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 83-year-old woman with type 2 diabetes mellitus presented with a 6-month history of painful rash. Physical examination findings are shown. The glycated hemoglobin level was 9.1% (reference value, <5.8), which had increased from a level of 6.6% measured 4 months earlier. What is the most likely diagnosis? You are offered: Acquired acrodermatitis enteropathica; Necrolytic acral erythema; Necrolytic migratory erythema; Staphylococcal scalded skin syndrome; and Stevens-Johnson syndrome. Hint, the rash looks awful and necrotic; the CT shows a pancreatic tumor, the HbA1C value recently got worse. Patients with muscle-invasive bladder cancer who are ineligible for cisplatin-based chemotherapy proceed directly to radical cystectomy with pelvic lymph-node dissection. Perioperative therapy may improve outcomes in this population. In a phase 3, open-label trial, participants with muscle-invasive bladder cancer who were ineligible for or declined cisplatin-based chemotherapy were randomly assigned to perioperative (neoadjuvant and adjuvant) enfortumab vedotin, an antibody–drug conjugate directed at nectin-4, plus pembrolizumab and surgery or surgery alone (control). The primary end point was event-free survival. Enfortumab vedotin plus pembrolizumab was decidedly superior to surgery alone. Catheter-based closure of the left atrial appendage is an alternative to oral anticoagulation for stroke prevention in patients with atrial fibrillation. The effectiveness of this strategy, as compared with physician-directed best medical care, in patients at high risk for stroke and bleeding is unknown. In a multicenter randomized trial conducted in Germany, investigators assigned patients with atrial fibrillation and a high risk of stroke and bleeding to undergo left atrial appendage closure or to receive physician-directed best medical care (including direct oral anticoagulants, if eligible). The primary end point, tested for noninferiority, was a composite of stroke (ischemic or hemorrhagic), systemic embolism, major bleeding, or cardiovascular or unexplained death, assessed in a time-to-event analysis. Appendage closure was not noninferior to DOACs; in other words, “not as good”. BCL11A (B-Cell CLL/Lymphoma 11A) is the transcription factor that shuts off gamma-chain production and starts beta-chain synthesis at birth so that

hemoglobin F is substituted by hemoglobin A after birth. The beta chain is mutated in sickle-cell anemia and in beta thalassemia, both devastating hemoglobinopathies. Reversing BCL11A could result in hemoglobin F synthesis that shifts the hemoglobin-oxygen saturation curve leftward to a higher saturation level at any given PO_2. With CRISPR-Cas9 editing technology, shutting BCL11A down in bone-marrow precursor cells is possible. The tradename of this strategy is called “reni-cell”. Reni-cell technique was performed in sickle-cell anemia patients and in beta-thalassemia-major patients. Hemoglobin F levels increased to about half of total in both groups and transfusion requirements largely disappeared. Major adverse events were not encountered. The role of long-term beta-blocker therapy after a myocardial infarction in patients without left ventricular systolic dysfunction or heart failure is unclear in the era of contemporary coronary-artery reperfusion and secondary prevention interventions. Investigators conducted an open-label, randomized, noninferiority trial at 25 centers in South Korea. Patients whose condition remained stable after a myocardial infarction, who had a left ventricular ejection fraction of at least 40% and no heart failure, and who had received beta-blocker therapy for at least 1 year after the myocardial infarction. Stopping the beta-blocker was non-inferior to (as good as) continuing the drug. The N Engl J Med review is on glucagon-like receptor (GLP)-1 agonists. The N Engl J Med mystery patient is an obese adult man who gorges himself at a US “all-you-can-eat” restaurant. Two-to-three days later he vomits, becomes confused, and lapses into coma. A marked increase in ammonia levels is found, although he does not have liver disease. What could be the explanation? In the Lancet, we confront child-hood cancer worldwide. The six most common are chronic lymphatic leukemia, Burkitt lymphoma, Hodgkin’s disease, retinoblastoma, Wilm’s tumor, and low-grade glioma. From world-wide registries a Cancer Survival Index was derived. In the next report, the Global Burden of Disease study reports for 2023. The Service Delivery Indicators (SDI) for health are a set of standardized metrics developed by the World Bank to assess the quality of primary health care services. The SDI predicts the years of life lost. As expected, poorer countries fare less well than richer countries. How best to repair critical left-main coronary disease? We inspect a 10-year outcome of a randomized trial of CABG versus drug-eluting stents. Modern stenting seems to be as good. The Lancet review is on stimulators of pyruvate kinase, which converts phospho-enol-

pyruvate to pyruvate. Recall that erythrocytes have no mitochondria and therefore cannot rely on the citric-acid cycle for energy. As a result of pyruvate-kinase stimulation, bis-phosphoglycerate levels are reduced, and the oxygen-saturation curve is shifted leftward. This effect would reduce sickling in sickle-cell anemia patients and even thalassemia patients could benefit. Perhaps, less gene-therapy would help these patients. The fibroblast activation protein (FAP) is a serine protease present in atherosclerotic plaques and contributes to plaque instability. An FAP inhibitor (FAPI) can be visualized with PET-CT. In Science Magazine, we learn that targeting modulated vascular smooth muscle cells in atherosclerosis via a FAP-directed immunotherapy with a BiTE antibody would be a potential therapeutic strategy. In the Washington Post, we observe the fascinating sex life of the octopus. The presentation is in English at 16:00, German at 17:00, and will take place will on Wednesday April 1, 2026.

Sincerely, Fred Luft

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