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ABOUT THE COVER

Pregnancy affects a woman’s breast cancer risk depending upon age at first pregnancy. Accumulating evidence indicates that pregnant women who have high circulating estrogen levels or who gain an excessive amount of weight, which is associated with high leptin levels, are significantly more likely to develop breast cancer after menopause. Using a preclinical model, the present study investigated whether excess estradiol (E2) or leptin during pregnancy increases later mammary tumorigenesis in rats. The cover micrograph depicts the effects of exposure to excess E2 (PCNA immunohistochemical staining; dark nuclei; 400× magnification) or leptin (not shown) during pregnancy on cell proliferation in representative mammary gland sections: the proliferation index was significantly higher in E2-treated parous rats compared to those of vehicle-treated parous control rats ($P < 0.001$). These findings suggest that an exposure to excess E2 or leptin during pregnancy prevents the parity-induced protective changes in mammary gland and increases subsequent breast cancer risk. This study further suggests that pregnant women should avoid being exposed to the highest levels of E2 and leptin during pregnancy, caused by either endogenous or life-style factors such as gaining excessive amounts of weight during pregnancy, which may not only put them at risk of developing gestational diabetes and hypertension but also increase later breast cancer risk. See the article by de Assis and colleagues (beginning on page 1194) for more information.