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### Natural Fluctuations in Progesterone Do Not Impact Endothelial Function in Healthy Premenopausal Women

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Endogenous sex hormone concentrations vary across the menstrual cycle of naturally menstruating premenopausal women and may elicit concomitant changes in vascular function. Specifically, estrogen (E2) may enhance vascular function partially by increasing nitric oxide bioavailability. In contrast, the influence of progesterone (P4) on endothelial function remains unclear, with some data suggesting it increases nitric oxide bioavailability and other data suggesting it antagonizes the dilatory effects of E2.

**PURPOSE:** To elucidate the effect of P4 on vascular function, in the presence of minimal fluctuations in E2 concentrations in healthy premenopausal women. **METHODS:** Sex hormones and endothelial function were measured in ten healthy premenopausal women (22±2 y) during the early follicular phase (EF, within 5 days of the onset of menstruation) and the early luteal phase (EL, 4±2 days post-ovulation) of a single menstrual cycle. Serum concentrations of E2 and P4 were analyzed using enzyme-linked immunosorbent assays. Independent concentrations of E2 and P4 were calculated, as well as the progesterone-to-estrogen ratio (P4:E2). Endothelial function was assessed via brachial artery flow-mediated dilation (FMD). %FMD was calculated as the percent change in brachial artery diameter following an ischemic stimulus. Data were compared between phases with paired t-tests.

**RESULTS:** Serum concentrations of E2 and P4 increased from the EF to the EL phase (91.8±34.5 vs. 120.9±32.6 pg/mL, p=0.01 and 1.4±0.6 vs. 5.1±3.6 ng/mL, p=0.01, respectively). As a result of the P4 surge in the EL phase, the P4:E2 was significantly higher in the EL phase as compared to the EF phase (42.9±30.5 vs. 15.5±4.8, p=0.02). %FMD did not vary between the EF and EL phases (9.6±4.4 vs. 9.5±3.5 %, p=0.97). **CONCLUSION:** The endothelial function of healthy premenopausal women is stable in the presence of significant fluctuation in P4 concentrations, despite minimal fluctuation in E2 concentrations.

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