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.

An 81-year-old man with a smoking history of approximately 60 pack-years was found to have a flank bulge. Twenty years earlier, he underwent surgical resection of three left ribs and a segment of lung for treatment of mesothelioma. He reported onset of the bulge as well as chronic cough a few years after the surgery. The protrusion was soft and compressible, and moved inward during inspiration and outward during expiration. Vesicular breath sounds were heard over the area. What is the most likely diagnosis? You are offered: Epidermal cyst, Flail chest, Lung hernia, Ruptured hemidiaphragm, and Subcutaneous emphysema. Hint: the phenomenon has been there for years and is not lethal. Retatrutide is a triple-receptor agonist of glucose-dependent insulinotropic polypeptide, glucagon-like peptide-1, and glucagon receptors. In a phase 3, randomized, double-blind trial, investigators assigned adults with obesity without diabetes to receive a once-weekly subcutaneous injection of retatrutide (at a dose of 4 mg, 9 mg, or 12 mg) or placebo for 80 weeks. Primary outcomes (evaluated in the 9-mg and 12-mg groups each vs. placebo) were the percent change in body weight and the change in the WOMAC pain score (ranging from 1 to 10, with higher scores indicating worse pain) in the subgroup of 574 participants with knee osteoarthritis and the change in the apnea–hypopnea index in the 243 participants with obstructive sleep apnea. Retatrutide resulted in a 20% weight loss, lowered inflammation markers, and alleviated symptoms without new safety signals. Many patients with suspected acute coronary syndrome in whom myocardial infarction has been ruled out in the emergency department remain at risk for cardiovascular events. Whether further investigation reduces this risk is unknown. In a multicenter, randomized, controlled trial, patients who presented to an emergency department in 14 hospitals across the United Kingdom were enrolled if myocardial infarction had been ruled out and high-sensitivity cardiac troponin testing indicated an intermediate risk of a cardiovascular event. Participants were randomly assigned to receive either outpatient computed tomographic (CT) coronary angiography–guided care or standard care. Adding CT did not reduce cardiovascular events. Severe

hypertriglyceridemia is associated with an increased risk of acute pancreatitis. Plozasiran, a small interfering RNA targeting APOC3 (inhibits lipoprotein lipase) messenger RNA, lowers triglyceride levels and potentially mitigates the risk of acute pancreatitis. In two double-blind, placebo-controlled trials, 757 adults with severe hypertriglyceridemia were randomly assigned in a 2:1 ratio to receive plozasiran (25 mg) or placebo at baseline and at months 3, 6, and 9. Plozasiran lowered triglycerides by 80% and sharply reduced pancreatitis. Atherosclerosis may begin in early adulthood and remain clinically silent for decades before cardiovascular disease manifests. Although silent atherosclerosis is associated with cardiovascular events and death independent of traditional cardiovascular disease risk factors, its age- and sex-specific prevalence, vascular territory distribution, and plaque volume across adult life remain incompletely defined. Investigators conducted a prospective cohort study in Denmark and Spain. Adults 18 to 70 years of age without known atherosclerotic cardiovascular disease were enrolled in five prespecified age strata that included balanced numbers of women and men. Silent atherosclerosis was assessed at baseline with three-dimensional vascular ultrasonography of the carotid and femoral arteries and with coronary computed tomographic angiography. The study of silent atherosclerosis showed that the disease was detectable in early adulthood, with age- and sex-associated increases in prevalence across arterial territories and marked increases in plaque volume. B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) have distinct roles in IgA-producing B-cell populations and appear to be central to the pathogenesis of IgA nephropathy. Povetacicept, an enhanced, variant transmembrane activator and calcium-modulator and cyclophilin-ligand interactor (TACI)–Fc fragment fusion therapeutic, is engineered for dual inhibition of BAFF and APRIL. In a double-blind, placebo-controlled trial, participants with biopsy-proven IgA nephropathy receiving stable background therapy were randomly assigned in a 2:1 ratio to receive povetacicept at a dose of 80 mg or placebo subcutaneously every 4 weeks. The primary end point of this prespecified interim analysis was the change in the 24-hour urinary protein-to-creatinine ratio at week 36. Secondary end points were the change at week 36 in galactose-deficient IgA1 levels and hematuria resolution at week 36 among participants with baseline hematuria. Povetacicept sharply reduced all endpoints. The N Engl J Med review is about thrombolysis in patients with acute

stroke. The mystery patient is the woman with a plasma calcium of 18 mg/dL that I discussed last week. In the Lancet, the strategy of testing troponin in patients suspected of having a coronary syndrome at onset and then again at 3 h, was compared to a repeat testing after only 1 h delay was tested in a randomized trial. Testing at 1 h was noninferior to testing at 3 h. However, time spent in the emergency department remained unchanged. In the next Lancet paper, a meta-analysis of all trials studying this issue, gave the same result. In short, cutting corners was safe but accrued no advantages in reducing health care issues including costs. Reultatug rezetecan combines an anti-HER3 antibody with a topo-isomerase inhibitor. A randomized trial from China shows that this new drug provides a novel treatment option for patients with non-small cell lung cancer. Lancet next reports on the 2026 “Lancet-Countdown” on health and climate change. We then encounter a Lancet patient with an eruptive histiocytosis mimicking lymphoma. In Science Magazine, GLP-1 agonists are the focus in this special issue. We inspect an article on obesity pharmacotherapies and the possible effects of GLP-1 agonists on cognition. Washington Post reports on exercises that lower blood pressure. We are steered to a BMJ report claiming that “wall sitting” lowers blood pressure. Try wall sits; they are not easy. I prefer swallowing candesartan. No oral presentation this week. We start again on Nov. 18.

Sincerely, Fred Luft

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