explanation of the interpretation of the results, the progestin has been implicated in the risk of breast cancer. It is known that MPA is not a pure progestin because it also has glucocorticoid and androgenic activity. Drospirenone is a progestin that does not have glucocorticoid activity and has modest antiandrogenic action. Otto et al used a mouse model to study the comparative effects of MPA and drospirenone maintenance of pregnancy and proliferation of the mammary gland and uterine epithelial mitogenic activity. MPA's stimulation of mammary gland compared with drospirenone's response similar to natural progesterone is consistent with a possible adverse effect of MPA on breast cancer. Clinical trials in humans will be needed to validate this possible adverse effect of MPA versus drospirenone on risk of breast cancer. However, such comparisons may not be justified.

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Recombinant LH (lutropin alfa) for the treatment of hypogonadotrophic women with profound LH deficiency: a randomized, double-blind, placebo-controlled, proof-of-efficacy study

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Objective.—To confirm the safety and efficacy of 75 IU lutropin alfa with concomitant follitropin alfa in inducing follicular development in women with profound gonadotrophin deficiency.

Design.—Double-blind, randomized, placebo-controlled trial conducted in 25 medical centres in four countries.

Patients.—Thirty-nine patients with LH < 1·2 IU/l and FSH < 5·0 IU/l were treated with concomitant 75 IU lutropin alfa and 150 IU follitropin alfa or concomitant placebo and 150 IU follitropin alfa.

Measurements.—Primary efficacy end-point (intent-to-treat): follicular development defined by (i) at least one follicle ≥ 17 mm; (ii) serum E_2 level ≥400 pmol/l on day of hCG administration (DhCG); and (iii) mid-luteal phase progesterone level ≥ 25 nmol/l.

Results.—In the analysis of evaluable patients, 66·7% (16 of 24) of patients given lutropin alfa achieved follicular development compared with 20·0% (2 of 10) of patients receiving placebo ($P = 0·023$). In the intent-to-treat analysis, follicular development was achieved in 65·4% (17 of 26) of patients receiving lutropin alfa and 15·4% (2 of 13) of patients receiving placebo ($P = 0·006$). The statistical difference between treatment groups was preserved when over-response leading to cycle cancellation was analysed as a failed response ($P = 0·034$). Lutropin alfa was well tolerated.

Conclusion.—Subcutaneous co-administration of 75 IU lutropin alfa with follitropin alfa is safe and effective in inducing follicular development in women with profound gonadotrophin deficiency.

▶ Hypogonadotrophic hypogonadism (HH) is an uncommon disorder, which is characterized by low serum concentrations of estradiol, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), arrested folliculogenesis, amenorrhea, infertility, and unresponsiveness to a progesterone challenge. The combined treatment with recombinant LH [recombinant human (r-h)LH] and FSH (r-hFSH) have been successful in inducing follicular development. The objective of this study was to determine the efficacy of 75 IU of r-hLH and 150 IU of r-hFSH in inducing follicular development in women with profound LH deficiency. The strength of the study was that it was a randomized, double-blind, placebo-controlled study. The combination of synthetic LH and FSH were much more effective in inducing follicular development than synthetic FSH alone. Although there were two resultant pregnancies in combined treatment group versus in the FSH treated group, further study will be required in a larger study to determine overall success in achieving pregnancy as an end point using this protocol.

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Female Reproductive Function and Menopause

Anti-Mullerian Hormone and Inhibin B in the Definition of Ovarian Aging and the Menopause Transition

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Context/Objective.—The objective of the study was to determine whether anti-Mullerian hormone (AMH) and inhibin B are viable endocrine biomarkers for framing the menopause transition from initiation to the final menstrual period (FMP).

Design.—We assayed AMH, inhibin B, and FSH in 300 archival follicular phase specimens from 50 women with six consecutive annual visits commencing in 1993 when all women were in the pre-and perimenopausal menopause stages. Subsequently each woman had a documented FMP. The assay results were fitted as individual-woman profiles and then related to time to FMP and age at FMP as outcomes.

Results.—Based on annual values from six time points prior to the FMP, (log)AMH longitudinal profiles declined and were highly associated with a time point 5 yr prior to FMP [including both observed and values below detection ($P < 0.0001$ and $P = 0.0001$, respectively)]. Baseline AMH profiles were also associated with age at FMP ($P = 0.035$). Models of declining (log)inhibin B profiles (including both observed and values below detection) were associated with time to FMP ($P < 0.0001$ and