

Dear friends of clinical journal club - load the file down at <https://www.mdc-berlin.de/cjc>:

The *N Engl J Med* image of the week concerns a 60-year-old woman, who presented to an oral surgery clinic with gum swelling. She had associated bleeding while brushing her teeth. She had a history of colorectal cancer treated with surgery and chemotherapy. On examination, a large, nontender, pedunculated mass was noted. What is the diagnosis? You are offered Zimmerman-Laband syndrome, Metastasis of colorectal cancer, Gingival hyperplasia secondary to chemotherapy, Alveolar soft part sarcoma, and Irritation fibroma. We review these conditions. The first paper in *N Engl J Med* concerns hydroxychloroquine and azithromycin in the treatment of Corona virus. We inspected this work already last week. Suffice it to say, hydroxychloroquine, with or without azithromycin, plays no role in the treatment of Covid-19. The subcutaneous implantable cardioverter-defibrillator (ICD) was designed to avoid complications related to the transvenous ICD lead by using an entirely extra-thoracic placement. Evidence comparing these systems has been based primarily on observational studies. Investigators conducted a non-inferiority trial in which patients with an indication for an ICD but no indication for pacing were assigned to receive a subcutaneous ICD or transvenous ICD. The primary end point was the composite of device-related complications and inappropriate shocks; the noninferiority margin for the upper boundary of the 95% confidence interval for the hazard ratio (subcutaneous ICD vs. transvenous ICD) was 1.45. A superiority analysis was prespecified if noninferiority was established. Secondary end points included death and appropriate shocks. The composite endpoint was the same. However, device-related complications were more common with the transvenous device. In 2015 and 2016, Colombia had a widespread outbreak of mosquito-borne Zika virus (single-stranded RNA Flavi-virus). Zika virus elicits a Dengue-like illness, but can also cause Guillain-Barré syndrome and birth defects. Data from two national population-based surveillance systems for symptomatic Zika virus disease (ZVD) and birth defects provided complementary information on the effect of the Zika virus outbreak on pregnancies and infant outcomes. Colombian investigators collected national surveillance data regarding cases of pregnant women with ZVD that were reported during the period from June 2015 through July 2016. The presence of Zika virus RNA

was identified in a subgroup of these women by means of real-time reverse-transcriptase–polymerase-chain-reaction (rRT-PCR) assay. Brain or eye defects in infants and fetuses and other adverse pregnancy outcomes were identified among the women who had laboratory-confirmed ZVD and for whom data were available regarding pregnancy outcomes. Among the pregnant women in this group who had laboratory-confirmed ZVD, 2% of their infants or fetuses had a brain or eye defect. Such defects were more common among infants carried by women who had an onset of ZVD symptoms during the first trimester of pregnancy than among those with a later symptom onset (3% vs. 1%). Colombia began official surveillance for Zika virus disease (ZVD) in August 2015. In October 2015, an outbreak of ZVD was declared after laboratory-confirmed disease was identified in nine patients. Using the national population-based surveillance system, Colombian investigators assessed patients with clinical symptoms of ZVD from August 9, 2015, to April 2, 2016. The outbreak of ZVD has spread rapidly throughout Colombia since the first cluster of laboratory-confirmed cases was identified in October 2015, with 65,726 cases reported, including in 11,944 pregnant women as of April 2, 2016. However, these numbers underestimate the total effect of the ZVD outbreak, since they do not account for asymptomatic infection or unreported clinical illness. Why these data were not published by *N Engl J Med* in 2017 instead of now, is unclear; there was no editorial comment on these papers. Multiple sclerosis is an auto-immune disease that attacks the central nervous system with demyelinating plaques. The disease generally features a relapsing course. Ofatumumab, a subcutaneous anti-CD20 monoclonal antibody, selectively depletes B cells. Teriflunomide, an oral inhibitor of pyrimidine synthesis (immune-modulatory thalidomide derivative), reduces T-cell and B-cell activation. The relative effects of these two drugs in patients with multiple sclerosis are not known. In two double-blind, double-dummy, phase 3 trials, investigators randomly assigned patients with relapsing multiple sclerosis to receive subcutaneous ofatumumab (20 mg every 4 weeks after 20-mg loading doses at days 1, 7, and 14) or oral teriflunomide (14 mg daily) for up to 30 months. The primary end point was the annualized relapse rate. The anti-B-cell strategy with ofatumumab was better than immune modulation with teriflunomide. The *N Engl J Med* review is on native-valve infective endocarditis. We review the latest in Duke criteria and antibiotic guidelines. The *N Engl J Med* case of

the week concerns a 34 year-old man from Vancouver, Canada, who presents with a 1-month history of constant diffuse abdominal pain, fatigue, and anorexia associated with a weight loss of 2.7 kg but no fevers or night sweats. He reported constipation but no diarrhea, melena, or hematochezia. The hemoglobin level was 7.7 g per deciliter, and the hematocrit 25%, with a mean corpuscular volume of 73 fl. Study of the peripheral blood smear reveals microcytic anemia with anisocytosis. Basophilic stippling is also observed. The doctors diagnose thalassemia (since he was born in India) and prescribe opiates for “pain”, decisions that I view as unconscionable. The patient clearly has lead poisoning, but the cause was news to me. In *J Am Soc Nephrol*, we learn that Covid-19 in two UK dialysis units was common, commonly also asymptomatic, and dialysis patients developed antibodies with high seroprevalence. Apparently, no one died. These findings are at variance with an online *Kidney Int* report indicating a 22% mortality in French dialysis patients. In the *Lancet*, we learn that admissions in the UK for acute coronary syndromes and myocardial infarction have dropped dramatically during the Covid-19 epidemic. Apparently, the patients are staying home and out-of-the hospital deaths are likely. Mortality from multi-drug-resistant tuberculosis remains high, but is higher still if HIV is not being treated, in those who have HIV. The scaphoid is the most commonly fractured carpal bone in hand trauma. How to manage scaphoid-waist fractures most appropriately is a matter of debate. We learn that if displacement is <2 mm, a conservative cast immobilization is appropriate and that surgery with fixation is indicated solely for non-union. The *Lancet* review (excellent in my view) is on dementia and its prevention. Yes, much can be done. We then review a *Science* paper on engineering human ACE2 to produce an optimally binding, soluble version with potential therapeutic utility. We close with a *Lancet* case of “wandering” spleen. The oral presentations will be in Wednesday at 16.00 English and 17.00 German.

Yours,

Fred Luft (Check out the file pdf at <https://www.mdc-berlin.de/cjc>)