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 33-year-old butcher presented with a 3-day history of painful ulcers on his left hand and several hours of worsening arm swelling. Three days before the ulcers appeared, he had slaughtered a sick cow. Ipsilateral arm edema and axillary lymphadenopathy were also noted. The lesions rapidly progressed to large hemorrhagic bullae 24 hours after presentation and subsequently ruptured 72 hours after presentation. Which of the following is the most likely diagnosis? You are offered: Cowpox, Cutaneous anthrax, Cutaneous brucellosis, Cutaneous *Mycobacterium bovis* infection, and Ulceroglandular tularemia. Hint: the condition used to be called: “malignant pustule”. There is controversy about venous thromboembolism (VTE) prophylaxis after major orthopedic surgery. Cutaneous low-molecular-weight heparin is no longer invariably used. Aspirin after an initial short course of rivaroxaban has been shown to be safe and effective for the prevention of venous thromboembolism after total hip or total knee arthroplasty, but uncertainty remains about the use of aspirin alone. In a multicenter, double-blind, randomized, controlled trial, investigators assigned patients to receive once daily thromboprophylaxis with either 81 mg of aspirin or 10 mg of oral rivaroxaban for the first 5 days after total hip or total knee arthroplasty. All the patients then received further thromboprophylaxis with 81 mg of aspirin daily for 9 additional days after knee arthroplasty and for 30 additional days after hip arthroplasty. Patients were followed for 90 days for symptomatic venous thromboembolism and for bleeding complications (primary safety outcome). Any differences were trivial, while events were few. The issue continues. Studies comparing aspirin with anticoagulants for VTE prophylaxis after total hip or knee arthroplasty have had conflicting results. In a comparative-effectiveness noninferiority trial, investigators randomly assigned patients undergoing elective hip or knee arthroplasty to receive aspirin (81 mg twice daily), warfarin (to a target international normalized ratio of 2.0), or rivaroxaban (10 mg daily) for 30 days. Endpoints were similar to those investigated in the first study. Events were few and differences were trivial. What to do? Is aspirin enough? As the baseline risk of venous thromboembolism (VTE) increases, the absolute benefits of anticoagulation for the

prevention of VTE may increase. As the risk of bleeding or wound complication increases, the net benefit of anticoagulation may decrease. When the bleeding risk with pharmacologic prophylaxis is deemed to be unacceptable, mechanical prophylaxis with intermittent pneumatic compression warrants consideration. What to do after management for acute coronary syndromes or acute MI after stenting? Clopidogrel is evidently “out”. Whether prasugrel or ticagrelor should be the preferred P2Y12 inhibitor for patients with an acute coronary syndrome is uncertain. Investigators conducted a registry-based, open-label, stepped-wedge, cluster-randomized trial in Sweden involving adults who had undergone percutaneous coronary intervention for an acute coronary syndrome. Seven regions, grouped into three clusters, switched from ticagrelor to prasugrel as the default P2Y12 inhibitor in a randomized sequence across four 9-month periods between 2021 and 2024. The primary end point was a composite of death from any cause, fatal or nonfatal myocardial infarction, or fatal or nonfatal stroke through 1 year, as well as bleeding, as ascertained from national registries. This large real-world registry study found that switching the default P2Y12 inhibitor policy from ticagrelor to prasugrel resulted in similar cardiovascular protection but a significantly lower rate of major bleeding (4.2% vs. 4.4%) but is 0.2% clinically important? In patients with IgA nephropathy, complement activation drives glomerular inflammation, which leads to hematuria, proteinuria, and nephron loss. Ravulizumab is a terminal complement inhibitor that prevents formation of C5a and C5b-9. In a phase 3 trial, investigators enrolled adults with IgA nephropathy who had an estimated glomerular filtration rate of at least 30 ml per minute per 1.73 m2 of body-surface area and proteinuria (24-hour urinary protein-to-creatinine ratio [with protein and creatinine both measured in grams] of ≥0.75 or total urinary protein excretion of ≥1.0 g per day), despite standard therapy. Patients were randomly assigned to receive an intravenous infusion of either ravulizumab or placebo every 8 weeks. In the prespecified interim analysis, the primary efficacy end point was the change from baseline in the 24-hour urinary protein-to-creatinine ratio at week 34. Blocking C5a sharply reduced proteinuria in these IgA-nephropathy patients. The N Engl J Med review is on malaria. The mystery patient is a man who develops a second bout of cardiomyopathy years after the first from which he has recovered. In the meantime, he develops decreased testosterone levels, and his gonads appear to

shrink. In the Lancet, we confront the combination of trifluridine/tipiracil (FTD-TPI), a DNA antimetabolite and degradation retardant in the treatment of refractory colorectal cancer. The question in the Lancet study was, should FTD-TPI be given as a 28-day cycle or are 14 days enough? A 14-day schedule of FTD-TPI was no worse than the 28-day schedule. Mismatch repair enzyme mutations are well known in colorectal cancers but also occur in other tumors such as endometrial cancer. Would pembrolizumab help here as it does in colorectal tumors? In a first-line study published in the Lancet, it clearly did. Huge numbers of HIV-positive small children in Africa get pneumonia. In addition to bacteria, pneumocystis prophylaxis treatment, TBC and cytomegalovirus (CMV) are commonly involved. To test any value in empirical treatment, a factorial superiority trial was performed. We learn from two papers that covering CMV is worthwhile treating, while covering TBC is probably not. Next, a Lancet commission reports on eliminating poverty in China. Then, Lancet comments on “ambient scribes”. These are recording programs that (AI supported) generate clinic notes after patient encounters. “Regulators” continually require longer written notes, can computer programs do it (or could the regulators also be replaced by computers)? Then, in Science Magazine we encounter the difficulty of making minute vascular anastomoses (transplanting mouse kidneys for example). The integrated microneedle-interlocking adhesive system (iMAS) is a bioinspired, sutureless surgical bioadhesive platform designed to connect small-caliber blood vessels (microvascular anastomosis) and continuously monitor tissue health. Chinese investigators report a revolutionary new method how to connect tiny blood vessels. In Washington Post, we meet dark chocolate which tastes better than dark matter I suppose. We meet on Nov. 18, 16:00 English; 17:00 German.

Sincerely, Fred Luft

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