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 22-year-old man presented to the emergency department with a 5-day history of painful lesions on his hands, feet, and mouth, with accompanying fever and malaise. Two months earlier, he had had a similar episode. PCR testing from a swab sample of the lip ulceration was positive for herpes simplex virus (HSV) type 1. Which of the following diagnoses best explains the lesions on the tongue and palm? We are offered: Bullous pemphigoid, Disseminated herpes infection, Erythema multiforme, Sweet syndrome, and Urticaria. The clues here are HSV and “bullseye” lesions. We know about human epidermal growth factor 2 (HER2) and its expression in breast cancer, but how about HER2 mutations? Until recently, no first-line targeted treatment options were available for patients with HER2–mutant (in about 2%) non–small-cell lung cancer (NSCLC). Zongertinib is an oral, irreversible tyrosine kinase inhibitor that selectively inhibits HER2 while sparing wild-type epidermal growth factor receptor (EGFR), thereby minimizing associated toxic effects. Investigators conducted a phase 1a–1b, multicohort trial to assess zongertinib in patients with advanced or metastatic nonsquamous HER2-mutant NSCLC. The primary end point was objective response. Zongertinib helped patients with HER2 mutations. Maternal infection and sepsis are major causes of maternal death and severe illness worldwide, particularly in low- and middle-income countries. Inconsistent implementation of evidence-based recommendations for infection prevention and management and delays in detection and treatment of maternal sepsis contribute to the number of preventable deaths. Investigators conducted a cluster-randomized trial to assess a multicomponent intervention, the Active Prevention and Treatment of Maternal Sepsis (APT-Sepsis) program. The program was designed to support health care providers in achieving three goals: adherence to World Health Organization (WHO) hand-hygiene standards; adoption of evidence-based practices for maternal infection prevention and management; and early detection of sepsis and use of the FAST-M (fluids, antibiotics, source control, transfer if required, and monitoring) treatment bundle. Usual care (presumably less of all these things) was provided in the control group, along with

dissemination of guidelines. The primary outcome was a composite of infection-related maternal outcomes. The interventions helped (a little). Factor VIII deficiency causes Hemophilia A. Factor VIII is large molecule and tough to approach with gene therapy. Binding Factor XIa to Factor X to activate the latter could treat Hemophilia A. Mim8 (denecimig), a bispecific antibody mimicking activated factor VIII, was developed for bleeding prophylaxis in patients with hemophilia A with or without factor VIII inhibitors. In a phase 3, randomized trial, investigators assigned patients 12 years of age or older with hemophilia A with or without inhibitors to receive subcutaneous Mim8 once weekly or once monthly at a dose tiered according to body weight and given in a fixed injection volume (0.8 ml). Patients who had been receiving on-demand treatment before the trial were assigned to continue on-demand treatment (group 1) or receive Mim8 once weekly (group 2a) or once monthly (group 2b). Briefly, Mim8 emerges as a credible and effective treatment for hemophilia A. Diagnosing tuberculosis with Ziel-Nielsen staining and culture is tedious and takes time (up to 6 weeks). Improved diagnostic tools for tuberculosis that are suitable for use in peripheral health centers are essential for reducing the persistent gap between estimated and notified cases. The diagnostic accuracy and usability of the MiniDock MTB test for detecting pulmonary tuberculosis is unknown. Investigators conducted a prospective, cross-sectional study at outpatient centers in India, Nigeria, the Philippines, South Africa, Uganda, Vietnam, and Zambia. The MiniDock MTB test looks like a real advance to combat this disease with a near instantaneous diagnosis in many cases. Barrett’s esophagitis is a precancerous lesion first described by the pioneering thoracic surgeon, Norman Barrett. N Engl J Med reviews the subject. The N Engl J Med mystery patient is a hepatitis-C-positive 76-year-old woman who develops a recurrent purpuric rash, severe proteinuria, and rapidly progressive renal failure. In the Lancet, the first study addresses alcohol-use disorder. Could this addiction be improved by GLP-1 agonists? A randomized controlled trial of semaglutide in obese heavy drinkers yields a positive result. Does ovarian ablation improve survival in breast cancer patients, even if they receive tamoxifen? A Lancet meta-analysis indicates that such is the case. Myasthenia gravis is (generally) caused by auto-antibodies directed against the nicotinergic acetylcholine receptor. Antibody depletion (rituximab etc.) does not always help. The complement system (including C-5) participates. Could an siRNA drug directed at C-5 help these

patients? A randomized, controlled trial indicates that this is the case. Papilloma virus (HPV) vaccination sharply reduces cervical cancer. Low and middle-income countries are poorly served with HPV vaccine administration. A Lancet report laments this state-of-affairs. Depression is a wide-spread chronic disease of endemic and epidemic proportions. Lancet reviews the topic. In Science Magazine, we learn about large language models (artificial intelligence or AI) applied to clinical medicine. Investigators applied various AI models (including Chat-GPT) to the N Engl J Med weekly "mystery-patient" exercise (goes back >100 years) and similar quizzes and compared the outcomes to "master" clinicians. AI beats the real doctors and gives us insight into the medicine of the future. Donald Trump puts his name on public buildings, academic institutions and the nation's coinage. In Washington Post, we learn that Trump has now put his picture onto US passports. Emperor Nero behaved similarly but at least the latter could play the fiddle.

The presentation is in English at 16:00, German at 17:00, and will take place will on Wednesday May 6, 2026.

Sincerely, Fred Luft

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