

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 57-year-old woman presented to the emergency department with a 3-day history of shortness of breath and dizziness. The physical examination was notable for pallor. Laboratory studies showed a hemoglobin of 4.4 g per deciliter (reference range, 11.6 to 15.5), an elevated reticulocyte count, an elevated lactate dehydrogenase level, and a low haptoglobin level. The results of hemoglobin electrophoresis and glucose-6-phosphate dehydrogenase testing were normal, and methemoglobin and direct antiglobulin tests were negative. A peripheral blood smear (left, Giemsa staining) showed poikilocytosis, nucleated red cells (black arrows), and polychromatic cells (white arrows). The peripheral blood smear also showed bite cells (left, red arrows), blister cells (left, asterisks), and erythrocyte inclusions (middle, Giemsa staining). The erythrocyte inclusions were identified as Heinz bodies, based on positive staining with methyl violet (right). Which of the following is the most likely etiology of this patient's hemolytic anemia? The mechanisms you are offered are: immune-mediated, infection, membrane defect, oxidative injury, and thrombotic microangiopathy. We review Heinz-body anemias. Pembrolizumab, a PD-1 humanized antibody, improves progression-free survival in patients with renal-cell carcinoma. Whether the results regarding overall survival from the third prespecified interim analysis of the trial would also favor pembrolizumab was uncertain. Indeed, pembrolizumab increased overall survival. However, side effects, including serious problems, were more common. The incidence of immune-mediated adverse events and infusion reactions (36.5% with pembrolizumab vs. 7.3% with placebo). Most trials that have shown a benefit of beta-blocker treatment after myocardial infarction included patients with large myocardial infarctions and were conducted in an era before modern biomarker-based diagnosis of myocardial infarction and treatment with percutaneous coronary intervention, antithrombotic agents, high-intensity statins, and renin–angiotensin–aldosterone system antagonists. In a parallel-group, open-label trial performed at 45 centers in Sweden, Estonia, and New Zealand, investigators randomly assigned patients with an acute myocardial infarction who had undergone coronary angiography and had a left

ventricular ejection fraction of at least 50% to receive either long-term treatment with a beta-blocker (metoprolol or bisoprolol) or no beta-blocker treatment. The presence or absence of beta-blockers made no difference in this patient population. The effects of temporary mechanical circulatory support with a microaxial flow pump on mortality among patients with ST-segment elevation myocardial infarction (STEMI) complicated by cardiogenic shock remains unclear. In an international, multicenter, randomized trial, investigators assigned patients with STEMI and cardiogenic shock to receive a microaxial flow pump (Impella CP) plus standard care or standard care alone. The primary end point was death from any cause at 180 days. Impella decreased mortality, but adverse events, severe bleeding, limb ischemia, hemolysis, device failure, or worsening aortic regurgitation, were common. Earlier, we learned that in non-diabetic severely obese heart failure with preserved ejection fraction (HFPEF) patients, semaglutide improved cardiac function and reduced symptoms. Now, we inspect a similar study but this time in obese type-2 diabetic patients. Again, semaglutide decreased body weight by 10% and improved cardiac performance. Characterization and cloning of the first tumor suppressor gene, retinoblastoma, is an important saga in oncology. N Engl J Med reviews what is happening with retinoblastoma currently. The N Engl J Med patient has a mitochondrial genetic disease that was first recognized at age 58 years. In the Lancet, we learn about the coronary sinus reducer. This approach to patients with stable angina pectoris is supposed to increase coronary venous pressure and thereby capillary gas transfer. In a randomized trial, the coronary sinus reducer reduced symptoms but did not improve myocardial perfusion. William Osler dedicated 30 pages to typhoid fever in his textbook of internal medicine. Now, in high-income countries the disease is largely forgotten, but not so elsewhere. We inspect a vaccine study from India that also covers paratyphoid, a less-severe disease. Anti VEGF antibodies or fusion proteins are effective in neovascular age-related macular degeneration. RGX-314 is a gene therapy, so that an anti-VEGF antibody is produced endogenously. The gene therapy was tolerated and at higher doses, produced protein. The Lancet case is a young woman with polyvinylpyrrolidone-induced histiocytosis. The Lancet next publishes two reviews on valvular heart disease. In Science Magazine, we learn how unscrupulous clever companies are now offering microbiome sequencing to the “worried well” for a hefty fee, although the

relevance of this information is totally unclear. In JAMA, we review a paper on Covid-19 excess deaths in Ohio and Florida amongst Democrats and Republicans. When the vaccines became available, these deaths decreased in Democrats but increased in Republicans. Vaccine denial was responsible, which is more prevalent among Republicans. A prominent vaccine denier is Robert F. Kennedy Jr. a previous Democrat, who holds several degrees from Harvard University. He should have taken more science courses. Join me on Wednesday, April 24, for this week's presentation. Best regards, Fred Luft, at <https://www.mdc-berlin.de/cjc>