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.

A 60-year-old man presented with a 3-month history of cough, dyspnea, and fatigue. On physical examination, decreased breath sounds over the left hemithorax were noted. Computed tomography of the chest showed a large pleural effusion associated with thickening and enhancement of both the parietal and visceral pleura — a finding known as the split pleura sign — and a partially calcified pleural rind. Pleural fluid analysis was consistent with empyema, with an elevated adenosine deaminase level. A polymerase-chain-reaction assay of the pleural fluid was positive for Mycobacterium tuberculosis. Which of the following is seen here microscopically in the fluid? You are offered the following: Acid-fast bacilli, Calcium pyrophosphate crystals, Cholesterol crystals, Monosodium urate crystals, and Talc. Hint, the crystals in the image do not look like calcium pyrophosphate or monosodium urate. Hereditary angioedema is a rare and potentially life-threatening genetic condition characterized by recurrent and debilitating swelling attacks driven by bradykinin. Prekallikrein (converted to kallikrein via Factor XII) is required to generate bradykinin via kallikrein's cleavage of high-molecular-weight kininogen. Lonvoguran ziclumeran (lonvo-z) — an investigational, in vivo gene-editing treatment based on clustered regularly interspaced short palindromic repeats (CRISPR) — is being developed as a single-dose treatment for hereditary angioedema. The idea is to knock down the gene encoding prekallikrein. In a phase 3, double-blind trial, investigators randomly assigned patients who were 16 years of age or older and had hereditary angioedema with C1 inhibitor deficiency to receive a single intravenous infusion of lonvo-z (at a dose of 50 mg) or placebo. The primary end point was the number of investigator-confirmed hereditary angioedema attacks per month. Lonvo-z sharply reduced angioedema attacks. The outcome of Philadelphia-positive acute lymphoblastic leukemia (Ph-positive ALL) has greatly improved with the use of tyrosine kinase inhibitors and immunotherapy. Investigators randomly assigned adult patients with Ph-positive ALL to receive ponatinib plus blinatumomab (intervention group) or imatinib plus chemotherapy (control group) as frontline treatment. The primary end point was event-free survival. The new Ph-inhibitor plus the engager

antibody beat imatinib and conventional chemotherapy in patients with Ph-positive ALL. Monoclonal antibodies targeting the interleukin-23 pathway are effective in treating inflammatory bowel disease. However, these therapies must be administered intravenously or by subcutaneous injection. Investigators conducted a phase 2b, double-blind, randomized trial of oral icotrokinra, a peptide that blocks the interleukin-23 receptor, in adults with moderately to severely active ulcerative colitis. Participants were assigned to receive icotrokinra at a once-daily dose of 400 mg, 200 mg, or 100 mg or placebo. The primary end point was clinical response at week 12. The oral icotrokinra beat placebo as expected. In eastern and southern Africa, approximately 1 million people living with human immunodeficiency virus (HIV) and receiving oral therapy do not have viral suppression because of adherence challenges. Investigators conducted a phase 3b, open-label, randomized trial to compare long-acting injectable cabotegravir plus rilpivirine with oral dolutegravir-based therapy among adults with virally suppressed HIV type 1 (viral load, <200 copies per milliliter) and suboptimal adherence or care engagement. The injectable cabotegravir plus rilpivirine combination was no worse than the daily oral regimen. Attention deficit–hyperactivity disorder (ADHD) is a medical condition that is present in approximately 2.5% of adults worldwide and manifests in a variety of different ways across the lifespan. N Engl J Med reviews adult ADHD. The mystery patient has a large paraspinal ganglioma and his father had one too. We learn how paragangliomas cause hypertension. Insulin has never been shown to reduce MACE in type-2 diabetic patients. Orforglipron, an oral GLP-1 agonist was tested against insulin glargine with MACE as the endpoint. Orforglipron was “no worse than” insulin in these type-2 diabetic patients. Yellow fever remains an important health issue below the equator. The vaccine is effective but expensive. Lancet presents a paper in which fractional one-fifth and one-half doses of the 17DD vaccine were compared to full-dose. The fractional doses appear to be effective. Fibrodysplasia ossificans progressiva is an ultra-rare genetic disease involving gain-of-function of the ACVR-1 gene encoding Activin-A. An antibody against Activin-A has been developed. Garetosmab was effective in reducing Activin-A and new heterotopic bone lesions in this disease. Sofosbuvir-velpatasvir for 12 weeks “cures” hepatitis C infection. A study from India suggests that 8 weeks might be enough. A Lancet Commission presents a 59-page report on 21st century global health

threats. Projections for the future do not inspire confidence. In Science Magazine, we learn that to maintain homeostasis, barrier epithelia—the body's first line of defense—undergo constant, rapid turnover. The process includes the inner surface of the mammalian intestine, where ongoing regeneration protects against daily wear and tear, preventing dangerous breaches and supporting gut health. Investigators report that cell type specification is encoded by the frequency of oscillations in expression of the transcription factor Hes1 (hairy and enhancer of split 1). They found that distinct oscillation time periods tracked with specific cell identities and that oscillating signaling dynamics, known to play a role in developmental processes, appear to control homeostatic processes as well. In the Washington Post, we learn about the surprising way walking can benefit the brain. Reporters claim that even Friedrich Nietsche profited from walking, which benefited his creative thinking. Indeed, a PLoS-One analysis suggests that walking improves divergent thinking. Load down the file and join me again on October 21 for a compilation of the last 2 weeks, 16:00 in English and 17:00 in German.

Sincerely, Fred Luft

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