

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 27-year-old woman presented with a 2-week history of joint pain, fever, sore throat, and a nonpruritic rash that worsened during febrile episodes. Physical examination was notable for generalized lymphadenopathy and swelling of the wrists, knees, and ankles. Laboratory studies showed neutrophilic leukocytosis, an elevated C-reactive protein level and erythrocyte sedimentation rate, and ferritin level of 4053 µg per liter (reference range, 10 to 200). An antinuclear antibody test was negative. Which of the following is the most likely diagnosis? You are offered: Adult-onset Still's disease, Drug reaction with eosinophilia and systemic symptoms, Parvovirus B-19, Sarcoidosis, and Scarlet fever. Hint, the very high ferritin level is the clue.

Despite guideline recommendations, evidence from randomized trials evaluating the appropriate low-density lipoprotein (LDL) cholesterol target for secondary prevention in patients with atherosclerotic cardiovascular disease remains limited. In an open-label superiority trial conducted in South Korea, investigators randomly assigned patients with atherosclerotic cardiovascular disease to a target LDL cholesterol level of less than 55 mg per deciliter (1.4 mmol per liter) (intensive-targeting group) or less than 70 mg per deciliter (1.8 mmol per liter) (conventional-targeting group). The primary end point was a composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, any revascularization, or hospitalization for unstable angina at 3 years. Down to 55 mg/dL beats 70 mg/dL. Uncontrolled hypertension disproportionately affects populations that have substantial health disparities (ie. poor people). Data regarding the effectiveness and implementation of multifaceted, team-based strategies for hypertension control among low-income patients are lacking. Investigators randomly assigned federally qualified health center clinics in Louisiana and Mississippi to use either a multifaceted implementation strategy (intervention group) or enhanced usual care (control group) for hypertension control. The intervention included team-based care, protocol-based intensive blood-pressure management, blood-pressure audit and feedback, health coaching on lifestyle changes, and medication adherence, and home blood-pressure monitoring. The intervention lowered systolic blood pressure

by about 5 mm Hg. Immune thrombocytopenia (ITP) is a disorder of increased platelet destruction and reduced platelet production and is associated with an increased bleeding risk and a compromised quality of life. Available therapies are ineffective in at least 20% of cases. Mezagitamab is an anti-CD38 antibody that targets plasma cells, plasmablasts, and natural killer cells. Investigators conducted a multicenter, double-blind, randomized, placebo-controlled trial to assess the safety and efficacy of mezagitamab at a dose of 100 mg, 300 mg, or 600 mg, as compared with placebo, administered subcutaneously once weekly for 8 weeks in adults with persistent or chronic ITP (mean platelet count on ≥ 2 measurements, $< 30,000$ per microliter). The primary end point was adverse events. A key secondary efficacy end point was a platelet response (defined by a platelet count of $\geq 50,000$ per microliter and $\geq 20,000$ per microliter above the baseline value) on at least two visits at any time through week 16. Mezagitamab improved outcomes in ITP. There is currently a very good vaccine against yellow fever (still common in Brazil and west Africa). However, stockpiles are low. A next-generation, live-attenuated yellow fever vaccine, vYF, was developed in Vero cells to improve vaccine supply and availability. The safety of and immune response to vYF as compared with those of the licensed yellow fever vaccine, YF-VAX, are unclear. In a year 1 interim analysis of a phase 2, observer-blinded, randomized, active-controlled trial, investigators randomly assigned healthy adults 18 to 60 years of age in a 2:1 ratio to receive vYF or YF-VAX as a single vaccine injection on day 1. Neutralizing antibody titers were measured on day 29, month 6, and year 1. The primary analysis focused on the per-protocol population, which included participants with no history of yellow fever infection or vaccination and with no protocol deviations. Immune responses of vYF were noninferior to YF-VAX and there were no safety issues. The KRAS p.G12D variant occurs in 5% of patients with non-small-cell lung cancer (NSCLC) and is the most common substitution variant in pancreatic ductal adenocarcinoma, occurring in 40% of patients, but no targeted therapies directed against this variant are currently approved for clinical use. Setidegrasib (ASP3082) is a first-in-class KRAS G12D-targeted protein degrader. Investigators conducted a phase 1 study to evaluate the safety, pharmacokinetics, pharmacodynamics, and antitumor activity of setidegrasib in patients with previously treated advanced solid tumors harboring KRAS p.G12D variants. The primary objectives were to evaluate the

safety profile, as indicated by dose-limiting toxic effects and adverse events (the primary end points), and to determine the phase 2 dose. Setidegrasib was administered intravenously once weekly at doses of 10 to 800 mg. The new protein degrader gave impressive results in these patients. The N Engl J Med review is on celiac disease. The weekly mystery patient underwent catheter ablation for atrial fibrillation and later develops heart failure symptoms and a pneumopericardium. In the Lancet, we confront catheter-conducted aortic valve (TAVR) replacement. Coronary angiography is routine and coronary stenoses, if present, are generally treated. Could the coronary repair be delayed? A randomized trial of TAVR with or without coronary PCI was conducted and a watch-and-wait approach appears warranted. Next, Lancet reports on a 10-year follow-up trial of long-term aspirin versus clopidogrel in patients undergoing PCI. Overall mortality was no different; however, clopidogrel exhibited some improved endpoints over aspirin. The Lancet reviews the development of liver fibrosis. Generally, this disease is attributed to alcohol intake. Alcohol is still important; however, obesity and type-2 diabetes mellitus are becoming more important. The Lancet reviews are about equitable preconception in men and women. I was not aware of this global-health issue. In Science Magazine we learn about “do not eat me” signals in acute myelogenous leukemia and possibly new approaches. In Washington Post, we are directed to a PNAS paper on detox to erase 10 years of social media-related brain damage.

The presentation is in English at 16:00, German at 17:00, and will take place will on Wednesday April 15, 2026.

Sincerely, Fred Luft

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