

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 60-year-old man with a 30-pack-year smoking history presented to the dermatology clinic for a 2-year history of a painful rash on his palms and soles. Previous treatment with various antibacterial agents had been ineffective. Laboratory studies revealed neutrophilic leukocytosis and an elevated C-reactive protein level. What is the diagnosis? You are offered: Contact dermatitis, Dyshidrotic eczema, Palmoplantar plaque psoriasis, Palmoplantar pustulosis, and Secondary syphilis. In chronic smokers only one of these diagnoses fit. The proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitor evolocumab reduces the risk of major adverse cardiovascular events (MACE) among patients with a previous myocardial infarction, stroke, or symptomatic peripheral artery disease (secondary prevention). The effect of evolocumab on the risk of MACE among patients without a previous myocardial infarction or stroke is unknown. Investigators conducted an international, double-blind, randomized, placebo-controlled trial of evolocumab in patients with atherosclerosis or diabetes and without a previous myocardial infarction or stroke who had a low-density lipoprotein cholesterol level of at least 90 mg per deciliter (primary prevention trial). Evolocumab reduced all MACE as a primary prevention. In fatty acids, the carboxy terminus is the alpha end and the methyl terminus is the omega end, from which the double bonds are counted. N-3 is the good fat in fish oil; N-6 from mammals is not so good. Most earlier fish oil studies sound good but have not been very convincing and were largely not significant. Cardiovascular disease is the leading cause of death in patients receiving hemodialysis, yet effective preventive therapies remain limited. Cardiovascular preventative studies in dialysis patients have also generally been negative. Supplementation with n-3 polyunsaturated fatty acids, especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), may have cardiovascular benefits in the general population, but efficacy among patients receiving hemodialysis is uncertain. In a double-blind, randomized, placebo-controlled trial conducted at 26 sites in Canada and Australia, investigators assigned adult patients receiving maintenance hemodialysis to daily supplementation with fish oil (4

g of n-3 polyunsaturated fatty acids [1.6 g of EPA and 0.8 g of DHA]) or corn-oil placebo. The primary end point was a composite of all MACE. Surprisingly, fish oil reduced MACE almost in half, compared to corn oil. Respiratory syncytial virus (RSV) can cause serious illness in older adults. The bivalent RSV prefusion F protein-based vaccine (RSVpreF) has been shown to prevent RSV-associated respiratory illness, but data from randomized trials regarding its effect on outcomes involving hospitalization are limited. In a pragmatic, open-label trial with individual randomization, participants who were 60 years of age or older were assigned in a 1:1 ratio to receive the RSVpreF vaccine (the RSVpreF group) or no vaccine (the control group) during the 2024–2025 winter season. RSVpreF sharply reduced hospitalizations but these were not very common anyway. T-cell leukemias are difficult to treat; CAR T cells are a good idea, but can we use CAR T cells against T cells? CD7 is an attractive target for chimeric antigen receptor (CAR) T-cell therapy in relapsed or refractory T-cell acute lymphoblastic leukemia (ALL). Supportive results of first-in-human studies of base-edited anti-CD7 CAR (BE-CAR7) T cells with triple C→T deamination-mediated knockouts of TCR $\alpha\beta$, CD52, and CD7 (to avoid fratricide) have been reported previously. Base-edited (BE) knockouts with Crispr-Cas9 is used. In a phase 1 study, investigators administered BE-CAR7 T cells to children (≤ 16 years of age) with relapsed or refractory T-cell ALL after they had undergone lymphodepletion with fludarabine, cyclophosphamide, and alemtuzumab. Adults with compassionate-use access arrangements were also eligible. Patients who had remission by day 28 after the BE-CAR7 T-cell infusion proceeded to allogeneic hematopoietic stem-cell transplantation. The primary outcome was safety. Secondary outcomes included duration of remission, disease-free survival, and overall survival. Safety was acceptable; efficacy looks very encouraging. The N Engl J Med review is on functional dyspepsia. The mystery patient has a chronic liver disease and then develops fever, abdominal pain, and shock after a trip to Brazil. In the Lancet, we encounter follicular-cell lymphoma, the second most common non-Hodgkin lymphoma. In a randomized trial, tafasitamab (anti CD19), lenalidomide, and rituximab (anti CD20) were assessed in refractory disease. Adding tafasitamab improved progression-free survival. In a second study against the same lymphoma type, eporitamab (a CD20-to-CD3 T-cell engager) was tested, also in the presence of lenalidomide and rituximab. Eporitamab

looked even better. Gonorrhea is becoming increasingly aggressive and resistant and now requires ceftriaxone. Could the new DNA gyrase inhibitor, zoliflodacin, be at least as good as ceftriaxone-plus-azithromycin for uncomplicated gonorrhea? It was. Radiation therapy commonly is based on high-energy photons (xrays). But how about proton particles that could cause less collateral damage? Patients with oropharyngeal cancer were randomized to protons versus photons, in addition to all other care modalities. Proton outcomes were non-inferior to photon outcomes and caused less collateral damage. Lancet next presents a countdown on health and climate change in Africa. Rumor has it that pain medicines interfere with bone fracture healing, but how come? In Science Magazine, we learn how bone fracture healing works. Investigators performed single-cell RNA-sequencing on limb-innervating dorsal root ganglia (DRG) neurons in mice and found that gene expression dramatically changes in response to fracture. They analyzed the data using a previously developed tool that infers intercellular communication networks from single-cell RNA-sequencing data (interactome analysis). From this analysis, they deduced that DRG neurons communicate with all the major cell types present in the fracture callus, particularly with the stem and progenitor cells that are important for osteogenesis and with endothelial cells involved in vascularization. Unexpectedly, the researchers identified neural-derived Fgf9 as a critical mediator of neural–bone crosstalk during repair. In the Washington Post we learn that ball-room dancing protects us from Alzheimer’s disease. The next oral presentation will be on January 14, 2026.

Sincerely, Fred Luft

Friedrich.luft@charite.de

<https://www.mdc-berlin.de/cjc>