggs, they may have just outgrown it or never developed the allergy in the first place!
- Pearl: negative predictive value of allergy testing is 97% while the positive predictive value is only 50% (meaning, people may test positive for it but not actually have an allergic reaction). Atopic conditions can lead to low levels of IgE to allergens that do not result in a true allergy.
- Order an allergy test for a specific allergen of concern as opposed to an entire panel or get to an allergist (if available) to let them handle testing
- **Recent updates in guidelines and the literature:**
 - Learning Early About Peanut (LEAP) in 2015 showed early introduction to peanut allergy was protective against developing a peanut allergy
 - Took infants age 4-11 months in the UK who had atopic predisposition (moderate to severe eczema, egg allergy or both)
 - Skin prick test for peanut had to be negative
 - Randomized to either avoid peanuts strictly or introduce peanut on a relatively frequent basis (1-3 times per week)
 - Kids who avoided peanuts had peanut allergy 35% v. 10% in those who introduced peanuts → 70% relative risk reduction
 - Follow-up study (LEAP-On) showed the effect was lasting
 - Early Introduction of Allergenic Foods (EAT) study
 - Took all infants starting at 3 months and pushed 6 foods (milk, egg, peanut, sesame, wheat, fish) until age 3
 - Found no difference in breastfeeding duration and no difference in allergies to these foods
 - HealthNut Study in Australia
 - Cohort of 5200 kids
 - Infants who got whole egg (not baked into things) had lower incidence of egg allergy at age one
 - AAP 2017 guidelines
 - Becoming increasingly less restrictive about allergen introduction
 - Recommend earlier introduction of peanut products in particular for kids:
 - Kids with severe eczema egg allergy or both - evaluation with IgE or skin prick test or oral food challenge at 4-6 months
 - Kids with mild to moderate eczema - introduce peanut-containing foods at 6 months
 - Kids with no eczema or allergy - introduce when age-appropriate
 - Bottomline: No food restrictions during pregnancy, no food restrictions during breastfeeding unless evidence of a food reaction and parents can

introduce solids at 4-6 months without restriction (unless evidence of food reaction)

- **Management:**
 - IgE testing for the specific allergens in question
 - Injectable epinephrine if concerned about a severe reaction like anaphylaxis
 - Counseling to avoid the food because even if the initial reaction is hives, they may end up having an anaphylactic reaction
 - Referral to allergist
 - May see at least annually to follow skin test or IgE levels because patient may outgrow it and tolerate an oral challenge
 - Acute management if you have eaten an allergen:
 - Mild (itching in mouth, runny nose, hive or two) → fast-acting antihistamine like diphenhydramine or cetirizine, observation
 - Progression of symptoms → injectable epinephrine → call 911 or go to the nearest emergency room
- **Emerging therapies:**
 - Peanut patch worn transdermally and peanut oral immunotherapy are designed to protect against small levels of cross-contamination NOT cure a peanut allergy
- **Tips for families:**
 - Parents should read labels
 - Avoid foods that have cross contamination labels
 - Roughly 5% of those foods may have some level of that protein
 - Roughly 2.5% of those foods may contain a level high enough that somebody may react
 - Good resources for parents:
 - [FARE](#) (Food Allergy Research Education) has tips about reading labels, eating out, travel

REFERENCES:

1. Bellach J, Schwarz V, et al. Randomized placebo-controlled trial of hen's egg consumption for primary prevention in infants. *J Allergy Clin Immunol* 2017; 139(5):1591-1599.
2. DuToit G, Roberts G, Sayre PH, et al for the LEAP Study Team. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med* 2015; 372:802-813.
3. DuToit G, Roberts G, Sayre PH, et al for the Immune Tolerance Network LEAP-ON Study Team. Effect of avoidance on peanut allergy after early peanut consumption. *N Engl J Med* 2016; 374:1435-1443.
4. Keet CA, Savage JH, et al. Temporal trends and racial/ethnic disparity in self-reported pediatric food allergy in the United States. *Ann Allergy Asthma Immunol* 2014; 112(3):222-229.e3
5. Lack G. Update on risk factors for food allergy. *J All Clin Immunol* 2012; 129(5):1187-1197.
6. Natsume O, Kabashima S, et al. Two-step egg introduction for prevention of egg allergy in high-risk infants with eczema (PETIT): a randomised, double-blind, placebo-controlled trial. *Lancet* 2017; 389(10066):276-286.

7. NIAID-Sponsored Expert Panel, Boyce JA, Assa'ad A, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. *J Allergy Clin Immunol*. 2010;126(6 Suppl):S1–S58.
8. Perkin MR, Logan K, et al for the EAT Study Team. Randomized trial of introduction of allergenic foods in breastfed infants. *N Engl J Med* 2016; 374:1733-1743.
9. Palmer DJ, Sullivan TR, et al. Randomized controlled trial of early regular egg intake to prevent egg allergy. *J Allergy Clin Immunol* 2017; 139(5):1600-1607.
10. Savage J, Sicherer S, Wood R. The natural history of food allergy. *J Allergy Clin Immunol Pract* 2016; 4(2):196-203.
11. Shek LP, Soderstrom L, et al. Determination of food specific IgE levels over time can predict the development of tolerance in cow's milk and hen's egg allergy. *J Allergy Clin Immunol* 2004; 114(2):387-391.
12. Sicherer SH, Munoz-Furlong A, et al. U.S. prevalence of self-reported peanut, tree nut, and sesame allergy: 11 year follow-up. *J Allergy Clin Immunol* 2010; 125(6):1322-1326.
13. Togias A, Cooper SF, Acebal ML, et al. Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases–sponsored expert panel. *World Allergy Organ J* 2017; 10(1):1.
14. Wei-Liang Tan J, Valerio C, et al. A randomized trial of egg introduction from 4 months of age in infants at risk for egg allergy. *J Allergy Clin Immunol* 2017; 139(5):1621-1628.

TIDBSI: Tramadol

Paul Simmons MD and Justin McCarthy, MD

Pearls:

- **Tramadol is a pain medication that has partial mu activity as well as serotonergic and norepinephrine system effects. The data about safety and efficacy is mixed.**
- **Some patients may not metabolize it very well or may be on common medications that inhibit metabolism, rendering it much less effective for them.**
- **It is not a black-and-white medication with clear indications for who will benefit. Consider the entire clinical picture and patient in front of you when trying to determine if this drug is right for your patient.**
- **Tramadol:**
 - Two differing opinions on tramadol:
 - Partial mu agonist that is considered (by some) to be safer, less addictive and less risk of respiratory depression.
 - Others view it as just as dangerous with active metabolites that are just as potent as a full mu agonist
 - FDA-approved in 1995
 - Became schedule 4 substance in 2014
- **How it works:**

- Tramadol gets metabolized by the cytochrome P450 2D6 enzyme. The enzyme has wide genetic variability leading to very different metabolism patterns → some people will have no effect and others will have tremendous effect
 - There are also many inhibitors to the P45 2D6 enzyme that are common drugs like fluoxetine, paroxetine and bupropion
- Partial agonist of mu receptor and affects norepinephrine and serotonin system
 - Analgesic effect comes from the M1 active metabolite, which has a 700 times stronger receptor affinity for the mu receptor than tramadol itself
- Pearl: When a patient says it is not working for them, it may be that they are a slow metabolizer of the drug
- **Recent studies:**
 - British Medical Journal 2019:
 - Analyzed 360,000 who underwent elective surgery and found that tramadol had 40% higher risk of prolonged opioid use compared to other opioids.
 - Middle Eastern study 2019:
 - 30% of youth prescribed tramadol develop dependence and a significant portion actually develop polysubstance abuse
 - Literature from France, Latin America have shown tramadol to be safe
- **Bottomline:**
 - Consider the patient in front of you: their comorbidities, what type of pain they have, other medicines they may be on
 - May be a an option for patient with a neuropathic component to their pain who is younger, not on other meds or with co-existing conditions

REFERENCES:

1. Bassiony, MM; Abdelghani, M; Salah El-Deen, GM; et al. Opioid use disorders attributed to tramadol among Egyptian university students. *J Addict Med* 2017; 12(2):150-155
2. Bravo, L; Mico, JA & Berrocoso, E (2017) Discovery and development of tramadol for the treatment of pain. *Expert Opinion on Drug Discovery*. 2017. 12(12):1281-1291
3. Chenaf, C; Kabor, J; Delorme, J; et al. Incidence of tramadol shopping behavior in a retrospective cohort study of chronic non-cancer pain patients in France. *Pharmacoepidemiology and drug safety*. 2016. 25: 1088-1098
4. Ekelin, E & Hansson, A The dilemma of repeat weak opioid prescriptions – experiences from swedish GPs, *Scandinavian Journal of Primary Health Care*, 2018. 36(2):180-188
5. Khosrojerdi, H; Talesh, GA; Danaei, GH; et al. Tramadol half life is dose dependent in overdose. *DARU Journal of Pharmaceutical Sciences*. 2015; 23:22
6. Miotto, K; Cho, AK; Khalil, MA; et al. Trends in Tramadol: Pharmacology, metabolism, and misuse. *Anesth Analg*, 2017. 124:44-51
7. Santos Garcia JB; Lecho O; Campos Krachete D; et al. The role of tramadol in pain management in Latin America: a report by the Change Pain Latin America. *Current medical research and opinion*, 2017: 33(9):1615-1621

8. Subedi, M; Bajaj S; Kumar, M; et al. An overview of tramadol and its usage in pain management and future perspective. *Biomedicine and Pharmacotherapy*. 2019; 111:443-451
9. Thiels, CA; Habermann, EB; Hooten, M; et al. Chronic use of tramadol after acute pain episode: cohort study. *BMJ* 2019; 365:l1849

Pre & Post Menopausal Vaginal Bleeding

Megan Jones, MD & Neda Frayha, MD

Neda sits down with Megan Jones, MD, a high risk OB/GYN. Dr. Jones breaks down an algorithmic approach for the *non-pregnant* pre vs. post menopausal patient with vaginal bleeding. What do we need to do in UC? What can be referred and managed down the road by a gynecologist? Dr. Jones explains!

Pearls:

- ❑ Post-menopausal vaginal bleeding is cancer until proven otherwise.
 - ❑ Transvaginal ultrasound should be obtained urgently as the initial study of choice to evaluate post-menopausal bleeding.
 - ❑ Avoid prescribing estrogen to post-menopausal women until cancer has been ruled out by US and/or endometrial biopsy.
 - ❑ Exclude pregnancy first in pre-menopausal women presenting with vaginal bleeding.
 - ❑ Speculum exam is useful to quantify bleeding and ensure that it is truly from the uterus.
 - ❑ A bulky uterus on bimanual exam suggests a structural cause of bleeding, whereas a non-palpable uterus is more likely due to hormonal issues.
 - ❑ A short course of an OCP with gyn follow-up in a week is recommended for premenopausal women with heavy bleeding.
- The differential diagnosis for non-pregnant women with vaginal bleeding will differ significantly depending on whether they are pre- or post-menopausal.
 - **Post-menopausal is defined as women who've not menstruated in >1 year.**
 - **Post-menopausal vaginal bleeding is never normal.**
 - The differential diagnosis for bleeding in post-menopausal women includes, most significantly, vaginal atrophy, endometrial hyperplasia, and cancer.
 - **Transvaginal ultrasound is the initial study of choice to differentiate between these entities.**
 - An endometrial stripe <5mm suggests vaginal atrophy which is treated with vaginal estrogens.
 - An endometrial stripe >5mm is worrisome for endometrial hyperplasia or cancer and requires urgent gynecological referral for endometrial biopsy.
 - **In pre-menopausal women, exclude pregnancy first with a urine HCG test and then obtain a detailed history of the pattern of bleeding.**
 - Important historical questions to ask include:
 - Do periods come regularly or unpredictably?

- Does the patient have other abnormal bleeding or coagulopathy or take medications that affect coagulation?
 - Does the patient have a structurally abnormal uterus (e.g. fibroids)?
- Quantifying bleeding can be challenging because it is highly subjective.
 - **In addition to inquiring about the number of pads/tampons used per day, it is helpful to discuss how saturated they are when changed.**
 - Patients who avoid going into public because they bleed through their clothing is a concerning piece of data suggesting significant hemorrhage.
- **Both speculum and bimanual exam are necessary aspects in the evaluation of vaginal bleeding.**
 - **A speculum exam is important for confirming that the bleeding is coming from the uterus and not from cervical or vaginal pathology (e.g. cervicitis, polyps, etc.) and for quantifying the bleeding.**
 - The bimanual exam provides an estimate for the size of the uterus.
 - A large and bulky uterus suggests that a structural cause of bleeding, such as a fibroid, is more likely.
 - A smaller uterus suggests that the cause is more likely to be hormonal (e.g. anovulation or exogenous hormone use).

Differential Diagnoses for Pre-Menopausal Abnormal Uterine Bleeding (AUB):

- PALM is a useful mnemonic for *structural* causes of AUB.
 - P - polyps
 - A - adenomyosis
 - L - leiomyoma
 - M - malignancy
- COEIN is a mnemonic for *hormonal and other non-structural* causes of AUB.
 - C - coagulation issues (including thyroid disorders and medications)
 - O - ovulatory disorders (e.g. anovulation, PCOS)
 - E - endometrial hyperplasia
 - I - iatrogenic (e.g. IUD or oral contraceptive prescriptions)
 - N - not otherwise classified (e.g. vascular malformations etc.)
- **Unlike in post-menopausal bleeding, urgent transvaginal ultrasound is not recommended for all pre-menopausal women with AUB.**
 - Ultrasound is most helpful if the uterus is palpably enlarged on exam because it can identify structural causes of bleeding.
 - The thickness of the uterine stripe changes throughout the menstrual cycle so the absolute magnitude of thickness is of less significance than in post-menopausal women.
 - Women >45 years or with risk factors for endometrial cancer with AUB will often require endometrial biopsy, so, for these patients, a gyn referral is recommended.
- It is generally safe and appropriate to prescribe hormonal treatment for pre-menopausal women with AUB from UC.
 - Dr. Jones recommends a combination estrogen & progestin oral contraceptive (OCP) with a higher dose of estrogen.
 - Norgestimate and ethinyl estradiol (trade name Sprintec™) with 35 mcg of estrogen *TID* for 1 week will help stabilize endometrium.

- Medroxyprogesterone acetate (trade name Provera™) 20mg TID x 1 week is similarly effective and preferred for patients with contraindications to estrogen (e.g. patients with a history of VTE, tobacco users, hypertension, and estrogen sensitive cancers).
 - **Patients should be counseled that there will be heavy bleeding when the OCP is stopped, so they should be seen within one week by a gynecologist to initiate a longer term plan.**
 - Nausea is also common with this high dose OCP regimen and prescribing an antiemetic (e.g. ondansetron etc.) will help prevent vomiting.
- Long term management options include hormonal IUD placement and endometrial ablation. Dilation and curettage (D&C) is the ultimate therapy for patients who do not respond to less invasive therapies, but is actually rarely necessary.

References:

1. Practice Bulletin No. 136: Management of Abnormal Uterine Bleeding Associated With Ovulatory Dysfunction. *Obstetrics & Gynecology*: July 2013 - Volume 122 - Issue 1 - p 176-185.
2. ACOG Committee Opinion No. 734: The Role of Transvaginal Ultrasonography in Evaluating the Endometrium of Women With Postmenopausal Bleeding. *Obstetrics & Gynecology*: May 2018 - Volume 131 - Issue 5 - p e124-e129.

Destigmatizing Therapy

Jay-Sheree Allen MD, Neda Frayha MD

Pearls:

- Mental health issues are very common in primary care and therapy is an evidence-based way to address them.
- Some tips to help encourage patients to seek therapy include a list of therapists in your area, routine screening for mental health issues and exploring telehealth options that may be a bridge to in-person therapy.
- **Why is it important for providers to feel comfortable talking about therapy with patients?**
 - Mental health issues are very common in primary care
 - Therapy is an important part of addressing these mental health issues
 - The more comfortable we are discussing it and foreseeing barriers for patients, the better able we are able to address them in the moment
- **Defining therapy:**
 - Psychotherapy is a way to help people with specific mental health disorders like depression and anxiety
 - Often includes shoring up coping healthy coping mechanisms
 - May intervene on patterns of thinking that lead to negative behaviors

- Types:
 - Cognitive behavioral therapy (CBT) is the most common
 - Helps change thinking and behavioral patterns that are harmful or ineffective. Replaces them with more accurate thoughts and functional behaviors.
 - Interpersonal therapy
 - Short-term form of therapy that helps patients understand underlying interpersonal issues. Learn healthy ways to express emotions and ways to improve communication
 - Dialectical behavioral therapy
 - Specific type of CBT that helps people regulate emotions for people with borderline personality disorder, eating disorders, PTSD
 - Psychodynamic therapy
 - Improve self-awareness by understanding childhood experiences
 - Psychoanalysis
 - Intensive form of psychodynamic therapy
- **Literature around therapy:**
 - Meta-analysis of psychotherapy and medication looking at unipolar depression showed about 75% of those who undergo psychotherapy benefit from it
 - Evidence psychotherapy has sustained effects over the long term
 - For treating OCD, psychotherapy may actually be better
 - For dysthymia, bipolar disorder and schizophrenia, medications are first-line
- **Perceived stigmas:**
 - 1. Cultural
 - Some people may think “just talking” is not an intervention/treatment like a pill
 - 2. Professional
 - Depending on the profession, may not want to appear incompetent or unable to cope
 - 3. Personal
 - People may have a bias about therapy or had a bad prior experience
- **Tips and tricks to achieve better outcomes:**
 - Create a list of local therapists for patients
 - Screen for depression with a PHQ-2
 - Explore telehealth options for therapy or as a bridge to in-person therapy
 - Encourage patients to focus on the process of therapy and try to trust the process

REFERENCES:

1. Mental Health Facts in America. National Alliance on Mental Illness. <https://www.nami.org/nami/media/nami-media/infographics/generalmhfacts.pdf> Accessed December 6, 2019.

2. Anxiety Disorder. National Institute of Mental Health. <https://www.nimh.nih.gov/health/statistics/any-anxiety-disorder.shtml> Published November 2007. Accessed December 5, 2019.
3. Depression. World Health Organization. <https://www.who.int/news-room/fact-sheets/detail/depression> Updated December 4, 2019. Accessed December 6, 2019.
4. Coffey SF, Banducci AN. Common Questions about Cognitive Behavior Therapy for Psychiatric Disorders. *American Family Physicians*. 2015 Nov 1;92(9):807-812.
5. Understanding Psychotherapy and How it works. American Psychological Association. <https://www.apa.org/helpcenter/understanding-psychotherapy> Accessed December 5, 2019.
6. What is Psychotherapy. American Psychiatric Association. <https://www.psychiatry.org/patients-families/psychotherapy> January 2019. Accessed December 4, 2019.
7. Imel ZE1, Malterer MB, McKay KM, Wampold BE. A meta-analysis of psychotherapy and medication in unipolar depression and dysthymia. *J Affect Disord*. 2008 Oct;110(3):197-206.
8. Cuijpers P, et al. The efficacy of psychotherapy and pharmacotherapy in treating depressive and anxiety disorders: A meta-analysis of direct comparisons. *World Psychiatry: Official Journal of the World Psychiatric Association (WPA)*. June 2013.
9. Eric L. Ross, MD; Sandeep Vijan, MD; Erin M. Miller, MS; Marcia Valenstein, MD; and Kara Zivin, PhD. The Cost-Effectiveness of Cognitive Behavioral Therapy Versus Second-Generation Antidepressants for Initial Treatment of Major Depressive Disorder in the United States: A Decision Analytic Model. *Ann Intern Med*. 2019;171:785-795.
10. Qaseem A, Barry MJ, Kansagara D, for the Clinical Guidelines Committee of the American College of Physicians. Nonpharmacologic Versus Pharmacologic Treatment of Adult Patients With Major Depressive Disorder: A Clinical Practice Guideline From the American College of Physicians. *Ann Intern Med*. 2016;164:350–359.

Precharting

Aisha Lofters MD

Pearls:

- **Precharting, reviewing the chart and starting documentation in advance of clinic, may help keep you on time, free you up in the exam room to engage more with the patient and save you time at the end of the day on charting.**
- **Reader question: Precharting - can it save time? Is it even useful?**
 - Pre-charting = reviewing the chart and starting documentation before the visit
 - Reviewing the chart in more detail - recent specialist visit, hospitalization, lab tests, removing outdated information
 - Documenting ahead of time to start off each section of the note

- **Subjective** - review chronic conditions and organize thinking about the chief complaint and chronic conditions
 - Note the chief complaint and questions you want to ask
 - **Objective** - document the exam findings you want to make sure to complete
 - **Assessment and Plan:** formulate your differential for a chief complaint, anticipate the plan for chronic conditions, prepare lab or imaging studies and referrals
- Can be very crucial for patient coming in after hospital discharge
- When to pre-chart?
 - Morning before seeing patients or even the day prior
- Benefits?
 - More likely to stay on time in visits so patients spend less time in the waiting room
 - More time to talk to patient instead of typing in the EMR
 - May allow you to finish day's work earlier since majority of charting has already been completed
 - May allow you to bill Medicare/Medicaid for CPT code 99358, 31 minutes or more spent reviewing medical records
 - Gives you opportunity to huddle with the nursing staff
- Disadvantages?
 - Carving out the chunk of time to do it

REFERENCES:

1. Allen, James. "Should A Physician Pre-Chart For Outpatient Visits?" *The Hospital Medical Director*, 28 Nov 2018.
hospitalmedicaldirector.com/should-a-physician-pre-chart-for-outpatient-visits/.
2. Sinsky, Christine A, et al. "Putting Pre-Visit Planning Into Practice." *Family Practice Management*, vol. 22, no. 6, Nov. 2015, pp. 34–38, www.aafp.org/fpm/2015/1100/p34.html.
3. Sinsky, Christine A. "Improving Office Practice: Working Smarter, Not Harder." *Family Practice Management*, vol. 13, no. 10, Nov. 2013, pp. 28–34, www.aafp.org/fpm/2006/1100/p28.html.

Paper Chase #1 - Metoprolol for the Prevention of Acute Exacerbation of COPD

Tom Robertson MD, Steve Biederman MD

Dransfield MT, Voelker H, Bhatt SP, et al. *Metoprolol for the Prevention of Acute Exacerbations of COPD. N Engl J Med.* 2019;381(24):2304-2314. doi:10.1056/nejmoa1908142

Pearls:

- **Addition of metoprolol did NOT reduce time to first exacerbation and exacerbations were more common among patients treated with metoprolol.**

- **Objective:** To evaluate beta blockers efficacy in preventing COPD exacerbations
- **Method:** double blind, placebo controlled, and prospective randomized trial of patients with COPD and randomized them to either metoprolol or placebo
 - Patients were 40-85 and had no other indication for beta-blockers
- **Results:**
 - 500 patients
 - No significant difference for time to first exacerbation (202 days)
 - Hazard ratio for time to first exacerbation was 1.5 and the metoprolol group also had more severe exacerbations
 - Trial was stopped prematurely because of futility
- **Bottomline:** Addition of metoprolol did NOT reduce time to first exacerbation and exacerbations were more common among patients treated with metoprolol who otherwise had no indication to be on a beta-blocker.

Paper Chase #2 - Dapagliflozin in Patients with Heart Failure and Reduced EF

Tom Robertson MD, Steve Biederman MD

McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. *N Engl J Med.* 2019;381:1995-2008. doi:10.1056/nejmoa1911303

Pearls:

- In patients with HFrEF, the risk of worsening CHF or death was less in dapagliflozin than placebo.
- **Objective:** To assess effect of dapagliflozin vs placebo in patients with HFrEF
- **Background:** SGLT2 inhibitors were initially developed for treating diabetes by preventing the reabsorption of glucose in the kidneys
- **Method:** placebo controlled randomized controlled trial among patients with HFrEF < 40% with NYHA2 symptoms or worse. Did not have to have diabetes. Followed for 18 months.
- **Results:**
 - 4700 patients
 - Less heart failure in treatment group (16%) v. placebo (21%) - hazard ratio of 0.74
 - Significant reductions in first worsening heart failure event, death from cardiovascular causes and all cause mortality
 - No excess in adverse events
- **Bottomline:** In patients with HFrEF, the risk of worsening CHF or death was less in dapagliflozin than placebo.

Paper Chase #3 - Results of a 6-week treatment with 10 mg prednisolone in patients with hand osteoarthritis (HOPE): a double-blind, randomised, placebo-controlled trial

Tom Robertson MD, Steve Biederman MD

Kroon FPB, Kortekaas MC, Boonen A, et al. Results of a 6-week treatment with 10 mg prednisolone in patients with hand osteoarthritis (HOPE): a double-blind, randomised, placebo-controlled trial. *Lancet*. 2019;394(10213):1993-2001. doi:10.1016/s0140-6736(19)32489-4

Pearls:

- **6-weeks of prednisolone was safe and efficacious in treating painful hand osteoarthritis but the difference between treatment groups tapered after 4 months.**
- **Objective:** To evaluate the safety and efficacy of 10 mg prednisolone for 6 weeks in treatment of patients with osteoarthritis and signs of inflammation
- **Method:** double blind randomized placebo controlled trial, recruited from a rheumatology clinic in the Netherlands. Had to have had osteoarthritis and 4+ joints with nodules. Followed for 4 months. Received a questionnaire assessing symptoms.
- **Results:**
 - 90 patients enrolled, most were women
 - Mean difference of 16 points lower on the pain scale among the treatment group that decreased after 3-4 months
 - Adverse events were similar between groups
- **Bottomline:** 6-weeks of prednisolone was safe and efficacious in treating painful hand osteoarthritis but the difference between treatment groups tapered after 4 months.

Paper Chase #4 - Does Scheduling a Postdischarge Visit with a Primary Care Physician Increase Rate of Follow-up and Decrease Readmissions?

Tom Robertson MD, Steve Biederman MD

Marcondes FO, Punjabi P, Doctoroff L, et al. Does Scheduling a Postdischarge Visit with a Primary Care Physician Increase Rates of Follow-up and Decrease Readmissions? *J Hosp Med*. 2019;14:E37-E42. doi:10.12788/jhm.3309

Pearls:

- **The rates of PCP f/u increased significantly with the assistance of a post-discharge appt service but did not result in significantly lower 30-day readmission rates compared to usual care.**
- **Objective:** To assess the effect of post-discharge scheduling assistance on PCP followup or readmissions
- **Background:** single center inpatient study where half of those discharged received a dedicated post-discharge appointment service that scheduled PCP follow-up appointments and the other half received usual care.
- **Method:**

- 17,500 hospitalizations
- Post-discharge primary care follow-up was 60% in the intervention group and 29% in the control group
- 30-day readmission rate was not significantly lower between the two groups
- **Results:**
- **Bottomline:** The rates of PCP f/u increased significantly with the assistance of a post-discharge appt service but did not result in significantly lower 30-day readmission rates compared to usual care.

Paper Chase #5 - Perioperative Management of Patients with Atrial Fibrillation Receiving a Direct Oral Anticoagulant

Tom Robertson MD, Steve Biederman MD

Douketis JD, Spyropoulos AC, Duncan J, et al. Perioperative Management of Patients With Atrial Fibrillation Receiving a Direct Oral Anticoagulant. JAMA Intern Med. 2019;179(11). doi:10.1001/jamainternmed.2019.2431

Pearls:

- **For patients with afib who had DOAC therapy interruption for elective surgery, a management strategy without heparin bridging or coagulant testing was associated with low rates of bleeding and embolism.**
- **Objective:** To investigate the safety of a standardized perioperative DOAC management strategy
- **Method:** prospective study of patients undergoing an elective surgery or procedure broken into three cohorts: apixaban, dabigatran, rivaroxaban. Followed an algorithm (below) and assessed major bleeding / clotting events

Figure. Perioperative Direct Oral Anticoagulant (DOAC) Management Protocol

DOAC	Surgical Procedure-Associated Bleeding Risk	Preoperative DOAC Interruption Schedule					Day of Surgical Procedure (No DOAC)	Postoperative DOAC Resumption Schedule			
		Day -5	Day -4	Day -3	Day -2	Day -1		Day +1	Day +2	Day +3	Day +4
Apixaban	High	→	→	→	→	→	Day of Surgical Procedure (No DOAC)	→	→	→	→
	Low	→	→	→	→	→		→	→	→	→
Dabigatran etexilate (CrCl ≥50 mL/min)	High	→	→	→	→	→		→	→	→	→
	Low	→	→	→	→	→		→	→	→	→
Dabigatran etexilate (CrCl <50 mL/min) ^a	High	→	→	→	→	→		→	→	→	→
	Low	→	→	→	→	→		→	→	→	→
Rivaroxaban	High	→	→	→	→	→		→	→	→	→
	Low	→	→	→	→	→		→	→	→	→

No DOAC was taken on certain days (shaded) and on the day of the elective surgery or procedure. The light blue arrows refer to an exception to the basic management, a subgroup of patients taking dabigatran with a creatinine clearance (CrCl) less than 50 mL/min. The orange arrows refer to patients having a high-bleed-risk surgical procedure. Dark blue arrows refer to patients having a

low-bleed-risk surgical procedure. The thickened orange part of arrows refer to flexibility in the timing of DOAC resumption after a procedure.

^a Cancer diagnosed within 3 months or has been treated within 6 months or metastatic.

- **Results:**
 - 3000 patients
 - 30 day major bleeding and clotting events was very low among all three cohorts (<1%)
- **Bottomline:** For patients with afib who had DOAC therapy interruption for elective surgery, a management strategy without heparin bridging or coagulant testing was associated with low rates of bleeding and embolism