 exceptionally high doses of insulin are warranted, ketoacidosis and hyperosmolarity for which exceptions of preexisting diabetes, including diabetic onset diabetes and severe metabolic complications, may cause pleiotropic alterations of glucose metabolism that could complicate the pathophysiology of preexisting diabetes, including diabetic ketoacidosis and hyperosmolarity for which exceptionally high doses of insulin are warranted, have been observed in patients with Covid-19. These manifestations of diabetes pose challenges in clinical management and suggest a complex pathophysiology of Covid-19–related diabetes. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes Covid-19, binds to angiotensin-converting enzyme 2 (ACE2) receptors, which are expressed in key metabolic organs and tissues, including pancreatic beta cells, adipose tissue, the small intestine, and the kidneys. Thus, it is plausible that SARS-CoV-2 may cause pleiotropic alterations of glucose metabolism that could complicate the pathophysiology of preexisting diabetes or lead to new mechanisms of disease.

There are also several precedents for a viral
cause of ketosis-prone diabetes, including other coronaviruses that bind to ACE2 receptors.\textsuperscript{5} Greater incidences of fasting glycemia and acute-onset diabetes have been reported among patients with SARS coronavirus 1 pneumonia than among those with non-SARS pneumonia.\textsuperscript{5}

In the aggregate, these observations provide support for the hypothesis of a potential diabetogenic effect of Covid-19, beyond the well-recognized stress response associated with severe illness. However, whether the alterations of glucose metabolism that occur with a sudden onset in severe Covid-19 persist or remit when the infection resolves is unclear. How frequent is the phenomenon of new-onset diabetes, and is it classic type 1 or type 2 diabetes or a new type of diabetes? Do these patients remain at higher risk for diabetes or diabetic ketoacidosis? In patients with preexisting diabetes, does Covid-19 change the underlying pathophysiology and the natural history of the disease? Answering these questions in order to inform the immediate clinical care, follow-up, and monitoring of affected patients is a priority.

To address these issues, an international group of leading diabetes researchers participating in the CoviDIAB Project have established a global registry of patients with Covid-19–related diabetes (covidiab.e-dendrite.com). The goal of the registry is to establish the extent and phenotype of new-onset diabetes that is defined by hyperglycemia, confirmed Covid-19, a negative history of diabetes, and a history of a normal glycated hemoglobin level. The registry, which will be expanded to include patients with preexisting diabetes who present with severe acute metabolic disturbance, may also be used to investigate the epidemiologic features and pathogenesis of Covid-19–related diabetes and to gain clues regarding appropriate care for patients during and after the course of Covid-19. Given the very short history of human infection with SARS-CoV-2, an understanding of how Covid-19–related diabetes develops, the natural history of this disease, and appropriate management will be helpful. The study of Covid-19–related diabetes may also uncover novel mechanisms of disease.

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TO THE EDITOR: In their trial of Lactobacillus crispatus CTV-05 (Lactin-V), Cohen et al. (May 14 issue) offered hope for the prevention of bacterial vaginosis.1 The protective effect of the treatment was modest, similar to twice-weekly metronidazole,2,3 but the L. crispatus CTV-05 strain could still be detected in 48% of participants 13 weeks after the last administration. This finding is encouraging, but in order to interpret the effects of Lactin-V properly, we would like to see additional data. First, previous trials of lactobacilli-containing vaginal probiotics have shown large variability in treatment responses among women, as well as fluctuations in response in individual women, over time.4 Cohen et al. report a cumulative incidence according to treatment group, thereby overlooking these variabilities. Second, sequencing or other data on the composition of the molecular vaginal microbiome — preferably quantified — are essential for interpretation.3,4 Unlike microscopy, molecular methods can differentiate between autologous and biotherapeutic lactobacilli, which enables microbiome data obtained at all trial visits, including those that occurred during treatment with Lactin-V, to be used in longitudinal modeling. Molecular methods also enable estimation of the relative abundance of lactobacilli and bacterial vaginosis–associated anaerobes over time. Clinical symptoms are important outcomes in their own right, but microscopy-based Amsel criteria and Nugent scores should be accompanied by molecular data.

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No potential conflict of interest relevant to this letter was reported.

Randomized Trial of Lactin-V to Prevent Recurrence of Bacterial Vaginosis

TO THE EDITOR: Cohen et al. report on a potential treatment for recurrent bacterial vaginosis. Women arrived at the trial screening clinic. (I could not find a description of the way in which they were recruited.) Bacterial vaginosis was diagnosed on the basis of the Amsel criteria and the Gram’s staining–based Nugent score; the presence of symptoms was not required for diagnosis. I could not find how many participants had symptoms at entry nor whether treatment affected the symptoms in the participants who had them. Some symptoms of bacterial vaginosis were reported as adverse events in some participants.

The U.S. Preventive Services Task Force recommends against screening for bacterial vaginosis in pregnant women who are not at risk for preterm delivery; for pregnant women who have such a risk, no recommendation is made, because current evidence is insufficient.1 I could find no recommendation for or against screening in nonpregnant women.

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