

## Correspondence



# Ovary is necessary to the health of uterus

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► See the letter “Embryos need a cozy house” in volume 27, e34.

### Correspondence to

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### Conflict of Interest

No potential conflict of interest relevant to this  
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### Reply to Fabio Martinelli:

We would like to express great thanks for the interest and comments on our review. We agree with Dr. Martinelli et al.'s opinion about the importance of the uterus with regards to pregnancy outcomes following radiation treatment [1]. Total body irradiation (TBI) or pelvic radiation can indeed affect the uterus, causing side effects like reduced uterine volume, endometrial injury, vascular impairment and myometrial fibrosis and thinning, as well as permanent damage dependent on dosage [2]. Therefore, it may ultimately affect the status of the uterus and lead to decreased pregnancy rates and complications during pregnancy. Currently, there is no clinically applicable way to protect the function of the uterus. Emerging options include uterus transplantation [3] or surrogacy for patients who have pregnancy complications after pelvic irradiation. Concern for uterine health and function as it relates to pregnancy is part of the current oncofertility discussion at National Physician Cooperative and Global Partner sites [4]. Thus we concur with the authors that personalized counseling for woman should include a multidisciplinary oncofertility team that discusses all aspects of treatment-related issues. We also agree that the goal of oncofertility interventions is the ability to protect as many reproductive functions as possible (pituitary, ovarian, fallopian tube, uterus, cervix) and that biological parenting with high quality gametes.

In addition to the direct effect of radiation or chemotherapy on uterine function, it is also important to evaluate the role of gonadal steroids in the loss of uterine health. Perhaps the best data regarding this topic comes from Bath and his colleagues [5] who showed that leukemia survivors with ovarian failure following TBI (14.4 Gy) had reduced uterine volume (myometrium), thickness (endometrial thickness) and impaired blood flow (vasculature). Perhaps not surprisingly, the data suggest that there is a correlation between ovarian failure and uterine size [5]. Indeed, physiological sex steroid replacement treatment improved uterus volume, implying that the uterus can be maintained or recovered with hormonal therapy, even after high levels of radiation.

Another case by the same group described a patient with ovarian failure caused by 14 courses of chemotherapy and direct radiation to the pelvic region (55 Gy); this patient achieved successful embryo implantation and pregnancy after spontaneous conception from the re-implantation of ovarian cortical tissue [6]. This case study shows that ovarian-derived hormones can recover uterine tissue, giving patients who had treatment of chemo- or radiation at childhood the hope of pregnancy.

It is also important to consider other ways to improve uterine health. For example, the combination of pentoxifylline and tocopherol (vitamin E) treatment [7-9] has been clinically successful in improving endometrial thickness, myometrial dimensions, and diastolic uterine artery suggesting that the uterus function can be recovered with adjuvant therapy.

Certainly the uterus is a central organ in female reproduction and direct damage can occur with cancer therapy. We all also agree that a functional ovary produces the hormones necessary for a healthy uterus. It is also not contested that the immature oocytes are exceptionally sensitive to damage-induced cell death [10,11]. It follows that if the ovarian follicles are protected, most radiation related uterine problems can be minimized [12]. In our review, we covered the existing and emerging technologies to preserve functional ovaries and fertility 'pre-, co-, and post' chemo- or radiation treatment. Further studies that define the direct and indirect effects of anti-cancer therapy on the uterus are essential. There is no doubt that preservation of ovarian function, preservation of a healthy uterus and strategies that limit exposure related effects are the goal of everyone working in the field of oncofertility.

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