Ann Robinson’s research reviews—27 October 2022

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Genital herpes: a sore subject
I was taught that herpes simplex virus type 1 (HSV-1) causes cold sores on the lip while HSV-2 causes genital sores. But that’s all changing, with HSV-1 fast becoming the leading cause of genital herpes in many countries, spread by oral sex or genital to genital contact. And genital herpes concerns us all: according to the World Health Organization, two thirds of the world’s population under 50 years old are infected with HSV-1, and half a billion people aged 15-49 have genital infection due to HSV-1 or HSV-2.

Most of what we know about genital herpes comes from studies on HSV-2, and we know much less about HSV-1. This small prospective cohort study of 82 people with their first episode of genital HSV-1 infection found significant levels of genital viral shedding after the initial infection (12.1% of days in a 30 day period at two months and 7.1% at 11 months) despite antiviral treatment for the initial episode. Prolonged genital shedding was more likely in those who hadn’t encountered HSV before.

Counterintuitively, viral shedding was mostly asymptomatic and was rare from genital and oral lesions, so you wouldn’t know to avoid sex unless, like the trial participants, you swabbed your mouth and genitals every day and sent the swabs off for PCR testing. The study was limited in scope, with no details on the use of antivirals outside the swabbing periods when they were banned, rates of shedding beyond one year, and genomics of the strains involved. More information is sorely needed to identify and counsel persistent shedsers and their sexual contacts.

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Back down
Around 30% of people who have lumbar spine surgery for their bad backs experience persistent or even worse radicular pain after their surgery. Spinal cord stimulation for this type of chronic pain is a growing and lucrative market, but there’s not much convincing evidence of its benefits. In this Norwegian crossover randomised trial of 50 people, two three-month periods of bursts of spinal cord stimulation using a subcutaneous implantable pulse generator with leads into the epidural space, resulted in no significant difference in self reported disability related to back pain, leg and back pain, quality of life, physical activity levels, or adverse events (18%) compared with placebo. However, the placebo effect was powerful, highlighting the need to treat claims made on the basis of open-label trials with caution if not scepticism. It is possible that other types of neuromodulation may be more effective in this scenario or in other clinical situations, but the case so far is underwhelming.

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The heart of the matter
Allopurinol is great for gout, but does it help the heart? This large, UK, prospective randomised study (ALL-HEART) found that allopurinol (600 mg/day) didn’t improve major cardiovascular outcomes in people over 60 years old with ischaemic heart disease (but not with gout) compared with usual care. There was no difference in the number of non-fatal heart attacks, strokes, or cardiovascular deaths over five years. Rates of cancer and adverse events were similar in both groups. Unfortunately, there was a very high dropout rate (57%) in the allopurinol group, which may have skewed results. The results may not be widely generalisable as 99.2% of participants were white, and most participants had had ischaemic heart disease for 10 years or more. As you’d expect, there was a lower than average rate of new cases of gout in the allopurinol group, but no cardiovascular or quality of life benefit to justify the use of allopurinol in ischaemic heart disease.

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Vitiligo promise
Vitiligo can be stigmatising and distressing, and, unfortunately, clinicians have little to offer except sympathy and camouflage creams. Ruxolitinib is a Janus kinase inhibitor that blocks cytokines and reduces inflammation. Ruxolitinib cream is licensed for use in eczema; the question is whether it can help in vitiligo. Two phase 3 trials (TRuE-V1 and V2) found that 1.5% ruxolitinib cream used twice a day resulted in more repigmentation of vitiligo patches than placebo (vehicle controls) over the course of a year (29.8% vs 7.4% in TRuE-V1 and 30.9% vs 11.4% in TRuE-V2). It did, however, cause adverse events in over half of the participants, including acne, nasopharyngitis, and itching. Half the patients who applied the active cream from day one had at least 75% facial repigmentation and at least 50% total body repigmentation at one year. Follow-up was limited by the covid-19 pandemic, and most participants were white, which limits generalisability to other skin types. Further head-to-head studies with other single therapies such as phototherapy and combinations of ruxolitinib cream with phototherapy are ongoing.


A for apixaban
Atrial fibrillation (AF) is common and increasingly identified in our ageing populations. Over 60% of people with AF also have valvular heart disease (VHD), and both conditions increase the risk of stroke. Anticoagulants reduce the risk of stroke by about two thirds, and direct oral anticoagulants (DOACs) such as apixaban and rivaroxaban have largely replaced...
warfarin as they’re so much easier to deal with. But how do we choose between the two DOACs?

This cohort study of nearly 20 000 people with AF and VHD registered on a US commercial health insurance database found that apixaban was associated with a lower rate of ischaemic stroke or systemic embolism and bleeding (gastrointestinal or cerebral) compared with rivaroxaban within the first year of treatment initiation (absolute reduction in probability 0.011 and 0.019). There was no difference in all-cause mortality between apixaban and rivaroxaban over the seven year study period. The study design meant that variables such as body mass index weren’t captured, which could have contributed to confounding. Longer follow-up and randomised controlled trials are needed to confirm whether apixaban has the edge.


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