

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 otherwise healthy 30-year-old man presented to clinic for a 2-year history of skin lesions on his right foot. He worked as an agricultural laborer and had sustained injuries to his feet over the years, including a puncture lesion in between the fourth and fifth toes of his right foot. What is the most likely diagnosis? You are offered: Chromoblastomycosis, Cutaneous tuberculosis, Mycetoma, Mycobacterium ulcerans, and Tetanus. The diagnosis is a “sight” matter that depends on whether-or-not you have experience about life in the tropics.

Blood-pressure reduction is the only proven treatment to prevent hemorrhagic stroke. Whether a single pill that combines three antihypertensive drugs at low doses, in addition to standard antihypertensive treatment, can lower blood pressure more than standard care alone and reduce the risk of recurrent stroke after intracerebral hemorrhage is uncertain. Investigators conducted a multinational, double-blind, randomized, placebo-controlled trial involving patients with a recent intracerebral hemorrhage. Patients were eligible for the trial if they had a systolic blood pressure of 130 to 160 mm Hg at baseline and were in clinically stable condition. After a 2-week active run-in phase during which all the patients received a once-daily pill containing three antihypertensive agents at low doses (telmisartan at 20 mg, amlodipine at 2.5 mg, and indapamide at 1.25 mg; the triple pill). The triple-pill lowered blood pressure and reduced hemorrhagic-stroke recurrence by half.

Nirmatrelvir–ritonavir was shown to reduce progression to severe illness from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in unvaccinated high-risk outpatients. The effectiveness of nirmatrelvir–ritonavir in persons who have been vaccinated, infected naturally, or both is unclear. In two open-label platform trials (PANORAMIC in the United Kingdom and CanTreatCOVID in Canada), investigators enrolled higher-risk adults (≥ 50 years of age or ≥ 18 years of age with coexisting conditions) in the community who tested positive for SARS-CoV-2 and had been unwell for 5 days or less. Nirmatrelvir did not keep more-recent Covid patients out of the hospital.

Transdermal estradiol (tE2) is an alternative to luteinizing hormone–releasing hormone (LHRH) agonists as androgen-deprivation therapy in

patients with prostate cancer. With tE2, testosterone is suppressed, and the side effects of estrogen depletion due to LHRH agonists and the thromboembolic side effects of oral estrogen are mitigated. In a phase 3, noninferiority, randomized trial, investigators assigned men with locally advanced (M0 and N0 or N+) prostate cancer to receive tE2 patches (100 µg of estradiol every 24 hours) or LHRH agonists. The primary outcome was 3-year metastasis-free survival. The simple (and much cheaper) estrogen patch was as good as the LHRH agonist. For critically ill adults undergoing tracheal intubation, observational studies suggest that the use of etomidate to induce anesthesia may increase the risk of death. Etomidate blocks 11-beta-hydroxylase that is important for cortisol synthesis. Whether the use of ketamine rather than etomidate decreases the risk of death is uncertain. In a randomized trial conducted in 14 emergency departments and intensive care units in the United States, investigators randomly assigned critically ill adults who were undergoing tracheal intubation to receive ketamine or etomidate for the induction of anesthesia. The primary outcome was in-hospital death from any cause by day 28. There was no difference in outcomes with these two induction strategies. The N Engl J Med review is on spinal epidural abscess. Imaging has emerged as the “game changer” here. The mystery N Engl J Med patient is an 86-year-old woman with anorexia, weight loss, and liver lesions. MALDI-TOF eventually determines the diagnosis. The Lancet first deals with simple urinary tract infections in women. A single large dose of fosfomycin is currently recommended as the treatment of choice. A phase 4, multicenter, parallel-group trial indicates that nitrofurantoin is probably better. The malaria sporozoite has a circumsporozoite protein. A humanized IgG antibody (L9LS) is available. The safety and efficacy of L9LS was tested in sub-Saharan children in a randomized, controlled trial. Both endpoints were shown, but results were not so impressive in my view. Lowering blood pressure in patients with chronic kidney disease (CKD) makes some clinicians nervous. Should blood pressure really be at 120/80 mm Hg in all CKD patients? A massive meta-analysis indicates that lowering blood pressure is indicated at all levels of CKD severity. The Lancet review is about the mitogen-activated (MAP) kinase/extracellular signal-regulated (ERK) kinase, commonly known as MEK. Inhibitors are available against MEK. How should this strategy be applied in cancer patients? Lancet reviews the topic. The heart is (almost) never involved in cancer. The question arises,

why not? In Science Magazine, we deal with a study that explains why not. We learn that Nesprin-2 is a key molecule in sensing cardiac mechanical forces, resulting in reduced histone methylation and chromatin compaction in cancer cells, overall halting their proliferation in the heart. In Washington Post, we are confronted with sea monsters, long thought to be merely mythology. The WP informed us about the sex lives of the octopus earlier. WP now draws our attention to another Science Magazine paper showing that 20 meters-long squids once romped the oceans 60 million years ago. Good thing we were not yet there. The presentation is in English at 16:00, German at 17:00, and will take place will on Wednesday April 22, 2026.

Sincerely, Fred Luft

Friedrich.luft@charite.de

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