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The N Engl J Med image of the week concerns a 5-year-old boy who presented to the dermatology clinic with a 2-week history of multiple painless and tense bullae containing clear to slightly hemorrhagic fluid and localized to the scrotum. What is the most likely diagnosis? You are offered fixed drug eruption, linear IgA bullous dermatosis, dermatitis herpetiformes, cutaneous bullous lupus, and bullous impetigo. We review these conditions. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can spread rapidly within skilled nursing facilities. After identification of a case of Covid-19 in a skilled nursing facility, investigators assessed transmission and evaluated the adequacy of symptom-based screening to identify infections in residents. They conducted two serial point-prevalence surveys, 1 week apart, in which assenting residents of the facility underwent nasopharyngeal and oropharyngeal testing for SARS-CoV-2, including real-time reverse-transcriptase polymerase chain reaction (rRT-PCR), viral culture, and sequencing. Symptoms that had been present during the preceding 14 days were recorded. Asymptomatic residents who tested positive were reassessed 7 days later. Residents with SARS-CoV-2 infection were categorized as symptomatic with typical symptoms (fever, cough, or shortness of breath), symptomatic with only atypical symptoms, presymptomatic, or asymptomatic. Twenty-three days after identifying the first resident with SARS-CoV-2 infection, the facility had a 64% prevalence of Covid-19 among residents, with a case fatality rate of 26% despite early adoption of infection-control measures. In addition, Covid-19 was diagnosed in 26 members of the staff (19%). In the investigation reported, more than half of the residents with positive tests were asymptomatic at the time of testing. Transmission from asymptomatic residents infected with SARS-CoV-2 most likely contributed to the rapid and extensive spread of infection to other residents and staff. Symptom-based infection-control strategies were not sufficient to prevent transmission after the introduction of SARS-CoV-2 into this skilled nursing facility. Covid-19 investigators conducted a randomized, open-label, phase 3 trial involving hospitalized patients with confirmed SARS-CoV-2 infection, oxygen saturation of 94% or less while they were breathing ambient air, and radiologic evidence of pneumonia. Patients were randomly assigned in a 1:1 ratio to receive intravenous remdesivir for either 5 days or

10 days. All patients received 200 mg of remdesivir on day 1 and 100 mg once daily on subsequent days. The primary end point was clinical status on day 14, assessed on a 7-point ordinal scale. There was no difference in the treatments; perhaps remdesivir did not work at all. Multiple loss-of-function alterations in genes that are involved in DNA repair, including homologous recombination repair, are associated with response to poly(adenosine diphosphate–ribose) polymerase (PARP) inhibition in patients with prostate and other cancers. Investigators conducted a randomized, open-label, phase 3 trial evaluating the PARP inhibitor olaparib in men with metastatic castration-resistant prostate cancer who had disease progression while receiving a new hormonal agent (e.g., enzalutamide or abiraterone). All the men had a qualifying alteration in prespecified genes with a direct or indirect role in homologous recombination repair. PARP inhibition almost doubled progression-free survival in these patients. Patients with PTEN hamartoma tumor syndrome (PHTS) have germline mutations in the tumor-suppressor gene encoding phosphatase and tensin homologue (PTEN). Such mutations have been associated with a hereditary predisposition to multiple types of cancer, including the Cowden syndrome. However, a majority of patients who have PHTS-related phenotypes have tested negative for PTEN mutations. In a previous study, investigators found that the E3 ubiquitin ligase WWP1 negatively regulates (suppresses) the function of PTEN. The investigators now expanded their findings. They found that germline WWP1 variants occur in patients with wild-type PTEN with characteristic PHTS-like phenotypes, particularly oligopolyposis. Patients with WWP1 germline mutations included those with Cowden-like syndrome, with the shared clinical diagnosis of at least five gastrointestinal polyps, including at least one hamartomatous polyp or a polyp that is hyperplastic or serrated. The findings are consistent with overactive WWP1 that interferes with the actions of PTEN. Obesity is a chronic disease with limited treatment options in pediatric patients. Liraglutide, a glucagon-like peptide 1 (GLP-1) analogue, increases the postprandial insulin level in a glucose-dependent manner, reduces glucagon secretion, delays gastric emptying, and induces weight loss through reductions in appetite and energy intake. Liraglutide may be useful for weight management in adolescents with obesity. In a randomized, double-blind trial, which consisted of a 56-week treatment period and a 26-week follow-up period, investigators enrolled adolescents (12 to <18 years of age)

with obesity and a poor response to lifestyle therapy alone. Participants were randomly assigned (1:1) to receive either liraglutide (3.0 mg) or placebo subcutaneously once daily, in addition to lifestyle therapy. The primary end point was the change from baseline in the body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) standard-deviation score at week 56. The kids lost 4 kg, which they regained when the drug was discontinued. Nephrologists quantified the SARS-CoV-2 viral load in autopsy tissue samples obtained from 22 patients who had died from Covid-19. Seventeen patients (77%) had more than two coexisting conditions, and a greater number of coexisting conditions was associated with SARS-CoV-2 tropism for the kidneys, even in patients without a history of chronic kidney disease. Between March 22 and April 4, 2020, a total of 215 pregnant women delivered infants at the New York–Presbyterian Allen Hospital and Columbia University Irving Medical Center. All the women were screened on admission for symptoms of Covid-19. Four women (1.9%) had fever or other symptoms of Covid-19 on admission, and all 4 women tested positive for SARS-CoV-2. Of the 211 women without symptoms, all were afebrile on admission. Nasopharyngeal swabs were obtained from 210 of the 211 women (99.5%) who did not have symptoms of Covid-19; of these women, 29 (13.7%) were positive for SARS-CoV-2. Thus, 29 of the 33 patients who were positive for SARS-CoV-2 at admission (87.9%) had no symptoms of Covid-19 at presentation. The N Engl J Med review concerns acute-on-chronic liver failure. We discuss a 63 year-old woman with osteopenia and fractures. Her calcium is normal but her phosphate concentration is reduced. Nevertheless, her phosphate fractional excretion is 34% (reabsorption only 66%). In the Lancet, we first inspect a study estimating excess 1-year mortality from the Covid-19 pandemic and the effects of intervention versus a do nothing scenario. Intervening is better than doing nothing. The next investigation addresses the use of renin-angiotensin-aldosterone inhibition and risk of Covid-19 requiring hospitalization. There was none. Then, we inspect a trial of interferon beta-1, lopinavir-ritonavir compared to lopinavir-ritonavir alone in Covid-19 patients. The triple therapy alleviated symptoms and reduced viral shedding. Since lopinavir-ritonavir alone does very little, presumably it was the interferon beta-1. The first Lancet review concerns collective isolation for indigenous populations in Brazil to protect from Covid-19. Apparently, the authors have not yet consulted President Bolsonaro. The

next review concerns Covid-19 and the plight of Africans. We then check out two Science papers. The first shows that rhesus monkeys re-infected with Covid-19 are protected from a second exposure. The report second concerns a DNA vaccine that seems to be effective in monkeys. We close with a patient who has drusen and dense-deposit disease. 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>)