Dear friends of clinical journal club - load the file down at <u>https://www.mdc-berlin.de/cjc</u>. 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 57-year-old man called emergency medical services to report a 1-hour history of chest pain. When he arrived at the hospital, his heart rate was 125 beats per minute, the blood pressure 128/84 mm Hg, and the oxygen saturation 99% while he was breathing ambient air. The physical examination was normal. An initial serum troponin I level was 35 ng per liter (reference range, 0 to 34). What does the (bizarre) electrocardiogram most likely represent? You are offered: Anteroseptal MI; Diffuse subendocardial ischemia, Pericarditis, Posterior myocardial infarction, and Wellen's syndrome. We discuss the options. Amino-acid infusions transiently increase renal blood flow and glomerular filtration rate (GFR). Acute kidney injury (AKI) is a serious and common complication of cardiac surgery, for which reduced kidney perfusion is a key contributing factor. Intravenous amino acids increase kidney perfusion and recruit renal functional reserve. However, the efficacy of amino acids in reducing the occurrence of AKI after cardiac surgery is uncertain. In a multinational, double-blind trial, investigators randomly assigned adult patients who were scheduled to undergo cardiac surgery with cardiopulmonary bypass to receive an intravenous infusion of either a balanced mixture of amino acids, at a dose of 2 g per kilogram of ideal body weight per day, or placebo (Ringer's solution) for up to 3 days. The primary outcome was the occurrence of AKI, defined according to the KDIGO guidelines. Secondary outcomes included the severity of AKI, the use and duration of kidney-replacement therapy, and all-cause 30-day mortality. AKI was slightly but significantly reduced. In an earlier study, azithromycin given to lower trachoma in African newborns and children seemed to reduce overall mortality (MORDOR Study). Twice-yearly mass distribution of azithromycin to children is a promising intervention to reduce childhood mortality in sub-Saharan Africa. The World Health Organization recommended restricting distribution to infants 1 to 11 months of age to mitigate antimicrobial resistance, although this more limited treatment had not yet been tested. Investigators randomly assigned rural communities in Niger to four twice-yearly distributions of azithromycin for children 1 to 59 months of age (child azithromycin group), four twiceyearly distributions of azithromycin for infants 1 to 11 months of age and placebo for children 12 to 59 months of age (infant azithromycin group), or placebo for children 1 to 59 months of age over the course of 2 years. Indeed, about a 2% absolute difference was achieved. After checkpoint and VEGF inhibitors for progressive renal cell cancer and then what? Belzutifan, a hypoxia-inducible factor 2a inhibitor, showed clinical activity in clear-cell renal-cell carcinoma in early-phase studies. In a phase 3, multicenter, open-label, active-controlled trial, investigators enrolled participants with advanced clear-cell renal-cell carcinoma who had previously received immune checkpoint and antiangiogenic therapies and randomly assigned them, in a 1:1 ratio, to receive 120 mg of belzutifan or 10 mg of everolimus orally once daily until disease progression or unacceptable toxic effects occurred. The dual primary end points were progression-free survival and overall survival. Progression free survival and overall responses were impressively reduced, compared to everolimus. Traumatic brain injury commonly features anemia. The effect of a liberal transfusion strategy as compared with a restrictive strategy on outcomes in critically ill patients with traumatic brain injury is unclear. Investigators randomly assigned adults with moderate or severe traumatic brain injury and anemia to receive transfusion of red cells according to a liberal strategy (transfusions initiated at a hemoglobin level of  $\leq 10$  g per deciliter) or a restrictive strategy (transfusions initiated at  $\leq 7$  g per deciliter). The primary outcome was an unfavorable outcome as assessed by the score on the Glasgow Outcome Scale-Extended at 6 months. Liberal transfusions did not help these patients; the contrary seemed to be the case. The N Engl J Med review is on sexual dysfunction in women. The weekly case is about a 59-year-old woman with severe anemia and a huge (neglected) breast mass. I saw this condition in medical school. Influenza is still with us and is lethal in patients >65 years. Vaccination is a good idea. A Lancet metaanalysis inspects the effects of antivirals (mostly neuraminidase inhibitors) as a treatment. Might help in severe cases, although certainty is low. Next comes the same idea with antivirals as prophylactic after exposure. Again, the answer is: "might" reduce risk. Next, Lancet presents a comprehensive review of GLP-1 agonist, semaglutide, in heart failure (SELECT Trial). Semaglutide reduced major adverse cardiac events (MACE) in obese patients, with or without heart failure, regardless of the heart failure type. The Lancet case is about a patient with "drop attacks" captured on closed-circuit television monitors. The Lancet review is on acute liver failure. A second Lancet review tackles non-small-cell lung cancer. The kyenurine pathway was not taught when I went to medical school but involves metabolism of tryptophan to NAD. In Science Magazine, we learn that beta-amyloid and tau proteins activate this pathway in glia, thereby reducing glucose availability. Alzheimer's disease in mice was markedly improved when this pathway was inhibited with currently available drugs. Deposits were reduced as well. In Washington Post, we learn that the anti-vaccine fringe presidential candidate, Robert F. Kennedy Jr., has opted out for Donald Trump. The Kennedy Legacy seems to be at an end. Read the file on-line and join me on August 28, in English and German.

Best regards, Fred Luft, at https://www.mdc-berlin.de/cjc