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 64-year-old woman with no known medical history presented to clinic with a 4-year history of worsening low back pain and difficulty walking. Exam was notable for a finding in the eyes, kyphosis, and a Trendelenburg gait. Radiographs of the lumbosacral spine and pelvis are shown. A urine sample turned black after being left at room temperature overnight. Which of the following is the most likely diagnosis? You are offered: Alkaptonuria, Ankylosing spondylitis, Hemochromatosis, Metastatic melanoma, and Porphyria. Hint: look at the urine; it is not porphyria! Heart failure and atrial fibrillation lead to atrial enlargement and tricuspid regurgitation. The effect of transcatheter tricuspid-valve repair on clinical outcomes, including death and hospitalization for heart failure, in patients with severe tricuspid regurgitation remains uncertain. Investigators randomly assigned patients with symptomatic severe tricuspid regurgitation and an increased risk of future heart-failure events in a 2:1 ratio to tricuspid-valve repair plus medical therapy (tricuspid-repair group) or medical therapy alone (medical-therapy group). The first primary end point was a hierarchical composite of death from any cause, hospitalization for heart failure, and quality-of-life improvement at 1 year. Tricuspid repair beat pills alone. The Galleri liquid-biopsy cancer test is recommended (by the company) for use in adults with an elevated risk for cancer, such as those age 50 or older. Whether screening with blood-based early-detection tests for multiple cancers in addition to usual care has clinical utility is unknown. In a randomized, controlled trial conducted in England, investigators obtained peripheral blood from persons 50 to 77 years of age at up to three annual visits. After baseline blood collection, participants were randomly assigned to the intervention group (participants whose blood was tested) or the control group (participants whose blood was stored). Participants and trial personnel were initially unaware of the group assignments. The primary end point was stage III or IV cancer among 12 prespecified types of cancer at three years. Galleri did not meet the primary endpoint but there is food for thought. The optimal approach to early resuscitation in septic shock is unknown. Equipoise exists between the use of larger volumes of

intravenous fluids to restore perfusion and the use of early vasopressor therapy along with smaller volumes of fluids to minimize potential harm from excess fluid. Investigators randomly assigned adult patients who presented to the emergency department with septic shock to receive either fluids at restricted volumes and early vasopressor therapy (vasopressor group) or higher volumes of fluids and later vasopressor therapy (fluids group) for at least 6 hours and up to 24 hours. The primary outcome was days alive and out of the hospital from randomization to day 90. Alas, equipoise remains; no difference was identified at 90 days. Retinitis pigmentosa is an inherited degenerative retinal disease that can lead to irreversible blindness. Optogenetic therapy has shown potential for restoring visual function at late stages of the disease. In an open-label study, investigators evaluated the safety of ganglion cell–directed optogenetic therapy in 10 participants with blindness due to advanced retinitis pigmentosa. Each participant received a single intravitreal injection of an adeno-associated viral (AAV) vector encoding the red-shifted channelrhodopsin, ChrimsonR, into the worse-seeing eye. Special goggles were then worn. The primary outcome was safety. ChrimsonR was safe and appears to have some efficacy. The N Engl J Med review is on therapy of breast cancer. The mystery patient has a sore throat, fever, and lymphadenopathy of unknown cause. ALAT, ASAT, and CRP are (somewhat) elevated. We learn about Kikuchi-Fujimoto disease. The Lancet presents the definitive trial of retatrutide (GLP-1, GIP, and Glucagon receptor agonist) versus placebo in obese type-2 diabetic patients. Weight loss was superior and diabetes was almost forced to disappear. Not all meningiomas are all that benign; grade 2 and worse commonly reappear after resection. Whether or not radiotherapy after resection could impede recurrence was tested in a randomized trial. It did. There are approximately 1.57 million to 2.4 million children and adolescents (ages 10–19) living with HIV globally. Lancet presents a trial where HIV children receiving daily suppression were switched to injectable cabotegravir-rilpivirine every 8 weeks. This approach was superior to the standard, daily triple combination. The Lancet reports on the (fine) arts as a global health resource. Appropriate road maps are presented. In Science Magazine, investigators tested whether vaccination had a deleterious effect on the microbiome. Turns out, they observed that things were the other way around. The investigators found that vaccine-associated fever had very little effect on the

microbiome; by contrast, fever-positive participants displayed chronic low-grade intestinal inflammation and a microbiome characterized by high expression of bacterial flagellins, both pre- and postvaccination. A bad microbiome was responsible for any adverse effects of vaccination, the authors surmised. Some helpful mice dutifully corroborated the findings. The “bad” microbiome was associated with a “Western” diet. No wonder Donald Trump does not want to be vaccinated! In the Washington Post, we learn that investigators have shown that weight regain after loss (yo-yo effect) is genetically determined, rather than being the result of patients’ will-power deficits. I checked it out. A Nature paper shows that the “fat-promoting” genes in obese persons are epigenetically modified to promote weight regain after weight loss. No oral presentation this week. Load down the file and join me again on October 21, 16:00 in English and 17:00 in German.

Sincerely, Fred Luft

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