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 52-year-old woman with hypertension presented to the hospital with a 1-month history of fatigue, as well as 6 days of vomiting and 1 day of confusion. Over the past 20 years, she had not received regular treatment for hypertension. Physical examination was notable for pallor of the conjunctiva and oral mucosa, as well as for powdery, crystalline deposits on the arms, legs, trunk, and scalp. Which of the following is the most likely diagnosis? You are offered: Contact dermatitis, Pityriasis versicolor, Psoriasis, Uremic frost, and Xerosis cutis. In the 1960's we saw this problem weekly. Digitalis (Foxglove) inhibits the sodium/potassium ATPase pump and was introduced in heart failure treatment 200 years ago. Digitalis gradually fell out of favor 30 years ago when renin-angiotensin-aldosterone inhibitors and beta blockers were introduced. The therapeutic efficacy of the cardiac glycoside, digitoxin, in patients with heart failure and reduced ejection fraction is not established. In an international, double-blind, placebo-controlled trial, investigators randomly assigned patients with chronic heart failure who had a left ventricular ejection fraction of 40% or less and a New York Heart Association (NYHA) functional class of III or IV or a left ventricular ejection fraction of 30% or less and an NYHA functional class of II in a 1:1 ratio to receive digitoxin (at a starting dose of 0.07 mg once daily) or matching placebo in addition to guideline-directed medical therapy. The primary outcome was a composite of death from any cause or hospital admission for worsening heart failure, whichever occurred first. Digitoxin reduced this composite endpoint. Will digitalis now make a comeback? The appropriate duration of anticoagulation for venous thromboembolism (VTE) in patients who have a transient provoking factor (e.g., surgery, trauma, or immobility) and concomitant enduring risk factors is uncertain. In a single-center, double-blind, randomized trial, adults with VTE after the occurrence of a transient provoking factor who had at least one enduring risk factor and had completed at least 3 months of anticoagulation were assigned to receive oral apixaban (at a dose of 2.5 mg twice daily) or placebo for 12 months. The primary efficacy outcome was the first symptomatic recurrent VTE. VTE occurred in about 10% of placebo patients and

apixaban reduced VTE to 1.3%. One episode of major bleeding occurred. Chronic lymphatic leukemia (CLL) has numerous treatment options. How best to hold the patients with no detectable minimal residual disease in complete remission? Investigators randomized CLL patients in remission to ibrutinib-venetoclax, ibrutinib alone, and fludarabine-cyclophosphamide-retuximab. The primary end points were undetectable measurable residual disease (MRD) in bone marrow within 2 years in the ibrutinib–venetoclax group as compared with the ibrutinib-alone group and progression-free survival in the ibrutinib–venetoclax group as compared with the FCR group. The ibrutinib-venetoclax (inhibiting the Bruton tyrosine kinase and BCL2 survival pathway) group fared best. Neutropenia was most common in this group. The platelet GPIIb-IIIa receptor binds to fibrinogen and causes the platelets to aggregate in clumps. The GPIIb-IIIa receptor can be inhibited with tirofiban. Intravenous thrombolysis remains a standard treatment for acute ischemic stroke within 4.5 hours after onset. Vascular reocclusion may occur after intravenous thrombolysis and may be preventable with an antiplatelet agent within the first 24 hours after thrombolysis. Tirofiban, a platelet glycoprotein IIb–IIIa receptor antagonist, has reduced macrovascular reocclusion in experimental models. In a phase 3, multicenter, double-blind, randomized, placebo-controlled trial conducted at 38 centers in China, investigators assigned patients with acute ischemic noncardioembolic stroke who presented within 4.5 hours after stroke onset and who were not eligible for thrombectomy to receive a 24-hour intravenous infusion of tirofiban or placebo within 60 minutes after intravenous thrombolysis. The primary efficacy outcome was an excellent functional outcome. Tirofiban improved the Rankin scale. Symptomatic intracranial hemorrhage occurred in 1.7% of tirofiban patients and in none receiving placebo infusions. Diagnostic equity is the principle that everyone should have an equal opportunity to receive an accurate and timely diagnosis, regardless of their race, gender, socioeconomic status, or other characteristics. N Engl J Med reviews this topic. We then review a patient who developed a gastric bezoar. The bezoar resolved with diet cola. Vericiguat is a compound that stimulates the soluble guanylate cyclase to produce cGMP. The effect reduces peripheral vascular resistance in vascular smooth muscle and thereby reduces afterload. Lancet presents a phase 3 randomized trial in heart failure patients with ejection fractions <40%. Vericiguat did not reduce the

primary endpoint of cardiovascular death and hospitalizations although fewer cardiovascular deaths were observed in the vericiguat group. Next, the results of the VICTORIA and VICTOR trials are analyzed and presented. Herein, vericiguat reduced the risk of hospitalization for heart failure and cardiovascular death in these HF-rEF patients. Next, Lancet addresses the problem of severe plaque psoriasis. Again, we learn that oral icotrokinra (IL-23 inhibition) and deucravatinib (Jak-Stat pathway blocker) can help these patients. Type-1 diabetes is an autoimmune disease caused by the immune system attacking and destroying insulin-producing beta cells in the pancreas. The autoantibodies commonly involved are Insulin Autoantibodies (IAA), Glutamic Acid Decarboxylase Autoantibodies (GADA), Insulinoma-Associated-2 Autoantibodies (IA-2A), and Zinc Transporter 8 Autoantibodies (ZnT8A). Given early on, anti-thymocyte globulin (ATG) can inhibit disease progression. Lancet presents the results of a phase 2 multicenter double-blind randomized trial of ATG addressing adaptive dose-ranging. The 2.5 mg/kg and 0.5 mg/kg doses addressed the desired endpoints most effectively. Next, the Lancet presents three position papers on Alzheimer's Disease. Artificial paper-"moth" prey are experimental tools used by scientists to study predator-prey interactions, primarily with birds. In Science Magazine, we find out how the camouflage strategy to avoid detection, and the aposematism strategy of frightening predators develop in insects to avoid being eaten. In Washington Post, we encounter the North American mountain lion, a predator dealing with camouflage and aposematism daily. Join me on Wednesday, October 1 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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