Articles That Could Change Your Practice

April 2016

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Jason Wilbur, MD
Che Guavera eating a hotdog
Which of the following has been shown to improve mortality in patients with systolic heart failure (HFrEF)?

A) Valsartan + Sacubitril
B) Ivabradine (Corlanor)
C) Azumumumab (Coregulator)
D) A and B
E) A and C
Answer: A

Approved this year, hence the article.
Background

• Ivabradine blocks the SA node leading to bradycardia.

• Thought is that it will help in angina, CHF similar to beta-blocker.

• Drops pulse *without* changing blood pressure
• 6500 adults with symptomatic left heart failure (HFrEF \rightarrow new terminology..heart failure with a reduced ejection fraction)
  – Terminology: HFpEF \rightarrow ”diastolic dysfunction”
• Initial heart rate of >70
• Endpoint cardiovascular death, cardiovascular hospitalizations
• Primary end point: 24% vs. 29%
• Death: 3% vs. 5%
Sounds great, right?

Not so fast, bucko.
• 90% on beta-blockers but only 50% adequately beta-blocked.
• No benefit if baseline pulse was <77 (so obviously not adequately beta-blocked)
Corlanor (ivabradine)

• NNT over 2 years *when added to ACE/ARB, beta-blocker, spironolactone*
  – Death 50
  – Hospitalization: 25

• But:
  – Only in patients who do not meet beta-blockade goal (HR 70 after other treatments).
• and..contd.
  – ONLY for sinus rhythm. Does not block down a-fib.
  – -1:100 will develop a-fib

• Maximize “standard” therapy first. Use as add-on if not quite to 70 BPM goal or if beta-blockade causes hypotension, CHF.
Sacubitril/Valsartan (Entresto)

September 11, 2014
DOI: 10.1056/NEJMoa1409077
• Inhibiting neprilysin increases vasodilatation and sodium loss.
• 8442 HFrEF <40% class II-IV, patients double blind, randomized to:
  – Sacubitril/Valsartan
  – Enalapril 10mg BID
• Followed for 27 months
• Endpoints include: cardiovascular death + hospitalization but powered to find changes in death.
• Stopped trial early because of benefit at 27 months.
• 22% combined endpoint vs. 27%
• Death from any cause: 17% vs. 20%
• Cardiac death 13.3% vs 16.5%.
• This can *replace* an ACE inhibitor or ARB.
• It cannot be given with an ACE inhibitor because of the risk of angioedema.
Flu Vaccine in Pregnancy

• Vaccination rate is <50% in pregnancy
  – Prevents serious maternal infection
  – Often cited concern for fetal wellbeing

• Australian retrospective Cohort Study
  – > 58000 births April 2012- December 2013
  – From statewide databases
  – 8.7% received RIV, highest in:
    • Women over 35
    • Higher SES
    • Live in accessible area
    • Preexisting medical disease
    • Primiparous
    • Multiple gestations

Flu Vaccine in Pregnancy

– Adjustment for
  • Maternal smoking
  • Indigenous status
  • Propensity for vaccination

• 507 vaccinated
  – Stillbirth aHR 0.49 (95% CI 0.29-0.84) in vaccinated mothers
  – Largest reduction in births just after flu season (aHR 0.33)
Interventional therapy for stroke

• Five trials published in NEJM in 2015 addressing endovascular intervention for acute ischemic stroke

• 1,300 patients total in the 5 trials
But...

• Earlier trials were inconclusive with regard to functional outcomes. What’s different?
• Retrievable stents employed in almost all of the interventions in the 2015 trials.
The trials

How were the trials similar?

• All assigned subjects randomly to endovascular intervention or no treatment.
• Most treated within 6 hours of symptom onset; one trial went up to 12 hours.
• All functionally independent prior to stroke.
• All strokes were intracranial ICA or MCA.
• Most received TPA.
Outcomes

• Significantly more patients in the intervention groups had Rankin scores in the range of 0-2, indicating functional independence.
  – 33% vs. 19% in MR CLEAN
  – 71% vs. 40% in EXTEND-1A
  – 53% vs. 29% in ESCAPE
  – 60% vs. 35% in SWIFT PRIME
  – 44% vs. 28% in REVASCAT
## Table 4. Selected Clinical Outcomes for Recent Randomized, Clinical Trials of Endovascular Treatments for Acute Ischemic Stroke

<table>
<thead>
<tr>
<th>Study</th>
<th>Primary End Point</th>
<th>Death (90 d/3 mo)</th>
<th>Symptomatic ICH</th>
<th>mRS 0 to 2 at 90 d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Active, %</td>
<td>Control, %</td>
<td>Comparison</td>
<td>Active, %</td>
</tr>
<tr>
<td>SYNTHESIS</td>
<td>mRS 0 to 1 at 3 mo</td>
<td>30.4</td>
<td>34.8</td>
<td>0.71</td>
</tr>
<tr>
<td>IMS III</td>
<td>mRS 0 to 2 at 90 d</td>
<td>40.8</td>
<td>38.7</td>
<td>1.5</td>
</tr>
<tr>
<td>MR RESCUE</td>
<td>Mean mRS</td>
<td>3.9</td>
<td>3.9</td>
<td>0.99</td>
</tr>
<tr>
<td>MR CLEAN</td>
<td>Improvement in mRS at 90 d</td>
<td>1.67</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>ESCAPE</td>
<td>Improvement in mRS at 90 d (shift analysis)</td>
<td>3.1</td>
<td>10.4</td>
<td>19</td>
</tr>
<tr>
<td>SWIFT PRIME</td>
<td>Improvement in mRS at 90 d 5 and 6 combined (shift analysis)</td>
<td>0.001</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>EXTEND-IA</td>
<td>Median reperfusion at 24 h</td>
<td>100</td>
<td>37</td>
<td>4.7</td>
</tr>
<tr>
<td>Decrease in NIHSS 8 or NHSS 0, 1 at 3 d</td>
<td>80</td>
<td>37</td>
<td>6.0</td>
<td>2.0 to 18.0)*</td>
</tr>
<tr>
<td>REVASCAT</td>
<td>Improvement in mRS at 90 d 5 and 6 combined (shift analysis)</td>
<td>1.7</td>
<td>18</td>
<td>16</td>
</tr>
</tbody>
</table>
• Cocktail napkin calculation:
  – Over the 5 trials, NNT for functional recovery = 4.5
  – Recent meta-analysis, NNT = 4.9
• Overall mortality was only significantly different in one trial
  – ESCAPE trial: 19% vs 10% 90-day mortality in non-intervention vs intervention group.
• No difference in ICH rates
AHA / ASA Guideline

• Online at http://stroke.ahajournals.org/content/46/10/3020.

• Class I, Level A recommendation to use stent retrievers in patients who meet criteria (next slide).

• But...it is estimated that only 10% of patients will meet the criteria.
Criteria for stent retriever intervention (AHA/ASA 2015)

- Pre-stroke mRS score 0 to 1
- Acute ischemic stroke receiving intravenous r-tPA within 4.5 hours of onset according to guidelines from professional medical societies
- Causative occlusion of the ICA or proximal MCA (M1)
- Age ≥18 years
- NIHSS score of ≥6
- ASPECTS of ≥6
- Treatment can be initiated (groin puncture) within 6 hours of symptom onset
Take away message

• There seems to be something better than tPA for stroke patients who meet criteria.
• Determine which stroke centers near you have stent retrieval therapy available 24-7.
• Be prepared to quickly move appropriate patients to stroke centers with this capability.
Pet Peeve Coming Up

Nietzsche

Dante
2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

Circulation. 2016;133:

Find it at:
http://circ.ahajournals.org/content/early/2016/03/28/CIR.000000000000000404. full.pdf+html
As we discussed in years past: Studies have shown that dual anti-platelet therapy does not incur any benefit after 1 year. Now we are getting updated guidelines.
For both bare metal stents and current generation drug eluting stents:
Guidelines: Dual Antiplatelet Therapy

• A Class I recommendation
  – (“should be given”) in most clinical settings is made for at least 6-12 months

• Class IIb recommendation (weak evidence)
  – (“may be reasonable”) is made for prolonged DAPT beyond this initial 6- to 12-month period

Stop the Non-Aspirin Drug
Recommendation

• Aspirin should be 81-100mg/day. No evidence higher doses are better and there is an increased bleeding risk.

• Caveat: If they have ongoing ACS, may want dual platelet therapy (the class IIB recommendation).

• Also assess bleeding risk, however.
Contraception: Choosing wisely

• LARC methods are safe, effective, and gaining popularity.
• Common patient concerns are weight gain and libido.
  – Patient reports of weight gain are frequent
  – Prior objective data does not support this except for DMPA (AJOG, March 2009)
    • OC did not cause weight gain
    • NH methods did not cause weight gain
    • DMPA: +5.1 kg over 36 mos
Progestin Implant and weight gain

• secondary data analysis from RCT in Jamaica
  – 2012-2014
  – 414 women
    • Implant
    • Delay

• Weight gain
  – Self-report- 15.3% vs. 4.3% in control arm (p=0.01)
  – One month – no difference (p= 0.44)
  – Three months- no difference (p=0.27)

Gallo MF et al. Obstet & Gynecol 2016
Hormonal Contraception and Libido

• Cross-sectional analysis of CHOICE subset 2011
• 1938 women
• 23.9% reported lack of interest after initiating new hormonal contraceptive
  – Copper IUD 18.3%
• Prior OCP data conflicting (some increase)
• Libido decrease more prevalent
  – Younger (OR 2.04)
  – Black (OR 1.78)
  – Married or cohabiting with partner (OR 1.82)

# Hormonal Contraception and Libido

<table>
<thead>
<tr>
<th>Method</th>
<th>OR</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>DMPA</td>
<td>2.61</td>
<td>1.47-4.61</td>
</tr>
<tr>
<td>Vaginal ring</td>
<td>2.53</td>
<td>1.37-4.69</td>
</tr>
<tr>
<td>Implant</td>
<td>1.60</td>
<td>1.03-2.49</td>
</tr>
<tr>
<td>OCP</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Hormonal IUD</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Patch</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

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New targets for hypertension?

  ...and...
SPRINT Trial

• 9,600 patients
• No diabetes
• Increased risk of CVD
  – Framingham 10-year CVD risk >/=15%
  – CKD
  – Clinical or “subclinical” CVD
• Baseline systolic BP >/= 130 mm Hg
• Mean age 68 years; 28% were >/=75 years
• Randomly assigned to target BP < 120 or < 140
• Primary outcome was a composite CVD outcome:
  – myocardial infarction, acute coronary syndrome not resulting in myocardial infarction, stroke, acute decompensated heart failure, or death from cardiovascular causes.

• Trial stopped early (after 3.2 years) for reaching threshold of significance.
### SPRINT Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients (%)</td>
<td>% per year</td>
<td>no. of patients (%)</td>
<td>% per year</td>
</tr>
<tr>
<td>All participants (N = 4678)</td>
<td></td>
<td></td>
<td>(N = 4683)</td>
<td></td>
</tr>
<tr>
<td>Primary outcome†</td>
<td>243 (5.2)</td>
<td>1.65</td>
<td>319 (6.8)</td>
<td>2.19</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>97 (2.1)</td>
<td>0.65</td>
<td>116 (2.5)</td>
<td>0.78</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>40 (0.9)</td>
<td>0.27</td>
<td>40 (0.9)</td>
<td>0.27</td>
</tr>
<tr>
<td>Stroke</td>
<td>62 (1.3)</td>
<td>0.41</td>
<td>70 (1.5)</td>
<td>0.47</td>
</tr>
<tr>
<td>Heart failure</td>
<td>62 (1.3)</td>
<td>0.41</td>
<td>100 (2.1)</td>
<td>0.67</td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>37 (0.8)</td>
<td>0.25</td>
<td>65 (1.4)</td>
<td>0.43</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>155 (3.3)</td>
<td>1.03</td>
<td>210 (4.5)</td>
<td>1.40</td>
</tr>
<tr>
<td>Primary outcome or death</td>
<td>332 (7.1)</td>
<td>2.25</td>
<td>423 (9.0)</td>
<td>2.90</td>
</tr>
</tbody>
</table>

Advertised as a 25% reduction in CVD outcomes. But let’s look at that a little closer...
SPRINT Outcomes

• Over the 3.2 year trial, the event rate decreased from 6.8% to 5.2%, or an absolute risk reduction of 1.6%.
• NNT = 62.5 patients for 3.2 yrs to prevent one CVD event.
• Adverse events were higher in the low blood pressure group, 4.7% vs 2.5%, or absolute risk of 2.2%.
• NNH = 40
Adverse Effects

- Hypotension
- Bradycardia
- Acute kidney injury
- Chronic kidney disease
- Electrolyte abnormalities
- Falls
Take away message

• A “one-size-fits-all-approach” is not appropriate.
• Consider the patient-specific risks.
• A healthier, non-diabetic patient at low risk of adverse events of more aggressive therapy may be a good candidate for a lower BP target.
• Frail patients or those at risk of AKI, falls, etc, should probably have a higher BP goal.
IUD’s and HPV clearance

• EMR review
  – IUD placed 2005-2012 (80% 2010-2012)
  – Pap and high risk HPV testing before and after insertion

• 302 women, similar at baseline
  – 150 copper IUD (30 HPV +, 20% )
  – 152 Levonorgestrel IUD (36 HPV +, 23.7% )

IUD’s and HPV Clearance

• Results
  – No significant differences in pap results
  – HPV clearance rates differed
    • 70% in Copper IUD (95% CI 53.6-86.4%)
    • 42% in Mirena IUD (95% CI 25.6-57.8%)
  – Trend toward lower rates of new HR HPV infection (p=0.056)
    • 2 (1.7%) in copper IUD
    • 8 (6.9%) in Mirena IUD
Anticoagulation for Venothromboembolism

• Newly published American College of Chest Physician guidelines:
Much ado about what?

- Two important points:
  - The clinical science has not changed drastically since the 2012 guideline.
  - The ACCP recommendation nomenclature:
    - Level 1 is a strong recommendation
    - Level 2 is a weak recommendation
    - Evidence is graded as high- (A), moderate- (B) and low-quality (C).
NOACs

• Novel oral anticoagulants (dabigatran, apixaban, etc.) are now recommended over warfarin for DVT/PE treatment in patients without cancer (Grade 2B).

  – This recommendation change is based on greater clinical experience with NOACs in the past 4 years and established acceptable safety record of these drugs.
Other Changes

- Do not routinely use compression stockings to prevent post-thrombotic syndrome (2B).
- For low-risk subsegmental PE with no proximal DVT, clinical surveillance is preferred over anticoagulation (2C). High-risk patients should be anticoagulated (2C).
- For recurrent VTE on an oral anticoagulant, LMWH is recommended over other oral anticoagulants (2C).
- For recurrent VTE on LMWH, the dose of LMWH should be increased by 25-33% (2C).
Oral Steroids for Gout Flair

• 416 individuals, average age 65
• Dx with gout on clinical criteria (one weakness).
• Randomized to 5 days of:
  – Indomethacin 50mg TID
  – Prednisolone 30mg QD
• Excluded CrCl<30, CHF, ACS, allergy, anticoagulated, etc.
Use a 10cm visual analog score at 2 hours and then over 2 weeks. Found no difference in pain reduction at any time during the study.
No Difference in Outcomes Regardless of Time or Activity
• Nausea, dizziness, fatigue greater with indomethacin (other studies have found > GI side effects as well).

• Why is this important? Used only 5 days of therapy and no differences in recurrence.

• Did not look at colchicine.
Molluscum: leave ‘em alone!

- Retrospective chart review/telephone survey
  - 170 Kids <16 yo
  - Johns Hopkins Children’s Center

<table>
<thead>
<tr>
<th>Clearance Rates</th>
<th>Treated</th>
<th>Untreated</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months</td>
<td>45.6%</td>
<td>48.4%</td>
</tr>
<tr>
<td>18 months</td>
<td>69.5%</td>
<td>72.6%</td>
</tr>
</tbody>
</table>

Basdag H et al. *Pediatric Derm* 2015
Send them home with meds

• Discharging asthma patients with medications in hand reduced odds of ED visit over the next 30 days. (OR 0.22, CI 0.05-0.99)

Reducing nerdiness nearsightedness

Background and Intervention

- Myopia is increasing in Asia.
- Study took place in China.
- About 2,000 students age 6 years in grade 1 involved.
- Half assigned to intervention (based on school location) and half had “usual care.”
- Intervention included an additional 40 minute outdoor class each day as well as education and encouragement to engage in outdoor activities at home.
Results

- Endpoint was cumulative incidence of myopia after 3 years in students without myopia at baseline.

- Cumulative incidence of myopia in the intervention group was 30.4% vs 39.5% in the control group (P<0.001).
Take away message

• Yet another reason for kids to get outdoors, get active and get away from screens (and books?)!
CT is not so great for PE

• 937 CT scans done over 1 year for rule out PE over 1 year.
• 174 read as positive by radiologist
• Had 3 chest radiologists read the CT.
• 26% were read as negative by all three chest radiologists.

• This is the same rate as when CT was compared to angiography in PIOPED 2 (but somehow we forgot this.....)
• More likely to be false positive if:
  – Single subsegmental PE
  – Single embolism
• Don’t do CT on “no-risk” patients
• Wells criteria + d-dimer or PERC rules can reliably rule out PE.
But wait, there’s more......

- Pulmonary Embolism Ruleout Criteria
- (PERC rules)
- Well tested
PERC RULES
(Pulmonary Embolism Rule Out Criteria)

• Age <50 years
• Heart Rate<100 bpm
• Oxygen saturation > 94%
• No unilateral leg swelling
• No hemoptysis
• No surgery or trauma within 4 weeks
• No prior DVT or PE
• No estrogen use

Negative? No need for d-dimer

Influenza Vaccines in Egg Allergy

• Open label intervention
• 779 children with egg allergy, age 2-18
  – 270 (34.7%) anaphylaxis to egg
    • 150 (20.1%) with respiratory/CV symptoms
  – 445 (57.1%) with asthma or recurrent wheeze
• Observed 30 minutes after vaccine
• Telephone FU 72 hrs later

Turner PJ et al. *BMJ* 2015
Influenza Vaccines in Egg Allergy

• LAIV did not cause any systemic allergic reactions
• 9% mild symptoms (IgE-mediated?)
• 221 with delayed events
  – 62 lower respiratory tract symptoms
    • 29 parent-reported wheeze
• No hospitalizations
• No increase in respiratory infections over 4 weeks
Return to School

• We tell kids to stay out of school for 24 hours after initiating treatment for strep throat.

• This study helps to answer the question, “Is this the right advice?”

This Study

- 111 children with a sore throat and positive streptococcal rapid antigen detection test (RADT).
- Treated with single dose amoxicillin.
- Returned the next day for RADT and strep culture.
- 91% had negative tests (12-23 hours after amoxicillin).
Take away message

• If you treat a child for strep throat by 5 PM, he/she is unlikely to be contagious the following morning.

• Where permissible by local policies, children can return to school/daycare the next day if they are afebrile and feeling better.
Another reason to avoid noisy toys

- Direct observation of parent-infant interaction in home environment
  - 3 toy sets (electronic, traditional, books)
  - 26 dyads
  - 2-15 minute sessions with each set

- Electronic toys (laptop, phone, talking farm)
  - Fewer words
  - Fewer conversational turns
  - Fewer parental responses
  - Children vocalized less

## Noisy toys (cont)

<table>
<thead>
<tr>
<th></th>
<th>Electronic</th>
<th>Traditional</th>
<th>Books</th>
<th>P (ANOVA)</th>
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</thead>
<tbody>
<tr>
<td>Adult words</td>
<td>39.62</td>
<td>55.56</td>
<td>66.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Content‐specific words</td>
<td>1.89</td>
<td>4.09</td>
<td>6.96</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Child vocalizations</td>
<td>2.90</td>
<td>3.74</td>
<td>3.91</td>
<td>0.04</td>
</tr>
<tr>
<td>Conversational turns</td>
<td>1.64</td>
<td>2.49</td>
<td>2.73</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Responses</td>
<td>1.31</td>
<td>2.09</td>
<td>2.18</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
What for neuropathic pain?

• Meta-analysis of 229 studies
• Likely biased by 10% towards effectiveness.
• So what should we use:
• Lowest NNT= Tricyclics-NNT 3.6
• Strong opiates: 4.3
• Tramadol strong opiates.
• Duloxetine/SNRIs: NNT 6.4
• Gabapentin: NNT 7.2→8.3
• Pregabalin: NNT 7.7
Others:

- No good data
  - Lidocaine patches
  - Carbamazepine
  - Capsalcin
  - SSRIs
- Don’t use
  - Valproic acid
  - Mexiletine
  - Lamictal
Head Lice

• Children should not be excluded from school because of head lice or nits
• Screening programs are not cost effective
• Treatment:
  – 1% permethrin or pyrethrins in low-resistance areas
    • Not completely ovicidal, apply twice
  – If resistance
    • Benzyl alcohol 5% (>6 mos age)
    • Malathion 0.5% (>2 yrs age)
  – Alternative treatments for three weeks
    • Occlusive methods
    • Wet-combing
  – New products may prove helpful, expensive
    • Spinosad
    • Topical ivermectin

AAP Guideline, Pediatrics  May 2015
Head Lice

• Infestations not affected by SES, hair length, combing, or shampooing
• No pet transmission
• Lice can only crawl (static electricity caveat)
• Identification
  – Eggs (nits)
  – Nymphs
  – Adult Lice
• Treat promptly
• Prevention: don’t share combs, brushes, hats
Should antibiotics be an option in appendicitis?

• 530 patients, 18-60,
  – “uncomplicated” appendicitis (no rupture, peritonitis, sepsis, etc.), appendicolith, elevated creatinine, “serious systemic illness”
• Dx confirmed using CT scan → not lactating, dye allergy
• Randomized to surgery or antibiotics
  – Ertapenem followed by levofloxacin+metronidazole X 7 days
• Followed for 1 year.
- Appendectomy was curative (of course).
- 27% of the antibiotic treated patients had an appendectomy in the first year.
- Nobody died.
- More wound infections and adhesions in the surgery group (as you would expect): 20% vs. 3%.
• Of course the people we want to avoid surgery in weren’t included.
  – Age > 60
  – Systemically ill
  – Elevated creatinine
• But….seems to be an option.
• Must know risk-benefit.
• We don’t have data for > 1 year......
About the same statistics for children 7-17 years of age.

JAMA Surg. Published online December 16, 2015.
doi:10.1001/jamasurg.2015.4534
• In Europe 4 species cause Lyme: B burgdorferi sensu lato, B afzelii, B garinii, B burgdorferi sensu stricto, and B bavariensis

• Now in upper Midwest: *Borrelia mayonii*. 
• Specimens from 2013-2014 analyzed at Mayo clinic. None from before this
• 6 of these had an atypical organism candidatus *Borrelia mayonii*. 
• The bad news.
  – Fever.
  – Diffuse macular rash
  – Neurologic symptoms including speech difficulties, visual difficulties.
  – Vomiting
  – Perhaps one swollen, painful, knee
  – Spirochetemia
• Not necessarily joint involvement on presentation (only 1 of 6 cases).
• **The good news:**
  – It is picked up on current Lyme titers.

• **Ticks**
  – 3% of ticks versus 30% of ticks with *B. burgdorferi*
Quick Points
Spironolactone is a great drug for resistant hypertension

(http://dx.doi.org/10.1016/S0140-6736(15)00257-3)
Early peanut butter reduces allergies. Result is sustained

(http://dx.doi.org/10.1056/NEJMoa1514209)
• No vena caval filters in patients who can be anticoagulated
• No oxygen for STEMI if sat>94%. May actually be harmful.
Filbanserin marginally effective (data below if you want it)

• 0.5 additional orgasms per month
• Sexual desire increased by 1.6 (on an 84 point scale).
• Patients essentially noticed no difference
• More
  – Dizziness
  – Somnolence
  – Fatigue
ARBS

A) Are just as effective in heart failure as ACE inhibitors.
B) Should be used in combination with ACE inhibitors but only in those with the worst CHF.
C) Obviate the need for beta blockers in CHF if you can get the dose high enough
D) Have a lower incidence of cough and angioedema when compared to ACE inhibitors.
Answer: D
Bangalore, et.al. ACE or ARB in Patients Without Heart Failure? Insights From 254,301 Patients From Randomized Trials

Background

• Multiple meta-analyses show that ARBs are inferior to ACEs even to the point of not being better than placebo.
• This is another analysis that informs us a bit more.....
How about this meta-analysis?
Metanalysis

• 106 studies with 254,000 patients
• ACE or ARB vs placebo, ACE vs. ARB
• Outcomes:
  – All cause mortality
  – Cardiovascular death
  – MI
  – CHF
  – Angina
  – Revascularization
  – New DM
<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. of Studies</th>
<th>Events</th>
<th>ACEi Participants</th>
<th>Events</th>
<th>Placebo Participants</th>
<th>Heterogeneity ( (I^2) )</th>
<th>RR (95% CI) (Random)</th>
<th>RR (95% CI) (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>40</td>
<td>2216</td>
<td>31,199</td>
<td>2424</td>
<td>31,199</td>
<td>37.5%</td>
<td>0.89 (0.80-1.00)</td>
<td>0.91 (0.86-0.96)</td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>31</td>
<td>1210</td>
<td>29,716</td>
<td>1408</td>
<td>29,716</td>
<td>50.3%</td>
<td>0.83 (0.70-0.99)</td>
<td>0.85 (0.79-0.92)</td>
</tr>
<tr>
<td>MI</td>
<td>24</td>
<td>1360</td>
<td>28,507</td>
<td>1632</td>
<td>28,507</td>
<td>0.0%</td>
<td>0.83 (0.78-0.90)</td>
<td>0.83 (0.78-0.90)</td>
</tr>
<tr>
<td>Angina</td>
<td>12</td>
<td>2022</td>
<td>19,730</td>
<td>2177</td>
<td>19,730</td>
<td>41.1%</td>
<td>0.95 (0.85-1.07)</td>
<td>0.93 (0.87-0.99)</td>
</tr>
<tr>
<td>Stroke</td>
<td>21</td>
<td>661</td>
<td>26,962</td>
<td>786</td>
<td>26,962</td>
<td>5.3%</td>
<td>0.85 (0.75-0.95)</td>
<td>0.85 (0.76-0.94)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>16</td>
<td>927</td>
<td>26,832</td>
<td>1196</td>
<td>26,832</td>
<td>25.3%</td>
<td>0.76 (0.67-0.87)</td>
<td>0.77 (0.71-0.84)</td>
</tr>
<tr>
<td>Revascularization</td>
<td>12</td>
<td>2741</td>
<td>23,685</td>
<td>2937</td>
<td>23,685</td>
<td>10.6%</td>
<td>0.93 (0.88-0.99)</td>
<td>0.93 (0.89-0.98)</td>
</tr>
<tr>
<td>New-onset diabetes</td>
<td>5</td>
<td>1010</td>
<td>14,911</td>
<td>1180</td>
<td>14,911</td>
<td>39.6%</td>
<td>0.84 (0.75-0.95)</td>
<td>0.86 (0.79-0.93)</td>
</tr>
<tr>
<td>Drug withdrawal</td>
<td>22</td>
<td>5075</td>
<td>24,574</td>
<td>4043</td>
<td>24,574</td>
<td>89.6%</td>
<td>1.50 (1.24-1.81)</td>
<td>1.24 (1.19-1.29)</td>
</tr>
<tr>
<td>ESRD</td>
<td>7</td>
<td>89</td>
<td>3121</td>
<td>157</td>
<td>3121</td>
<td>0.0%</td>
<td>0.57 (0.44-0.74)</td>
<td>0.57 (0.44-0.74)</td>
</tr>
<tr>
<td>Doubling of creatinine</td>
<td>4</td>
<td>105</td>
<td>3028</td>
<td>171</td>
<td>3028</td>
<td>47.3%</td>
<td>0.59 (0.41-0.86)</td>
<td>0.62 (0.49-0.80)</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>10</td>
<td>16</td>
<td>1148</td>
<td>11</td>
<td>1148</td>
<td>0.0%</td>
<td>1.29 (0.62-2.68)</td>
<td>1.29 (0.62-2.68)</td>
</tr>
</tbody>
</table>
• Compared with *placebo*, ACEis but not ARBs reduced the outcomes:
  – All-cause mortality
  – Cardiovascular death
  – MI.

• So.....they looked back to see if the new studies (mostly ARBS) differed from the old studies (mostly ACEs).
• What they found: The rate of placebo events was higher in the older studies. Thus the bar wasn’t as high for ACEs as it is for ARBs.
• However, CHF was still worse in the ARB group (and remember they excluded patients with CHF as much as possible).
Do I believe this?

• Sort of......
• It is assuming that people are otherwise maximally treated and thus have a low rate of events (beta-blocker, statin, diuretics, ASA, etc.).
• If people are not optimally treated they will have the same event rate as in the ACE trials.
• In this case ACE does seem superior to ARB.
• 2100 adolescent girls (11-18) in Britain about how their perception of their breasts effect exercise.

• 73% related some concern about breasts and exercise

• Larger chested girls did not participate in sports at the same rate as those with smaller breasts.
• 63% vs 45% (large vs small) had concerns about their breasts and sports activities (primarily bouncing).
  – Includes pain, bouncing, changing in locker room.
• >50% had never used a sport’s bra
• 40% large breasted girls though that their breasts were too large to exercise.
• We need to educate girls a bit better on breasts and exercise.