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.

N Engl J Med is on summer break this week, but we are not. I present N Engl J Med mystery cases instead. A 33-year-old man with systemic lupus erythematosus presented with a 1-week history of pruritic, burning plaques. Examination showed pink, edematous plaques on the hands, elbows, knees, and feet. Laboratory testing showed elevated antinuclear and anti–double-stranded DNA antibody levels and low complement levels. Skin biopsy showed leukocytoclastic vasculitis. Treatment with oral and topical glucocorticoids was started. One week later, the lesions evolved into fixed, urticarial, annular, and targetoid plaques with rims of purpura on the thighs, chest, abdomen, and back. Which of the following is the most likely diagnosis? You are offered: Chronic spontaneous urticaria, Erythema multiforme, Secondary syphilis, Subacute cutaneous lupus erythematosus, and Urticarial vasculitis. Pick the palpable rash with the lowest complement levels. The N Engl J Med mystery cases now follow. A 76-year-old man is found crawling on the sidewalk. He is disheveled, disoriented and then stuporous. In emergency, his blood pressure is 183/113 mm Hg and his respiratory rate is 27/min. A “drug screen” reveals nothing. Routine labs show Na, 140, K 4.3, Cl 106, and HCO3 15 (mmol/L). Ultrasound, CT and much more shows nothing much. On the next day, blood gases are done that show pH 7.5 and pCO2 21. The patient is still breathing at 22/min. What is the most likely diagnosis? You are offered: Central hypothyroidism, Herpes simplex virus encephalitis, Hypertensive encephalopathy, Salicylate toxicity, Seizure disorder, and Wernicke’s encephalopathy. An 80-year-old woman is admitted with fatigue and weight loss, pancytopenia, and identification of schistocytes on a peripheral-blood smear. Her hemoglobin is low, reticulocyte count is 2%, haptoglobin is normal, LDH and ferritin are two-fold elevated. An earlier bone marrow aspirate had revealed slightly hypercellular marrow with maturing trilineage hematopoiesis but with some erythroid abnormalities and occasional hyperchromatic megakaryocytes; cytogenetic analysis had shown a loss of chromosomes 3 and 5 and a gain of chromosome 8 in 65% of the cells. What is the most likely diagnosis? You are offered: Anaplasmosis, Myelodysplastic syndrome,

Myelophthisis, Thrombotic thrombocytopenic purpura, Toxin exposure from chemical cleaning agents, and Vitamin B12 deficiency. A 29-month-old boy is admitted because of a seizure and is found to have hypocalcemia (around 5 mg/dL). On examination, the cover-up test — in which the distal lower leg is covered, and the alignment of the proximal lower leg is compared with that of the upper leg — was negative, a finding consistent with physiologic bowing of the leg. He has rather severe atopic dermatitis and several food allergies. His mother suffers from obsessive-compulsive disorder and refuses to allow any vaccinations for her son. The child's PTH is elevated and an x-ray shows splayed metaphyses of both femurs. What is the diagnosis? You are offered: Autoimmune polyglandular syndrome type 1, Chronic kidney disease, 22q11.2 deletion syndrome (DiGeorge syndrome), Pseudohypoparathyroidism, Tumor lysis syndrome, and Vitamin D deficiency. A 72-year-old woman is admitted to the hospital with altered mental status. Her story is complicated and she suffers from >10 chronic diseases (including severe lung disease with sleep apnea treated with CPAP). She is treated with more than 20 medicines that happen to include metformin and dapagliflozin for type-2 diabetes. While in the intensive care unit, her anion gap increases, blood sugar is normal urine ketone is only +1, and she becomes somnolent. What is the diagnosis? You are given: Chronic acetaminophen use causing elevated level of 5-oxoproline, Ethylene glycol ingestion, Euglycemic diabetic ketoacidosis, Salicylate toxicity, Type A lactic acidosis, and Type B lactic acidosis. A 22-year-old man comes to emergency because of pain and rapidly spreading erythema of the left hand. Over a period of several hours, the pain progressed and bullae began to form. He began to have pain with movement of the second and fourth fingers, and the bullae turned dark purple. On examination, the patient appeared well. The temperature was 38.6°C, the blood pressure 126/63 mm Hg, the heart rate 101 beats per minute, the respiratory rate 18 breaths per minute, and the oxygen saturation 100% while he was breathing ambient air. He lives in rural New England and recently began a new hobby as a taxidermist. The consulting hand surgeon is very nervous about the hand. What is the most likely diagnosis? You are offered: Cellulitis due to infection with Streptococcus pyogenes, Contagious ecthyma due to infection with orf virus, Cutaneous anthrax due to infection with Bacillus anthracis, Erysipeloid due to infection with Erysipelothrix rhusiopathiae, Plague due to infection with Yersinia pestis, and

Ulceroglandular tularemia due to infection with Francisella tularensis. We solve all these mysteries! In the Lancet, we are confronted with beta radioactive decay. ^{177}Lutetium emits high-energy electrons over short distances and when coupled with prostate-specific membrane antigen (PSMA) could be useful to treat prostate cancer. A randomized trial of LuLu-PSMA added to androgen deprivation with androgen-receptor pathway inhibitor provided a modest improvement in outcomes. HIF-2alpha steers erythropoiesis in renal cells and plays a role in renal cancer. Belzutifan is a HIF-2alpha inhibitor. Lenvatinib inhibits VEGF pathway. Cabozantinib is a multi-inhibitor of receptor tyrosine kinases. Belzutifan plus Lenvatinib were compared to cabozantinib in renal cancer patients. The combination drugs achieved a modest advantage over cabozantinib. Islatravir inhibits reverse transcriptase while lenacapvir impairs capsid production in HIV. Once-a-week might revolutionize maintenance treatment for HIV suppression. A Lancet study supports that point of view. Rezpegaldesleukin is a novel compound that stimulates regulatory T cells (Tregs), which in turn signal further via IL2. Thus, an IL-2 agonist effect is achieved. Lancet presents a study of rezpegaldesleukin in atopic-dermatitis patients. The Lancet review is on preeclampsia, a mismatch between between placental delivery and fetal demand. Otherwise, not much new here. Transfer RNA (tRNA) are RNA hairpin loops that carry aminoacids to ribosomes and insert them via a fitting codon on the mRNA strip in the process of protein synthesis. Many Mendelian diseases are caused by stop codon mutations in mRNA (cystic fibrosis for example). Suppressor tRNAs (sup-tRNAs) can be constructed that forcibly insert an aminoacid and override stop codons. In Science Magazine, we inspect a study of inhaled sup-tRNAs via lipid nanoparticles as a novel approach to fix stop-codon CFTR mutations in cystic fibrosis. In the US, deaths from measles disappeared in the 1980's. Now, deaths are back. Ribert Kennedy Jr. is largely responsible for this trend. In the Washington Post, we learn that the governor of Pennsylvania holds the anti-vaxxer Kennedy responsible. Load down the file and join me again on September 2, 16:00 English and 17:00 German.

Sincerely, Fred Luft

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