

Dear friends of clinical journal club - load the file down at <https://www.mdc-berlin.de/cjc>:

The *N Engl J Med* image of the week concerns a 78-year-old man with end-stage renal disease, diabetes mellitus, and microscopic polyangiitis, for which he was taking glucocorticoids. He presented to the rheumatology clinic with fever, painful glossitis, and taste abnormalities that had persisted for 1 month. Examination of the tongue showed a large, punched-out, painful ulcer. What is the diagnosis? You are offered: cytomegalovirus infection, syphilitic chancre, herpes simplex, Behcet's disease, and eosinophilic ulcer. We discuss the differential diagnosis. Uric acid levels are implicated in the progression of chronic kidney disease (CKD). Higher serum urate levels are associated with an increased risk of diabetic kidney disease. Lowering of the serum urate level with allopurinol may slow the decrease in the glomerular filtration rate (GFR) in persons with type 1 diabetes and early-to-moderate diabetic kidney disease. In a double-blind trial, investigators randomly assigned participants with type 1 diabetes, a serum urate level of at least 4.5 mg per deciliter, an estimated GFR of 40.0 to 99.9 ml per minute per 1.73 m² of body-surface area, and evidence of diabetic kidney disease to receive allopurinol or placebo. The primary outcome was the baseline-adjusted GFR, as measured with iohexol, after 3 years plus a 2-month washout period. Secondary outcomes included the decrease in the iohexol-based GFR per year and the urinary albumin excretion rate after washout. Safety was also assessed. Lowering uric acid did not help. In another randomized, controlled trial, investigators randomly assigned adults with stage 3 or 4 chronic kidney disease and no history of gout who had a urinary albumin:creatinine ratio of 265 or higher (with albumin measured in milligrams and creatinine in grams) or an eGFR decrease of at least 3.0 ml per minute per 1.73 m² of body-surface area in the preceding year to receive allopurinol (100 to 300 mg daily) or placebo. The primary outcome was the change in eGFR from randomization to week 104, calculated with the Chronic Kidney Disease Epidemiology Collaboration creatinine equation. Again, lowering uric acid levels improved no outcomes. These studies are counter to a much smaller earlier investigation of febuxostat. The effects on patient safety of eliminating extended-duration work shifts for resident physicians remain controversial. All believe that "physician fatigue" is responsible for errors (as opposed perhaps to poor training or too many "hand-offs").

Investigators conducted a multicenter, cluster-randomized, crossover trial comparing two schedules for pediatric resident physicians during their intensive care unit (ICU) rotations: extended-duration work schedules that included shifts of 24 hours or more (control schedules) and schedules that eliminated extended shifts and cycled resident physicians through day and night shifts of 16 hours or less (intervention schedules). The primary outcome was serious medical errors made by resident physicians, assessed by intensive surveillance, including direct observation and chart review. Interestingly, the doctors with the shorter working hours were worse than the ones doing the longer shifts.

Hydroxy-urea inhibits ribonucleotide reductase that converts ribose to deoxyribose. The cytostatic drug is also used in patients with sickle-cell anemia (Hemoglobin SS), because it results in more fetal hemoglobin that does not sickle. Investigators compared hydroxyurea at a fixed dose (approximately 20 mg per kilogram of body weight per day) with dose escalation (approximately 30 mg per kilogram per day). The primary outcome was a hemoglobin level of 9.0 g or more per deciliter or a fetal hemoglobin level of 20% or more after 24 months. Secondary outcomes included the incidences of malaria, vaso-occlusive crises, and serious adverse events. The kids tolerated the higher hydroxy-urea dose fine and were clinically improved.

We next inspect a study from the Ochsner health system in New Orleans and learn that African-American patients with Covid-19 do much worse than whites. The *N Engl J Med* review is on salicylate toxicity. The patient of the week is a 7-year-old girl who had immigrated (fled) to the United States from Central America with her mother. She was evaluated in the asylum clinic of a Boston hospital — where forensic medical evaluations of asylum seekers are performed to document evidence of persecution. In this case, the persecution is related to psychological distress after family separation from parents while in U.S. immigration detention. The current US policy evidently is that children are separated from their parents and institutionalized (placed in camps) if apprehended by United States Immigration and Customs Enforcement (ICE). We review this very sad state-of-affairs. We leave *N Engl J Med* with a video of how to don and doff personal protective equipment in the corona age. The amount of plastic and paper refuse is astounding. In the *Lancet*, physical distancing, face masks, and eye protection for Covid-19 are reviewed in a large meta-analysis. We hope that Tony Fauci explains the results of this paper to the Donald and

his side kick, Mr. Sixpence. Mosquito saliva proteins play a role in facilitating mosquito-borne diseases. Humans with antibodies against mosquito proteins show resistance to mosquito-borne diseases. We review a study on safety and immunogenicity of a mosquito saliva peptide-based vaccine. As we reviewed recently, persons with trisomy 21 (Down syndrome) develop Alzheimer's dementia at a very early age (about age 50 years). We learn that clinical and biomarkers in such patients may have utility as a population screening measure for early preventative treatments. Covid-19 patients develop antibodies; however, the utility of these antibodies in terms of subsequent protection is uncertain. In *Nature*, we inspect a paper on antibodies from convalescent patients. Not all patients develop effective neutralizing antibodies. The authors found two patients with outstanding responses in terms of receptor-binding domain antibodies. Their antibodies are a scientific model for vaccines. In *Science*, we find a paper on susceptibility of ferrets, cats, dogs, and other domestic animals to SARS-CoV2. Fortunately, swine do not appear to contract Corona virus. The *Lancet* review is on pancreatic carcinoma. The *Lancet* case is a 16 year-old with Covid-19 myocarditis. We close with a brief *JAMA* editorial about "Arrowsmith", a novel by the Nobel prizewinning author, Sinclair Lewis. The book reflects Lewis' contact with the Influenza pandemic of 1918 and is very relevant to our current Covid-19 pandemic. The oral presentations will be in Wednesday at 16.00 English and 17.00 German.

Yours,

Fred Luft (Check out the file pdf at <https://www.mdc-berlin.de/cjc>)