

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 28-year-old woman presented to the hospital with a 6-month history of dry cough. She was a lifetime nonsmoker and reported no fevers, joint aches, eye pain, or rashes. On physical examination, auscultation of both lower lungs revealed fine crackles. High-resolution computed tomography (CT) of the chest showed mediastinal lymphadenopathy and diffuse ground-glass opacities (left, axial view). Also visible were areas of superimposed interlobular and intralobular septal thickening, a pattern known as crazy paving (left, box). A subsequent transbronchial lung biopsy showed multiple noncaseating granulomas (middle, inset showing granuloma; hematoxylin and eosin stain). Bronchoalveolar lavage cultures, histopathological analysis, and molecular testing were negative for infectious organisms, including *Mycobacterium tuberculosis*. Which of the following is the most likely diagnosis? You are offered: Foreign body granulomatosis, Granulomatosis with polyangiitis, Pulmonary alveolar proteinosis, Pulmonary Langerhans cell histiocytosis, and Pulmonary Sarcoidosis. We review crazy pavements. The biopsy helps! CAR T-cell therapy for cancers is established. Could CAR T-cell therapy also help in refractory autoimmune disease? Treatment for autoimmune diseases such as systemic lupus erythematosus (SLE), idiopathic inflammatory myositis, and systemic sclerosis often involves long-term immune suppression. Resetting aberrant autoimmunity in these diseases through deep depletion of B cells is a potential strategy for achieving sustained drug-free remission. Investigators evaluated 15 patients with severe SLE (8 patients), idiopathic inflammatory myositis (3 patients), or systemic sclerosis (4 patients) who received a single infusion of CD19 chimeric antigen receptor (CAR) T cells after preconditioning with fludarabine and cyclophosphamide. Efficacy up to 2 years after CAR T-cell infusion was assessed by means of ARA Definition of Remission. In this case series, CD19 CAR T-cell transfer appeared to be feasible, safe, and efficacious in three different autoimmune diseases. Thrombolytic agents, including tenecteplase, are generally used within 4.5 hours after the onset of stroke symptoms. Information on whether tenecteplase confers benefit beyond 4.5 hours is limited. Investigators

conducted a multicenter, double-blind, randomized, placebo-controlled trial involving patients with ischemic stroke to compare tenecteplase (0.25 mg per kilogram of body weight, up to 25 mg) with placebo administered 4.5 to 24 hours after the time that the patient was last known to be well. Patients had to have evidence of occlusion of the middle cerebral artery or internal carotid artery and salvageable tissue as determined on perfusion imaging. The primary outcome was the ordinal score on the modified Rankin scale. Sadly, late Tenecteplase (after 4.5 hours) did not improve outcomes. Biomarker changes that occur in the period between normal cognition and the diagnosis of sporadic Alzheimer's disease have not been extensively investigated in longitudinal studies. Investigators conducted a multicenter, nested case-control study of Alzheimer's disease biomarkers in cognitively normal participants who were enrolled in the China Cognition and Aging Study from January 2000 through December 2020. A subgroup of these participants underwent testing of cerebrospinal fluid (CSF), cognitive assessments, and brain imaging at 2-year-to-3-year intervals. A total of 648 participants in whom Alzheimer's disease developed were matched with 648 participants who had normal cognition, and the temporal trajectories of CSF biochemical marker concentrations, cognitive testing, and imaging were analyzed in the two groups. In this case-control study, biomarkers diverged long before clinical symptoms. Polycythemia vera is a chronic myeloproliferative neoplasm characterized by erythrocytosis. Rusfertide, an injectable peptide mimetic of the master iron regulatory hormone hepcidin, restricts the availability of iron for erythropoiesis. The safety and efficacy of rusfertide in patients with phlebotomy-dependent polycythemia vera are unknown. Hepcidin indeed reduced hematocrits and lowered the need for phlebotomy. The review in N Engl J Med is on wearable digital health technology for epilepsy patients. The N Engl J Med case has a severe anemia with multilobed granulocytes and red cells with basophilic stippling. In the Lancet, we inspect endovascular thrombectomy plus medical care (mostly Alteplase and Tenecteplase), versus medical care alone within 24 hours in patients with proximal occlusion and large core. Thrombectomy was better. In patients with uncomplicated urinary tract infection, gepotidacin proved to be "no worse than" nitrofurantoin. Next, we review a cluster trial of sun-powered oxygen delivery for hypoxemic infants in Uganda. The sun came through. The Lancet review is on hyperthyroidism. The N Engl J Med board

examination question concerns an Alzheimer patient with a decline after ingesting diphenhydramine. SOX9 is an HMG-box transcription factor important in development. In Science Magazine, we learn about a SOX9 switch that links regeneration and fibrosis in the kidney. In the Washington Post, we are told that Viagra reduces the risk of Alzheimer's disease in a dose-dependent fashion over time. I cannot be here on February 28. But join me again on March 6 for this, and next week's fascinating reports. Best regards, Fred Luft, at <https://www.mdc-berlin.de/cjc>