

Dear friends of clinical journal club - load the file down at <https://www.mdc-berlin.de/cjc>. This website also gives you access to my seminar on Wednesdays 16:00 English and 17:00 German. You need to click on *Besprechung beizutreten*. If it fails to work immediately, keep on clicking.

A 23-year-old man with autism spectrum disorder and chronic constipation presented to the emergency department with a 1-week history of abdominal pain on his left side, nausea, and vomiting. Physical examination was notable for abdominal distention and mild tenderness to palpation on the left side of the abdomen. Computed tomography of the abdomen and pelvis is shown. What is the most likely diagnosis? You are offered: Hirschsprung's disease, Simple fecal impaction, Stercoral colitis, Toxic megacolon, and Ulcerative colitis. Clinical experience and common sense are helpful here. Aldosterone dysregulation plays an important pathogenic role in hard-to-control hypertension. In several studies, baxdrostat, an aldosterone synthase inhibitor, reduced the seated systolic blood pressure of patients with uncontrolled or resistant hypertension. In a phase 3, multinational, double-blind, randomized, placebo-controlled trial, investigators recruited patients with a seated systolic blood pressure of between 140 mm Hg and less than 170 mm Hg despite the receipt of stable treatment with two antihypertensive medications (uncontrolled hypertension) or three or more such medications (resistant hypertension), including a diuretic. The primary efficacy end point was the change in the seated systolic blood pressure from baseline to week 12, as assessed for each baxdrostat group as compared with placebo. We learn that yes indeed, baxdrostat lowers blood pressure. Potassium sneaked up a bit in some. But could not low-dose spironolactone have done as well? Transthyretin (TTR) primarily functions as a transport protein, carrying thyroid hormones (thyroxine) and vitamin A (retinol) throughout the body. It is produced mainly in the liver and choroid plexus, and it plays a critical role in nerve and brain health by moving hormones and potentially protecting against neurodegenerative diseases. Some people have genetic mutations in TTR causing amyloidosis, heart failure, and crippling neuropathy (ATTR). Since TTR is solely produced in liver, could we just knock it out? Nexiguran ziclumeran (nex-z) is an investigational in vivo therapy based on CRISPR-Cas9 (clustered regularly interspaced short palindromic repeats and associated Cas9 endonuclease) that is designed to reduce serum TTR levels through selective

inactivation of TTR in the liver. In a phase 1, open-label study, investigators administered one infusion of nex-z to patients with ATTRv-PN. Primary objectives included assessment of the safety and pharmacodynamics of nex-z. Secondary end points included changes in the familial amyloid polyneuropathy stage, polyneuropathy disability score, serum neurofilament light chain (NfL) level, modified body-mass index (modified BMI, defined as the conventional BMI [weight in kilograms divided by square of height in meters] multiplied by the albumin level in grams per liter), and modified Neuropathy Impairment Score+7 (mNIS+7; range, 0 to 304, with higher scores indicating more impairment). A single administration of nex-z in patients with ATTRv-PN was associated with rapid, deep, and durable reductions in serum TTR levels. The results support further investigation of nex-z to treat ATTRv-PN.

Targeted indoor residual spraying focuses insecticide applications on common resting surfaces of *Aedes aegypti* mosquitoes (an arboviral disease vector) in houses, such as exposed lower sections of walls and under furniture. Investigators conducted a two-group, parallel, unblinded, cluster-randomized trial in Merida, Mexico, to quantify the efficacy of targeted indoor residual spraying for preventing aedes-borne diseases (chikungunya, dengue, or Zika). Children 2 to 15 years of age were enrolled from households in 50 clusters of five-by-five city blocks. The primary end point was laboratory-confirmed, symptomatic aedes-borne disease. Community effects were assessed with the use of geolocated national surveillance data. Targeted indoor spraying lowered insect body counts but did not reduce disease.

On the other hand, could permethrin-treated baby wraps reduce infant malaria? In a double-blind, randomized, placebo-controlled trial conducted in Uganda, we enrolled adult women with a child who was 6 to 18 months of age. The mother-child pairs were randomly assigned in a 1:1 ratio to use permethrin-treated wraps (intervention group) or sham-treated wraps (control group). The wraps underwent retreatment every 4 weeks. All the participants received a new, pyrethroid-only long-lasting insecticide-treated bed net. The participants visited the trial clinics every 2 weeks for 24 weeks and made unscheduled visits in the case of febrile illness in the children. The primary outcome was clinical malaria in the children, as defined by fever and a positive malaria rapid diagnostic test. The pyrethroid-treated body wraps reduced malaria in these children.

The N Engl J Med review is about idiopathic intracranial hypertension (pseudotumor

cerebri). In the weekly patient presentation, we have an extremely complicated clinical scenario discussed by a seasoned clinician and reasoned out with an AI program. I believe the clinician won. The person unknowingly swallowed a toothpick that penetrated the duodenum to the right renal vein. In the Lancet, the Global Burden of Disease investigators studied cancer worldwide since 1990 until the present and made projections to 2050. Cancer is increasing. Cancer could be reduced by 30% if people stopped smoking, overeating and lowered environmental hazards. C3 (complement C3) glomerulonephritis is a rare disease. However, we can now manipulate the complement cascade. Iptacopan reduces C3 activation and decreases progression of this disease. C-reactive protein (CRP) was discovered in the 1930's and binds pneumococci. CRP has become a universal marker of inflammation. We learn that using CRP as a clinical decision tool can reduce the use of antibiotics in children presenting with a febrile illness. Next, in a final analysis, we learn that simvastatin does not favorably influence the activity of multiple sclerosis. The EAT Commission reports that healthy, sustainable, and just food systems are a goal worth pursuing but hardly attainable. In Science Magazine, we learn about mycoheterotrophic plants. Mycoheterotrophic plants are thieves. Found in forests worldwide, they entwine their roots with the threadlike hyphae of soil fungi. These fungi acquire carbon from trees and shrubs while providing nutrients in a mutually beneficial exchange. The mycoheterotrophs then steal some of that carbon from the fungi, instead of relying on sunlight and chlorophyll to power photosynthesis. The Washington Post reports on the 20th anniversary of the introduction of cell phones. They now outnumber persons on the planet. Their negative effects are frightening. No oral presentation this week but please review the files. Join me on Wednesday, October 22 for the above and more in another stunning, orally presented, clinical journal club, 16:00 in English and 17:00 in German.

Sincerely, Fred Luft

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