Inflammation appears to play an important role in atherosclerosis. In the past three years, studies have looked at the role of anti-inflammatory agents in CV disease: injectable monoclonal antibody canakinumab led to a 15% lower risk of CV events compared with placebo, but also increased the risk of fatal infections (NEJM 2017; 377:1119-31); on the other hand, methotrexate did not affect cardiovascular outcomes or plasma markers and inflammation (NEJM 2019; 380:752–62).

Tardif et al. (NEJM 2019, Nov 16) randomly assigned 4745 patients (mean age, 61 years) to receive either colchicine (0.5 mg daily) or placebo after myocardial infarction; the mean follow-up was 22.6 months. The risk of the primary composite end-point (death from cardiovascular causes, resuscitated cardiac arrest, myocardial infarction, stroke, or urgent hospitalization for angina leading to coronary revascularization) was lower in the colchicine group than in the placebo group (5.5% vs 7.1%, NNT=62) This result was driven predominately by lower risks of angina (NNT=100) and stroke (NNT=166). A significant effect on death from cardiovascular causes or myocardial infarction was not shown.
The common adverse events observed were gastrointestinal. Diarrhea was reported in 9.7% of the patients in the colchicine group and an 8.9% of those in the placebo group. No deaths from infection occurred in either group. Colchicine did not lower the high-sensitivity C-reactive protein level more than placebo in the small subgroup of patients with available data.

**My Take:**

- The first time I read this paper I got excited-- a cheap, safe approach to CV disease! A more in-depth perusal…19% of each group dropped out and a lack of a tenable mechanism of action (failure of the inflammatory markers to fall in the colchicine group) led to a reality check.

- An interesting observation in this trial was the lower risk of stroke in the colchicine group than in the placebo group. Dr. Newby in an editorial (NEJM 2019; 380: 752-62) comments that similar findings were reported in a systematic review and meta-analysis of four other randomized trials and colchicine (Clinical Therapeutics 2019; 41 (3): 582 – 590.) Does colchicine have a unique mechanistic effect on the cerebrovasculature or is this just the play of chance?

And speaking of a simple, cheap, safe approach to a difficult problem, read on.

**Aromatherapy for Nausea and Vomiting**

Everything about this study… small size (n=120) single-site and a title that includes the word “aromatherapy” made me want to dismiss this research out of hand. Yet this simple, safe, inexpensive intervention warrants attention. April et al. in Ann Emerg Med 2018 Feb 17, in an emergency room setting, randomized 120 adults (not requiring IV access) who presented with nausea or vomiting into three groups:

- Inhaled isopropyl alcohol + 4 mg oral ondansetron
- Inhaled isopropyl alcohol + oral placebo
- Inhaled saline + 4 mg oral ondansetron

Isopropyl alcohol was provided in the form of a standard isopropyl alcohol swab. Patients received a single dose of the oral intervention, but could sniff alcohol or saline swabs repeatedly. Nausea was measured on a 100 mm visual analog scale at baseline and in 30 minutes.

**Results:**

(recall that a change of 13 mm on a 100 point scale is the minimum change that is thought to be clinically significant)

- Mean nausea scores decreased by 30 mm in the alcohol/ondansetron group
- Decreased 32 mm in the alcohol/placebo group
- Decreased 9 mm in the saline/ondansetron group
- Rescue antiemetic therapy was given to 28%, 25% and 45% of each group, respectively.
- Patients in the inhaled alcohol groups had better nausea control at the time of discharge and reported higher satisfaction scores with nausea treatment. No adverse events occurred. The mechanism of action is unknown, although olfactory distraction has been suggested.
Other studies (Beadle et al. Ann Emerg Med 2016 July) have noted rapid onset of nausea alleviation with isopropyl alcohol, but a high incidence of symptom recurrence particularly beyond six hours post intervention. A Cochrane Database Systematic Review 2012 (16 studies and 1036 patients) concluded that in patients with post-op nausea and vomiting, isopropyl alcohol and placebo were equally effective in relieving symptoms. This review also suggested that participants who received aromatherapy needed fewer antiemetic medications.

My Take:

- Until recently I considered ondansetron as the first-line agent for nausea and vomiting. After doing this review and looking at the broad spectrum of antiemetics,
  - I learned:
    o ondansetron works extremely well in cancer patients, but not so well in non-cancer patients
    o there is low to moderate level evidence that the etiology of the nausea and vomiting may help direct treatment
    o that in randomized controlled trials of non-cancer patients, none of the antiemetics consistently work significantly better than placebo
  - Given the overall consistent lack of effectiveness of antiemetics in general and the simple, cheap, safe nature of isopropyl alcohol swabs, this is worth a try!

In the category of:

What is Big Pharma thinking?

or

How gullible do they think we are?

Three newly introduced drugs lend credence to the idea that contemporary drug pricing is simply based on “what the market will bear, no matter how ridiculous.”

- Drizalma (duloxetine DR)
  This is Cymbalta (available as a generic) marketed as sprinkles for ages seven and up. There were no new studies to bring this boondoggle to market. Generic venlafaxine is available to sprinkle on food.

  Drizalma $7/cap vs venlafaxine $0.61/cap

- Katerzia (oral suspension of amlodipine)
  The patient or a PharmD can crush generic tablets of amlodipine.

  Katerzia solution $17 for 5 mg
  vs
generic 5 mg tab of amlodipine $0.17

Yes, that’s a 100 fold difference in cost or a $1000 a month for a 10 mg/ day dose of Katerzia.

- Relafen DS (nabumetonr) 1000mg tablet.
  The clinical trial information in the package insert is the same as for the 1991 approval of Relafen (500 mg). In late January 2020, there is no website to advertise this drug. What are the folks at Carwin Pharma up to?
Relafen DS $48/tab ($1440/mo)

vs

nabumetone $0.25/tab ($15/mo)

Baqsimi (glucagon nasal)

Baqsimi (glucagon nasal) is an important addition to the pharmacopeia. This is a single use dry powder device that is non-inferior to GlucaGen HypoKit IM in terms of mean time to hypoglycemic relief. It does not need to be inhaled to be effective. And the really good news is that it is priced comparably to the existing product at $336 per dose. Coming soon is an auto-injector device for Gvoke, an already reconstituted drawn up glucagon sub-q product. ($336 per dose)

Follow up

Finally, in follow up of my inability to discover the hospital lab charges for a urine culture (Prudent Prescriber December 2019) neurologist Dr. Logan McDaneld uncovered this data from St. Mary’s Hospital in Grand Junction. “Urine culture. The full charges are estimated at $91. The discounted rate is estimated at $63.70. If the culture results in a positive, there would be additional charges attached.” Thanks, Logan.