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 48-year-old man who presented to the dermatology clinic with a 2-month history of an itchy rash that began in the genital region and then progressed to his torso, hands, and legs. He also noted a 13 kg weight loss over the past few months. On examination, he had erythematous patches and plaques at various stages of healing. What is the diagnosis? You are offered herpes simplex virus, acrodermatitis enteropathica, paraneoplastic pemphigus, discoid lupus, and necrolytic migratory erythema. You should be able to narrow the diagnosis down quickly. On-line in *N Engl J Med* is a vaccine study performed in non-human primates (Rhesus monkeys). An mRNA vaccine encoding the prefusion-stabilized spike protein of SARS-CoV2 was given to monkeys at two doses. Antibodies and T-cell responses were monitored. Then the monkeys were challenged with viral particles and viral replication was monitored. Neutralizing antibodies were robust and the monkeys did not get pneumonia. A second on-line report from Brazil tested whether or not hydroxychloroquine with or without azithromycin is of value in Covid-19 disease. Hydroxychloroquin did not improve clinical status. Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infection in infants, and a need exists for prevention of RSV in healthy infants. A monoclonal antibody, Palivizumab, exists to provide passive immunity to RSV; however, that antibody requires multiple dosing. Nirsevimab is a monoclonal antibody with an extended half-life that is being developed to protect infants for an entire RSV season with a single intramuscular dose. A randomized controlled trial was performed in premature infants. Medically attended RSV-associated lower respiratory tract infection occurred in 2.6% of the participants (25 participants) in the nirsevimab group and in 9.5% (46) in the placebo group. Hospitalization for this condition occurred in 0.8% of those in the nirsevimab group (8 participants) and in 4.1% (20) in the placebo group. But perhaps vaccinating pregnant women against RSV would be better. Healthy pregnant women, at 28 weeks 0 days through 36 weeks 0 days of gestation, with an expected delivery date near the start of the RSV season, were randomly assigned in an overall ratio of approximately 2:1 to receive a single intramuscular dose of RSV fusion (F) protein nanoparticle vaccine or placebo. Unfortunately, the results with respect to the primary end point did not meet

prespecified criteria for vaccine efficacy. Uterine fibroids, the most common type of tumor among women of reproductive age, are associated with heavy menstrual bleeding, abdominal discomfort, subfertility, and a reduced quality of life. For women who wish to preserve their uterus and who have not had a response to medical treatment, myomectomy and uterine-artery embolization are therapeutic options. Investigators conducted a multicenter, randomized, open-label trial to evaluate myomectomy, as compared with uterine-artery embolization, in women who had symptomatic uterine fibroids and did not want to undergo hysterectomy. Procedural options included open abdominal, laparoscopic, or hysteroscopic myomectomy. The primary outcome was fibroid-related quality of life, as assessed by the score on the health-related quality-of-life domain of the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire (scores range from 0 to 100, with higher scores indicating a better quality of life) at 2 years; adjustment was made for the baseline score. Actually, myomectomy led to slightly better results compared to uterine-artery embolization. But back to viruses. Yellow fever virus has a remarkable history (Panama Canal etc). An attenuated viral vaccine exists that is effective. However, the vaccine (YF17D-204) is not trivial and also results in symptoms, albeit usually mild. Investigators assessed the safety, side-effect profile, and pharmacokinetics of TY014, a fully human IgG1 anti–yellow fever virus monoclonal antibody. In a double-blind, phase 1b clinical trial, they assessed the efficacy of TY014, as compared with placebo, in abrogating viremia related to the administration of live yellow fever vaccine (YF17D-204). The primary safety outcomes were adverse events reported 1 hour after the infusion and throughout the trial. Efficacy was tested by injecting the participants with the attenuated YF17D-204 vaccine. The primary efficacy outcome was the dose of TY014 at which 100% of the participants tested negative for viremia within 48 hours after vaccine infusion. Indeed, the antibody was well tolerated, abrogated viremia, and reduced the incidence of YF17D-induced symptoms. The *N Engl J Med* review is about chronic lymphocytic leukemia, the most common leukemia in Western countries. Remarkable progress has been made here. The patient of the week has Covid-19 multisystem inflammatory syndrome (discussed last week in children), and requires treatment with ECMO. She recovers cardiac function. In the *Lancet* we review a trial of cytosponge-trefoil factor 3 to identify Barrett's esophagus. The cytosponge is swallowed by the

patients and has a string attached. After the sponge expands in the stomach, the operator pulls the device up by the string and thereby harvests cells in the lower esophagus. The cells are prepared in a paraffin block, sectioned, and stained. Quite a clever idea! We next learn about seroprevalence of anti-SARS-CoV2 antibodies in Geneva, a city that had a high prevalence of Covid-19. Unfortunately, the seroprevalence has remained low, so that Covid-19 outbreaks remain possible. Next, we review histopathological and ultrastructural findings of fatal Covid-19 infections from the state of Washington, US. The results are largely similar to other such studies we have discussed earlier. An extensive *Lancet* review focusses on atopic dermatitis. Clustered, regularly-interspaced short palindromic repeats (CRISPR) and CRISPR-associated (CAS) enzymes are a part of a remarkable defense system (Star Wars) developed by bacteria to combat DNA viruses (phage). Crispr/Cas9 has developed into a gene-editing platform. In *Science*, we review a report on phage-encoded anti-CRISPR. This viral defense enables complete evasion of CRISPR-Cas immunity in *Listeria*. Thus, the empire strikes back! The work reveals anti-Crispr mechanisms that have potential utility as a CRISPR effector control switch. This knowledge should allow us to bring the Crispr/Cas technology to a higher level. Finally, we inspect a Lancet case report on tear gas, allergy, and severe tracheobronchitis (for any demonstrators in the audience). The oral presentations will be in Wednesday at 16.00 English and 17.00 German.

Yours,

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