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 56-year-old woman presented to the emergency department with a 3-week history of leg swelling. On physical examination, pitting edema in both legs was seen and a urine sample was collected. Laboratory studies were notable for a low serum albumin level and a very elevated urinary protein-to-creatinine ratio. Which of the following diagnostic tests is most likely to explain the appearance of the patient's urine? You are offered: Urinary chylomicron and triglyceride levels, Urine culture, Urine microscopy for dysmorphic red cells, Urine microscopy for white cell casts, and Urine protein electrophoresis. The urine is a urinary classic, mostly seen "as the worm turns". Massive pulmonary embolism causing shock is treated with a lysis therapy, namely a recombinant plasminogen activator and then anticoagulation. Secondary hemorrhage is a problem. But how about less severe pulmonary embolism? Investigators conducted a multinational, adaptive-design trial with blinded outcome adjudication to test a novel approach. Patients with intermediate-risk pulmonary embolism (with a ratio of right ventricular end-diastolic diameter to left ventricular end-diastolic diameter of ≥1.0 and an elevated troponin level) were eligible if they had at least two indicators of cardiorespiratory distress. Patients were randomly assigned to undergo ultrasound-facilitated, catheter-directed fibrinolysis with alteplase plus anticoagulation (the intervention group) or anticoagulation alone (the control group) according to prespecified treatment protocols. The primary outcome was a composite of pulmonary embolism–related death, cardiorespiratory decompensation or collapse, or symptomatic recurrence of pulmonary embolism within 7 days. The novel technique was better and safer than merely heparinization alone. Several years back, augmenting left ventricular function with various cardiac "stem-cell" approaches in patients with severe heart failure appeared promising and then disappeared from the scene but hope springs eternal. Biologic ventricular assist tissue (BioVAT) is formulated from engineered heart muscle composed of cardiomyocytes and stromal cells derived from allogeneic induced pluripotent stem cells for cardiac remuscularization in patients with heart failure and a reduced left ventricular ejection

fraction. In the BioVat study, the progenitor cells (cardiomyocytes and supporting stromal cells) are allogeneic. They originate from a standardized bank of healthy, human induced pluripotent stem cells (iPSCs) rather than being harvested from each individual patient. Investigators conducted an open-label, phase 1–2 study of tissue-engineered heart repair by means of BioVAT transplantation. All the study patients had symptomatic heart failure with a reduced left ventricular ejection fraction of 35% or less that was refractory to guideline-directed medical therapy. The dose-finding part of the study identified BioVAT assembled from 20 engineered-heart-muscle units as the safe maximal dose. The transplant recipients had increases in measures of the target heart-wall thickness in diastole, the left ventricular ejection fraction, and quality of life at the prespecified 3-month interim analysis. Of the 20 patients who underwent BioVAT transplantation, all had adverse events. Zanidatamab, a dual human epidermal growth factor receptor 2 (HER2)–targeted bispecific antibody, plus chemotherapy both with and without tislelizumab (anti–programmed death 1), showed encouraging efficacy and safety as first-line therapy in phase 2 studies involving patients with HER2-positive gastroesophageal adenocarcinoma. Investigators randomly assigned (three groups), patients with previously untreated, centrally confirmed HER2-positive advanced gastroesophageal adenocarcinoma to receive zanidatamab and tislelizumab plus chemotherapy, zanidatamab plus chemotherapy, or trastuzumab plus chemotherapy. Anti HER2 plus PD1 receptor blockade carried the day. In children with Chiari type I malformation and syringomyelia, neurosurgical posterior fossa decompression (PFD) provides clinical improvement, but whether duraplasty (incising the dura and placing a dural graft) improves outcomes is unclear. Neurosurgeons conducted a multicenter, cluster-randomized, controlled trial of PFD with duraplasty (PFD-D) as compared with PFD alone. Dispensing with duraplasty reduced adverse events; however, noninferiority of the simpler approach could not be shown. Systemic leishmaniasis (Kala Azar) remains an important clinical challenge. N Engl J Med reviews leishmaniasis. The N Engl J Med patient is a 64-year-old woman with fatigue, memory changes, and falls. MRI of the head showed numerous hyperintensities on FLAIR images. In the Lancet, we first confront the efficacy of ocrelizumab (Anti CD20) in the treatment of relapsing and progressive multiple sclerosis. A higher antibody dose does not beat the standard dose. In a second study, ocrelizumab shows efficacy in multiple-

sclerosis patients who are older and have progressed to more severe disease. Prasinezumab is an antibody directed at alpha-synuclein that causes Parkinson's disease. Alas, prasinezumab did not meet required endpoints in a randomized Lancet trial. Lancet next presents two papers on Alzheimer's disease, the first looks at biomarkers already at an early age in a cohort study, the second examines modern MRI imaging options. Then, in a disappointing trial, semaglutide as an oral formulation did not favorably alter the course of Alzheimer's disease. The Lancet review is directed at Alzheimer's disease. In Science Magazine, we learn that in the US, NIH and NASA are placing limits on non-US co-authors on scientific papers. The Trump administration is apparently now going after international scientific cooperations. In the Washington Post, we encounter how Trump appointees are pushing to put his face on the US currency. The next presentation will be in English at 16:00, German at 17:00, and will take place will on Wednesday May 27, 2026.

Sincerely, Fred Luft

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