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 previously healthy 4-year-old boy presented to the emergency department with leg pain and an inability to bear weight on his left side. While jumping on a trampoline with his father at home, he had leaped higher than usual, landed on his feet, and then felt the leg pain. Physical examination was notable for knee swelling and tenderness to palpation on the left side. Radiographs of the left tibia and fibula are shown. We observe a subtle curving fracture line at the tibial plateau. What is the most likely mechanism of this injury? You are offered: Avulsion of the patellar tendon, Bending of the bone, Blunt trauma, Compressive axial forces on the bone, and Twisting around a planted foot. An axial force is a load that acts directly parallel to the longitudinal (center) axis of a structural member or object. The 250 million persons infected with hepatitis B virus cannot be cured; suppression therapy is all we can offer. Or could they? Treatment with bepirovirsen, an antisense oligonucleotide targeting hepatitis B virus (HBV) transcripts, has the potential to result in a functional cure, defined by at least 24 weeks of a sustained HBV DNA level below the lower limit of quantification (LLOQ) and hepatitis B surface antigen (HBsAg) loss after fixed-duration therapy. Investigators randomly assigned adults with noncirrhotic chronic HBV infection in a 2:1 ratio to receive subcutaneous bepirovirsen (at a weekly dose of 300 mg) or placebo for 24 weeks. All the patients were receiving stable nucleoside or nucleotide analogue (NA) therapy and had an HBsAg level of more than 100 to 3000 IU per milliliter. Eligible patients discontinued NA therapy at 48 weeks. The primary outcome was a functional cure at week 72. Bepirovirsen cured 20%; control infusion cured no-one. The results look promising. Pulse-field ablation for atrial fibrillation takes much less time, is easier to perform and could be better. But first we need to know that pulse-field ablation is effective and safe. Cardiologists conducted an international, randomized trial involving patients with previously untreated persistent atrial fibrillation. The patients were randomly assigned in a 2:1 ratio to receive PFA performed with a pentaspline catheter or to receive antiarrhythmic-drug therapy. All the patients received an insertable cardiac monitor. The primary effectiveness end point was the short-term and long-term

success of treatment through 12 months. Short-term success was defined as procedural success in the PFA group and the absence of ablation during the blanking period (90 days after treatment initiation) in the antiarrhythmic-drug group. Long-term success was defined as freedom from recurrence of atrial arrhythmias, repeat ablation, or need for antiarrhythmic drugs from 90 days through 12 months (in the PFA group) and freedom from amiodarone use at any time. The primary safety end point was device- and procedure-related serious adverse events. One year later, the PFA group did much better than the drug therapy group with acceptable safety issues. Tranexamic acid inhibits the binding of plasmin to fibrin. Whether a hospital policy of tranexamic acid administration for patients undergoing major noncardiac surgery safely reduces the need for red-cell transfusion is uncertain. Investigators conducted a multicenter, double-blind, cluster-randomized, placebo-controlled trial involving patients undergoing noncardiac surgery who were at high risk for red-cell transfusion. Hospitals were randomly assigned at 4-week intervals to a hospital-wide policy of intraoperative tranexamic acid or placebo. The coprimary effectiveness and safety outcomes were transfusion of red cells during the index hospitalization and diagnosis of venous thromboembolism within 90 days, respectively. The safety outcome was assessed for noninferiority. Tranexamic acid reduced transfusions and caused no adverse events compared to placebo. Safer, more effective treatment regimens for rifampicin-resistant tuberculosis are needed. Investigators conducted a phase 3, open-label, pragmatic, randomized, controlled noninferiority trial in South Africa to assess a 6-month treatment strategy for pulmonary rifampicin-resistant tuberculosis. Participants with pulmonary rifampicin-resistant tuberculosis who were 6 years of age or older were randomly assigned to a regimen consisting of bedaquiline, linezolid, delamanid, and levofloxacin or clofazimine or both for 6 months (trial-strategy group) or the 9-month standard-of-care treatment regimen that was current in South Africa (control group). The new regimen for six months was “non-inferior” to the old regimen that requires 9 months treatment time. Anti-CD19 chimeric antigen receptor (CAR) T-cell therapy (now called tisagenlecleucel) is a standard treatment for relapsed or refractory B-cell non-Hodgkin lymphomas. Long-term results and curative potential remain uncertain. The University of Pennsylvania group report their results in patients followed 10 years after CAR T-cell therapy. Among patients with heavily pretreated B-cell non-Hodgkin

lymphoma, a single infusion of tisagenlecleucel led to decade-long remissions (lymphoma-free survival) in approximately one third of the patients with large B-cell lymphomas and in nearly one half of those with follicular lymphoma. The N Engl J Med review is about peanut allergy. Much has changed here and prophylactic strategies generally highly effective. The mystery patient this week is a middle-aged man who is discovered to be diabetic with HbA1C at 14%. The patient develops weight loss, profound weakness in his lower extremities without real signs of muscle inflammation. We used to call this disease “amyotrophy”. Now it has a new name. In the Lancet, we inspect the OptiTROP trial. This study assesses the efficacy of an antibody directed against TROP2 protein (present on non-small-cell lung cancer cells) that carries a tropoisomerase I inhibitor as a Trojan-Horse strategy. Combined with pembrolizumab (checkpoint inhibitor) the strategy should beat conventional chemotherapy plus pembrolizumab alone for non-small-cell lung cancer. And it did. Next comes the HORMONi-6 trial; the study addresses the same disease. Ivonescimab is an antibody directed against the T-cell checkpoint while also inhibiting VEGF. This antibody was compared to (anti-checkpoint-alone) tislelizumab (both with standard chemotherapy. Again, a modest advance could be shown. Next, the Lancet addresses the issue of food-labeling. Can we get the kiddies from becoming fat by telling them (or their mums) that the yummies inside are toxic? A study from Chile suggests that food labeling could be helpful. Most of us will die of cardiovascular disease (heart failure, coronary disease and stroke). We have known for generations that smoking, hypertension, cholesterol, obesity, type-2 diabetes and aging drive cardiovascular disease. These risk factors have been now relabeled as “cardiometabolic multiple long-term conditions (MLTC). Now there is a wonderful opportunity for “commissions” to be formed (experts with not enough to do) to ruminate on this state-of-affairs. The Lancet presents not-one but-three reviews on MLTC. We learn that integration of traditional disease biomarkers with multimodal data including genomic profiles, electronic health records (EHR), clinical measurements, wearable-derived metrics, and imaging phenotypes will enable the identification of disease subtypes and improve prediction of disease trajectories. At age 69 years in 1944, Oswald Avery proved that bacterial virulence is transferred in the form of DNA. He died and the Nobel Prize went to others. However, the interbacterial shuttling of proteins via double-membrane vesicles is still appreciated,

as we learn in Science Magazine this week. Vesicle donors and recipients actively cooperate to benefit the entire bacterial population when an antibiotic treatment comes along. In Washington Post, we encounter a couple both receiving semaglutide (GLP-1 agonist) for weight loss. Is it socially proper for them to share a single entre, instead of the usual two, in a restaurant? No oral presentation this week. The next presentation will be in English at 16:00, German at 17:00, and will take place will on Wednesday July 8, 2026.

Sincerely, Fred Luft

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