RAP #4, 12/15 Regions RAP (Heme/ Onc)

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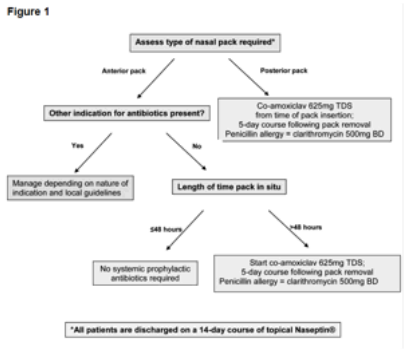
Influenza & Epistaxis (CoreEM 10/19/15, Authored by Anand Swaminathan) - Reviewed by Brad Hansen

- Vent basics: Link in show notes to EMCrit dominating the vent
  - http://emcrit.org/lectures/vent-part-1/
  - http://emcrit.org/podcasts/vent-part-2/
- Respiratory viral panel testing
  - Test done for cohorting patients when admitted and to treat with Tamiflu
  - Rapid turn around
  - High specificity but low sensitivity (no citation)
    - Only studied when endemic flu present and flu symptoms
    - Can miss patients if cohort only + tests
  - Costly if we test everyone
- Tamiflu
  - Bottom line reduce symptoms 12-16 hours, lots of side effects
  - Only uses if patient is critically ill, questionable benefit
  - http://www.aliem.com/neuraminidase-inhibitors-influenza/
    - Symptoms shortened by 16.8 hours
    - No difference in admissions, pneumonia, transmission prophylaxis, or other complications
    - Side effects: Nausea (NNH 28), Vomiting (NNH 22), Psychiatric events (NNH 94), Headache (NNH 32)
  - http://www.emlitofnote.com/2015/02/which-review-of-tamiflu-data-do-you.html
- Epistaxis
  - Posterior bleeds
    - Uncommon 5-10% of all epistaxis
    - Posterior sphenopalatine arteries or rarely internal carotid
    - Difficult to identify
      - Recent nasal surgery, brisk bleeding, dripping into oropharynx
      - Bleeding not stopped with anterior packing
    - Rapid rhino for tamponade
    - Low resources? Foley catheter
      - Insert in nose until tip visualized in posterior pharynx
      - Inflate balloon and pull back
      - Temporizing until ENT or IR in to fix bleed
  - Anterior bleeds
    - Topical TXA?
      - 1 RCT: http://www.ncbi.nlm.nih.gov/pubmed/23911102 (AJEM 2013)
      - 216 patients with anterior epistaxis, randomized clinical trial
      - Topical application of 500 mg TXA in 5 cc's vs. anterior nasal packing
      - Bleeding cessation w/in 10 min (71% TXA, 31.2% packing)
      - Discharge w/in <2 hours (95.3% TXA, 6.4% packing)
      - Rebleed w/in 1st 24 hours (4.7% TXA, 12.8% packing)
      - Rebleed w/in 1 week (2.8% TXA, 11% packing)
      - Patient satisfaction (8.5 TXA, 4.4 packing) (1-10 scale, higher is better)
      - TXA application:
        - "15-cm piece of cotton pledget soaked in injectable form tranexamic acid (500 mg in 5 mL) was inserted in the nostril of the bleeding side. It was removed after bleeding arrest was determined by examining the blood-soaked pledgets and the oropharynx."
    - Prophylactic antibiotics for nasal packing?
      - Concerned for acute otitis media, sinusitis, toxic shock syndrome
      - May cause diarrhea, allergic reactions, antibiotic resistence
      - Does not routinely use antibiotics for anterior packing
      - Will consider antibiotics if immunosuppressed, diabetes, etc
      - 3 relevant articles, poor studies, no adequate evidence for prophylactic antibiotics in anterior bleeds (no evidence whatsoever for posterior bleeds)
        - http://www.ncbi.nlm.nih.gov/pubmed/2923686 (Archives Otolaryngeal Head and Neck Surgery, 1989)
          - 20 patients prospective, randomized, blinded, placebo controlled
          - Packing examined after removal, foul smelling and heavily colonized with gram- bacteria in placebo, odor free and lightly colonized in antibiotic group
        - http://www.ncbi.nlm.nih.gov/pubmed/22214602 (Journal of Laryngology and Otology, 2012)
          - Prospective 6 month study of 149 patients, first 3 months antibiotics, final 3 months no antibiotics
          - Monitoring for otitis media, sinusitis, toxic shock via exam and survey
          - No patients with evidence of any infection

- http://www.ncbi.nlm.nih.gov/pubmed/23317726 (Annals of the Royal College of Surgeons, 2013)
  - 57 patients, 2 audit cycles, 1st cycle usual care, 2nd cycle new antibiotic guideline
  - Telephone surveys at 6 weeks to assess infective symptoms, re-bleeding rates, re-admission rates



  - Systemic antibiotic use decreased by 58.2%, no statistically significant increase in any of the outcome measures

- **Evaluation**
  - AIR Grade:

Tier 1: BEEM Rater Scale	Score-choose only 1	Tier 2: Content accuracy	Score-choose only 1	Tier 3: Educational Utility	Score-choose only 1	Tier 4: EBM	Score-choose only 1	Tier 5: Referenced	Score-choose only 1
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Useless information	○	Yes, many concerns from many inaccuracies	○	Low value: No valuable pearls	○	Not EBM based, only expert opinion (and thus more biased)	○	No	○
Not really interesting, not really new, changes nothing	○		○		○		○		○
Interesting and new, but doesn't change practice	○	Yes, a major concern about few inaccuracies	○	Yes, but there are only a few (1-2) valuable or multiple (>=3) less-valuable educational pearls	○	Minimally EBM based	○		○
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Your Score	6		6		4		5		6

Supratherapeutic INR (ALiEM PV Card 8/10/12, Authored by Michelle Lin) - Reviewed by Maria Bergstrand

- If interested check out these Paucis Verbis Cards (Quick, helpful clinical overviews that can be downloaded to evernote, dropbox, AgileMD; look on the top right of the website for directions)
- Guidelines for management of patients with supratherapeutic INR
  - INR ≤10 and no bleeding – hold Coumadin, restart INR when therapeutic
  - INR > 10 and no bleeding – hold Coumadin, oral Vitamin K (2.5 mg)
  - Major bleeding – hold Coumadin, IV vitamin K 5-10 mg, four factor PCC
  - Minor bleeding – hold Coumadin, oral vitamin K and 15 cc/kg FFP
  - Pearl: No FFP unless high INR with minor bleeding
  - Limitations: All grade 2B or 2C recs. Only RCT done in patients with INR 4.5-10 without bleeding.
- What causes increased bleeding risk when on Coumadin?
  - NSAIDS
  - Antiplatelet agents (aspirin and plavix)
  - Clotrimoxazole
  - Antibiotics (especially quinolones)
  - Pearl: Risk of ICH doubles for every 1 point increase in INR
- Why would you have supratherapeutic INR >6
  - Greatest risk: advanced malignancy
  - Acetaminophen intake
  - New medications (60% of cases due to abx)
  - Extra Coumadin intake
  - Decreased oral intake (decreased vitamin K)
  - Diarrhea

- Alcohol use (stimulates p450 system)

- **Evaluation**
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Your Score	6		6		3		5		7

Thrombosis Infographic (Boring EM 10/19/15)/ NOAC Infographic (Boring EM 7/27/15) - Reviewed by Brian Hahn

- Infographic 1: Thrombosis and Hemostasis
  - Breaks it down into arterial (MI and stroke) and venous (DVT and PE)
  - Discusses treatment of arterial with antiplatelets and venous with anticoagulants
  - Provides pathophysiology behind these as well
  - Also has a good review of ASA, clopidogrel, heparin, and warfarin on mechanism of action and tying it back into what is specifically being targeted
  - Overall it is very easy to understand and broken down well. It helps to remind you about the differences between arterial and venous clots and why we treat them differently. Its not terribly clinical or practice changing as these are things we were already doing. This is more of a simple way to look at these things when you are just learning, or perhaps a way to explain things to patients if they have questions about blood clots.
  - AIR Grades (3,5,5,3,1) (no sources listed)

- Infographic 2: New Oral Anticoagulants (NOACs)
  - VTE Epidemiology
  - Breaks down what the aims of therapy are in the Immediate (heparin/lovenox/fondaparinux), Long term and extended (warfarin) timeline and addresses most of the familiar problems of warfarin including bleeding risk, inconsistent levels, diet restriction, and frequent monitoring
  - NOACs as a potential option instead of warfarin
  - Direct thrombin (Dabigatran) and Factor Xa (Apixaban, Rivaroxaban) inhibitors
    - These have been validated in phase III trials for venous thromboembolism and stroke prevention in non-valvular atrial fibrillation
    - Pros: Some data to support less bleeding risk, fewer drug/food interactions, faster onset without the need for frequent monitoring
    - Cons: Expensive, lack of reversal (for now, see below), renal clearance, and not currently indicated anticoagulation for artificial heart valves
  - Nice chart breakdown breakdown comparing each NOAC warfarin
  - 2nd chart with suggestions/ considerations on when to use the different anticoagulants including patients with poor access to anticoagulation clinic, poor compliance, pregnancy, renal/ liver impairment, active cancer, etc.
  - Overall this is a good intro to the new anticoagulants. It has good explanations of their pros/cons and provides good suggestions for when to use them. This is more clinically relevant and practice influencing information than the first one.

- **Evaluation**

- AIR Grade:

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Your Score	5		5		5		3		1

Iron Toxicity (EMBlog Mayo Clinic 5/12/14, Authored by Daniel Baalmann) - Reviewed by Alan Sazama

- Iron is NOT benign.
  - High incidence of overdose
  - Something we need to know about.
- 3 main forms of iron:
  - Ferrous Gluconate (12% elemental iron)
  - Ferrous Sulfate (20% elemental iron)
  - Ferrous Fumarate (33% elemental iron)
  - A mnemonic that was mentioned from the tox folks:
    - 10, 20, 30; Oh Good (Gluconate), Oh F*** (Fumarate)
- Amount of elemental iron ingestion:
  - <20 mg/kg: usually not clinically significant
  - 20-60 mg/kg: moderate toxicity
  - >60 mg/kg: severe toxicity
- Mechanism of toxicity
  - Free radical formation
  - Uncouples oxidative phosphorylation
- Clinical Presentation (Of note, hours since ingestion not as big a deal as which clinical stage they present in)
  - Stage 1 (30 min-6 h): Nausea, vomiting, diarrhea, GI bleed
  - Stage 2: (4-12 h)Loving life, clinical improvement
  - Stage 3: (6-72 h) Coma, shock, coagulopathy, Hyperventilation, Seizures
  - Stage 4: (12-96 h)Liver failure, Jaundice, Hypoglycemia
  - Stage 5: (2-4 weeks)Pyloric stenosis, small bowel obstruction
- Diagnostics
  - CBC: can show leukocystosis (remembering that this is incredibly non-specific)
  - BMP: can show metabolic acidosis, hypoglycemia
  - Type and screen (concern of possible GI hemorrhage)
  - Serum iron (>500 mcg/dL----BADNESS)
  - Plain films: Radioopaque tablets can be seen
    - CHIPES mnemonic for radioopaque tablets
      - C-calcium carbonate,chloral hydrate
      - H- Heavy metals- mercury, lead
      - I- Iron and Iodine
      - P-Phenothiazines
      - E- Enteric coated pills
      - S-Sustained release preparations.
- Treatment
  - ABCs
  - No real role for activated charcoal
  - Potential role for whole bowel irrigation (500 cc/hr for children, 2 L/hr adults of go lytely).
  - No role for dialysis
  - Antidote: Deferoxamine

- Deferoxamine Indications:
  - >60 mg/kg ingestions
  - >350 mcg/dL serum iron level
  - shock, coma, etc.
- Dose: 15mg/kg /h IV (6 g/day max dose)
  - Keep giving until urine is no longer orange (Iron turns the urine orange)

- **Evaluation**
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Your Score	7		5		7		5		1

Calf Clots (ERCast 9/2/15, Authored by Rob Orman) - Reviewed by Sakib Motalib

- Propagation to proximal veins
  - Without anticoagulation: around 15%. Wide variation in numbers
  - Propagation with anticoagulation: around 2%
  - Propagation is probably higher with risk factors such as malignancy and an unprovoked clot
  - Caveat: isolated gastrocnemius and soleal vein clots progress at about 3% untreated. Felt to be lower risk than the other deep veins of the calf. Lower risk of extension. No clear evidence on what to do.
- Pulmonary Embolism
  - Without anticoagulation up to 6%
  - With anticoagulation 0-6%, biggest study 3%, but PEs mostly asymptomatic
  - 1 reported fatal PE, but unknown if this patient was anticoagulated
- Recurrence
  - Short term recurrence without treatment: up to 30%
  - Short term treatment with treatment 0-3%,
  - Recurrence is higher if two calf veins involved, increased clot burden
- Compression stockings and post thrombotic syndrome (PTS)
  - Incidence of post thrombotic syndrome in proximal DVTs is around 50%, depending on the source you read. In calf DVTs, it's lower: somewhere around 10 to 24%.
  - There is good evidence that compression stockings can decrease the incidence of PTS. The big lancet study that suggested no benefit wasn't well designed (blind side of study also got socks)
- Duration of Treatment
  - For proximal DVTs, 3 months of treatment but for calf DVTs, no benefit found if treatment extended beyond 6 weeks.
  - The ACCP, American College of Chest Physicians, kind of recommends 6 weeks. Mostly of a discussion in the evidence review that there's no benefit in treatment beyond 6 weeks.
  - Post surgical patients with 2 or more veins involved, 12 weeks (3 months of treatment)
- Type of treatment:
  - No superior agent. Unfractionated heparin, LMWH, vitamin K antagonists - no data suggesting superiority.
  - No discussion of NOACs.
- Different Treatment Recommendations and Guidelines
  - 2012 ACCP: serial ultrasound for low risk clots and treat high risk clots (cancer, close to the popliteal vein, history of prior DVT)
  - National Clinical Guideline Centre
    - did not mention the treatment of isolated distal DVT because the guideline "… focused on proximal DVT rather than isolated calf vein DVT as the latter is less likely to cause post thrombotic syndrome than proximal DVT and also less likely to embolize to the lungs."

- International Consensus Statement on Prevention and Treatment of Venous Thromboembolism: 3 months of oral anticoagulants for all calf clots
- Up to date: Treat for 3 months (based on poor evidence) versus 2 weeks of serial US

- **Evaluation**
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Edited by Joe Walter