Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

the gut microbiota area. This review concluded, "The sum of the data provides clear evidence that changes in the diet unrelated to LNCS consumption are likely the major determinants of change in gut microbiota numbers and phyla, confirming the viewpoint supported by all the major international food safety and health regulatory authorities that LNCS are safe at currently approved levels."

As for the statement in Section 2a (NNS regulation and labeling), "The FDA's [U.S. Food and Drug Administration] regulatory processes for NNS are controversial due to concerns with unknown effects of long-term consumption," citing Chattopadhyay et al,[3] the authors of that paper indicated that global regulatory authorities had approved all the NNSs they discussed. ■

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The author was a member of the PureCircle Stevia Institute and was a consultant of the Calorie Control Council.

The author reports no conflict of interest.

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REPLY

Check for updates

We thank Dr Ayoob for his interest in our Clinical Opinion paper entitled "Consumption of non-nutritive sweeteners during pregnancy" and his comments.

We state that this article intends to present the prevalence of nonnutritive sweetener (NNS) consumption in pregnant women and highlight pieces of literature that have been overlooked by health professionals. We also cited several professional societies, including the Academy of Nutrition and Dietetics, and reported that they state that NNS consumption is safe during pregnancy and childhood. We then highlighted the fact that the United States Institute of Medicine and the American College of Obstetricians and Gynecologists have not made any statement on NNS consumption during pregnancy.

In addition, it must be noted that we have no conflict of interest in terms of NNS research and that the food industry did not fund our research. Therefore, we are merely advising caution and emphasizing the need for more research on NNS exposure during healthy gestation or pregnancy complications.

Furthermore, we acknowledge the comment emphasizing the recent article by Lobach et al.[1] However, this is the only piece supporting a safe effect of NNS consumption on the microbiome. It also poses a conflict of interest as being financially supported by the Calorie Control Council, preventing objectivity.

Once again, we appreciate the supplementary information provided and welcome their addition to our Clinical Opinion paper. ■

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Confirmatory evidence of the visualization of severe acute respiratory syndrome coronavirus 2 invading the human placenta using electron microscopy

Check for updates

TO THE EDITORS: In May 2020, our article reporting on the visualization of the invasion of the human placenta by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using electron microscopy, was published online in the *American Journal of Obstetrics and Gynecology*.[1] In a subsequent Reply to a Letter to the Editors, we provided further

evidence to support the findings of our original article, proving that it was indeed SARS-CoV-2 virions that were visualized.[2] The evidence we have presented includes the following: (1) the virus was visualized with transmission electron microscopy showing that the extracellular structures that were visualized were identical to those seen within the cells, thus indicating that these were not clathrin-coated vesicles; (2) immunohistochemical analysis of the placental samples was positive for SARS-CoV-2 glycoprotein using a specific antibody in conjunction with positive and negative controls; (3) the virus was immunolocalized using immunogold electron microscopy; and (4) the virus was detected in the placenta using real-time polymerase chain reaction (RT-PCR)—specific primers. Our aforementioned findings are very consistent with subsequent reports that also documented the visualization of SARS-CoV-2.[3,4]

With the current letter, we would like to provide additional information regarding the detection of the virus in our placental sample. A fresh piece of the placenta from our case was tested for SARS-CoV-2 by RT-PCR by our neonatal research team, led by Dr. Nazeeh Hanna, who is also conducting coronavirus disease 2019 related research, funded by the National Institute of Child Health and Human Development (NICHD), R01 HD098258-01A1. Fresh placental tissues were collected immediately after birth. The total RNA was isolated with a miRNeasy mini kit (QIAGEN Sciences Inc, Germantown, MD). The SARS-CoV-2 nucleocapsid (N) 1 and N2 genes were assayed for by a 2-step RT-PCR test. Reverse transcription was carried out using the High-Capacity cDNA Reverse Transcription Kit (Applied Biosystems, Foster City, CA), with primers specific for the N1, N2, and RNase P genes.[5] The presence of the viral RNA was assayed for using a 2019-nCoV RUO Kit (Integrated DNA Technologies, Coralville, IA) and a sample with a cycle threshold value less than 40 was considered positive. The results were positive for the presence of viral RNA in the placenta of our case report.[1]

In conclusion, we want to emphasize that literature published after our case report[1] has shown unequivocally that there is scientific and clinical evidence that placental invasion by SARS-CoV-2 is valid.[3,6–8] As a matter of fact, when vertical transplacental transmission occurs, the viral load in the placenta is severalfold higher than in the other maternal and fetal compartments.[8] For all the reasons outlined in this letter, we are convinced that we have successfully reported on the visualization of SARS-CoV-2 in the human placenta.[1] ■

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