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 11-year-old girl presented to the orthopedic clinic with a 1-month history of right thigh pain that worsened at night. Physical examination was notable for soft-tissue swelling over the distal thigh and limited range of motion of the knee on the right side. You are shown roentgenograms of the right knee. Which of the following is the most likely diagnosis? You are offered: Aneurysmal bone cyst, Chondrosarcoma, Osteoid Osteoma, Osteomyelitis, and Osteosarcoma. Hint, when clueless always pick the worst prognosis. For patients with atrial fibrillation, the use of oral anticoagulant therapy to prevent stroke is limited by the risk of bleeding. Left atrial appendage closure is considered for patients who are unsuitable candidates for long-term anticoagulation, but its role in patients who are eligible for anticoagulants has not been established. The primary efficacy end point — a composite of death from cardiovascular causes, stroke, or systemic embolism — was tested for noninferiority (noninferiority margin, 4.8 percentage points) after 3 years of follow-up. The primary safety end point, non–procedure-related bleeding, was tested for superiority. We recently saw a study from Germany in which “noninferiority” for left atrial appendage study could not be shown. This study was run by Boston Scientific. Noninferiority made it for the first endpoint, as did superiority for the second endpoint. Data are needed on the effect of oxygen delivered through a high-flow nasal cannula, as compared with standard oxygen therapy, on intubation and mortality in patients with acute hypoxemic respiratory failure. In a multicenter, open-label trial, investigators randomly assigned patients who had acute hypoxemic respiratory failure to receive high-flow-oxygen or standard-oxygen therapy. All the patients had a ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen of 200 or less, a respiratory rate of more than 25 breaths per minute, and pulmonary infiltrate on chest imaging. The primary outcome was death by day 28. High-flow nasal cannula that uses about 10-times more oxygen, was not superior to standard therapy with a simple rebreathing mask. For patients with acute myeloid leukemia (AML) who are 75 years of age or older or who are ineligible for intensive induction chemotherapy, azacitidine or decitabine plus venetoclax is the

standard of care, but parenteral administration imposes a burden on patients and providers. Oral decitabine–cedazuridine, approved in Europe for AML, has pharmacokinetic properties equivalent to those of intravenous decitabine but provides limited survival benefit as monotherapy. In a phase 1–2, open-label, multicenter, nonrandomized trial, investigators assigned patients with newly diagnosed AML who were 75 years of age or older or who were ineligible for intensive chemotherapy to receive oral decitabine–cedazuridine plus oral venetoclax. The old people with AML did pretty well with this treatment. HLA sensitization poses a major challenge to kidney transplantation for patients with end-stage kidney disease, especially for highly sensitized candidates. Attempts at antibody elimination (desensitization) have had inconsistent efficacy and have often failed to produce sustained reductions in anti-HLA antibodies in patients with the highest level of sensitization (calculated panel-reactive antibody score, ≥99.9%). CAR T-cell therapy could represent an answer to this dilemma. We inspect two reports suggesting that CAR T-cell therapy could be a solution for highly sensitized transplant patients. Recombinant adeno-associated virus (AAV) vectors are predominantly nonintegrating, but rare genomic integration events have been associated with oncogenesis in neonatal murine models. Investigators now report a case of a neuroepithelial tumor that developed in a 5-year-old boy with severe mucopolysaccharidosis type I (MPSI, Hurler subtype) 4 years after intracisternal magna administration of AAV serotype 9 gene therapy. The two-centimeter brain tumor was removed. The child is doing quite well, and the gene therapy has met its goal. Molecular analysis of the tumor showed clonal integration of rearranged AAV vector elements into the gene PLAG1 and expression of a chimeric AAV-PLAG1 transcript. The AAV vector was evidently responsible for the tumor. the U.S. Secretary of Health and Human Services (HHS), Robert F. Kennedy Jr. has used his position to aggressively reshape (i.e. hinder and limit) federal vaccine policy and public health recommendations. The N Engl J Med review is on childhood vaccine hesitancy. The mystery patient is 53-year-old man with Crohn's disease and psoriasis, both treated with immunosuppression. He develops endocarditis and a series of complications ensue. In the Lancet, we encounter a randomized controlled trial of the CD40 ligand dapiroliizumab pegol in conventionally treated systemic lupus erythematosus patients. CD40 ligand inhibitions appears to enable better control. What to do after obese people

have lost >20% of their body weight after GLP-1 inhibition? Lancet presents a tirzepatide study where patients were randomized to discontinue treatment, continued treatment or reduced treatment. All received life-style counseling. As expected, the placebo regained the most weight, the treatment group held their weight, and reduced treatment patients found a middle ground. At coronary angiography, fractional flow reserve identifies coronary patients with small vessel disease. The condition is called “coronary microvascular dysfunction”. Do these patients really do worse longitudinally? Lancet presents a long-term study suggesting that this is indeed the case, even after a two-year follow-up. The Lancet review is about polyendocrine metabolic ovarian syndrome (PMOS), previously called polycystic ovarian syndrome (PCOS). The name change is justified. Science Magazine shows us a single-cell study in cardiomyocytes elucidating heart failure with preserved ejection fraction (HFpEF). The study implicates faulty troponin I phosphorylation. Washington Post reports ejection of diabetes researchers from an annual American Diabetes Association meeting for distributing leaflets critical of Trump-and-Co’s eviscerating NIH. We also learn that contributors to Trump’s “ball room” have been awarded $50 billion in US government contracts. The next presentation will be in English at 16:00, German at 17:00, and will take place will on Wednesday June 10, 2026.

Sincerely, Fred Luft

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