

Dear friends of clinical journal club - load the 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 6-month-old girl was brought to the emergency department with a 3-day history of redness and swelling of a toe. A physical examination is shown. Which of the following is the most likely underlying cause of the findings? You are offered: Allergic reaction, Cellulitis, Hair tourniquet, Nonaccidental trauma, Insect bite. The lesion has the appearance of a constrictive band. Daratumumab, an anti-CD38 monoclonal antibody, has been approved for the treatment of multiple myeloma. Data are needed regarding the use of daratumumab for high-risk smoldering multiple myeloma, a precursor disease of active multiple myeloma for which no treatments have been approved. A randomized controlled trial suggests that smoldering multiple myeloma may not just be smoldering after all. In a previous phase 2 trial, bacille Calmette–Guérin (BCG) revaccination was not shown to provide protection from primary *Mycobacterium tuberculosis* infection but prevented sustained *M. tuberculosis* infection, defined by an initial conversion on a QuantiFERON-TB (QFT) test (an interferon- $\gamma$  release assay) from negative to positive, followed by two additional positive QFT tests at 3 and 6 months after the initial conversion (a secondary end point). A vaccine efficacy of 45% (95% confidence interval [CI], 6 to 68) was observed. To test the idea that a booster BCG vaccination could have efficacy, investigators performed a phase 2b, double-blind, randomized, placebo-controlled trial to evaluate the efficacy of BCG revaccination, as compared with placebo, for the prevention of sustained QFT test conversion (primary end point) in QFT test–negative, human immunodeficiency virus (HIV)–negative adolescents. Alas, BCG did not prevent primary tuberculosis infection in these children. Automated insulin delivery (AID) systems have been shown to be beneficial for patients with type 1 diabetes, but data are needed from randomized, controlled trials regarding their role in the management of insulin-treated type 2 diabetes. In a 13-week, multicenter trial, adults with insulin-treated type 2 diabetes were randomly assigned in a 2:1 ratio to receive AID or to continue their pretrial insulin-delivery method (control group); both groups received continuous glucose monitoring (CGM). The primary outcome was the glycated hemoglobin level at 13 weeks. The AID

system was better than insulin injections and usual care in these type 2 diabetic patients, as it was in persons with type 1 diabetes. In lymphoma patients the question arises what to do when your CAR T-cell therapy fails. A promising strategy to improve CAR T-cell efficacy involves developing fourth-generation, “armored”-CAR T cells that secrete proinflammatory cytokines to bolster antitumor activity. This approach is currently being explored in solid tumors according to the hypothesis that cytokine secretion enhances the cytotoxicity of CAR and tumor-infiltrating T cells while modifying the immunosuppressive tumor microenvironment. One such cytokine, interleukin-18, is a proinflammatory molecule that is primarily produced by macrophages and dendritic cells. We learn that armored CAR T cells are an improvement over non-armored-CAR T cells. The N Engl J Med review is on nutrition “dark matter”. The topic involves biochemicals or bio active compounds within food. The N Engl J Med patient of the week is a 70-year-old man with weight loss, weakness, and anorexia. He has a past history of hairy-cell leukemia, gastric bypass surgery, and exhibits respiratory alkalosis and progressive encephalopathy with delta and theta waves. Finally a lumbar puncture is performed. In the Lancet, we learn that a new clade of Monkey Pox in Africa is looking more-and-more like smallpox with increased lethality. Commonly, children are involved. Atopic dermatitis of the hands can be crippling and is treatment resistant. A randomized trial suggests that delgocitinib (JAK-STAT inhibitor directed at IL-31) could be helpful. Negative pressure wound therapy is a vacuum-assisted closure method that uses suction to promote healing in wounds. A randomized controlled trial, however, fails to show efficacy of this method. The Lancet review is on “President’s Emergency Plan for AIDS Relief” (PEPFAR). This program, promoted by Anthony Fauci and initiated by George W. Bush, has saved millions of African kids from AIDS. The current US administration appears less impressed with PEPFAR. The taste receptors on the tongue are mysterious G protein-coupled receptors. “How we taste sweetness”: the long-sought structure of the human sugar receptor has been mapped and completely elucidated at last. This research, announced in both *Nature* and *Science Magazine*, was published in *Cell*. In the Washington Post, we find out that Scandinavian epidemiological studies find a relationship between tattoos and lymphoma. One third of Americans have them and half have more than one. Armored CAR T cells may have a sustained future.

No presentation this week. Join me on Wednesday, May 21 for another stunning, orally presented, clinical journal club, 16:00 in English and 17:00 in German.

Sincerely, Fred Luft

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