Rap #16, 3/17 Regions Rap Overview (GU/ Neurology)

Wednesday, March 29 2017, 8:42 PM

Rap #16, 3/17 Regions Rap Overview (GU/ Neurology)

IV Contrast (EM Lit of Note 02/01/17, Authored by Ryan Radecki) – Reviewed by Mark Bergstrand

- Conventional wisdom: IV contrast®risk of renal insufficiency
- A lot of the data is from high-doses of angiography and old high-osmolar contrast
- Developing consensus is that this is not a significant risk with CT modern contrast agent
- Difficult to study d/t confounding of sicker patients getting contrast, ethics of randomizing sick patients to no contrast
- Report/comment on "Risk of Acute Kidney Injury After Intravenous Contrast Media Administration" -- www.annemergmed.com/article/S0196-0644(16)31388-9/abstract
    - Propensity-matched study of ~15k pt's who underwent noncon CT, contrast CT or no CT
    - Stratified by comorbidities, meds given, illness severity, baseline renal function
    - After weighting, conclusion: No effect of contrast on risk of AKI if baseline Cr <4
- Conclusion: minimize imaging when possible, but often morbidity of missed diagnosis outweighs risk from IV contrast
- **Evaluation**
    - Air Grade:

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Your Score	7		7		3		4		6

UTI Sans Abx (EM Lit of Note 01/15/16, Ryan Radecki) - Reviewed by Noah Maddy

- Summary: The post is only 329 words long. I recommend investing 90 seconds in reading it.
- If you cannot, then:
    - You may not need antibiotics for simple UTI, but a few people will get pyelonephritis.
    - Possibly using a "wait-and-see" approach of 1-2 days such as in otitis media may be useful.
    - How much of what we do (i.e. medicine) is necessary?
- **Evaluation**

- Air Grade:

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tPA in Stroke Review (St.Emlyn's 02/02/17) - Reviewed by Jenny Bennett

- Stroke and EM doctors disagree about TPA's usefulness and the interpretation of the literature
- History of TPA Research
    - *NINDS trial in 1995*
        - TPA given within 180 minutes of symptom onset
        - Improved functional outcomes
        - Increased rates of symptomatic ICH (SICH) and early mortality in those treated with TPA
        - Questions regarding methods / results, real world application, drug manufacture involvement
    - *IST-3 trial in 2012*
        - Biggest TPA versus placebo trial (n=3035); 1617 over 80 years old
        - Window for TPA extended to 6 hours
        - Polarizing results:
            - No increase in alive and independent patients at 6 months.
            - 7x more fatal and non-fatal SICH in the treatment group.
            - 50% increase in 7 day mortality.
            - Authors concluded …
                - "between 7 days and 6 months no fewer deaths in TPA versus placebo"
                - TPA within 6 hours of symptoms onset improved functional outcomes
                - The benefit was not diminished in the elderly — questionable at best.
    - Most recently …
        - ***Review article: Why is there still a debate regarding the safety and efficacy of intravenous thrombolysis in the management of presumed acute ischemic stroke? A systemic review and meta-analysis.***

- *Meant to be an independent systemic and meta-analysis to assess harms and benefits for TPA in stroke*
- Well done MA and SR, planned and registered by the team, very thorough search strategy, bias was well recorded and established tools were used to determine bias
- *Outcomes: primary good functional outcome at follow up — Rankin score of 3 or less (able to walk and care for personal needs, may need some assistance)*
  - *Initially had 20,296 studies —> narrowed to 26 studies with a total of 10,431 participants*
  - *COMMENTARY — from the article directly, questions the studies included there methods, data and results*
    - *"of the 16 studies that nominated a specific primary outcome, only two studies reported a significant treatment effect in favour of thrombolysis and five studies were stopped early after interim analyses demonstrated either harm or lack of benefit… The largest study did not use any method of blinding, and ascertainment of the primary outcome was conducted in an unblinded fashion via telephone or postal survey. Both studies reporting a positive treatment effect based on the primary outcome reported significant baseline imbalance. While the majority of studies were sponsored by pharmaceutical companies, the most influential study did not declare any such sponsorship. Notably, few studies provided details regarding anticoagulant and antiplatelet agent use after 24 h, nor did they specify that patients were cared for in a stroke unit post randomisation. Only four studies had specific protocols for the management of blood pressure"*
- Results:
  - *Key table from study*
  -

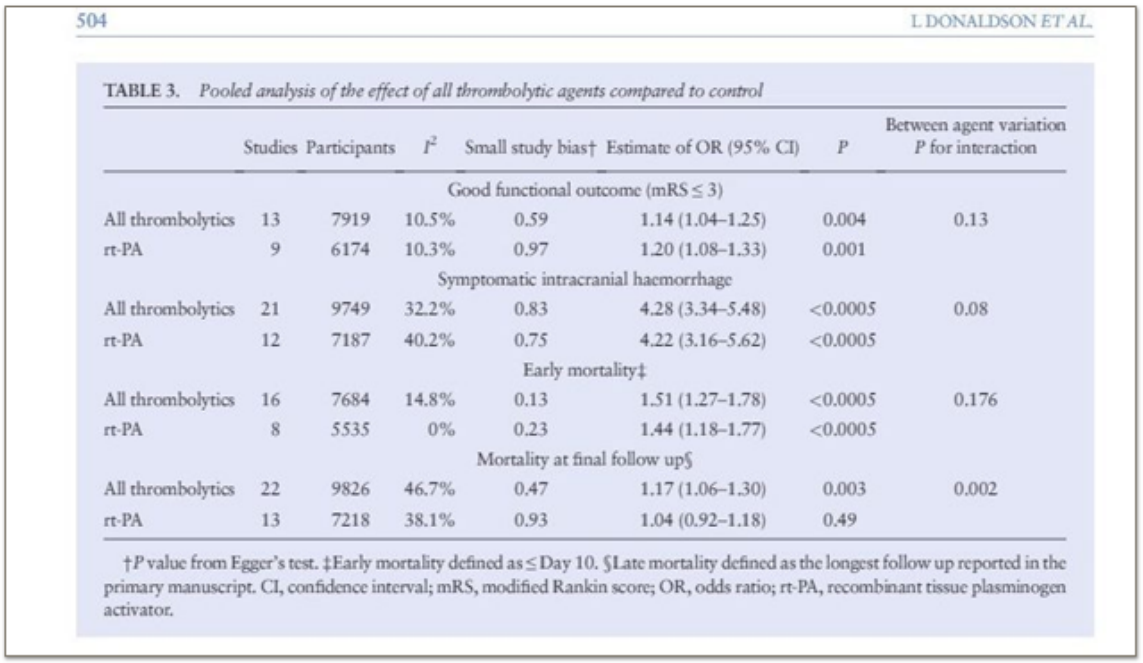

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TABLE 3. *Pooled analysis of the effect of all thrombolytic agents compared to control*

	Studies	Participants	I^2	Small study bias†	Estimate of OR (95% CI)	*P*	Between agent variation *P* for interaction
Good functional outcome (mRS ≤ 3)							
All thrombolytics	13	7919	10.5%	0.59	1.14 (1.04–1.25)	0.004	0.13
rt-PA	9	6174	10.3%	0.97	1.20 (1.08–1.33)	0.001	
Symptomatic intracranial haemorrhage							
All thrombolytics	21	9749	32.2%	0.83	4.28 (3.34–5.48)	<0.0005	0.08
rt-PA	12	7187	40.2%	0.75	4.22 (3.16–5.62)	<0.0005	
Early mortality‡							
All thrombolytics	16	7684	14.8%	0.13	1.51 (1.27–1.78)	<0.0005	0.176
rt-PA	8	5535	0%	0.23	1.44 (1.18–1.77)	<0.0005	
Mortality at final follow up§							
All thrombolytics	22	9826	46.7%	0.47	1.17 (1.06–1.30)	0.003	0.002
rt-PA	13	7218	38.1%	0.93	1.04 (0.92–1.18)	0.49	

†*P* value from Egger's test. ‡Early mortality defined as ≤ Day 10. §Late mortality defined as the longest follow up reported in the primary manuscript. CI, confidence interval; mRS, modified Rankin score; OR, odds ratio; rt-PA, recombinant tissue plasminogen activator.

  - *Thrombolytics causes greater risk for SICH and early mortality*
  - *Thrombolytics lead to better functional outcome at final follow up*

- *Increased mortality at final follow up for thrombolytics (trend towards increased mortality at final follow up for TPA too)*
- *TPA is better than streptokinase*

- **Bottom line — number needed to …**
  - ***NNT is 21.7 (for good functional outcomes)***
  - ***NNH 17.6 (used the SICH rates)***
  - ***NNKill 39.5 (early mortality)***
  - ***NNKill (final follow up) 333 (if you think world wide thats actually a huge number)***
  - *Plus its very expensive*

- Conclusions directly from the paper —
  - *"The current summary of evidence for the use of thrombolysis in presumed acute ischaemic stroke shows clear early harm, in terms of increased rates of symptomatic intracranial haemorrhage and increased early mortality. There is no evidence of late reductions in mortality, but an improvement in late functional outcomes that is largely reliant on one small trial and one large trial with significant methodologic limitations. As such, it is very likely that those skeptical of the relative benefits of this therapy have foremost in their minds the avoidance of adding further harm to patients with an already devastating condition. It should be noted although that withholding a treatment that could lead to improved functional outcomes might also leave patients with significant functional deficits that could have been avoided. The available data are unlikely to resolve this controversy, and replication studies with robust methods are urgently required.*
  - Thrombolysis appears to cause MORE harm than good

- So lots of questions:
  - *What do you do when a person has a devastating stroke in front of you ? Is there a need to "Do something"?*
  - *How do you consent a lay person with this data? Who's also having a stroke?*
  - *Need more / better clinical studies instead of this being the standard of care.*

- **Evaluation**

- Air Grade:

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anti-NMDA Encephalitis (First10EM 01/17) – Reviewed by Sarah Schroeder

- What is it: an auto-immune encephalitis caused by antibodies targeting the NMDA receptor
- It's rare but actually more common than HSV encephalitis
- For boards: the prompt would probably be a young female with a teratoma (this is the population where it was first found, though it can occur without a teratoma)
- Symptoms:
  - Vague prodrome (viral symptoms)
  - Psych symptoms (often in a patient without psych history, acute onset, rapidly progressive)
  - Neuro symptoms (movement/speech problems, seizures, coma)
  - Autonomic instability (dysrhythmias, hyper/hypothermia, slow RR)
- Diagnosis: LP with anti-NMDA antibody titer (CT/MRI not usually helpful, EEG might show abnormalities or might be normal)
- Treatment:
  - Supportive care in the ED, treat for possible meningitis (empiric antibiotics or antivirals)
  - Definitive treatment = IVIG, steroids or plasmapheresis (likely done on the floor)
- Relatively high morbidity (20%) and mortality (4-5%) even with treatment
- Bottom line: keep it on your radar and send the test when you get the LP in the ED!
- **Evaluation**

- Air Grade:

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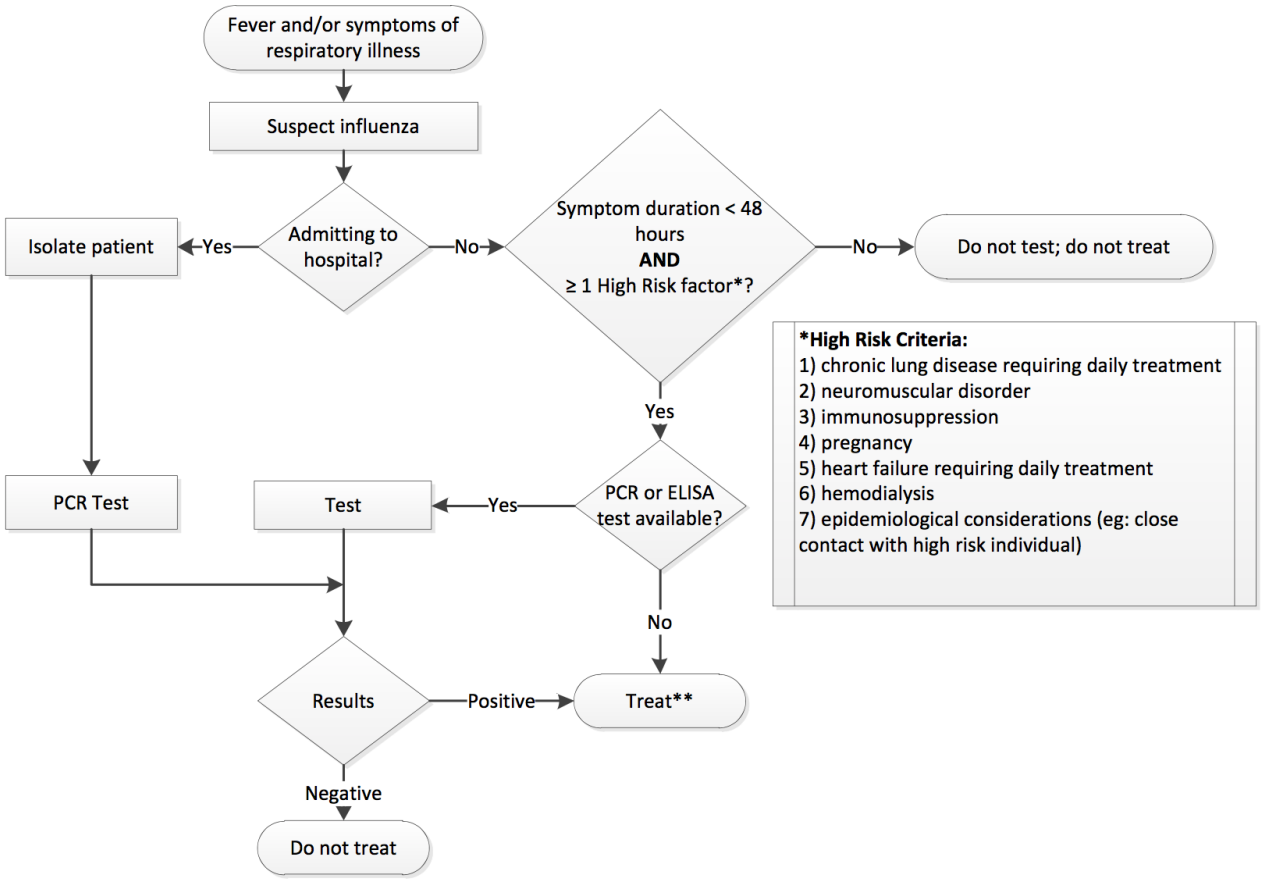
Influenza Pathway (EMRAP 02/17) - Reviewed by Robert Welborn

- Background: Summary of history of drugs and how current recommendations came into play
  - Neuraminidase inhibitors (NAI) are the only class of drugs that we have currently approved to treat Influenza.
  - Oseltamivir is the only NAI that we should be considering for treatment.
  - 2009 – H1N1 Swine Flu pandemic brought the topic of influenza treatment medications to the forefront. Though it wasn't a particularly lethal pandemic, CDC, WHO, and EMA published guidelines recommending widespread treatment of influenza. Public health recommendations to stockpile NAIs
  - Recently the Cochrane Collaboration has been assessing the validity of these recommendations.
    - The pharmaceutical industry: Roche and Glaxo-Smith-Kline profited heavily from the recommendations – high degree of publication bias
      - 107 randomized trials of NAIs, suppressed trial data, only ~20 were published
      - Only trials published were those with positive outcomes. These trials were done in otherwise healthy people. No good data on sick people
      - 53 biggest trials were not published
      - CC has petitioned to get unpublished data released
  - Treatment effect:
    - Decrease in symptom duration by 16 hours when initiated within the 1st 48 hours of symptoms
      - Also decreases "viral shedding" and spread of disease to close contacts
      - Average symptoms duration is 7-10 days
  - Treatment Downsides
    - Cost, GI, psychiatric side-effects
    - Does not decrease hospitalization, death, multi-organ failure, or other badness.
  - Treatment Algorithm



- First decision is: Does this person need to be admitted or not? This changes testing and treatment protocol regardless of symptom duration and risk factors
  - If the person is going to be admitted for a suspected flu-like illness, get the PCR test regardless of symptoms duration.
  - Treat all hospitalized patients with confirmed influenza.
    - Several reasons:
      - It affects isolation precautions
      - It may decrease spread to other hospitalized patients
      - There is a paucity of data on whether or not these populations will have a benefit with regard to their symptoms, mortality or morbidity.
- For all patients who do not need to be hospitalized and do not have “High Risk Criteria” do not test and do not treat.
  - "Rational to avoid a costly and potentially dangerous medication in healthy people who we know will not benefit"
- For patients with at least 1 “High Risk Criteria” (see algorithm above) and symptoms <48 hours, get the test.
  - Though the algorithm lists PCR and ELISA, the podcast has significant reservations about ELISA testing – our clinical judgement might be better. For clinicians working in a setting without adequate testing, they recommend treating this population if high enough clinical suspicion for disease.
  - Cited literature has additional “High Risk Criteria”

- Persons with sickle cell anemia and other hemglobinopathies
- Persons with diseases that requiring long-term aspirin therapy, such as rheumatoid arthritis or Kawasaki disease
- Persons with cancer
- Adults aged >65 years
- Residents of any age of nursing homes or other long-term care institutions

- Cited literature does not recommend treatment for hospitalized patients presenting >48h after symptom onset however states this population "may also benefit from treatment"
- Cited literature also recommends treatment for outpatients with "high risk criteria" >48h
- Cited literature also recommends treatment for outpatient without high risk criteria presenting <48h

- **Evaluation**
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Edited by Zlata Vlodaver, Brian Hahn, Matt Bogan and Joe Walter