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proinflammatory cytokines also increased in mice on a HFD. The effects of HFD on litter production rate and number of pups per litter were independent of obesity. High fat diet seems to activate primordial follicles and promote a kind of premature ovarian aging by activating inflammation, independent of obesity itself. This paper demonstrates that increased fat consumption,

even without obesity, is detrimental to fertility and ovarian function. To date, most studies in women have studied the effects of body mass index on reproduction. Futures studies need to examine the effects of dietary content on reproductive function in women, and whether anti-inflammatory agents may counter the effects of HFD on reproduction.—DK)

## Randomized Trial of a Lifestyle Program in Obese Infertile Women

**Meike A. Q. Mutsaerts, Anne M. van Oers, Henk Groen, Jan M. Burggraaff, Walter K. H. Kuchenbecker, Denise A. M. Perquin, Carolien A. M. Koks, Ron van Golde, Eugenie M. Kaaijk, Jaap M. Schierbeek, Gerrit J. E. Oosterhuis, Frank J. Broekmans, Wanda J. E. Bemelmans, Cornelis B. Lambalk, Marieke F. G. Verberg, Fulco van der Veen, Nicole F. Klijn, Patricia E. A. M. Mercelina, Yvonne M. van Kasteren, Annemiek W. Nap, Egbert A. Brinkhuis, Niels E. A. Vogel, Robert J. A. B. Mulder, Ed T. C. M. Gondrie, Jan P. de Bruin, J. Marko Sikkema, Mathieu H. G. de Greef, Nancy C. W. ter Bogt, Jolande A. Land, Ben W. J. Mol, and Annemieke Hoek**

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### ABSTRACT

Obesity is a prevalent health condition that affects 14% to 20% of women of reproductive age. Some of the adverse affects of obesity on reproductive health include increased risks of menstrual dysfunction, anovulation, and infertility, especially resulting in failure of assisted reproductive techniques. There are various guidelines that advocate lifestyle intervention programs aimed at weight loss of 5% to 10% of body weight as the first step in caring for obese infertile women. There is, however, a dearth of randomized controlled trials assessing the effectiveness of lifestyle intervention programs. The objective of this study was to assess the effectiveness of a lifestyle intervention preceding infertility treatment. A multicenter randomized trial was conducted at 6 university medical centers and 17 general hospitals in the Netherlands. Infertile women with a body

mass index (the weight in kilograms divided by the square of the height in meters) of 29 or higher were randomly assigned to a 6-month lifestyle intervention program preceding treatment for infertility or to prompt treatment for infertility. Primary outcome was the vaginal birth of a healthy singleton at term within 24 months after randomization. Prespecified secondary outcomes included a change in the woman's weight, waist circumference, and blood pressure. The participants were assigned to 2 treatment groups. A total of 290 women were assigned to a 6-month lifestyle intervention program preceding 18 months of infertility treatment (intervention group), and 287 were assigned to prompt infertility treatment for 24 months (control group of which 3 women withdrew consent, resulting in 289 women in the intervention group and 285 women in the control group). The study revealed that in intention-to-treat analyses, the mean weight loss was 4.4 kg in the intervention group and 1.1 kg in the control group ( $P < 0.001$ ). Whereas the primary outcome occurred in 27.1% of the women in the intervention group, it was 35.2% in the control group (rate ratio in the intervention group, 0.77; 95% confidence interval, 0.60–0.99). The findings of the study show that in obese infertile women, a lifestyle intervention preceding infertility treatment, as compared with prompt infertility treatment, did not result in higher rates of a vaginal birth of a healthy singleton at term within 24 months after randomization.

#### EDITORIAL COMMENT

(Obesity disrupts reproduction by causing menstrual dysfunction, anovulation, and infertility. Even assisted reproductive techniques, which tightly control ovarian stimulation and endometrial development, are less effective in obese women. Can lifestyle intervention mitigate the effects of obesity on reproduction in women? This paper reports the results of a multicenter randomized trial from the Netherlands of the efficacy of a 6-month lifestyle intervention program before fertility treatment in obese women. The primary outcome was vaginal birth of a healthy singleton at term within 24 months after randomization. Secondary

outcomes included change in weight, waist circumference, and blood pressure. In this intention-to-treat analysis, women in the intervention group lost more weight, 4.4 kg, compared to 1.1 kg in the control group. However, lifestyle intervention before infertility treatment did not result in higher delivery rates (27% vs 35%, respectively). These results could mean that obesity itself is not a cause but rather a marker for some other process contributing to infertility in women. Alternatively, the effects of the 6-month delay, imposed by the lifestyle intervention, may counter any beneficial effects deriving from weight loss.—DK)

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## Use of Effective Contraception 6 Months After Emergency Contraception With a Copper Intrauterine Device or Ulipristal Acetate—A Prospective Observational Cohort Study

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