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# Primary Care RAP January 2020 Written Summary

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EDUCATION

### **INTRO: WOUND DRESSINGS**

Matthew DeLaney MD, Paul Simmons MD, Neda Frayha MD

- The key to wound healing is the 3 W's: wet, warmth, well kept.
- Foam dressings generally meet these criteria with little downside other than cost, making them a good default for most wounds.
- What wounds need to heal:
  - WET not overly wet but also don't want to dry it out
  - WARMTH too much cooling at the cellular level can slow things down
  - WELL KEPT keep the world/bacteria off the wound
- What about wet-to-dry dressing?
  - Accounts for 40% of home health orders
  - 70% of the time this type of dressing is ordered inappropriately
  - True indication: mechanical debridement of a wound. When the dressing becomes dry and you remove it, the wound is debrided
  - For most other wounds, it does keep it wet but also dries out, causes cooling when initially applied and does not keep bacteria out
  - Bottomline: Wet-to-dry dressing not a go-to dressing for most wounds
- Good dressing for most wounds  $\rightarrow$  foam dressings
  - More than 300 companies
    - Some good examples Mepilex, Aquacel
  - Hits all 3 W's:
    - Wet absorbs 5-7 times weight in liquid, which means a couple of days of good moisture control
    - Warmth don't have to take off, which keeps the wound from cooling
    - Well kept fairly impermeable material
  - Few downsides other than cost more expensive than gauze wraps. You're not going to harm the patient and may be able to bridge them to a wound care clinic
  - Minimal good data to support one foam dressing or product over the other 0

 No special way to apply the dressings. Can usually wrap the foam with an ACE bandage or kerlix

#### **REFERENCE:**

- Ubbink DT, Brölmann FE, Go PM, Vermeulen H. Evidence-Based Care of Acute Wounds: A Perspective. Adv Wound Care (New Rochelle). 2015;4(5):286–294
- 2. Game FL, et al. A systematic review of interventions to enhance the healing of chronic ulcers of the foot in diabetes. Diabetes Metab Res Rev 2012; 28 Suppl 1:119.
- 3. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 2012; 54:e132.

### **Respiratory Failure: Pre- and Post-ICU**

#### Nirav Shah MD, Mizuho Morrison DO, Tom Robertson MD

- There are two types of respiratory failure: hypoxic and hypercarbic. Distinction between the two types determines differential diagnosis and treatment.
- The spectrum of respiratory support is nasal cannula → face mask +/- non-rebreather → high flow nasal cannula v. non-invasive ventilation (CPAP/BiPAP) → mechanical ventilation.
- Remember pulmonary rehabilitation (guided breathing exercises, upper body strengthening and dietary counseling) as an important tool both for post-disease exacerbation and as a means of prevention.
- Respiratory failure is a spectrum:
  - Clinical diagnosis
    - <u>Observation</u> accessory muscle use, difficulty completing a sentence due to breathlessness, sitting forward trying to catch their breath
  - Types narrows your differential and determines your treatment
    - 1. Hypoxic respiratory failure: low oxygen, no problem ventilating (getting rid of carbon dioxide)
      - Examples pneumonia, interstitial lung disease
      - Five causes of hypoxia
        - $\circ$  1. High altitude
        - 2. Hypoventilation
        - 3. Diffusion disorder
        - 4. Shunting
        - 5. V/Q mismatch
    - 2. Hypercarbic respiratory failure: elevated PCO2, more an issue of ventilation and not oxygenation (but they can have lower oxygen levels, too)

- **Treatment:** nasal cannula → face mask +/- non-rebreather → high flow nasal cannula v. non-invasive ventilation (CPAP/BiPAP)
  - Nasal Cannula
    - Fast
    - Readily available
    - Delivers up to 5-6L/min of oxygen
      - <u>Pearl</u>: pushing this amount of flow leads to turbulent flow instead of laminar flow → not really getting as much benefit and need to use a different method of delivery
  - Face Mask
    - Control the FiO2 (fractional content of oxygen) up to 60%
      - Room air is 21% FiO2
    - Can also use with a non-rebreather face mask that allows even higher oxygen content
      - A good temporizing measure until you figure out a next step. If used in someone with COPD can actually make things worse if left on.
  - High flow nasal cannula
    - Another way to increase both flow and oxygen content up to 100% FiO2
    - Also get some ventilation support
    - Does not have to be done in the ICU, and they may even be able to walk around
  - Non-invasive ventilation
    - Delivery up to 100% FiO2
    - Provides some ventilation support
    - Good evidence supports use in: acute exacerbations of COPD and CHF, immunosuppressed hypoxemic respiratory failure, obstructive sleep apnea, obesity hypoventilation syndrome, neuromuscular disease-related respiratory failure, asthmatics (data is limited)
    - Contraindications:
      - Hemodynamic instability
      - Poor seal on the mask (facial hair or facial trauma)
      - Impaired mental status
      - Nausea/vomiting, ileus, abdominal distension
      - Untreated pneumothorax
    - Other considerations:
      - Comfort for the patient it's like sticking your head out the window of a car driving 60 miles an hour
      - Spend 15-20 minutes in the room helping the patient get through the initial transition period
      - <u>Pearl</u>: Evaluate after 2 hours to ensure the patient is improving with this therapy
    - Types: CPAP and BiPAP
      - CPAP continuous positive airway pressure

- Used for sleep apnea to stent open airways and in CHF exacerbations to offload work of the heart
- BiPAP -
  - Used for ventilatory issues to help patients get rid of carbon dioxide by adding a differential expiratory pressure
  - Mainly used for COPD exacerbations
- Post-recovery from respiratory failure
  - Consider what was the cause of the exacerbation and address that issue (ie: environment, medications, infection)
  - Patients will be deconditioned after prolonged hospitalization and may need pulmonary rehab
    - Pulmonary rehab:
      - 2-3 times per week meetings to learn breathing exercises and other exercises to improve the strength of their upper body
      - Also learn about dietary modifications because carbohydrates generate carbon dioxide
      - Don't have to have an exacerbation to do pulm rehab. If they qualify for the program, the earlier the better!

### **References:**

- Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med*. 2000 May 4. 342(18):1301-8.
- Rochwerg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. *Eur Respir J.* 2017 Aug. 50 (2). <u>http://erj.ersjournals.com/content/50/2/1602426.long</u>

### **Cholestasis of Pregnancy**

### Matthew Zeitler MD, Neda Frayha MD

- ICP is a disease characterized by generalized pruritus without rash and liver function abnormalities typically in the 2nd or 3rd trimester of pregnancy.
- There are significant risks to the mother and fetus (including stillbirth) with no clear guidelines around monitoring or timing of delivery.
- Intrahepatic cholestasis of pregnancy (ICP):
  - Liver disease of pregnancy characterized by generalized pruritus without the presence of a rash + elevated serum bile acids +/- abnormal liver function tests
  - Most common pregnancy specific liver disease
  - Typically presents in 2nd or 3rd trimester with about 80% after 30 weeks

- Incidence ranges from 0.32% to 5.6%, higher incidence in Latina population with some reports as high as 15% in some Latin American countries
- Risk Factors:
  - Advanced maternal age (>35)
  - Multiple gestations
  - Conception after in vitro fertilization
  - Preexisting liver disease
  - Personal or family history of cholestasis
- Etiology:
  - Environmental
  - Genetic
    - Low dietary selenium and vitamin D
  - Hormonal estrogens have a cholestatic effect (ie: third trimester, ovarian hyperstimulation, twin pregnancies)
- Pathophysiology:
  - Bile acids are the end products of hepatic cholesterol metabolism and inherently cytotoxic. They may cause unbearable itching for the mother and increase risk for comorbid conditions for mother:
    - Gestational diabetes
    - Preeclampsia, HELLP
    - Acute fatty liver of pregnancy
  - $\circ$   $\,$  Also bad for the baby:
    - Intrauterine demise
    - Meconium-stained amniotic fluid
    - Preterm delivery
    - Neonatal respiratory distress syndrome
  - $\circ$   $\;$  The higher the bile acids, the more severe the complications for mother and baby
    - Bile acids > 40 = increased risk for meconium-stained amniotic fluid
    - Bile acids > 100 = increased risk for stillbirth
- Presentation:
  - Itching classically started in the palms and soles that then generalizes and is worse at night
  - Absence of rash differentiates from other dermatoses of pregnancy
  - May also have dark urine and pale chalky stools
  - Rarely you can get jaundice
  - If you see encephalopathy or other stigmata of liver failure, think about other causes of liver disease, NOT ICP
- Diagnosis:
  - Elevated bile acids in about 90% of cases → symptoms may precede lab abnormality by several weeks
  - Elevated AST/ALT/alk phos/bilirubin
    - Liver function tests are changed in pregnancy
  - Imaging (ultrasound, CT) should be normal

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- Differential:
  - Other dermatoses of pregnancy (if there is rash)
  - HELLP, preeclampsia, acute fatty liver of pregnancy
- Treatment:
  - Ursodeoxycholic acid or UDCA: 300-500mg twice daily but can titrate up to three times per day up to a max dose of 2000mg daily
    - Unclear mechanism but reduces bile acid in mom, baby and amniotic fluid
    - Start once you have bile acids > 10
    - Improves symptoms, lab abnormalities and potentially fetal outcomes
  - Other options (best in consultation with OB or maternal fetal medicine specialists):
    - Cholestyramine
    - Rifampin
    - S-Adenosyl Methionine
  - Antihistamines like hydroxyzine can also help with symptoms
- Timing of delivery:
  - Up to delivery would measure LFT's weekly because when bile acids > 100, there is a dramatic increase in risk of stillbirth
  - Very limited evidence and lots of practice variation around fetal monitoring and delivery → even with testing, nothing has been shown to predict who will have an adverse outcome
    - Typically at 34 weeks, weekly neonatal stress test or biophysical profiles
    - Instructions for mothers to do kick counts
  - Delivery is generally around 36 to 37 weeks that takes into account shared decision making
- Postpartum:
  - Typically symptoms and lab tests normalize days after delivery
  - Good to check labs 6-8 weeks to make sure things are normalizing
  - Very likely to recur (60-90%) but is hard to know if it will be as severe
  - Be careful with high dose estrogen-containing contraceptives because it can increase the risk of cholestasis

- 1. Puljic A, Kim E, Page J, Esakoff T, Shaffer B, LaCoursiere DY, et al. The risk of infant and fetal death by each additional week of expectant management in intrahepatic cholestasis of pregnancy by gestational age. *Am J Obstet Gynecol.* 2015 May;212(5):667.e1–5.
- 2. Geenes V, Chappell LC, Seed PT, Steer PJ, Knight M, Williamson C. Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: a prospective population-based case-control study. *Hepatology.* 2014 Apr;59(4):1482–1491.
- 3. Brouwers L, Koster MPH, Page-Christiaens GCML, Kemperman H, Boon J, Evers IM, et al. Intrahepatic cholestasis of pregnancy: maternal and fetal outcomes associated with elevated bile acid levels. *Am J Obstet Gynecol.* 2015 Jan;212(1):100.e1–7.

- Kawakita T, Parikh LI, Ramsey PS, Huang C-C, Zeymo A, Fernandez M, et al. Predictors of adverse neonatal outcomes in intrahepatic cholestasis of pregnancy. *Am J Obstet Gynecol.* 2015 Oct;213(4):570.e1–8.
- 5. Henderson CE, Shah RR, Gottimukkala S, Ferreira KK, Hamaoui A, Mercado R. Primum non nocere: how active management became modus operandi for intrahepatic cholestasis of pregnancy. *Am J Obstet Gynecol.* 2014 Sep;211(3):189–196.
- Bacq Y, Sentilhes L, Reyes HB, Glantz A, Kondrackiene J, Binder T, et al. Efficacy of ursodeoxycholic acid in treating intrahepatic cholestasis of pregnancy: a meta-analysis. *Gastroenterology.* 2012 Dec;143(6):1492–1501.
- Ozkan S, Ceylan Y, Ozkan OV, Yildirim S. Review of a challenging clinical issue: Intrahepatic cholestasis of pregnancy. World J Gastroenterol. 2015 Jun 21;21(23):7134–7141.
- 8. Williamson C, Geenes V. Intrahepatic cholestasis of pregnancy. *Obstet Gynecol.* 2014 Jul;124(1):120–133.
- UNC School of Medicine Center for Infant and Maternal Health. Intrahepatic Cholestasis of Pregnancy Algorithm [Internet]. UNC School of Medicine Center for Infant and Maternal Health. 2018 [cited 2019 May 23]. Available from: http://www.mombaby.org
- 10. Sabrina Craigo, MD. Intrahepatic cholestasis of pregnancy explained. SMFM Opinion Article. April 2011.
- 11. ACOG Committee Opinion: Medically Indicated Late-Preterm and Early-Term Deliveries. Feb 2019.
- 12. Royal College of Obstetricians and Gynecologists: Obstetric Cholestasis. Green-top Guideline No. 43. April 2011.

### Breast Cancer Screening: When to Begin?

### Alison Chetlen DO, Neda Frayha MD

- Dr. Chetlen leans into earlier annual mammography at age 40 given:
  - Improved technology (radiography and cancer treatment) since the time of the randomized control trials that societies still use to develop guidelines
  - Seriously flawed data from a Canadian trial that influenced USPSTF guidelines
  - New studies that have long-term follow-up showing clear mortality benefit from earlier screening
- Goals of screening to reduce deaths from breast cancer by:
  - Detecting earlier when smaller and when more effective to treat
    - If a woman waits until the cancer is palpable, usually it is larger and more likely to have spread to the lymph nodes (especially for premenopausal women)
  - Largest and longest running breast cancer trials found that the annual mammography screening cuts breast cancer deaths by <sup>1</sup>/<sub>3</sub> in all women ages 40 and over

- Studies are all Scandinavian with well over 100,000 women with follow-up times of 10-29 years
- All conclude that screening for breast cancer earlier results in earlier detection and reduced mortality
- Statistics that Dr. Chetlen uses to talk with patients and colleagues:
  - In the US, 1 in 8 women will be diagnosed with breast cancer over their lifetime
  - Number of breast cancer cases in 2017 was 253,000 with an estimated 40,600 deaths
  - No decade of life (ie: 40's, 50's, 60's) accounts for more than 25% of cancers diagnosed each year → there are no sudden jumps in incidence beyond the age of 50
  - Breast cancer incidence increases steadily with age
    - Age 40: 1 in 1000 will be diagnosed with breast cancer
    - Age 50: 2 in 1000 will be diagnosed with breast cancer
    - Age 60: 3 in 1000 will be diagnosed with breast cancer
  - The breast cancer found in women less than 40 are smaller in size, lower stage, less likely to receive chemotherapy
  - 75% of women diagnosed with breast cancer have no identifiable risk factors
- <u>Pearl</u>: Facts and figures can be found on the Society of Breast Cancer Imaging's website (<u>https://www.sbi-online.org/endtheconfusion/Home.aspx</u>)
- Guidelines:
  - <u>ACOG</u>: annual mammograms starting at age 40
  - <u>USPSTF, AAFP, ACP</u>: biennial screening mammography for women 50-74. Decision to start before age 50 should be an individual one. Women who place higher value of potential benefit over the potential harms may choose biennial screening between ages 40-49.
  - <u>American College of Radiology and Society of Breast Imaging</u>: women at average risk should begin annual screening at age 40. Women of higher risk and African American women should begin risk assessment and screening at age 30.
  - <u>American Cancer Society</u>: annual screening mammography at age 45, biennial at age 55.
- Benefits of early detection: Likely to exceed that of data from early randomized control trials because significant improvement since the 1970's
  - Technology has improved
    - Early trials relied on single-view mammogram → standard today is two-views which increased detection by 20%
    - New improvements in mammo grids, newer target materials, automatic exposure control
    - Film screen to digital mammography
    - 2D to 3D mammography (tomosynthesis)
  - Longer term trials more recently found a greater mortality benefit than older, shorter term trials
- Controversy around the USPSTF recommendations:

- In 2009, they argued the benefit of screening before 40 did not outweigh the potential harms
- Used data from randomized control trials to estimate a mortality reduction of only 15% in women aged 40-49 vs. 32% for women ages 60-69.
- The data included a significantly flawed Canadian national breast cancer screening study trial that showed no benefit for women women 40-60.
  - Randomization occurred after a physical exam and palpation of the breasts, which meant blinding was not guaranteed
  - Women with palpable masses should not have been included in the screening trial because screening by definition means asymptomatic women (ie: no breast mass)
  - The physicist rated the mammography quality as far below state of the art at the time (ie: older equipment with out-of-date technology leading to poorer detection of cancer)

• Concerns about overdiagnosis:

- We can't yet tell reliably which cancers will be aggressive and lead to death versus those cancers which are more benign
- Women do experience short-term anxiety regarding breast cancer screening in general but it rapidly declines and has no measurable effect on their health
  - 96% of women who experienced a false positive screening mammogram support screening and would continue screening mammography
  - False positive actually increased their intention to undergo future breast cancer screening
- A scenario of 1000 women receiving screening mammograms:
  - 100 are asked to come back for additional mammogram views, physical exam, ultrasound → 81 are called negative → 19 may undergo invasive needle biopsy → 5 diagnosed with breast cancer
  - Out of the 1000 women, 90% of those called back do NOT result in biopsy. Many centers offer same-day biopsy. Biopsy takes a few minutes with results returning in 2-3 days.
- To the reader than says, "You're talking to a radiologist what about financial gain?"
  - 3D mammography is <u>cost effective</u> compared with 2D with recent study reporting overall savings of \$28 per woman screened due to better images leading to less recall for further imaging and better less costly treatment (ie: early detection of breast cancer may mean no need for more expensive chemotherapy)

- American College of Obstetricians and Gynecologists. ACOG Statement on Breast Cancer Screening Guidelines. Published January 2016. <u>https://www.acog.org/About-ACOG/News-Room/Statements/2016/ACOG-Statement-on-Breast-Cancer-Screening-Guidelines</u>
- 2. American College of Radiology. ACR Appropriateness Criteria <sup>®</sup>: Breast Cancer Screening. Revised 2017. https://acsearch.acr.org/docs/70910/Narrative/

- American College of Radiology/Society of Breast Imaging. USPSTF Breast Cancer Screening Recommendations Could Endanger Women. Published December 2016. https://www.sbi-online.org/Portals/0/Position%20Statements/2016/SBI%20ACR%20Response%20to%20USPSTF%20Recommendations.pdf
- American College of Radiology/Society of Breast Imaging. New ACR/SBI Breast Cancer Screening Guidelines Call for Significant Changes to Screening Process. Published April 2018.

https://www.sbi-online.org/Portals/0/Position%20Statements/2018/New-2018-BCS-Guidelines.pdf

- 5. Arleo EK, Henrick RE, Helvie MA, Sickles EA. Comparison of recommendations for screening mammography using CISNET models. *Cancer* 2017;123(19):3673-3680.
- 6. Gabriel CA, Domchek SM. Breast cancer in young women. *Breast Cancer Res.* 2010;12(5):212. doi:10.1186/bcr2647
- 7. Gotzche PC, Jorgensen K. Screening for breast cancer with mammography. Cochrane Database of Systematic Reviews 2013, Issue 6. DOI: 10.1002/14651858.CD001877.pub5
- Hellquist BN, Duffy SW, Abdsaleh S et al. Effectiveness of population–based service screening with mammography for women ages 40 to 49 years. *Cancer* 2011;117:714-722. doi:10.1002/cncr.25650
- Hendrick RE, Helvie MA. United States Preventive Services Task Force Screening Mammography Recommendations: Science Ignored. American Journal of Roentgenology 2011;196(2):W112-116.
- 10. Kalager M, Zelen M, Langmark F, et al. Effect of Screening Mammography on Breast Cancer Mortality in Norway. N Engl J Med 2010; 363:1203-1210.
- Lind E, Nakamura A, Thalabard JC. No overdiagnosis in the Norwegian Breast Cancer Screening Program estimated by combining record linkage and questionnaire information in the Norwegian Women and Cancer study. European Journal of Cancer 2018; 89:102-112. <u>https://doi.org/10.1016/j.ejca.2017.11.003</u>
- Miller AB, Wall C, Baines CJ, et al. Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial. *BMJ* 2014; 348 :g366
- 13. Myers ER, Moorman P, Gierisch JM et al. Benefits and Harms of Breast Cancer Screening: A Systematic Review. JAMA 2015;314(15):1615-34.
- 14. National Cancer Institute's Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: Female Breast Cancer. https://seer.cancer.gov/statfacts/html/breast.html
- Oeffinger KC, Fontham ETH, Etzioni R, et al. Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society. JAMA 2015;314(15):1599–1614. doi:10.1001/jama.2015.12783
- Partridge AH, Goldhirsch A, Gelber S, Gelber RD. Chapter 85: Breast Cancer in Younger Women, in Harris JR, Lippman ME, Morrow M, Osborne CK. Diseases of the Breast, 5th edition, Lippincott Williams & Wilkins, 2014.
- 17. Pearlman MD. Breast cancer screening: is the controversy of benefits vs harms resolved? OBG Manag 2017;29(11):24-28.

https://www.mdedge.com/obgmanagement/article/150334/breast-cancer/breast-cancer-s creening-controversy-benefits-versus-harms

- Saadatmand S, Bretveld R, Siesling S, Tilanus-Linthorst MA. Influence of tumour stage at breast cancer detection on survival in modern times: population based study in 173,797 patients *BMJ* 2015;351:h4901
- Tabár L, Vitak B, Hsiu-Hsi Chen T, et al. Swedish Two-County Trial: Impact of Mammographic Screening on Breast Cancer Mortality during 3 Decades. Radiology 2011; 260(3):658-663.
- Tosteson ANA, Fryback DG, Hammond CS, et al. Consequences of False-Positive Screening Mammograms. JAMA Intern Med 2014;174(6):954–961. doi:10.1001/jamainternmed.2014.981
- 21. United States Preventive Services Task Force. *Final Recommendation Statement: Breast Cancer: Screening.* May 2019. https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/breast-cancer-screening1
- 22. Wilt TJ, Harris RP, Qaseem A, for the High Value Care Task Force of the American College of Physicians. Screening for Cancer: Advice for High-Value Care From the American College of Physicians. *Ann Intern Med* 2015;162:718–725. doi: 10.7326/M14-2326

### Marijuana and Lung Disease

### Kathryn Robinett MD, Tom Robertson MD, Neda Frayha MD

- If people have respiratory issues, smoking MJ is going to make it worse; but conclusive data linking it to COPD, pneumonia and lung cancer does not exist.
- Recreationally (ie: a bit on the weekends) is probably not putting you at risk for lung cancer based on the data we have currently.
- Marijuana use and COPD:
  - Hard to know if MJ use is an independent risk factor because some studies didn't really look at concurrent tobacco use. Other studies that did look at tobacco and MJ use with COPD did not find an association.
- Marijuana use and other lung changes:
  - Although no FEV1 does not drop, daily users of MJ still have same symptoms associated with chronic bronchitis: productive cough, shortness of breath
    - Still hard to tease out of with available data
  - There is some data showing people who smoke MJ have higher forced vital capacities potentially because they are taking deep breaths from water pipes and holding it in, much like physiology seen in swimmers. Unlike swimmer, this is not good for your lungs.
  - Increased risk of spontaneous pneumothorax and pneumomediastinum barotrauma
- Marijuana use and HIV

- 2019 prospective cohort study of 2700 men, half with HIV, found that MJ use was associated with increased risk of infectious pulmonary disease and chronic bronchitis independent of tobacco use. This risk was additive with tobacco use. No such risk in those without HIV.
  - Theory is that HIV may predispose someone to be more vulnerable to marijuana

### • Marijuana use and pneumonia

- Not an independent risk factor but the challenge is quantifying people who smoke "enough" MJ and enough data
- THC is an immunosuppressant
- MJ joints are often contaminated with aspergillus or some pathogenic gram-negative rod
- Biopsies of lung from those who are daily smokers show changes like goblet cell hyperplasia consistent with inflammation seen in tobacco smokers
- Marijuana use and lung cancer
  - One study showed a signal for an association while another showed synergy between MJ and tobacco use
  - $\circ$   $\:$  No study that shows MJ use as an independent risk factor
- Bottomline for primary care providers:
  - If people have respiratory issues, smoking MJ is going to make it worse
  - Recreationally (ie: a bit on the weekends) is probably not putting you at risk for lung cancer based on the data we have currently

- Aldington S, Harwood M, Cox B et al on behalf of the Cannabis and Respiratory Disease Research Group. Cannabis use and risk of lung cancer: a case-control study. *Eur Respir J* 2008; 31(2):280-286.
- 2. Chang SW, Wellmerling J, Zhang X, et al. The psychoactive substance of THC negatively regulates CFTR in airway cells. *Biochimica et Biophysica Acta* 2018; 1862(9):1988-1994.
- Ghasemiesfe M, Ravi D, Vali M, et al. Marijuana use, respiratory symptoms, and pulmonary function: a systematic review and meta-analysis. *Ann Intern Med* 2018; 169:106–115. doi: 10.7326/M18-0522
- Lorenz DR, Uno H, Wolinsky SM, Gabuzda D. Effect of marijuana smoking on pulmonary disease in HIV-infected and uninfected men: a longitudinal cohort study. *EClinicalMedicine* 2019; 7:55–64. doi:10.1016/j.eclinm.2019.01.003
- 5. Tashkin, DP. Marijuana and lung disease. *Chest* 2018; 154:653-63.
- Underner M, Urban T, Perriot J, et al. [Spontaneous pneumothorax and lung emphysema in cannabis users]. *Rev Pneumol Clin* 2018; 74(6):400-415. doi: 10.1016/j.pneumo.2018.06.003.



### Anaphylaxis

Jason Liebzeit MD, Neda Frayha MD

- Epinephrine (0.3-0.5mg) is the treatment for anaphylaxis. Everything else is adjunctive. Don't withhold that epinephrine if you're thinking anaphylaxis!
- **Clinical Scenario:** 27 year old woman who had driven in and she is red as a beet, is kind of diaphoretic throwing up actively, and the one thing that she keeps saying is "Don't intubate me. Don't intubate me."
- Anaphylaxis:
  - No one consistent definition → allergic reaction that involves multisystem severe reactions with life threatening symptoms like low blood pressure or throat swelling
  - Diagnostic criteria from The National Institute of Allergy and Infectious Disease includes 2 out of the 4 symptoms after exposure to either unknown or likely allergen:
    - Hypotension
      - Lightheadedness, dizziness
    - Involvement of skin or mucosal tissues
      - Hives
      - Urticarial rash
      - Swelling of eyes, lips tongue
    - Respiratory compromise
      - Wheezing
      - Shortness of breath
    - GI symptoms
      - Nausea
      - Vomiting
      - Diarrhea
- Presentation:
  - Adults tend to present with typical symptoms
  - <u>Pearl</u>: Children uncommonly manifest with any respiratory / airway involvement at their initial presentation. More likely to present with fatigue and lethargy, low blood pressure.
- Common causes:
  - 1. Food (0.3% to 7.5% of kids, 3 million people in the US)
    - Peanuts
    - Tree nuts
    - Shellfish
    - Fruits in particular mangoes
  - 2. Bee stings, wasp stings, fire ant bites
  - 3. Medications
- Pathophysiology:

- Cross-linking immunoglobulins after exposure to an antigen → mast cell degranulation → release of inflammatory modulators (histamine, platelet aggregator factor), cytokines
- Release of inflammatory modulators leads to:
  - Vasodilation
  - Swelling of lips and tongue
  - Smooth muscle contraction
  - Direct cardiotoxicity leading to decreased cardiac index
- Either Ig-E dependent (anaphylaxis) or Ig-E independent (anaphylactoid)
- Diagnosis:
  - Clinical diagnosis
  - Serum histamine and tryptase levels will be elevated but none of them will be helpful
- Treatment:
  - ABC's
  - Epinephrine
    - For adults: 1mg/ml 1:1000 solution 0.3 to 0.5mg, must be given intramuscularly NOT subcutaneously because it takes longer to reach peak concentrations (8 min IM v. 34 minutes SubQ)
    - For children, minimum 0.1mg (0.01mg/kg)
    - Spring-loaded epinephrine auto-injector use:
      - Remove the caps on both ends
      - Make sure you know which end of the device the needle comes out before sticking your hand on either end of the device
      - Press the end of where the needle comes on the lateral thigh
      - <u>Pearl</u>: designed to penetrate through clothing but ideally you would have bare clean skin
      - Administers 0.3mg of epinephrine intramuscularly
    - Repeat every 5-15 minutes as needed → if you find yourself repeating it more than once, you should be thinking about what is preventing the epi from working or that the reaction is severe enough to warrant a drip
  - Antihistamines and H2-blockers may help with cutaneous symptoms but not with GI or respiratory symptoms
  - Fluids if hypotensive
  - Albuterol in hopes of alleviating bronchospasm
  - Antiemetic if in GI distress (though the body's response to getting rid of the allergy may be vomiting in the case of something ingested)
  - Glucagon to reverse the effect of someone potentially on beta blockers who is not responding to epinephrine
  - Steroids does not treat the initial reaction but may help blunt a biphasic reaction
- Post-treatment
  - Epi lasts for about 1-2 hours so may be a good idea to watch them until it is out of system to make sure there isn't immediate return of symptoms

- <u>Biphasic reaction</u>: return of anaphylactic reaction anywhere from 1-72 hours, incidence is 3-20% with no clear indicator of who will have one or not
- Patient should always have an epi auto-injector on-hand
- Referral to allergist especially if unsure what triggered the reaction

### **REFERENCES:**

- 1. Sampson HA et al. Second symposium on the definition and management of anaphylaxis: summary report. Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol* 2006; 117(2): 391-397.
- 2. Brown GSA. Clinical features and severity grading of anaphylaxis. *J Allergy Clin Immunol* 2004; 114:371-376.
- 3. Yocum MW et al. Epidemiology of anaphylaxis in Olmsted County: a population-based study. J Allergy Clin Immunol 1999; 104: 452-456.
- 4. Yocum MW, Khan DA. Assessment of patients who have experienced anaphylaxis: a 3-year survey. *Mayo Clin Proc* 1994; 69: 16-23.
- 5. Thomas M, Crawford I. Best evidence topic report. Glucagon infusion in refractory anaphylactic shock in patients on beta-blockers. *Emerg Med J* 2005; 22: 272-273.
- 6. Simons FER. Anaphylaxis pathogenesis and treatment. *Allergy* 2011; 66 (Suppl. 95): 31–34.
- Anchor J. Appropriate use of epinephrine in anaphylaxis. *Am J Emerg Med* 2004; 22(6): 488-90.
- 8. Douglas DM, Sukenick E et al. Biphasic systemic-anaphylaxis—an inpatient and outpatient study. *J Allergy Clin Immunol* 1994; 93: 977-985.
- 9. Brazil E, MacNamara AF. "Not so immediate" hypersensitivity—the danger of biphasic anaphylactic reactions. *J Accid Emerg Med* 1998; 15: 252-253.

### **Medical Assistants, Please**

### Michael Baca-Atlas, MD, Neda Frayha MD

- Medical assistants are the largest occupational group in US ambulatory clinics with a broad scope of practice that varies by geography and clinic.
- Some of the key strategies for successfully working with MA's is to create a safe environment for open communication to build trust and foster mutual respect.
- **Reader question:** How do you respectfully navigate the relationship with your medical assistants?
- Medical Assistants (MA's):
  - Largest occupational group in US ambulatory clinics
  - Average annual salary is \$40,000 and many are hourly wage workers
  - Training is usually bachelor's or below
  - Approximately 15% are certified with the American Association of Medical Assistants
- Potential impact of MA's:

- 50% of patients leave a visit without understanding physician advice
- 25% of patients are unable to express their concerns at all
- 42% of primary care physicians reported lack of adequate time with patients
- Growth in this workforce driven by:
  - $\circ \quad \text{Complexity of office-based practice} \\$
  - Shift or nursing to the inpatient setting
  - Cost containment and focus on value-based care has led to a focus on team-based care
  - Relative ease of training and predictable hours while working in a field that helps people
- What can MA's do?
  - Out of scope: independent assessments, providing medical advice, administering medications to patients
  - In scope: scheduling appointments, managing records, billing insurance, calling in pharmacy refills, obtaining/recording vital signs, assisting in medical examinations, immunizations, obtaining basic labs tests and ECGs
- Ideas for working with MA's:
  - 2014 study from Annals of Family Medicine put forth a framework → Be nice and respectful to everyone!
    - Complex responsive process of relating between clinicians and MAs: humans are naturally reciprocal in our interactions so an environment that fosters mutual respect and communication is ideal
    - Trust and verify: build trust by socializing and creating a safe place for collaboration/communication so that there is less and less need to verify
  - Huddle before each patient
- Pitfalls to watch for:
  - Frustration around inequality of financial compensation
  - Feeling that MA's are not able to build trust
- Expanding role of MA's:
  - Ultrasound in point-of-care testing
  - New point-of-care lab testing
  - Detailed protocols that allow MA's to operate more independently within a defined scope
  - Compensation models for MA's doing high level work as a means to retain and provide professional advancement opportunities

- Ferrante JM, Shaw EK, Bayly JE, et al. Barriers and Facilitators to Expanding Roles of Medical Assistants in Patient-Centered Medical Homes (PCMHs). J Am Board Fam Med. 2018;31(2):226-235. doi:10.3122/jabfm.2018.02.170341
- Taché S, Chapman S. The expanding roles and occupational characteristics of medical assistants: overview of an emerging field in allied health. *J Allied Health*. 2006;35(4):233-237. https://www.ncbi.nlm.nih.gov/pubmed/17243439.

 Taché S, Hill-Sakurai L. Medical assistants: the invisible "glue" of primary health care practices in the United States? *J Health Organ Manag.* 2010;24(3):288-305. doi:10.1108/14777261011054626

### **Sexual Assault**

### Mizuho Spangler DO & Kari Sampsel MD

Pearls:

- Sexual assault victims are trauma patients and should be evaluated for associated injuries.
- □ The pelvic examination should not be deferred if there is concern for genitourinary trauma.

#### History

- Give yourself the time and space to allow the patient to tell you their story.
- Re-victimization occurs when a patient is shamed or judged for being a victim of sexual assault Do not use victim-blaming statements or perpetuate rape myths.
- Our responses can have a profound psychological impact on patients for years afterwards.

### Exam

- Remember that patients who are involved in a sexual assault are victims of trauma and should be evaluated thoroughly for other injuries.
- The pelvic exam should be best performed by a sexual assault expert who has access to a sexual assault evidence kit and can perform a forensic exam.
- Do not defer pelvic examination in order to preserve a forensic exam if you think the patient has a significant pelvic injury (i.e. vaginal laceration).

### Prophylaxis

- Pregnancy
  - Levonorgestrel (Plan B) can be used to prevent pregnancy within 72 hours
  - Ulipristal (Ella) is effective up to 5 days of intercourse
- Gonorrhea/Chlamydia
  - Azithromycin 1gm PO PLUS Cefixime 800 mg PO OR Ceftriaxone 250 mg IM.
- HIV
  - Post-exposure prophylaxis (PEP) must be started within 72 hours to be effective.
  - The quicker PEP is started the more likely it is to be effective
  - PEP includes dolutegravir, 50 milligrams, once a day along with the combination pill, emtricitabine and tenofovir, which is 200 milligram and 300 milligrams, respectively, once per day.
  - Patients should be discharged with a prescription for a 28 day course.

### **References:**

- ACEP Statement on Care of the Sexually Assaulted Patient in the ED https://www.acep.org/patient-care/policy-statements/management-of-the-patient-with-t he-complaint-of-sexual-assault/ #sm.0000aip8gzdhzdjds7v2a05t7wfic
- Evaluation and Management of the Sexually Assaulted or Sexually Abused Patient https:// www.acep.org/globalassets/new-pdfs/sexual-assault-e-book.pdf
- National Guidelines for Post Exposure Prophylaxis after non-occupational and occupational exposure to HIV: Australasian Society for HIV medicine http://www.ashm.org.au/pep-guidelines/ NPEPPEPGuidelinesDec2013.pdf
- Center for Disease Control and Prevention (CDC) http://www.cdc.gov/hiv/law/pdf/ Hivtranmsmision.pdf
- https://www.forensicnurses.org/search/custom.asp?id=2100
- Characteristics associated with sexual assault at mass gatherings. PMID: 26315648 PMCID: PMC4752638 DOI: 10.1136/emermed-2015-204689

## **Chiropractic Care**

### John Allen MD, Tom Robertson MD, Neda Frayha MD

Pearls:

- Chiropractic care for lower back pain has mixed data about its effectiveness compared to standard of care. It is generally safe (except for specific conditions listed below) with minimal side effects and is covered by insurance.
- **Reader question:** "What is the evidence behind chiropractic care for back pain?"
- Background:
  - Chiropractic is a form of complementary and alternative medicine with a broad scope of practice dependent on where you train and where you practice
    - Some states allow ordering of lab tests, interpreting lab tests, prescription of medications and delivery of babies
    - Some feel they are primary care providers
  - Started in 1895 with the idea that misregulation of the spine due to subluxation / misalignment led to disease. Reduction of that subluxation through spinal adjustment leads to better health.

### • Two schools of thought:

- 1. Vitalism innate intelligence of the body and ability to heal. Changes in nerves due to spine subluxation lead to organic disease like diabetes and hypertension
  - May dissuade patients from seeking allopathic medical treatment
  - May also not believe in germ theory so dissuade against vaccination
- 2. Mixed chiropractic care blend of modern medicine that is complementary to allopathic care
- Training and education:
  - Minimum of 3 years of undergrad with a minimum 3.0 GPA in the sciences for a 4-year chiropractic school

- 4000 hours of hands-on clinical training
- Treatment types: manipulation and mobilization
  - <u>Manipulation</u>: vigorous adjustments, shorter distance, high velocity applied directly to a spinal process
  - <u>Mobilization</u>: gentler, something that could be resisted if uncomfortables
- Literature for chiropractic care:
  - $\circ$   $\$  Lots of literature of varying quality
  - Some good evidence for the following indications:
    - Headache three arm randomized blinded trial showed both the spinal manipulation and sham arms had improvements in headache over medication along, suggesting a large placebo effect.
    - Back pain decent evidence for acute back pain that is not better than standard care; VA systematic review of evidence found trend towards effect for spinal manipulative therapy with a good deal of study heterogeneity. No predictive decision tools around which patients may benefit and which will not.
  - AAFP and ACP support spinal manipulation therapies of osteopathic colleagues but have not recommended chiropractic care for chronic or acute low back pain
- Safety?
  - Patients who should NOT seek our chiropractic care:
    - C1C2 instability
    - Rheumatoid arthritis
    - Osteoporosis
    - Known fractures
    - Multiple myeloma
    - Paget's disease
    - Spinal tumors
    - Unstable bleeding disorders
  - 40-60% of patients are going to experience some sort of adverse outcome, most of them minor (ie: soreness at site of manipulation, headache)
  - $\circ$   $\;$  Other risk: vertebrobasilar accident and dissections  $\;$
- Payment?
  - Covered by almost all insurances

- 1. Ernst E. Spinal manipulation: Its safety is uncertain. *CMAJ: Canadian Medical Association Journal*. 2002;166(1):40-41.
- Miangolarra-Page JC. Methodological Quality of Randomized Controlled Trials of Spinal Manipulation and Mobilization in Tension-Type Headache, Migraine, and Cervicogenic Headache. *Journal of Orthopaedic and Sports Physical Therapy*. 2006.
- 3. Chaibi A, Benth JŠ, Tuchin PJ, Russell MB. Chiropractic spinal manipulative therapy for migraine: a three-armed, single-blinded, placebo, randomized controlled trial. *European Journal of Neurology* 2016;24(1):143–53.

- 4. Jüni P, Battaglia M, Nüesch E, *et al.* A randomised controlled trial of spinal manipulative therapy in acute low back pain. *Annals of the Rheumatic Diseases* 2009;68:1420-1427.
- 5. Gouveia LO, Castanho P, Ferreira JJ. Safety of Chiropractic Interventions. *Spine* 2009;34(11).
- Hurwitz EL, Morgenstern H, Vassilaki M, Chiang L-M. Frequency and Clinical Predictors of Adverse Reactions to Chiropractic Care in the UCLA Neck Pain Study. *Spine*. 2005;30(13):1477-1484
- 7. Rothwell DM, Bondy SJ, Williams JI, Bousser M-G. Chiropractic Manipulation and Stroke : A Population-Based Case-Control Study. *Stroke* 2001;32(5):1054–60
- 8. Cote P, Cassidy JD, Haldeman S, et al. Spinal manipulative therapy is an independent risk factor for vertebral artery dissection. *Neurology* 2003;61(9):1314–5.
- Flynn T, Fritz J, Whitman J, et al. A Clinical Prediction Rule for Classifying Patients with Low Back Pain Who Demonstrate Short-Term Improvement With Spinal Manipulation. *Spine*. 2002;27(24):2835-2843.
- The Effectiveness and Harms of Spinal Manipulative Therapy for the Treatment of Acute Neck and Lower Back Pain: A Systematic Review. Department of Veterans Affairs Evidence-Based Synthesis Program. April 2017.
- Qaseem A, Wilt TJ, McLean RM, Forciea MA, for the Clinical Guidelines Committee of the American College of Physicians. Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain: A Clinical Practice Guideline From the American College of Physicians. *Ann Intern Med.* 2017;166:514–530. doi: 10.7326/M16-2367
- 12. Globe G, et al. Clinical Practice Guideline: Chiropractic Care for Low Back Pain. *Journal of Manipulative and Physiological Therapeutics* 2016;39(1):1-22.

### Paper Chase #1 - Outcomes Associated with Apixaban Use in Patients with End-Stage Kidney Disease and Atrial Fibrillation in the United States Tom Robertson MD, Steve Biederman MD

Siontis KC, Zhang X, Eckard A, et al. Outcomes Associated With Apixaban Use in Patients With End-Stage Kidney Disease and Atrial Fibrillation in the United States. Circulation. 2018;138(15):1519-1529. doi:10.1161/CIRCULATIONAHA.118.035418

- In ESRD patients on dialysis with atrial fibrillation, apixaban was associated with a lower risk of major bleeding compared with warfarin.
- **Objective:** To determine patterns of apixaban use and its outcomes in dialysis-dependent patients with ESRD and atrial fibrillation.
- **Method:** Retrospective cohort analysis of Medicare patients with ESRD who were taking off-label apixaban for atrial fibrillation compared to matched controls on warfarin.
- Results:
  - 25,000 patients

- Stroke event rate and survival free of strokes was similar with hazard ratio favoring apixaban non-significantly
- Statistically significant lower rates of bleeding in apixaban group
- Trend toward reduced mortality in the apixaban group
- Standard dose 5mg BID had lower rates of stroke and embolic events while the 2.5mg BID had lower rates of bleeding and non-inferior rates of stroke or embolic events compared to warfarin
- **Bottomline:** In ESRD patients on dialysis with atrial fibrillation, apixaban was associated with a lower risk of major bleeding compared with warfarin.

### Paper Chase #2 - An Open, Randomized, Comparative Study of Oral Finasteride and 5% Topical Minoxidil in Male Androgenetic Alopecia Tom Robertson MD, Steve Biederman MD

Arca E, Açikgöz G, Taştan HB, Köse O, Kurumlu Z. An open, randomized, comparative study of oral finasteride and 5% topical minoxidil in male androgenetic alopecia. Dermatology (Basel, Switzerland). 2004;209(2):117-125. doi:10.1159/000079595

- Both drugs were effective and safe in treating androgenic alopecia but oral finasteride was more effective.
- **Objective:** To compare the efficacy of oral finasteride and topical minoxidil for males with androgenic alopecia
- **Background:** Androgenic alopecia is the most common form of male pattern baldness in men 95% of the time. Pathogenesis involves increased conversion of testosterone to dihydrotestosterone (DHT), which is inhibited by finasteride
- Method: open randomized control trial of finasteride v. minoxidil for treatment of androgenic alopecia
- Results:
  - 60 patients
  - 80% of the finasteride group had hair growth compared to just 52% of the minoxidil group
  - Side effects were minimal and went away after discontinuation of drug
- **Bottomline:** Both drugs were effective and safe in treating androgenic alopecia but oral finasteride was more effective.

## Paper Chase #3 - Polypill for Cardiovascular Disease Prevention in an Underserved Population

### Tom Robertson MD, Steve Biederman MD

Muñoz D, Uzoije P, Reynolds C, et al. Polypill for Cardiovascular Disease Prevention in an Underserved Population. N Engl J Med. 2019;381(12):1114-1123. doi:10.1056/nejmoa1815359

- A polypill-based strategy led to greater reduction in systolic blood pressure and LDL cholesterol level compared with usual care in a socioeconomically vulnerable minority population as well as reduction in prescription of other blood pressure and lipid medications.
- **Objective:** To evaluate the efficacy of a polypill containing atorvastatin amlodipine losartan and hydrochlorothiazide for lowering blood pressure and LDL
- Background:
  - Fewer than half of adults with hypertension are being treated and have their hypertension controlled
  - <sup>1</sup>/<sub>3</sub> of adults are eligible in the US for statin therapy with only a minority receiving it
- **Method:** Two group open label randomized control trial comparing polypill with usual care. Participants were adults without a known history of cardiovascular disease, stroke, cancer, or diabetes
  - Polypill =
    - Atorvastatin 10mg
    - Amlodipine 2.5mg
    - Losartan 25mg
    - HCTZ 12.5mg
- Results:
  - 300 patients in each arm
  - 96% black
  - 75% had annual income below \$15,000
  - Median adherence was 86%
  - In the polypill group:
    - 44% had a reduction in their blood pressure or lipid medication
    - 9mmHg reduction in sBP
    - 15mg/dL reduction in LDL
- **Bottomline:** A polypill-based strategy led to greater reduction in systolic blood pressure and LDL cholesterol level compared with usual care in a socioeconomically vulnerable minority population as well as reduction in prescription of other blood pressure and lipid medications.

# Paper Chase #4 - Effect on Treatment Adherence of Distributing Essential Medicines at No Charge - The CLEAN Meds Randomized Clinical Trial

Tom Robertson MD, Steve Biederman MD

Persaud N, Bedard M, Boozary AS, et al. Effect on Treatment Adherence of Distributing Essential Medicines at No Charge. JAMA Intern Med. October 2019. doi:10.1001/jamainternmed.2019.4472

### Pearls:

- There was increased adherence and improvement in some but not all disease-specific outcomes.
- **Objective:** To determine whether providing essential medicines at no charge to outpatients who reported not being able to afford medicines improves adherence
- **Background:** Estimated 40-60% of patients are not adherent to their medications with one common cited barrier being cost.
- Method: multicenter unblinded randomized control trial in Canada. Adults who self-reported med non-adherence related to costs, randomized them to receive essential meds for free versus usual medication access. Followed patients for one year looking at adherence (self-report) as well as disease-specific markers (ie: A1c, LDL, systolic blood pressure)
- Results:
  - 800 patients
  - 38% adherence in the free medicine group, 27% in the usual care group
  - Disease-specific markers:
    - sBP lower by 7mmHg
    - LDL unchanged
    - A1c down 0.38% (p-value of 0.05)
- **Bottomline:** There was increased adherence and improvement in some but not all disease-specific outcomes.

### Paper Chase #5 - Frequently Hospitalized Patients' Perceptions of Factors Contributing to High Hospital Use

### Tom Robertson MD, Steve Biederman MD

O'Leary KJ, Chapman MM, Foster S, O'Hara L, Henschen BL, Cameron KA. Frequently Hospitalized Patients' Perceptions of Factors Contributing to High Hospital Use. J Hosp Med. 2019;14(9):E1-E6. doi:10.12788/jhm.3175

### Pearls:

• Participants perceived fluctuations in their course to be related to psychological, social and economic factors. They also found episodes of illness uncontrollable and unpredictable.

- **Objective:** To obtain patients' perspectives of factors associated with the onset and continuation of high hospital use
- **Method:** Semi-structured interviews of patients who were frequently readmitted and specifically in this study broken down between sickle cell and non sickle cell patients
- Results:
  - 26 enrolled (10 with sickle cell and 16 without)
  - Themes:
    - All patients had at least one major chronic medical problem
    - Psychological stress, social support and financial constraints were identified as factors influencing the course of their illness
    - Having social support was perceived as helpful in keeping them out of the hospital
    - Participants found their symptoms to be sudden, unpredictable and outside their control
    - They tried to control their symptoms and only sought care only when clear this approach was not going to work
    - None had a desire to be back in the hospital
- **Bottomline:** Participants perceived fluctuations in their course to be related to psychological, social and economic factors. They also found episodes of illness uncontrollable and unpredictable.