

Dear friends of clinical journal club - load the latest 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 19-year-old man who had undergone splenectomy at 5 years of age for hereditary spherocytosis presented to the emergency department with a 1-day history of sharp pain in the right wall of the chest. Physical examination was unremarkable. Serum laboratory studies showed compensated chronic hemolysis. A peripheral-blood smear showed sporadic Howell–Jolly bodies and spherocytes. Computed tomography of the abdomen and pelvis and a technetium-99m–labeled heat-damaged red-cell scan are shown. Which of the following is the most likely diagnosis? You are offered: Accessory spleens, Extramedullary hematopoiesis, Lymphoma, Peritoneal carcinomatosis, and Splenosis. Hint, it's a bit like endometriosis of the spleen. Patients are at increased risk for recurrent ischemic events after an acute coronary syndrome event. Factor XI increase and stay up for months. Milvexian, an oral factor XIa inhibitor, may reduce the risk of major adverse clinical events with minimal bleeding risk. In a phase 3, randomized, placebo-controlled trial, investigators evaluated the efficacy and safety of milvexian when added to standard antiplatelet therapy within 7 days after an acute coronary syndrome event. Patients were assigned to receive oral milvexian (25 mg twice daily) or matched placebo. The primary efficacy outcome was a composite of cardiovascular death, myocardial infarction, or ischemic stroke as evaluated in a time-to-event analysis. The principal safety outcome was bleeding. Milvexian did not reduce events but caused no major bleeding. Sjögren's disease is a complex, systemic autoimmune disease with no approved targeted therapies. Ianalumab is an IgG1 monoclonal antibody with a dual mechanism of action, depleting B cells through antibody-dependent cellular cytotoxicity and inhibiting B-cell activation and survival through blockade of B-cell activating factor receptor (BAFF). Investigators conducted two 52-week, double-blind, randomized, placebo-controlled trials involving patients with active Sjögren's disease. The primary end point was the change from baseline in the score on the European Alliance of Associations for Rheumatology (EULAR) Sjögren's Syndrome Disease Activity Index (ESSDAI) at week 48. Ianalumab improved the index but not by very much. In patients with infective endocarditis on the

left side of the heart, the current recommendation of up to 6 weeks of antibiotic therapy is based largely on expert consensus opinion. Whether a clinical response–tailored antibiotic management strategy can shorten treatment duration without compromising safety is unclear. In an international, open-label, randomized trial, investigators assigned adults in stable condition with infective endocarditis caused by *Staphylococcus aureus*, *Enterococcus faecalis*, or streptococcus species to receive either response-tailored or standard-duration antibiotic therapy. Before randomization, all the patients received at least the prespecified 2 to 4 weeks of therapy and met criteria for clinical stabilization. After randomization, patients in the tailored-therapy group discontinued antibiotics and those in the standard-therapy group continued standard treatment (total duration, 4 to 6 weeks). The primary efficacy end point was days alive without antibiotic treatment for infective endocarditis or bacteremia within 6 months after randomization (tested for superiority). Four weeks was “no worse” than 6 weeks but was associated more commonly with relapse. Tambotatug pelitecan (known as Tam-Peli, a new antibody–drug conjugate that targets the immune-checkpoint molecule B7-H3) showed promising clinical efficacy in patients with relapsed extensive-stage small-cell lung cancer in early-phase trials. In a phase 3, multicenter, open-label, randomized trial, investigators assigned eligible patients with small-cell lung cancer that had progressed after first-line platinum-based therapy to receive tambotatug pelitecan or topotecan. The primary end point was overall survival. The key secondary end points were progression-free survival and objective response as assessed by investigators. Tam-Peli was better than topotecan. In 1984, Barry Marshall swallowed a culture of *Helicobacter pylori* and developed gastritis, as diagnosed by Robin Warren; they received the Nobel Prize. The rest is history as reviewed by N Engl J Med this week. The N Engl J Med mystery patient this week has small-cell lung cancer and develops unilateral vision loss. The retina looks more like CMV retinopathy. In the Lancet, we again confront mirapivat, a stimulator of erythrocyte pyruvate kinase. Stimulation increases ATP and decreases 2,3BPG shifting the hemoglobin-oxygenation curve leftward and increasing PaO<sub>2</sub> slightly. Mirapivat improved the lot of patients with beta thalassemia major. Now, we learn that patients with homozygous sickle cell anemia can also profit. Oral deucritibant blocks the bradykinin B2 receptor. Angioedema due to C1 esterase deficiency is bradykinin driven. Last week, we learned

that knocking down prekallikrein helps patients with C1 esterase deficiency. This week, we learn that a “pill-in-the-pocket” strategy with deucritibant would be far cheaper and is also helpful. Next, Lancet presents a randomized trial of the artificial medical intelligence explorer (AMIE - an AI program) and contact with a primary care physician (PCP). We glimpse into the future. Lancet next presents three review articles on the Digital Determinants of Health, a view of global public health in the future. In Science Magazine we learn about a nonbiological graphite felt matrix with platinum-decorated gold nanoclusters as an electrocatalyst that promotes the selective electrochemical oxidation of glucose to gluconate. Gluconate is quickly excreted by the kidneys, thereby lowering blood sugar values to normal. The device can be steered by available glucose sensors. In mice, the device normalized blood sugar in animals with type 2 diabetes and shifted their metabolism to burning fat, causing weight loss. Thus, a device could compete with GLP-1 agonists. In Washington Post, we learn that Pete Hegseth wanted Dwight Eisenhower’s world globe for his own office. In the process, his staff wrecked Eisenhower’s globe. It’s the least damage Pete Hegseth has done lately. Load down the file and join me again on October, 16:00 in English and 17:00 in German.

Sincerely, Fred Luft

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