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 26-year-old man presented with sudden onset of severe pain in the legs and inability to move the left leg. On physical examination, he had complete loss of motor function in the left leg. Bedside ultrasonographic examination with color Doppler showed no blood flow in the distal aorta. Computed tomographic angiography of the abdomen revealed a saddle embolus at the aortoiliac junction. Emergency aortoiliac embolectomy was performed, and a gelatinous mass was removed. A subsequent transthoracic echocardiogram identified a heterogeneous mass in the left atrium. On hospital day 2, cardiothoracic surgery was performed to remove the left atrial mass, and a villous, friable lesion was excised. Histopathology of the cardiac mass showed abundant mucopolysaccharide matrix with scattered nests of lepidic cells. What is the diagnosis? You are offered: Cardiac myxoma; Cardiac sarcoma; Intracardiac thrombus; Marantic endocarditis; Papillary fibroelastoma. The presentation is classic.

In bronchiectasis, neutrophilic inflammation is associated with an increased risk of exacerbations and disease progression. Dipeptidyl peptidase 1 (DPP-1) is an enzyme that activates elastase, proteinase 3, and cathepsins in neutrophils. Brensocatib, an oral, reversible DPP-1 inhibitor, targets neutrophil serine proteases, key mediators of neutrophilic inflammation. In a phase 3, double-blind trial, investigators randomly assigned patients with bronchiectasis (in a 1:1:1 ratio for adults and a 2:2:1 ratio for adolescents) to receive brensocatib (10 mg or 25 mg once per day) or placebo. The primary end point was the annualized rate of adjudicated pulmonary exacerbations over a 52-week period. DPP-1 inhibition decreased pulmonary exacerbations (slightly).

Baloxavir inhibits the cap-dependent endonuclease in influenza virus and is said to reduce viral shedding by influenza-infected persons. Investigators conducted a multicountry, phase 3b trial to assess the efficacy of single dose baloxavir treatment to reduce influenza transmission from index patients to household contacts. Influenza-positive index patients 5 to 64 years of age were randomly assigned in a 1:1 ratio to receive baloxavir or placebo within 48 hours after symptom onset. The primary end point was transmission of influenza virus from an index patient to a household contact

by day 5. The first secondary end point was transmission of influenza virus by day 5 that resulted in symptoms. Indeed, baloxavir reduced influenza-virus transmission to household contacts (odds ratio 0.68). Clonal hematopoiesis of indeterminate potential (CHIP) is an age-related condition first associated with hematological cancers, then with cardiovascular disease risk, and-also with progression of solid tumors. Thus, CHIP reflects an increased mortality among patients with cancer. CHIP mutations with high variant-allele frequencies can be detected in tumors, a phenomenon investigators term, tumor-infiltrating clonal hematopoiesis (TI-CH). The frequency of TI-CH and its effect on tumor evolution are unclear. The investigators characterized CHIP and TI-CH in 421 patients with early-stage non–small-cell lung cancer (NSCLC) from the TRACERx study and in 49,351 patients from the MSK-IMPACT pan-cancer cohort. They studied the association of TI-CH with survival and disease recurrence and evaluated the functional effect of TET2-mutant CHIP on the biologic features of lung tumors. Their study showed that TI-CH increased the risk of disease recurrence or death among patients with NSCLC and the risk of death from any cause among patients with solid tumors. Metachromatic leukodystrophy (MLD) is an ultrarare, severe lysosomal storage disorder caused by a deficiency of arylsulfatase A (ARSA). Hematopoietic stem cells (CD34) are responsible for microglia, which could perhaps be modified to express normal ARSA. Investigators treated patients who had MLD with atidarsagene autotemcel (arsa-cel), a hematopoietic stem-cell–based gene therapy, in two prospective open-label clinical studies and expanded-access programs. They compared their outcomes with those of untreated patients (natural history cohort). Indeed, the therapy resulted in an improvement, compared to the historical controls. The N Engl J Med review is about the neonatal Fc receptor. This receptor transfers IgG antibodies from mother to fetus and thus, is vital for neonatal immunity. We learn that the neonatal Fc receptor is responsible for many immune responses in adult life and plays a role in autoimmunity. The neonatal Fc receptor has become an important therapeutic drug target. The weekly N Engl J Med patient is a homeless woman with a rash that proves to be chicken pox. In medical school we learned that the four most common causes of postpartum hemorrhage are uterine atrophy, birth canal trauma, placental debris, and coagulopathy. Now, a worldwide systemic review and meta-analysis in the Lancet shows that what we were taught in medical school was correct.

Twenty years ago, a lively debate concerned whether-or-not coronary bypass surgery or percutaneous stenting resulted in better outcomes. Since then, both procedures have been technically improved. Now, in the Lancet we confront an open-label randomized trial and learn that both procedures are good; however, which is better remains a toss-up. Percutaneous stenting is commonly augmented by angiography-derived fractional flow reserve or intravascular ultrasound. From a randomized non-inferiority trial we learn that both procedures are non-inferior to the alternative. Next, a Lancet Commission presents a massive 2025 report on women's, children's, and adolescents' health. Not too much encouraging news is presented here. Those of us who are increasing in age have observed a progressive abdominal "spread". Is the cause overeating, fat-cell hypertrophy, or new adipogenesis? A report from Science Magazine implicates a population of adipocyte progenitor cells (APCs) that emerges in middle-aged visceral adipose tissue, which then drives adipogenesis. Since a "driver" was identified, perhaps there is subsequent hope. In the Washington Post, we are introduced to a 77-year-old woman who is the best female runner (1500 meters to marathon at 3.5 h) of her age. Her $VO_2$max is almost 50 ml/kg/min in case you were wondering. Join me on Wednesday, April 30 for another stunning, orally presented, clinical journal club, 16:00 in English and 17:00 in German.

Sincerely, Fred Luft

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