frozen vs fresh embryo transfers (16/512 [3.1%] vs 4/401 [1.0%]; relative risk 3.13, 95% confidence interval 1.06−9.30, $P = .029$), where the only important difference between the groups was the preparation of the embryos.

Close examination of the data presented in Tay et al[1] as regards maternal cardiovascular functional parameters shows that their findings are at odds with other studies, including from their group[5]: while they describe a state of increased cardiac output (CO) and decreased peripheral vascular resistance (PVR) in cases with preeclampsia, Foo et al[5] described decreased CO and increased PVR, ie, there is no consensus whether preeclampsia is a hyper- or hypo-dynamic state. Moreover, Tay et al[1] show that compared to control pregnancies, CO was increased in "pure" preeclampsia (without FGR), but decreased in FGR alone or with preeclampsia, and PVR was reduced in "pure" preeclampsia and increased in FGR alone or with preeclampsia. This shows a lack of continuum among these degrees of severity of the clinical presentation. It would appear that we are looking at a group of disorders that are characterized by similar clinical presentation but different pathophysiology; mixing them in epidemiological studies produces confusing results.

Taken together with decades-long research into the placental origins of preeclampsia, it would appear that although maternal cardiac adaptation has an important place in the development of the clinical syndrome, there is significant heterogeneity in preeclampsia, as recently described by Benton et al.[6] The investigators found that the clinical heterogeneity of preeclampsia correlates with both gene expression and placental histopathology.[6]

Therefore, future studies on the role of fetal/placental vs maternal cardiovascular factors in the development of preeclampsia should be multicenter, multidisciplinary endeavors with sufficiently large numbers to allow cogent subgroup analysis, in order to reach valid conclusions regarding the pathophysiology of preeclamptic disorders of pregnancy, with or without FGR. ■

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UTERINE AND FETAL PLACENTAL DOPPLER INDICES ARE ASSOCIATED WITH MATERNAL CARDIOVASCULAR FUNCTION: REPLY

TO THE EDITORS: We thank Professor Yagel for his observations. We report that uterine and fetal Doppler indices are associated with maternal cardiovascular function,[1] and have previously found that cardiovascular function prior to pregnancy in healthy women is associated with the development of preeclampsia or fetal growth restriction.[2] Although we do not discount a role for the placenta in these pathological processes, the question is whether cardiovascular function or placental maldevelopment initiates them.

There are few or no data on maternal cardiovascular dysfunction in trisomic, triploid, and twin pregnancies in relation to preeclampsia. In these cases, one might hypothesize that a very abnormal placenta could indeed influence maternal cardiovascular function, in turn leading to perturbations that then drive fetal vascular responses. The theories are not mutually exclusive.

Hence we suggest that it is not a case of "fetal/placental vs maternal cardiovascular factors" as Professor Yagel suggests, but rather "fetal/placental AND cardiovascular factors." Although no one would disagree with the concept of more multicenter, multidisciplinary studies, Professor Yagel does not expand on which questions would be answered by them, and his suggestion should not diminish the value of carefully phenotyped cohort studies designed to answer basic mechanistic questions. ■

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Revitalizing research in genitourinary syndrome of menopause

Check for updates

TO THE EDITORS: The call to action by Chang and Paraiso[1] highlighted the many barriers to women wishing relief of postmenopausal sexual dysfunction stemming from genitourinary syndrome of menopause (GSM). Even when gaining advice from knowledgeable care providers, women find the costs of effective local and systemic therapies to be prohibitive. Therapies now too expensive for many women include hormonal options that have been available for decades, as well as new energy-based therapies whose efficacy and safety have not passed FDA muster.[2]

The authors repeated a now-challenged prohibition against low-dose local estrogen products in women with a history of estrogen-sensitive breast cancer, but these were deemed safe by experts in the American College of Obstetricians and Gynecologists.[3] Despite this shift in recommendations, most survivors choose to forego hormones even after developing very difficult genitourinary symptoms.

Physicians should realize that there is an inexpensive, self-applied option that has been shown to be extremely helpful in a randomized controlled trial.[4] Patients successfully used a topical numbing solution to prevent moderate and severe dyspareunia after menopause. After a 3-minute application using cotton balls, penetration pain scores dropped on average from 8 out of 10 to 1 out of 10 with use of lidocaine 4% topical solution applied to the vulvar vestibule just before intimacy. GSM is not simply atrophy, but includes a pain condition specific to the vulvar vestibule. Numbing therapy may seem counterproductive for pleasure, but the location is discrete and small, and women can extinguish mucosal pain but still enjoy wider genital sensations. Arousal success and orgasm quality increased when pain was prevented. Partners did not note any numbing, and couples rejoiced at being able to return to pain-free coitus after half of them had previously abandoned painful penetrative sex.

Even lidocaine is not without its price explosion in the last several years. This old off-patent medication that used to cost $8.50 by prescription for a 50 mL bottle now approaches a 10 times higher price. There are over-the-counter gel and cream products with the same 4% concentration of lidocaine, but studies have not been published on use in this population.

While the health care system in the United States grapples with prescription drug costs, patients can be directed to this effective, low-cost, nonhormonal option rather than sitting out penetrative intimacy during postmenopausal years. The lidocaine option was studied in breast cancer survivors because they so typify the difficulties that arise with estrogen deprivation. But any GSM patient may find this therapy beneficial. I wonder if the authors agree that it is time to share information about self-applied anesthetic products for GSM and continue studying outcomes. ■

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REPLY

Check for updates

We would like to thank Dr Goetsch for her Letter to the Editors (L19-053AR1). In our Call to Action—"Revitalizing research in genitourinary syndrome of menopause"[1]—we discussed the barriers and limitations to the treatment of genitourinary syndrome of menopause (GSM) in light of the FDA 2018 statement cautioning women against vaginal rejuvenation devices.

We discussed the limitations with the use of vaginal estrogen in women with a history of hormone-sensitive breast cancer. The American College of Obstetricians and Gynecologists recommends trialing nonhormonal treatment options for vaginal atrophy in this population, owing to the lack of long-term data on hormone treatments (level C recommendation).[2,3]