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The N Engl J Med image of the week concerns a 26-year-old man who presented to the emergency department with a 2-month history of an altered sense of taste associated with malaise, weight loss, and muscle cramps. Physical examination showed white, sharply demarcated, adherent plaques on the sides of the tongue. What is the diagnosis? You are offered: Oral hairy leukoplakia, Oral lichen planus, Human papillomavirus infection, Candidiasis, and Uremic stomatitis. We review the options.

There is considerable variation in disease behavior among patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (Covid-19). Genomewide association analysis may allow for the identification of potential genetic factors involved in the development of Covid-19. Investigators conducted a genomewide association study involving 1980 patients with Covid-19 and severe disease (defined as respiratory failure) at seven hospitals in the Italian and Spanish epicenters of the SARS-CoV-2 pandemic in Europe. After quality control and the exclusion of population outliers, 835 patients and 1255 control participants from Italy and 775 patients and 950 control participants from Spain were included in the final analysis. In total, the investigators analyzed 8,582,968 single-nucleotide polymorphisms and conducted a meta-analysis of the two case-control panels. On chromosome 3p21.31, the peak association signal covered a cluster of six genes (SLC6A20, LZTFL1, CCR9, FYCO1, CXCR6, and XCR1), several of which have functions that are potentially relevant to Covid-19. On chromosome 9, the ABO locus showed up. Harboring A was worse than harboring O. The authors did not say, but according to allele frequencies and other considerations, the effects of age, sex, co-morbidities, and body-mass index are far more important. In regions with high burdens of tuberculosis and human immunodeficiency virus (HIV), many HIV-infected adults begin antiretroviral therapy (ART) when they are already severely immunocompromised. Mortality after ART initiation is high in these patients, and tuberculosis and invasive bacterial diseases are common causes of death. Investigators conducted a 48-week trial of empirical treatment for tuberculosis as compared with treatment guided by testing in HIV-infected adults who had not previously received ART and had CD4+ T-cell counts below 100 cells per cubic

millimeter. Patients recruited in Ivory Coast, Uganda, Cambodia, and Vietnam were randomly assigned in a 1:1 ratio to undergo screening (Xpert MTB/RIF test, urinary lipoarabinomannan test, and chest radiography) to determine whether treatment for tuberculosis should be started or to receive systematic empirical treatment with rifampin, isoniazid, ethambutol, and pyrazinamide daily for 2 months, followed by rifampin and isoniazid daily for 4 months. The primary end point was a composite of death from any cause or invasive bacterial disease within 24 weeks (primary analysis) or within 48 weeks after randomization. Death or invasive infectious disease was about 20% in both groups; thus, the strategies were about the same in efficacy. Trastuzumab deruxtecan (DS-8201) is an antibody-drug conjugate consisting of an anti-HER2 (human epidermal growth factor receptor 2) antibody, a cleavable tetrapeptide-based linker, and a cytotoxic topoisomerase I inhibitor. The drug may have efficacy in patients with HER2-positive advanced gastric cancer. In an open-label, randomized, phase 2 trial, investigators evaluated trastuzumab deruxtecan, as compared with chemotherapy, in patients with HER2-positive advanced gastric cancer. Patients with centrally confirmed HER2-positive gastric or gastroesophageal junction adenocarcinoma that had progressed while they were receiving at least two previous therapies, including trastuzumab, were randomly assigned in a 2:1 ratio to receive trastuzumab deruxtecan (6.4 mg per kilogram of body weight every 3 weeks) or physician's choice of chemotherapy. The primary end point was the objective response, according to independent central review. Trastuzumab deruxtecan beat the physicians' choice regimen. We next glance at three Covid-19 studies that we reviewed earlier, examining whether or not cardiovascular drugs influence risks or outcomes. Although the Mehra study has been retracted, cardiovascular drugs do not negatively influence Covid-19 outcomes. At Montefiore Medical Center, nephrologists identified 36 consecutive adult kidney-transplant recipients who tested positive for Covid-19 between March 16 and April 1, 2020. Ten of the 36 kidney-transplant recipients (28%) and 7 of the 11 kidney-transplant patients who were intubated (64%) died. The N Engl J Med review is on RNA vaccine development – we inspect the latest ideas. The N Engl J Med case concerns a 74 year-old man with mantle-cell lymphoma. At an earlier hospitalization, he had accepted “do not resuscitate” (DNR) status. Now, Covid-19 is suspected and he needs to be intubated. Is he still DNR? Should we ask

him or his wife? Is the question very important? A lively discussion follows. In Nat Med, we inspect the epidemiology of Covid-19 amongst children. We learn that there are very few Covid-19 cases in children. Those under 20 years, have half the susceptibility and their chances of being asymptomatic or pauci-symptomatic appears greater than in older individuals. In the Lancet, we inspect two papers on Covid-19 in cancer patients. Cancer does not appear to have a major influence on Covid-19 outcomes. Tranexamic acid is a lysine-like amino acid derivative that inhibits plasminogen activation and clot dissolution. In a major far-eastern study, we learn that tranexamic acid does not favorably influence outcomes of major gastrointestinal bleeding episodes. The Lancet review is on novel approaches to opioid abuse management. Next, in Cell, we inspect the proteomic and metabolomic characterization of Covid-19 from patient sera. We close with a Lancet case of marked breast hypertrophy related to pseudo-angiomatous stromal hyperplasia. 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>)