



Primary Care RAP June 2020 Written Summary

Editor-in-Chief: Neda Frayha MD

Associate Editor: Kenji Taylor MD, MSc

Intro: Death Certificates

Neda Frayha MD, Aisha Lofters MD

Pearls:

- Death certificates should be completed within 3 days and completely filled out with no abbreviations.
- Terms like cardiac arrest, respiratory failure and asystole are not causes of death and should not be listed as such in the death certificate. They refer more to circumstances surrounding death.
- The cause of death may be probable or presumed - its an “informed opinion - more likely than not with a greater than 51% chance of being correct”.

- Reader question - death certificates:
 - What is it?
 - Official statement signed by a clinician of the cause, date, and place of a person's death
 - Why is it important?
 - Provide information used by policymakers to set public health goals and determine priorities for funding healthcare research
 - Used for basis of national mortality database
 - Surveillance for outbreaks and pandemics
 - Sometimes help settle estates of the deceased
 - Needs to be completed prior to cremation or burial
 - Provide closure for family members
 - Who completes it?
 - Most often filled out by the hospital or hospice provider
 - If a person dies at home of suspected natural causes, it is the primary care provider that completes the certificate
 - If there is suspicion about cause of death at home, then the coroner’s office gets involved and is responsible for filling out
 - Who can complete varies by state. Some states do allow advanced practice providers to fill out

- When is it completed?
 - Most states in the US require it be done within 3 days
- How to complete?
 - Fine to use probable or presumed death as the point of the certificate is to solicit an “informed opinion - more likely than not with a greater than 51% chance of being correct”
 - Sections:
 - Date of death
 - Time of death
 - Death pronouncement
 - Cause of death
 - Line A: Immediate cause - specific cause
 - Line B: Final complications relating to death listed in order of most recent to longest established
 - Pearl!: Terms like cardiac arrest, respiratory failure and asystole are not causes of death, rather circumstances surrounding death.
 - Referral to coroner
 - Injuries
- Examples of Line A (immediate cause of death)
 - Gastric hemorrhage caused by gastric ulcer caused by H pylori infection
 - Mesenteric thrombosis caused by colectomy caused by adenocarcinoma of a sigmoid colon
 - Pulmonary embolism caused by deep vein thrombosis caused by metastatic non-small cell lung cancer
- Examples for Line B (complications)
 - Atherosclerotic disease
 - COPD
 - Diabetes
 - Smoking
- Common Pitfalls to avoid
 - Use black ink
 - Don't erase anything
 - Don't white-out anything
 - No abbreviations
 - Leaving nothing blank
 - In Part 1, put only one cause per line
 - Terms like renal failure, sepsis, hypotension, hepatic failure, “old age”, “senescence” are generally thought of as too vague and have to be attributed to specific causes
 - Be specific as possible (ie: left upper lobe, primary small cell lung cancer)
- Resources:
 - Mobile app - “Cause of Death”
 - CDC instructions (see references below)

- CDC training module
- Local coroner's office or office of the medical examiner

REFERENCES:

1. *Instructions for Completing the Cause-of-Death Section of the Death Certificate.*; 2004. https://www.cdc.gov/nchs/data/dvs/blue_form.pdf
2. Nowels D. Completing and Signing the Death Certificate. *Am Fam Physician.* 2004;70(9):1813. <https://www.aafp.org/afp/2004/1101/p1813.html>. Accessed March 4, 2020.
3. Swain GR, Ward GK, Hartlaub PP. Death Certificates: Let's Get It Right. *Am Fam Physician.* 2005;71(4):652. <https://www.aafp.org/afp/2005/0215/p652.html>. Accessed March 4, 2020.
4. Prentice N, Arnold R. Completing a Death Certificate. Palliative Care Network of Wisconsin. <https://www.mypcnow.org/fast-fact/completing-a-death-certificate/>. Published May 2007. Accessed March 4, 2020.
5. Death Certification. *National Association of Medical Examiners.* <https://www.thename.org/death-certification>. Accessed March 6, 2020.
6. Cina S. *Death Certification: A Final Service to Your Patient.*; 2014. <https://name.memberclicks.net/assets/docs/81c91419-9186-4727-a1cc-356713e613d8.pdf>

TIDBSI: Knee Injections

Paul Simmons MD, Justin McCarthy MD

Pearls:

- The evidence for steroid injections to treat pain for knee osteoarthritis suggests a very modest benefit with side effects that include capsular calcification, hypopigmentation, infection and transient hyperglycemia.
- The evidence for hyaluronic acid is weak and shows modest benefit, predominantly in younger patients with less severe osteoarthritis. It is not recommended by the AAOS.
- The evidence for other modalities (PRP, stem cells, prolotherapy) is very weak and not endorsed by any major medical organizations.
- **Latest evidence on corticosteroid injections (CSI) in the knee for osteoarthritis:**
 - Cochrane review 2015 of 27 randomized control studies comparing steroids v. saline placebo
 - 1700 patients
 - Most common steroid triamcinolone, 50mg prednisone equivalents
 - Pain improved by one point on a 10-point scale
 - Risks: pericapsular or capsular calcification, hypopigmentation, infection risk and transient hyperglycemia in adults
 - **Bottomline:** only evidence for short-term benefit
 - JAMA 2017 article

- 2-year double-blind RCT of steroid injection v. saline placebo every 3 months
 - No difference in pain control, cartilage loss in the steroid group
- **Latest evidence on hyaluronic acid injections**
 - Several systematic reviews and RCTs that showed trend toward a 3-6 month modest benefit of one point on a 10-point scale
 - Strongest evidence for use was actually in younger patients < 65 with less severe osteoarthritis
 - Less side effects than steroids but very expensive
 - Per AAOS: “The AAOS cannot recommend use of intraarticular hyaluronic acid for patients with symptomatic OA of the knee based on a lack of efficacy with low likelihood of achieving clinically important benefits”
- **Latest evidence for other options: stem cells, platelet rich plasma, prolotherapy**
 - Most evidence in younger patients, low powered studies
 - None are recommended by any major organizations yet

REFERENCES:

1. Jüni P, Hari R, Rutjes AW, et al. Intra-articular corticosteroid for knee osteoarthritis. *Cochrane Database Syst Rev*. 2015;10. doi:10.1002/14651858.cd005328.pub3
2. McAlindon TE, LaValley MP, Harvey WF, et al. Effect of Intra-articular Triamcinolone vs Saline on Knee Cartilage Volume and Pain in Patients With Knee Osteoarthritis. *JAMA*. 2017;317(19):1967. doi:10.1001/jama.2017.5283
3. Jevsevar D, Donnelly P, Brown GA, Cummins DS. Viscosupplementation for Osteoarthritis of the Knee: A Systematic Review of the Evidence. *J Bone Joint Surg Am*. 2015;97(24):2047–2060. doi:10.2106/JBJS.N.00743
4. Bannuru RR, Schmid CH, Kent DM, Vaysbrot EE, Wong JB, McAlindon TE. Comparative effectiveness of pharmacologic interventions for knee osteoarthritis: a systematic review and network meta-analysis. *Ann Intern Med*. 2015;162(1):46-54. doi:10.7326/M14-1231

Acute Gastroenteritis (AGE), Parts 1 & 2

Matthieu DeClerck MD & Sol Behar, MD

Pearls:

- ❑ Due to the rotavirus vaccine, norovirus is now the most common cause of viral AGE in the US.
- ❑ Because it is usually self-limited, stool testing for suspected AGE should be reserved for those with bloody diarrhea, severe presentation, or history of other medical/endocrine disorders.
- ❑ Before treating an infant < 1 year old for C difficile, consult ID or GI. Up to 40% in this age group are colonized with C diff .
- ❑ Oral hydration with a balanced electrolyte solution is the cornerstone of therapy for AGE. Avoid lactose containing and sugary liquids as they can exacerbate the diarrhea

- **Definition:**
 - Acute gastroenteritis (AGE) is a common intestinal ailment in children of all ages presenting with vomiting, diarrhea, abdominal pain, and +/- fevers.
 - Most *viral* causes present with non-bloody, non-bilious vomiting and watery, non-bloody diarrhea.
- **We are taught to think twice before sending a pediatric patient home with the diagnosis of AGE. But why?**
 - Many jump to the diagnosis of AGE before all the symptoms (vomiting + diarrhea) are present.
 - You don't want to get trapped into assuming a patient with vomiting and/or diarrhea has AGE. These patients need a thorough history and exam to ensure you're not missing more serious entities.
- **Differential diagnosis:**
 - Viral
 - Norovirus -- most common viral cause of AGE in US children
 - Rotavirus -- decreasing incidence due to rotavirus vaccine [1, 2]
 - Enterovirus -- more common in summer
 - Bacterial
 - Consider especially in those with bloody diarrhea or if travel history suggests risk.
 - Parasitic
 - Foodborne illness
 - Milk protein allergy or food sensitivities -- consider if diarrhea > 14 days in a child <2 years old
 - Primary immune deficiency may present with chronic diarrhea
 - Antibiotic associated diarrhea
 - Post-antibiotic Clostridium difficile
 - Malabsorptive processes (ie. celiac, IBS, Crohn's)
- **Diagnostic confirmation**
 - **Viral AGE is usually a clinical diagnosis.**
 - Consider stool testing for those with bloody diarrhea, severe presentation, or history of other medical/endocrine disorders.
 - PCR assays
 - Rapid detection of viral, bacterial and parasitic etiologies.
 - Often not necessary as most viral and bacterial causes are self-limited.
 - Cost-effectiveness has not been established.
 - Stool cultures
 - Limited utility given long turnaround times.
 - Ova and parasites
 - Can be helpful if history of travel, outdoor swimming, camping, etc.

- Both giardia and cryptosporidium can also be detected with an enzyme immunoassay (EIA) or direct fluorescent antibody (DFA) blood test.
 - C difficile testing
 - Consider if history of antibiotic exposure or recent hospitalization.
 - Should only be performed in infants if evidence of toxic megacolon, pseudomembranous colitis, or clinically significant diarrhea and other causes have been ruled out [6].
 - **Up to 40% of infants < 1 year old are colonized with C diff [7].**
 - C diff treatment decisions for infants should be made in consultation with an ID or GI specialist.
- **Management**
 - **Oral hydration with a balanced electrolyte solution is the cornerstone of therapy.**
 - Can be purchased (ie. Pedialyte) or homemade (1 liter water + 6 tsp sugar + ¼ teaspoon salt).
 - Avoid fluids with excess sugar (ie. undiluted juice, sports drinks), as the sugar is osmotically active and can exacerbate diarrhea by pulling water into the intestine. Juice or sports drinks diluted 50:50 with water should be safe [15].
 - Lactose containing fluids (ie. milk products, breastmilk, formula) may be difficult to absorb since the lining of the small intestine villi which contains the lactase enzyme is sloughed off during AGE.
 - Younger infants (< 6 months) should continue to breastfeed ad lib through the illness.
 - For prolonged diarrhea in older infants, a temporary trial of lactose-free formula or milk may be helpful.
 - While there is plenty of historical experience with the BRAT diet (bananas, rice, applesauce, and toast), there is no evidence to say it helps.
 - **Antiemetics**
 - Ondansetron (0.15 mg/kg IV, PO, or oral dissolving tablet)
 - Safe and effective in reducing need for IV fluids [9, 10].
 - May prescribe a 1-2 days supply for kids > 2 years.
 - FDA approved for children older than 2, but commonly given to younger children in a clinic setting.
 - Other antiemetics (metoclopramide, promethazine, etc)
 - Avoid in kids < 12 years due to extrapyramidal side effects.
 - **Antimotility agents should be avoided.**
 - Loperamide has been associated with respiratory depression/death in kids.
 - Bismuth compounds can turn the stool black.
 - **Probiotics**

- One study showed that in children prescribed an antibiotic, the co-administration of a probiotic was associated with lower rates of antibiotic-associated diarrhea. [18].
 - Other studies, including a Cochrane review, showed no benefit [16, 17, 19, 20].
 - **IV fluids**
 - IV rehydration may be necessary for kids who are clinically dehydrated with ongoing frequent stool output and/or emesis.
 - Tachycardia is often the only vital sign manifestation of dehydration in kids. Blood pressure can remain normal.
 - Children seem to feel better overall after hydration.
 - Consider external jugular, scalp vein, or subcutaneous rehydration (aka hypodermoclysis) if peripheral venous access is challenging [8].
 - For severe dehydration, resuscitate with isotonic fluids, rapidly giving boluses of 20 cc/kg.
 - **Antibiotics**
 - Treatment should be guided by specific pathogens; the Red Book is an excellent resource for guiding antibiotic therapy [11].
 - Do not give empiric antibiotics for bacterial infections until you've identified the bug.
 - More specifically, do not treat E coli O157:H7 with antibiotics due to an association with hemolytic uremic syndrome [13, 14].
 - C difficile treatment:
 - Oral vancomycin 7.5 mg/kg/dose tid or qid OR
 - Metronidazole 10 mg/kg/dose qid for 10 days
 - In more severe illness, oral or rectal vancomycin is preferred over metronidazole.
 - Recurrent episodes can be treated with a longer course of oral vancomycin, oral rifaximin or fecal transplant.
 - Giardia treatment:
 - Nitazoxanide or tinidazole for 1-3 days [21].
 - Cryptosporidium treatment:
 - Can be self-resolving.
 - For severe cases → nitazoxanide (100 mg PO bid x 3 days for children age 1-3 years, 200 mg PO bid x 3 days for age 4-11 year) [22].
- **Red flags questions which help with disposition:**
 - Has there been bloody diarrhea?
 - Does the history or exam suggest severe dehydration (ie. no tears, decreased urine output, tachycardia)?
 - Has there been vomiting as an isolated symptom, without diarrhea?
 - Consider appendicitis, intracranial pathology, intussusception/obstruction, diabetes, UTI/pyelonephritis, testicular or ovarian torsion.

References:

1. Shah MP, et al. Decline in Emergency Department Visits for Acute Gastroenteritis Among Children in 10 US States After Implementation of Rotavirus Vaccination, 2003 to 2013. *Pediatr Infect Dis J*. 2016 Jul;35(7):782-6. [PMID: 27088585](#).
2. Desai R, et al. All-cause gastroenteritis and rotavirus-coded hospitalizations among US children, 2000-2009. *Clin Infect Dis*. 2012 Aug;55(4):e28-34. [PMID: 22543022](#).
3. Chhabra P, et al. Etiology of viral gastroenteritis in children <5 years of age in the United States, 2008-2009. *J Infect Dis*. 2013 Sep 1;208(5):790-800. [PMID:23757337](#).
4. Rha B, et al. Emergency department visit data for rapid detection and monitoring of norovirus activity, United States. *Emerg Infect Dis*. 2013Aug;19(8):1214-21. [PMID:23876432](#).
5. Thiagarajah JR, et al; PediCODE Consortium. Advances in Evaluation of Chronic Diarrhea in Infants. *Gastroenterology*. 2018 Jun;154(8):2045-2059.e6. [PMID: 29654747](#)
6. McDonald LC, et al. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clin Infect Dis*. 2018 Mar 19;66(7):987-994. [PMID: 29562266](#).
7. Schutze GE, et al. Clostridium difficile infection in infants and children. *Pediatrics*. 2013 Jan;131(1):196-200. [PMID: 23277317](#).
8. Spandorfer PR, et al. A randomized clinical trial of recombinant human hyaluronidase-facilitated subcutaneous versus intravenous rehydration in mild to moderately dehydrated children in the emergency department. *Clin Ther*. 2012 Nov;34(11):2232-45. [PMID: 23062548](#).
9. Tomasik E, et al. Systematic review with meta-analysis: ondansetron for vomiting in children with acute gastroenteritis. *Aliment Pharmacol Ther*. 2016 Sep;44(5):438-46. [PMID: 27401959](#).
10. Rutman L, et al. Clinical Pathway Produces Sustained Improvement in Acute Gastroenteritis Care. *Pediatrics*. 2017 Oct;140(4). pii: e20164310. [PMID: 28882877](#).
11. Committee on Infectious Diseases, in *Red Book: 2018-2021 Report of the Committee on Infectious Disease*, D. Kimberlin, BRady MT, Jackson MA, Long SS, Editor. 2018, American Academy of Pediatrics. p. 352-54.
12. Diseases, C.o.I., in *Red Book: 2018-2021 Report of the Committee on Infectious Disease*, D. Kimberlin, BRady MT, Jackson MA, Long SS, Editor. 2018, American Academy of Pediatrics. p. 304-06.
13. Bruyand M, et al. Hemolytic uremic syndrome due to Shiga toxin-producing Escherichia coli infection. *Med Mal Infect*. 2018 May;48(3):167-174. [PMID: 29054297](#).
14. Wong CS, et al. The risk of the hemolytic-uremic syndrome after antibiotic treatment of Escherichia coli O157:H7 infections. *N Engl J Med*. 2000 Jun 29;342(26):1930-6. [PMID: 10874060](#).
15. Freedman SB, et al. Effect of Dilute Apple Juice and Preferred Fluids vs Electrolyte Maintenance Solution on Treatment Failure Among Children With Mild Gastroenteritis: A Randomized Clinical Trial. *JAMA*. 2016 May 10;315(18):1966-74. [PMID: 27131100](#).

16. Hong Chau TT, et al. A Double-blind, Randomized, Placebo-controlled Trial of Lactobacillus acidophilus for the Treatment of Acute Watery Diarrhea in Vietnamese Children. *Pediatr Infect Dis J*. 2018 Jan;37(1):35-42. [PMC5681247](#).
17. Goldenberg JZ, et al. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. *Cochrane Database Syst Rev*. 2015 Dec 22;(12):CD004827.PMID: 26695080.
18. Johnston BC, et al. Probiotics and the Prevention of Antibiotic-Associated Diarrhea in Infants and Children. *JAMA*. 2016 Oct 11;316(14):1484-1485. [PMID: 27727371](#).
19. Freedman SB, et al. Multicenter Trial of a Combination Probiotic for Children with Gastroenteritis. *N Engl J Med*. 2018 Nov 22;379(21):2015-2026. [PMID: 30462939](#).
20. Schnadower D, et al. Lactobacillus rhamnosus GG versus Placebo for Acute Gastroenteritis in Children. *N Engl J Med*. 2018 Nov 22;379(21):2002-2014. [PMID: 30462938](#).

Continuous Glucose Monitors

Elizabeth Lamos MD, Paul Simmons MD

Pearls:

- **As continuous glucose monitors (CGMs) become more widely available, consider them for primary care patients who check their blood sugar levels multiple times a day, have complex insulin regimens or have a history of hypoglycemia.**
- **What are continuous glucose monitors (CGMs)?**
 - Continuously monitor glucose with a sensor on the body usually the size of a quarter that has a small (couple millimeter) plastic catheter on it sitting underneath the skin in the interstitial space
 - Transmits wirelessly
 - Historically had been used in patients with complex diabetes but as the technology has advanced is more applicable to patients seen in primary care
 - Accurate within about 10% of a fingerstick glucose
 - Lag time of 5 to 10 minutes
- **Good candidates:**
 - Type 1 and 2 diabetics that require intensive insulin titration
 - Those with multi-injection daily insulin regimens
 - Those with issues of hypoglycemia regardless of insulin regimen
 - Those struggling with fingersticks
- **Relative Contraindications:**
 - Pregnancy
 - Critically ill / hospitalized
 - Dialysis
- **Functions of CGM's:**
 - Catheters last 7-14 days
 - May transmit intermittently to continuously to a device (ie: phone, watch, separate device)

- Set alarms for different glucose levels
- **Different use cases:**
 - Can be used for short-term periods borrowed from the office to monitor a patient who you're worried about has significant hypoglycemia. Can be checked out from the office.
 - May unblind monitoring so the patient can use the data to change behavior as they see it
 - May blind monitoring to review with the patient to provide feedback retrospectively
- **FreeStyle Libre:**
 - Place sensor on the arm every 10-14 days and usually takes 12 hours before its ready to give accurate readings
 - Good for those with Type 1 or 2 diabetes who have to check sugar frequently
 - Does not have hypoglycemia alarm so isn't good for people who have hypoglycemia unawareness or frequent hypoglycemia
 - Data can be downloaded by provider to show percent time spent at different glucose levels
- **Eversense:**
 - The only implanted CGM on the market
 - Implanted in the upper arm under local anesthesia in the office every 90 days
- **Other devices:**
 - Dexcom G5 and G6
 - Medtronic Guardian Sensor can pair with insulin pumps
- **Reimbursement:**
 - CPT codes (99250) can pay for the review of CGM data

REFERENCES:

1. Chamberlain JJ, Doyle-Delgado K, Peterson L, Skolnik N. Diabetes Technology: Review of the 2019 American Diabetes Association Standards of Medical Care in Diabetes. *Ann Intern Med.* 2019;171(6):415. doi:10.7326/m19-1638
2. Carlson AL, Mullen DM, Bergenstal RM. Clinical Use of Continuous Glucose Monitoring in Adults with Type 2 Diabetes. *Diabetes Technol Ther.* 2017;19(S2):S4–S11. doi:10.1089/dia.2017.0024
3. Tamborlane W, Beck R, Bode B, et al. Continuous Glucose Monitoring and Intensive Treatment of Type 1 Diabetes. *N Engl J Med.* 2008;359(14):1464-1476. doi:10.1056/nejmoa0805017
4. Klonoff DC, Buckingham B, Christiansen JS, et al. Continuous Glucose Monitoring: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2011;96(10):2968-2979. doi:10.1210/jc.2010-2756
5. Longo R, Sperling S. Personal Versus Professional Continuous Glucose Monitoring: When to Use Which on Whom. *Diabetes Spectr.* 2019;32(3):183–193. doi:10.2337/ds18-0093

Flashes and Floaters

Will Flanery, MD, Neda Frayha, MD, & Mike Weinstock, MD

Flashes and floaters can be a worrisome visual complaint. Ophthalmologist and comedian, Dr. Glaucomflecken (aka Will Flanery), is back to discuss how to evaluate patients with these complaints in the UC setting.

Pearls:

- ❑ New onset of flashes and floaters can represent an ophthalmologic emergency. Patients require evaluation by an ophthalmologist within 24 hours.
 - ❑ Flashes and floaters, especially in older patients, most likely represent vitreous detachment, which can be a precursor to retinal tear, vitreous hemorrhage, and, most concerning, retinal detachment.
 - ❑ Acute complaints of visual field cuts should raise concern for stroke, especially if visual fields in BOTH eyes are affected.
 - ❑ Performing a dilated fundoscopic exam with phenylephrine and tropicamide ophthalmic drops is safe and allows for any meaningful examination of the retina.
-
- Flashes refer to brief, lightning like patterns of illumination, most often in a patient's unilateral, peripheral visual field.
 - Flashes are a consequence of posterior vitreous detachment (PVD) which occurs predominantly in patients >50 years.
 - The more severe the flashes appear, the more tension the vitreous detachment is causing on the retina, which can lead to retinal tears.
 - Floaters are caused by the hardened and detached vitreous disrupting the path of light to the retina and can last for years.
 - Floaters can take many different shapes and may be described as strands, dots, spiderwebs, etc.
 - Patients can be reassured that, over time, the prominence and nuisance of floaters will dissipate.
 - Patients with new-onset flashes and floaters require an urgent dilated fundoscopic exam.
 - The greater the magnitude of floaters, the greater the likelihood of an underlying retinal tear.
 - Nearsightedness/myopia is a significant risk factor for retinal tear and detachment.
 - Many patients do not know if they are nearsighted, so this can be determined by looking at the refractive error on their glasses or contacts. A negative prescription (e.g. -1.75) implies nearsightedness.
 - Alternatively, if patients wear glasses or contacts, you can ask if they need them to drive.

- Other indicators of nearsightedness are needing corrective lenses beginning in their teenage years or if they have had LASIK.
 - History of prior retinal tear or detachment is also a significant risk factor.
- Retinal tears can be seen and treated with laser within 24 hours without risking permanent visual impairment.
- **Retinal detachments are a more significant ocular emergency than retinal tears.**
 - Orbital ultrasound, in the hands of experienced providers, is a sensitive and rapid means of ruling out retinal detachment.
- **When there is a high suspicion for retinal detachment, the patient should be seen immediately by an ophthalmologist to coordinate surgery within 24 hours.**
 - If the patient is being seen in the evening hours, arranging for ophthalmology clinic follow-up first thing the next morning is also reasonable.
- **Retinal tears do not typically cause more than flashes and floaters, however, if there is a “curtain” appearance or a visual field cut/partial loss of monocular vision, this should raise serious concern for retinal detachment.**
 - CVA/Stroke is a more common cause for partial vision loss than retinal detachment.
 - **Differentiating CVA from retinal detachment can be easily achieved on physical exam by determining if there are homonymous visual field cuts in both eyes.**
 - Binocular visual loss symptoms are suggestive of stroke.
- **The presence of vitreous hemorrhage in patients presenting with flashes and floaters is most commonly due to the concomitant presence of a retinal tear.**
 - Flashes and floaters without vitreous hemorrhage will only have a retinal tear in ~15% of cases.
 - **Vitreous hemorrhage can only be diagnosed by dilated fundoscopic exam.**
 - Vitreous hemorrhage is virtually indistinguishable from vitreous detachment on US.
- A non-dilated fundoscopic exam has little clinical utility.
 - **Dilating the eye with a drop of 2.5% phenylephrine and 1% tropicamide is almost always safe and will not affect the ophthalmologists subsequent ability to evaluate the patient.**

References:

1. Johnson D, Hollands H. Acute-onset floaters and flashes. *CMAJ* 2012;184(4):431. doi:10.1503/cmaj.110686
2. Hollands H, Johnson D, Brox AC, Almeida D, Simel DL, Sharma S. Acute-onset floaters and flashes: is this patient at risk for retinal detachment? *JAMA* 2009; 302(20):2243–2249. doi:10.1001/jama.2009.1714
3. Kahawita S, Simon S, Gilhotra J. Flashes and floaters: a practical approach to assessment and management. *Australian Family Physician* 2014; 43(4):201-203.

New GINA Guidelines for Asthma

Paul Simmons MD

Pearls:

- **The latest asthma guidelines (GINA 2019) have the following major changes:**
 - Asthma defined by medications necessary to control it rather than symptoms
 - No more intermittent category
 - For mild asthma, recommend ICS or ICS with LABA whenever there is an exacerbation of symptoms or they have to use a SABA
- **U.S. National Asthma Education and Prevention program guidelines (NAEPP), 2007:**
 - Prior guidelines in 2007 favored stepwise treatment approach starting at intermittent asthma to persistent asthma (mild, moderate, severe)
 - Start with short-acting bronchodilators (SABA) to long-acting bronchodilators (LABA), inhaled corticosteroids (ICS), muscarinic agonists, leukotriene inhibitors and oral steroids based on those steps of severity
- **Why the change in guidelines:**
 - People with even mild intermittent asthma or mild persistent asthma can have severe exacerbations
 - Studies have shown that inhaled corticosteroids can prevent severe exacerbations and preserve lung function
 - Five RCTS confirmed as needed ICS combined + bronchodilator is non-inferior to daily inhaled corticosteroid
 - Large study in Lancet 2019 of pragmatic study of albuterol prn + ICS was superior to daily ICS for prevention of exacerbations
- **The Global Initiative for Asthma Management and Prevention (GINA) guidelines, 2019:**
 - Defines severity of disease based on the medications you need to control it, not symptoms
 - No intermittent category → just mild (intermittent or persistent)
 - For mild asthma: recommend ICS or ICS with LABA when they have an exacerbation of symptoms or whenever they use their SABA
- **Caveats to the GINA guidelines:**
 - Not FDA approved yet
 - Don't apply to people under 12
 - The studies that GINA are based off of used a ICS-LABA turboinhaler device that is not available in the US
 - Cost may be prohibitive for some (ie: \$300 for Symbicort v. \$50 for albuterol)

REFERENCES:

1. Hardy J, Baggott C, Fingleton J, et al. Budesonide-formoterol reliever therapy versus maintenance budesonide plus terbutaline reliever therapy in adults with mild to moderate

- asthma (PRACTICAL): a 52-week, open-label, multicentre, superiority, randomised controlled trial. *Lancet*. 2019;394(10202):919–928. doi:10.1016/S0140-6736(19)31948-8
2. Global Initiative for Asthma. Global strategy for Asthma Management and Prevention (2019): Main Report. Available at: <https://ginasthma.org/gina-reports/>.
 3. National Asthma Education and Prevention Program (2007): Expert Panel Report Accessed at <https://www.nhlbi.nih.gov/sites/default/files/media/docs/asthsumm.pdf> on 17 February 2020.
 4. National Asthma Education and Prevention Program Expert Panel Report 3 Guidelines for the Diagnosis and Management of Asthma; 2007. <https://www.nhlbi.nih.gov/sites/default/files/media/docs/asthsumm.pdf>.
 5. Papi A, Brightling C, Pedersen SE, et al. Asthma. *Lancet*. 2018;391(10122):783-800. doi:10.1016/s0140-6736(17)33311-1
 6. 4.Amrol D. NEJM Journal Watch: Summaries of and commentary on original medical and scientific articles from key medical journals. www.jwatch.org. <https://www.jwatch.org/na50011/2019/09/26/new-approach-treating-patients-with-intermittent-mild>. Published September 26, 2019. Accessed February 17, 2020.

Medications in Breastfeeding

Elizabeth Lavery MD, Neda Frayha MD

Pearls:

- **Avoid the pump and dump method because it has real downsides and many medications are fine to use while breastfeeding.**
- **Check out the LactMed (free) and Infant Risk apps (paid) apps for more information about medication safety if breastfeeding.**
- **Breastfeeding in the US:**
 - 83% of women in the US breastfeed at some point during postpartum hospitalization but that drops off significantly at 3- and 6-months
 - Many women take medications immediately after delivery and it isn't known what the effects of those medications are
- **Pump and Dump:**
 - Many problems:
 - In order for a mother to maintain milk supply while not providing breast milk to her infant, she would need to continue pumping at the same frequency.
 - Pumping takes longer than feeding, incompletely empties the breasts, ties you to an electrical outlet and generates dishes
 - Incomplete emptying of the duct predisposed to mastitis
 - You still have to feed the infant
 - Formula can cause changes in the infant gut microbiome
- **Breast milk production and medications:**

- Milk production is a very dynamic process → drugs can diffuse in and out of breast milk. It is NOT reliant on emptying the breast.
- Two factors are important to consider: breast milk content and oral bioavailability
 - 1. Factors affecting drug diffusion into breast milk:
 - Maternal serum level of a medication (most important)
 - Size of drug molecule (larger has harder time diffusing in and out)
 - Lipid solubility
 - Protein binding
 - 2. Oral bioavailability
 - Relative infant dose (RID): measure of infant's dose (mg/kg/day) divided by mother's dose (mg/kg/day)
 - Pearl: RID < 10% is generally safe and accepted
- **Information on medications and breastfeeding:**
 - Most labels on medications do not have reliable information on breastfeeding because breastfeeding women were often excluded from the original safety studies.
 - Warnings from your electronic medical record or from pharmacists are often derived from the medication labels, so also not the most helpful
 - LactMED is a free website with evidence-based pharmacologic information
 - Infant Risk (app that costs \$9.99) is another resource
- **Antibiotics:**
 - Sulfamethoxazole-trimethoprim is acceptable in full term healthy infants but avoid in those with G6PD deficiency. Caution against long-term use.
- **Narcotics:**
 - Hydrocodone, oxycodone and hydromorphone have a risk of infant sedation so recommended dosage is <30mg per day
 - Avoid codeine and tramadol because some women may be rapid metabolizers that can lead to adverse effects with infants
 - NSAIDS are a safe alternative
- **Anticoagulants:**
 - DOACs are new so there's less evidence out there. RID < 1% but there's no information on impact to infants. Best to avoid if possible.
 - Warfarin is fine
 - Heparin doesn't enter the breast milk because it is such a large molecule it doesn't enter breast milk and also has no oral bioavailability
- **Off-label med use for breast milk production:**
 - Make sure to really diagnose the true issue: breast milk supply, overfeeding of the infant?
 - No medication or herb will make up for skipping pumps
 - Metoclopramide and fenugreek do not appear to have adverse effects in infants. Data for use isn't strong (not many studies that are well designed).
- **Imaging and radiation exposure:**

- CT scan or magnetic resonance will not make the milk radioactive
- Contrast agents for both CT and MRI have an RID < 1% and per ACOG are fine during breastfeeding

REFERENCES:

1. Byrne JJ, Spong CY. “Is It Safe?” - The Many Unanswered Questions about Medications and Breast-Feeding. *N Engl J Med* 2019;380(14):1296-7.
2. Breastfeeding Report Card.
<https://www.cdc.gov/breastfeeding/pdf/2018breastfeedingreportcard.pdf>. Published 2018.
3. Saha MR, Ryan K, Amir LH. Postpartum women’s use of medicines and breastfeeding practices: a systematic review. *Int Breastfeed J*. 2015;10(1). doi:10.1186/s13006-015-0053-6
4. Task force on research specific to pregnant women and lactating women: report to Secretary, Health and Human Services, Congress. Washington DC: National Institute of Child Health and Human Development, September 2018
(https://www.nichd.nih.gov/sites/default/files/2018-09/PRGLAC_Report.pdf)
5. Hale T. Drug entry into Human Milk | InfantRisk Center. www.infantrisk.com.
<https://www.infantrisk.com/content/drug-entry-human-milk>. Accessed March 24, 2020.
6. Medications and Mothers’ Milk Online: <https://www.medsmilk.com/pages/about>
7. Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK501922/>
8. *ACR Manual On Contrast Media 2020 ACR Committee on Drugs and Contrast Media*; 2020.
https://www.acr.org/-/media/ACR/Files/Clinical-Resources/Contrast_Media.pdf#page=106. Accessed March 24, 2020.
9. Eglash A, Leeper K. *The Little Green Book of Breastfeeding Management for Physicians & Other Healthcare Providers*. The Institute for the Advancement of Breastfeeding and Lactation Education; 6th edition (2017); 2017
10. Brodribb W. ABM Clinical Protocol #9: Use of Galactogogues in Initiating or Augmenting Maternal Milk Production, Second Revision 2018. *Breastfeeding Medicine*. 2018;13(5):307-314. doi:10.1089/bfm.2018.29092.wjb

Prior Authorizations

Ashish Patel MD, Neda Frayha MD

Pearls:

- **Prior authorizations is the process we go through for approval of treatments that are problematic as they may delay care, result in adverse events and require a great deal of staff time.**
- **Prior authorization:** A decision by your health insurer or plan that a health care service treatment plan, prescription drug or durable medical equipment is medically necessary, sometimes called prior authorization, prior approval or pre-certification, pre-authorization

or prior authorization. It is not a promise that your health insurance or plan will cover the cost.

- **Process:**
 - 1. Provider orders a test, drug or procedure. Routed to billing team who submits (usually fax) to insurance company to determine if pre-certification is necessary.
 - 2. Insurance company reviews the request
 - 3. Insurance company submits a judgement of approval or denial
 - 4. Provider can appeal the denial, usually phone conversation with another physician
 - 5. Schedule the appeals process
 - 6. If denied again, you appeal again to the company's medical director in writing. May take up to a month.
 - The physician may or may not be off the same specialty
 - Often times the physician has covering guidelines put out by the insurance company
 - The guidelines by the insurance company are opaque
- **Issues with the process:**
 - Denial of a recommendation the patient and doctor have already discussed is incredibly anxiety-producing
 - Unclear who the doctors are doing the peer reviews and their qualifications to be making these decisions
 - What is the liability of the insurance company or doctor if there is an adverse event
- **The impact of prior auths on our practice:**
 - Data from AMA 2018 study:
 - Resulted in delay or wait time by 3-5 business days
 - 91% reported these kind of delays in patient care and in terms of impact on clinical outcomes
 - 91% said prior auths have negative impact on patient clinical outcomes
 - 29% report prior auths have led to serious adverse events
 - 86% found prior auth burden to be high or extremely high
 - Physician and office staff spend 2 days per week on average doing prior auths
 - Data from American Society of Radiation Oncology
 - 63% noted delay of more the 4 days
 - Other data:
 - Delays in initiating cancer treatment were associated with 1.2-3.2% increase in mortality depending on cancer type per week
 - Community practices were longer than for academic practices
 - 66% of radiation denials were overturned on appeal
 - Health Affairs study in 2009 showed prior auths cost healthcare system \$21-31 billion based on average spend of \$68,000 per physician per year in prior auth process
- **Advocacy:**

- **Coalition of multiple health care groups that center around 5 principles:**
 - 1. Clinical validity
 - 2. Continuity of care
 - 3. Transparency and fairness
 - 4. Timely access and administrative efficiency
 - 5. Alternative and exemptions
- Other groups:
 - AMA has great information, toolkits → check out fixpriorauth.org
 - AAFP has a position statement
 - ACP has a Patients Before Paperwork initiative

REFERENCES:

1. Prior authorization research & reports. American Medical Association. <https://www.ama-assn.org/practice-management/sustainability/prior-authorization-research-reports>.
2. *2018 AMA Prior Authorization (PA) Physician Survey*. American Medical Association; 2019. <https://www.ama-assn.org/system/files/2019-02/prior-auth-2018.pdf>
3. Casalino LP, Nicholson S, Gans DN, et al. What Does It Cost Physician Practices To Interact With Health Insurance Plans? *Health Aff.* 2009;28(Supplement 1):w533-w543. doi:10.1377/hlthaff.28.4.w533
4. Morley CP, Badolato DJ, Hickner J, Epling JW. The Impact of Prior Authorization Requirements on Primary Care Physicians' Offices: Report of Two Parallel Network Studies. *The Journal of the American Board of Family Medicine*. 2013;26(1):93-95. doi:10.3122/jabfm.2013.01.12006
5. Khorana AA, Tullio K, Elson P, et al. Time to initial cancer treatment in the United States and association with survival over time: An observational study. Ahmad A, ed. *PLoS ONE*. 2019;14(3):e0213209. doi:10.1371/journal.pone.0213209

Paper Chase #1 - Open-label randomised pragmatic trial (CONTACT) comparing naproxen and low-dose colchicine for the treatment of gout flares in primary care

Tom Robertson MD, Steve Biederman MD

Roddy E, Clarkson K, Blagojevic-Bucknall M, et al. Open-label randomised pragmatic trial (CONTACT) comparing naproxen and low-dose colchicine for the treatment of gout flares in primary care. *Ann Rheum Dis*. 2019;79(2):annrheumdis-2019-216154. doi:10.1136/annrheumdis-2019-216154

Pearls:

- **There was no difference in patient pain between groups but naproxen was associated with fewer side effects.**
- **Objective:** To compare the effectiveness and safety of naproxen vs low dose colchicine for treating acute gout flares in primary care

- **Background:** first paper directly comparing colchicine versus NSAIDs both for efficacy and side effect profile for an acute gout flare
- **Method:** multicenter, open-label pragmatic randomized control trial of adults with gout flares from over 100 different primary care practices randomized to two different drug options, either naproxen with a loading dose Q8 hours for seven days or low-dose colchicine at 0.5 milligrams TID for four days
 - Exclusion criteria: ischemic heart disease, GFR < 30 or anticoagulant use
 - Primary outcome: change in baseline of pain intensity over the last 24 hours on a daily basis
- **Results:**
 - 350 patients included
 - No statistical differences in average pain scores
 - In the colchicine group, diarrhea and headache were more common
 - No statistical difference between the groups at four weeks of reporting recurrent flares or seeking further medical care
- **Bottomline:** There was no difference in patient pain between groups but naproxen was associated with fewer side effects.

Paper Chase #2 - Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial

Tom Robertson MD, Steve Biederman MD

de Koning HJ, van der Aalst CM, de Jong PA, et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. NEJM. 2020;382(6):503-513. doi:10.1056/nejmoa1911793

Pearls:

- **Lung cancer mortality was significantly lower among those who underwent CT screening.**
- **Objective:** To investigate if a low-dose CT screening can reduce lung-cancer mortality among male former and current smokers
- **Background:** 15% of patients with lung cancer are alive five years after diagnosis because nearly 70% of people have advanced cancer at diagnosis. USPSTF currently recommends screenings those age 55 to 80 with at least a 30 pack-year smoking history who currently smoke or have quit within the past 15 years
- **Method:** RCT done in Belgium and Netherlands of those aged 50-74 who were current smokers or heavy smokers. Randomized to four CT scans (year 0, 1, 3, 5.5) or none. Followed for 10 years and looked at incidence of lung cancer
- **Results:**
 - 16,000 patients
 - 2.5 deaths per 1000 person-years (CT group) v. 3.3 deaths per 1000 person-years (control group)

- Lung cancer mortality rate ratio of 0.76 in favor of screening
- **Bottomline:** Lung cancer mortality was significantly lower among those who underwent CT screening.

Paper Chase #3 - Risk of Acute Kidney Injury Following Contrast-enhanced CT in Hospitalized Pediatric Patients

Tom Robertson MD, Steve Biederman MD

Gilligan LA, Davenport MS, Trout AT, et al. Risk of Acute Kidney Injury Following Contrast-enhanced CT in Hospitalized Pediatric Patients: A Propensity Score Analysis. *Radiology*. 2020;294(3):548-556. doi:10.1148/radiol.2020191931

Pearls:

- **Hospitalized children with stable kidney function who underwent contrast CT scan had a similar frequency of AKI compared with matched unexposed group**
- **Objective:** To evaluate the association between IV iodinated contrast exposure and AKI in hospitalized pediatric patients with stable kidney function
- **Method:** Retrospective study of hospitalized patients under age 18 at a single academic center who had stable kidney function. One group underwent contrast-enhanced CT scan while the control group was propensity matched who did not undergo CT scan.
- **Results:**
 - 900 kids in each group
 - No statistical difference in the frequency of AKI between the two groups even stratifying by GFR > 60 or < 60
 - Low incidence of AKI in either group at around 2%
- **Bottomline:** Hospitalized children with stable kidney function who underwent contrast CT scan had a similar frequency of AKI compared with matched unexposed group

Paper Chase #4 - Effect of Sunscreen Application on Plasma Concentration of Sunscreen Active Ingredients

Tom Robertson MD, Steve Biederman MD

Matta MK, Florian J, Zusterzeel R, et al. Effect of Sunscreen Application on Plasma Concentration of Sunscreen Active Ingredients: A Randomized Clinical Trial. *JAMA*. 2020;323(3):256-267. doi:10.1001/jama.2019.20747

Pearls:

- **All 6 of the tested active ingredients were systemically absorbed and had plasma concentrations that surpassed FDA threshold for potentially waiving additional safety studies**

- **Objective:** To assess the systemic absorption and pharmacokinetics of the 6 active ingredients (avobenzone, oxybenzone, octocrylene, homosalate, octisalate, and octinoxate) in 4 sunscreen products under single and maximal use conditions
- **Background:** In February 2019 the FDA released a proposal for increased clarity in studies surrounding sunscreen. Of the 16 kinds of marketed active ingredients, only 2 (zinc oxide and titanium dioxide) are recognized as safe and effective, while 2 are not (PABA and trolamine salicylate).
- **Method:** Randomized adults to a group with a lotion, a group with an aerosolized spray, a group with non-aerosolized spray, and lastly a pump spray. Kept patients in clinic for 7 straight days and were not exposed to direct sunlight during that time. Measured blood levels of chemicals over the next 3 weeks.
- **Results:**
 - 48 people enrolled
 - No serious adverse events
 - All of the ingredients with all of the formulations had systemic absorption even after just one administration
 - Absorption into the blood was greater than the FDA threshold for potentially waiving additional safety studies for sunscreens
- **Bottomline:** All 6 of the tested active ingredients were systemically absorbed and had plasma concentrations that surpassed FDA threshold for potentially waiving additional safety studies

Paper Chase #5 - Screening for Hepatitis C Virus Infection in Adolescents and Adults USPSTF recommendation statement

Tom Robertson MD, Steve Biederman MD

US Preventive Services Task Force, Owens DK, Davidson KW, et al. Screening for Hepatitis C Virus Infection in Adolescents and Adults: US Preventive Services Task Force Recommendation Statement. JAMA. March 2020. doi:10.1001/jama.2020.1123

Pearls:

- **The USPSTF concluded with moderate certainty that screening for HCV infection in adults aged 18-79 has substantial benefit**
- **Objective:** To update the evidence related to screening for HCV infection
- **Background:** Hepatitis C virus is now associated with more deaths in the United States than the top 60 reportable infectious diseases combined, including HIV.
- **Method:** Systematic evidence review
- **Results:**
 - Moderate evidence supporting routine screenings for those 18-79 and more frequently for those with ongoing risk factors

- **Bottomline:** The USPSTF concluded with moderate certainty that screening for HCV infection in adults aged 18-79 has substantial benefit