

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 54-year-old woman presented with a 4-month history of progressively worsening asthenia, falls, and 5 days of dyspnea. On exam, there was also head drop and mild symmetric weakness of the proximal upper and lower limbs. The creatine kinase level was 373 U per liter (reference range, 24 to 173). Magnetic resonance imaging of the head and cervical spine was notable for fatty infiltration of the tongue and paravertebral muscles. Which of the following is the most likely disease category? You are offered: Age-related sarcopenia, Cervical myelopathy, Hypercholesterolemia, Infectious myositis, and Lysosomal storage disease. What makes large tongues in adults?

Exagamglogene autotemcel (exa-cel) is a cell therapy in which autologous CD34+ hematopoietic cells are engineered through ex vivo clustered regularly interspaced short palindromic repeats–Cas9 editing of the erythroid-specific enhancer region of BCL11A to express fetal hemoglobin. In phase 3 studies involving participants 12 to 35 years of age with sickle cell disease or transfusion-dependent β -thalassemia, exa-cel eliminated vaso-occlusive crises and the need for red-cell transfusions. Investigators evaluated exa-cel in children 5 to 11 years of age with transfusion-dependent β -thalassemia or sickle cell disease. Before exa-cel infusion, participants underwent myeloablative conditioning with pharmacokinetically dose-adjusted busulfan. The primary end points were transfusion independence for at least 12 consecutive months in children with transfusion-dependent β -thalassemia and freedom from severe vaso-occlusive crises for at least 12 consecutive months in children with sickle cell disease. Exa-cel excelled in both diseases. HbF comprised about 50% of total hemoglobin. Studies of obinutuzumab, a type II anti-CD20 antibody, have shown efficacy in the treatment of hematologic cancers and autoimmune diseases. An evaluation of the efficacy and safety of obinutuzumab in patients with primary membranous nephropathy is needed. Investigators randomly assigned adults with primary membranous nephropathy to receive intravenous obinutuzumab or oral tacrolimus. The primary end point was complete remission (defined as a urinary protein-to-creatinine ratio of 0.3 or lower and a stable estimated glomerular filtration

rate [eGFR]) at week 104. In an earlier study of this disease rituximab beat cyclosporin so success came as no surprise. Complete coronary-artery revascularization is recommended in patients with ST-segment elevation myocardial infarction (STEMI) and multivessel disease, but the preferred strategy for identifying nonculprit lesions that warrant treatment remains uncertain. Investigators assigned patients with STEMI and multivessel disease in whom the culprit lesion had been successfully treated to undergo complete coronary-artery revascularization guided by functional coronary angiography (physiology-guided group) or by conventional angiography (angiography-guided group). The primary outcome was a composite. Functional coronary angiography won hands down. Migrants crossing the Central Mediterranean Sea route travel in overcrowded vessels, where fuel may leak and contaminate seawater accumulating on the vessel floor, result in prolonged dermal exposure and fuel-related skin injuries. Since March 2024, clusters of severe acquired methemoglobinemia (>50%) with no apparent cause have been identified by clinicians in Lampedusa at disembarkation among migrants arriving in Italy. Investigators identified dermal absorption of the gasoline additive N-methylaniline from fuel-contaminated seawater as responsible. G6PD deficiency was a major contributor. The N Engl J Med review is on multiple myeloma. The mystery case has palpable purpura and hematuria. In the Lancet, the first topic is atrial fibrillation. Ablation therapy beats rate control but in evenly matched patients does it really improve quality of life that much or at all? A European study suggests that it does not. Mitapivat stimulates pyruvate kinase, increases ATP production in erythrocytes (slightly), and shifts the hemoglobin-oxygen dissociation curve (a bit) to the left. A randomized trial in Thalassemia patients suggests that mitapivat reduces transfusion requirements in patients already receiving hydroxyurea. So not everyone with sickle cell anemia or thalassemia may need exa-cel. Vesicular stomatitis virus-Zaire ebola is a currently available vaccine against Ebola virus that worked in Zaire. Could it work in Democratic Republic of Congo on Bundibugyo virus (BDBV), an Ebola disease? Persisting titers in vaccinated patients from Zaire suggest that this could be the case. The vaccine is currently being applied against BDBV. The xenograft kidney from porcine to man reported earlier worked about a month until the patient died of heart disease. Lancet now reports a pig kidney that worked for 9 months until it was replaced by a human kidney. No pig-related issues

occurred. Graft failure involved innate immunity involving T-cell activations. The Lancet review is on small-cell lung cancer. This neuro-endocrine derived tumor is responding to some newer therapies. Ferroptosis is an iron-dependent form of apoptosis. In Science Magazine, investigators wondered why fat women have a higher risk of breast cancer than thin women. The same is true of breast cancer in mice. Either fat cells from fat patients make something that stimulates tumors or thin fat cells from thin people are somehow responsible for cancer protection via tumor suppression. Perhaps adipocytes produce lipid mediators that regulate tumor growth and contribute causally to obesity-accelerated breast cancer. The lean mammary adipocyte secretome (fat cells from thin mice) inhibited breast cancer cell growth by inducing ferroptotic cell death, characterized by oxidative lipid damage and increased intracellular ferrous iron. Fat cells from fat mice had no such effect. Thus, fat cells from thin mice (or hopefully people) are protective by driving malignant cells into ferroptosis. In Washington Post we learn that in the USA, ICE officials are now outfitted with shocking gloves that deliver >350-volt jolts when suspects are handled. Hope no one gets ventricular fibrillation, but maybe it beats being shot dead. Load down the file and join me again on September 16, 16:00 English and 17:00 German.

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