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 46-year-old man with chronic kidney disease presented with a 2-year history of painless shortening and rounding of the fingertips. Ten years earlier, he had received a diagnosis of chronic kidney disease due to obstructive nephropathy from nephrolithiasis. Since then, he had been intermittently lost to follow-up. On physical examination, all the fingertips were short, broad, and bulbous, with a pseudo-clubbing appearance. The toes had similar but less severe changes. What do the findings on the exam and imaging represent? You are offered: Acro-osteolysis, Arthritis mutilans, Clubbing (Trommelschlägelfinger), Hypertrophic osteoarthropathy, and Sclerodactyly. We discuss the options. Mucoactive agents (slime looseners) are widely used in patients with acute respiratory failure despite limited evidence of their effectiveness or safety. Investigators conducted a multicenter, open-label, randomized trial with a 2-by-2 factorial design that involved critically ill, mechanically ventilated participants 16 years of age or older with acute respiratory failure and difficult-to-clear secretions. All participants received usual care along with carbocisteine (750 mg three times daily enterally), 6% or 7% nebulized hypertonic saline (HTS) (4 ml four times daily), both interventions, or usual care alone for up to 28 days. The primary outcome was duration of mechanical ventilation. Both these time-honored slime loosening interventions were useless and caused harm. Wheezing illnesses are a leading cause of hospitalization for preschool-age children and are frequently treated with antibiotics. Observational studies have shown more frequent isolation of three pathogenic bacteria (Streptococcus pneumoniae, Moraxella catarrhalis, and Hemophilus influenzae) from nasopharyngeal samples from children with recurrent episodes of wheezing than from those without such illnesses. In a multicenter trial, investigators randomly assigned patients 18 to 59 months of age who presented to an emergency department with a moderate-to-severe episode of wheezing to receive azithromycin once daily at a dose of 12 mg per kilogram of body weight or matching placebo for 5 days. The primary outcome was the sum of scores on the Asthma Flare-up Diary for Young Children (ADYC) over 5 days. Azithromycin did not improve outcomes (with or without the

putative pathogens). Sunvozertinib received accelerated approval for use in later lines of therapy for patients with advanced non–small-cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon-20 insertion mutations. Data are needed on the efficacy and safety of sunvozertinib as a first-line treatment for NSCLC. In a phase 3, international trial, investigators randomly assigned, in a 1:1 ratio, patients with advanced nonsquamous NSCLC with EGFR exon-20 insertions to receive sunvozertinib or chemotherapy (carboplatin–pemetrexed). The primary end point was progression-free survival. These patients with an exon-20 EGFR mutation were helped by sunvozertinib. Although medications with glucagon-like peptide-1 (GLP-1) receptor agonist activity have transformed the management of obesity and shown substantial cardiometabolic benefits, unmet needs remain. Survodutide, an investigational glucagon receptor–GLP-1 receptor dual agonist (also addresses the glucagon receptor), led to substantial weight reduction in a phase 2 trial involving adults with obesity without diabetes. In a phase 3, double-blind trial, investigators randomly assigned adults with a body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) of 30 or higher, or 27 or higher with at least one obesity-related complication (excluding diabetes), in a 1:1:1 ratio to receive once-weekly survodutide administered subcutaneously at a dose adjusted up to 3.6 mg or 6.0 mg or placebo, in addition to counseling for lifestyle modification. The two primary end points were the percent change in body weight and a reduction in body weight of at least 5% from baseline to week 76. Survodutide caused weight loss and met goals. The safety issues were about the same as with earlier GLP-1 agonists. Classic myeloproliferative neoplasms, including essential thrombocythemia, polycythemia vera, and primary myelofibrosis, are chronic, clonal hematopoietic stem-cell disorders. These disorders are driven by gain-of-function mutations in the genes Janus kinase 2 (JAK2), calreticulin (CALR), or the thrombopoietin receptor (MPL) that activate cytokine signaling. N Engl J Med reviews these diseases. The mystery patient is a 74-ear-old man who develops myasthenia gravis and is treated with conventional immunosuppression. His weakness gets worse and he develops hypoxemia. In the Lancet, we confront hepatocellular carcinoma, a very common cancer in the orient. This cancer is treated routinely with checkpoint inhibitors and VEGF inhibitors. Does primary tumor resection help? I randomized trial suggests it does. The next study

involves key-hole approaches for coronary bypass surgery. A randomized trial suggests that (if possible) key-hole surgery causes less morbidity than conventional sternotomy. About 80% of patients in both groups were managed “off-pump”. Dystrophin is a rod-shaped cytoplasmic protein, and a vital part of a protein complex that connects the cytoskeleton of a muscle fiber to the surrounding extracellular matrix through the cell membrane. Duchenne muscular dystrophy (mutated dystrophin) is a devastating muscle disease with no (or very few) therapeutic options. Deramiocel (also known as CAP-1002) is an investigational cell therapy to treat Duchenne muscular dystrophy (DMD) and its associated cardiomyopathy. It uses donor-derived heart cells to reduce inflammation, protect heart function, and slow the loss of upper limb strength in patients. These cells allegedly release micro-vesicles responsible for the effects. The cells are infused intravenously at periodic intervals. Lancet reports a randomized trial, which suggests efficacy of this immune-modulatory treatment. However, earlier an FDA advisory committee voted 9-3 that available data failed to show substantial evidence of effectiveness in treating Duchenne cardiomyopathy. The Lancet review is on psoriasis; lots of recent good news here. In Science Magazine, we inspect how cardiac vessels construct collaterals, at least in mice. The Washington Post features the recent solar eclipse.

Load down the file and join me again on August 19, 16:00 English and 17:00 German.

Sincerely, Fred Luft

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