

MATERNAL OBESITY IN PREGNANT RATS IS ASSOCIATED TO INCREASED LEVELS OF ESTRADIOL DURING EARLY POSTNATAL LIFE AND ALTERED OVARIAN FOLLICULAR DEVELOPMENT IN THE OFFSPRING

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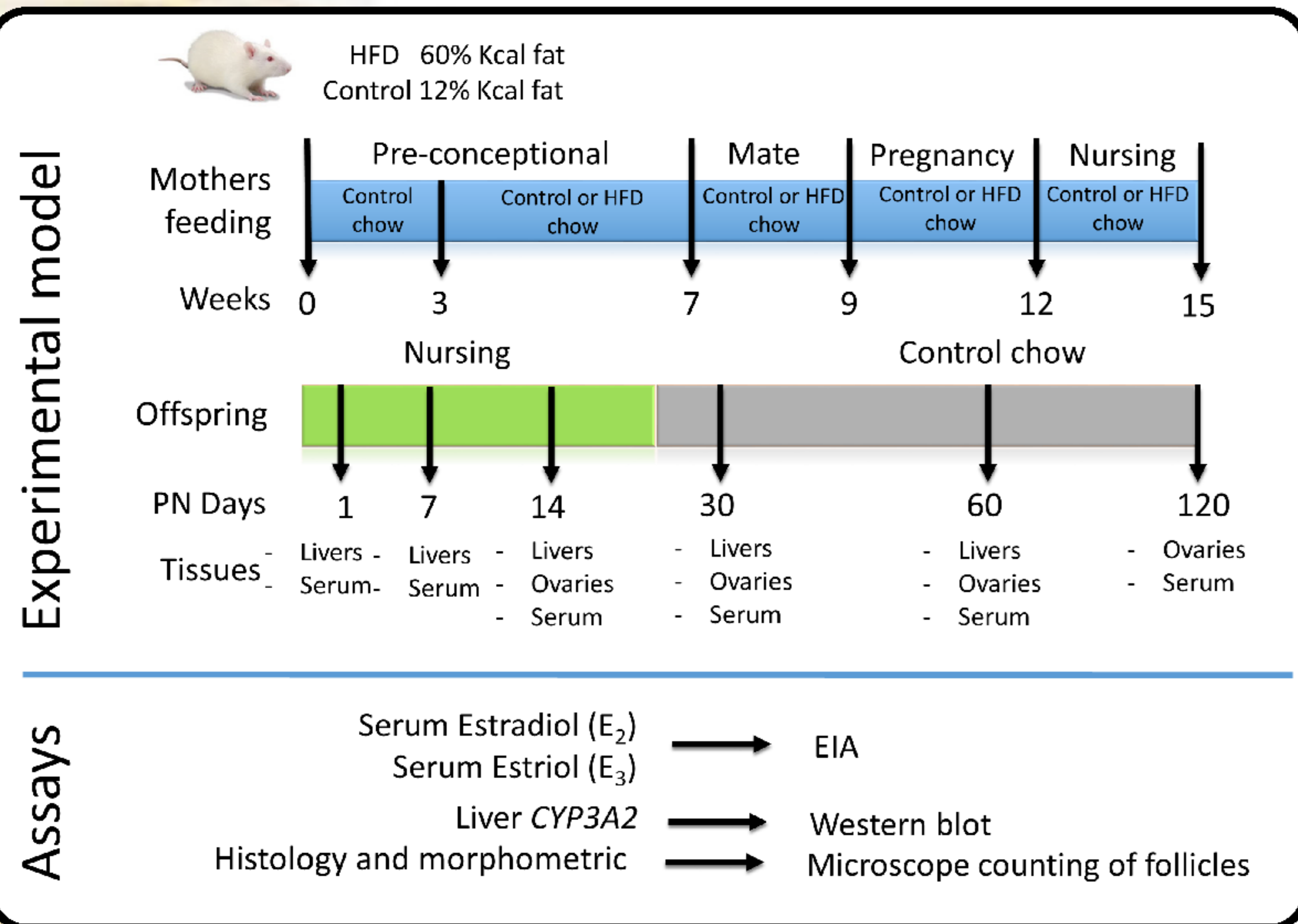
Introduction

Obesity during gestation is related to predisposition to endocrine and metabolic diseases in the offspring. Regarding reproductive effects, an increase in body mass index in pregnant mothers is associated with precocious puberty in their offspring. This has been replicated in animal models of high fat diet administration to mothers. Also, gestational obesity has been associated to higher susceptibility to developing breast cancer in the offspring. As both precocious puberty and breast cancer are strongly related to higher estrogens levels, we studied if offspring of rats exposed to a high fat diet (HFD) had increased levels of endogenous estradiol from neonatal until adult age. In addition, we evaluated ovarian follicular development in adult rats because early exposure to estrogens alters ovarian follicular development.

Purpose

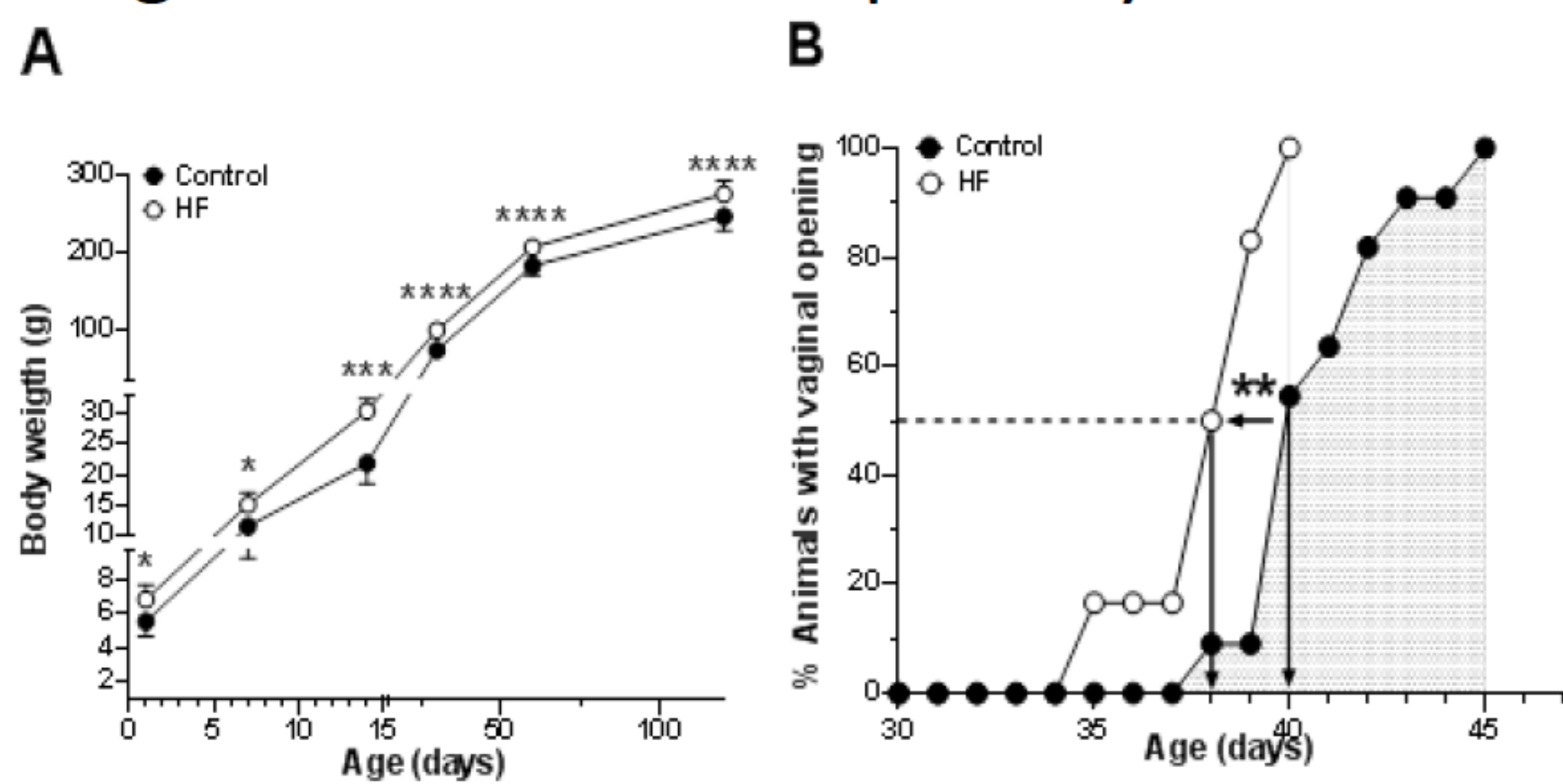
To evaluate reproductive effects of maternal obesity on the offspring and associate these alterations to increased levels of estradiol

Methods



Results

1 Maternal obesity relates with an increase in body weight and an advance puberty in the female offspring



2 Offspring of obese mothers showed less antral follicles and follicular cyst in the ovary.

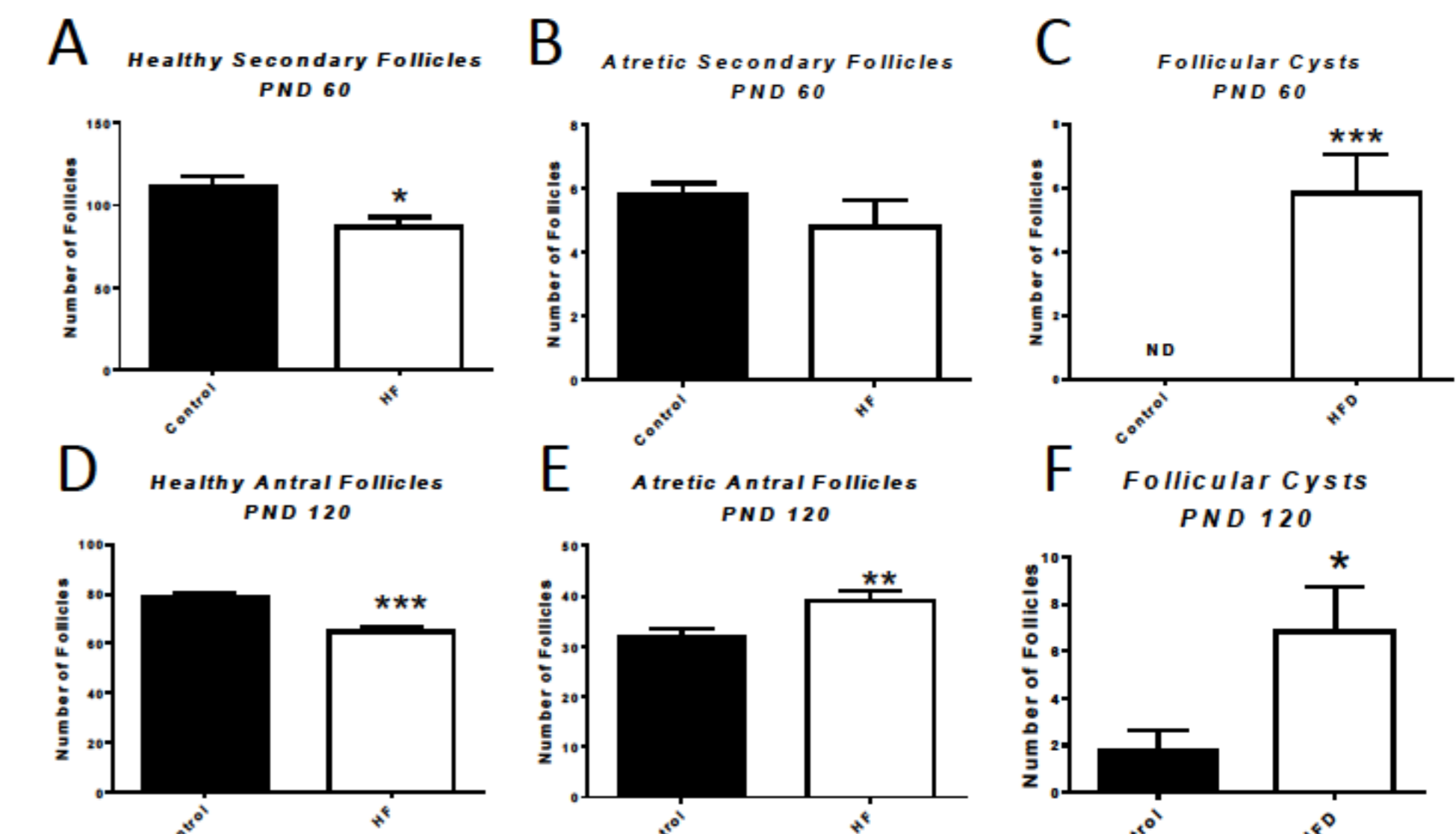


Figure 2.- The figure represents follicular quantification. Graphs shows the total number of follicles. Results are mean ± SEM of N=5 Ovaries. Significance was obtained by a Student t-test. p<0,05 = *, p<0,01 = ** and p<0,001 = *** for control (black bars) vs HFD (white bars) in each condition.

3 Maternal obesity produces an increase in serum E₂ levels in the offspring

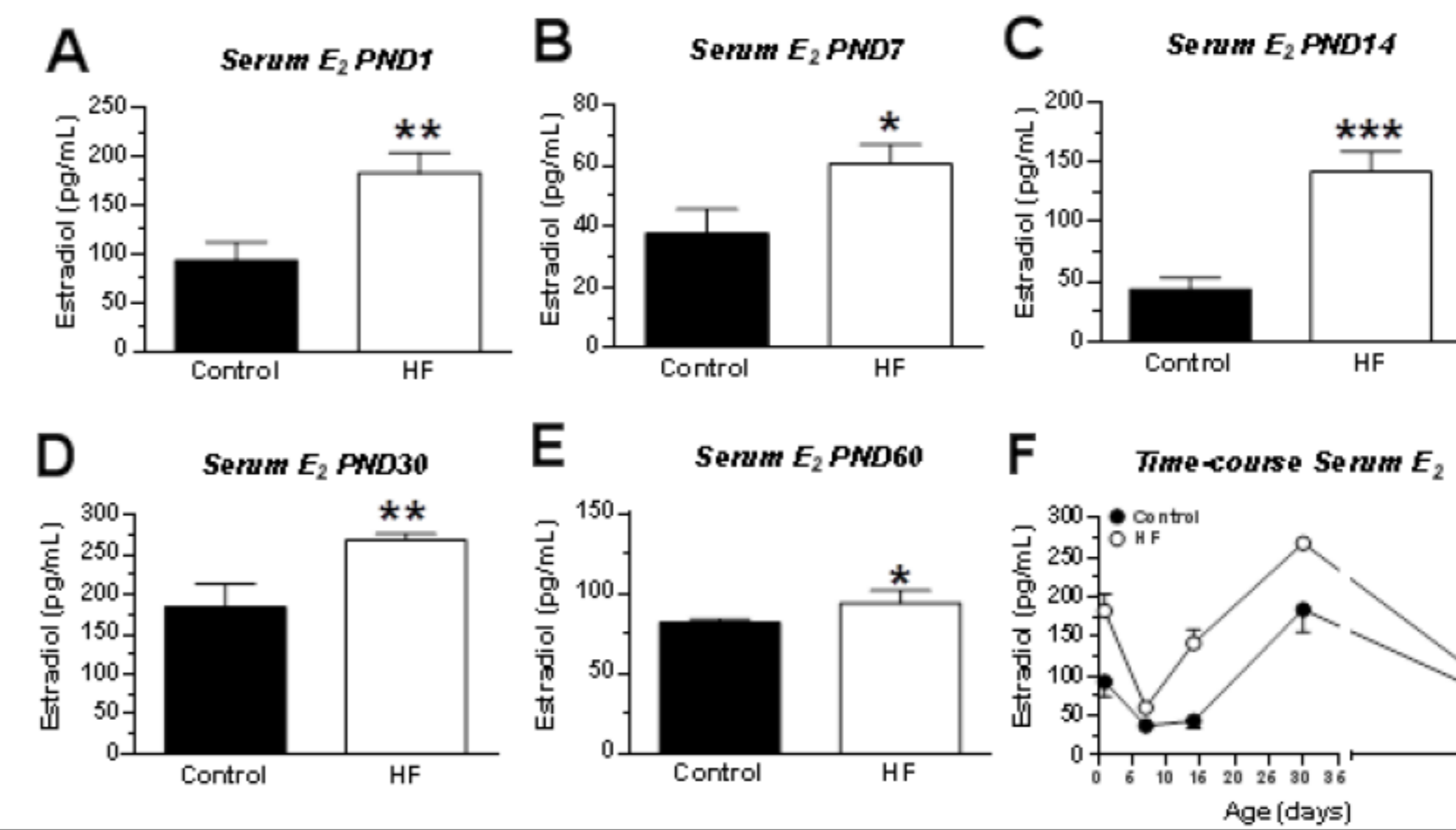


Figure 3.- A) E₂ at PND1, control, black bar (N=5) and HFD, white bar (N=4), B) E₂ at PND7, control N=6 and HFD N=5, C) E₂ at PND14, control N=6 and HFD N=10, D) E₂ at PND30, control N=4 and HFD N=8, E) E₂ at PND60, control N=7 and HFD N=4 and F) Changes in time course serum of E₂ through the life span of the rats, control (closed circles) and HFD (open circles). Serum samples were measured in triplicate. Data are shown as mean ± SEM. Significance was obtained by a Student t-test. p<0,05 = *, p<0,01 = ** and p<0,001 = *** for control vs HFD in each age

4 Increase in serum estradiol relates to a decrease in hepatic CYP3A2 expression

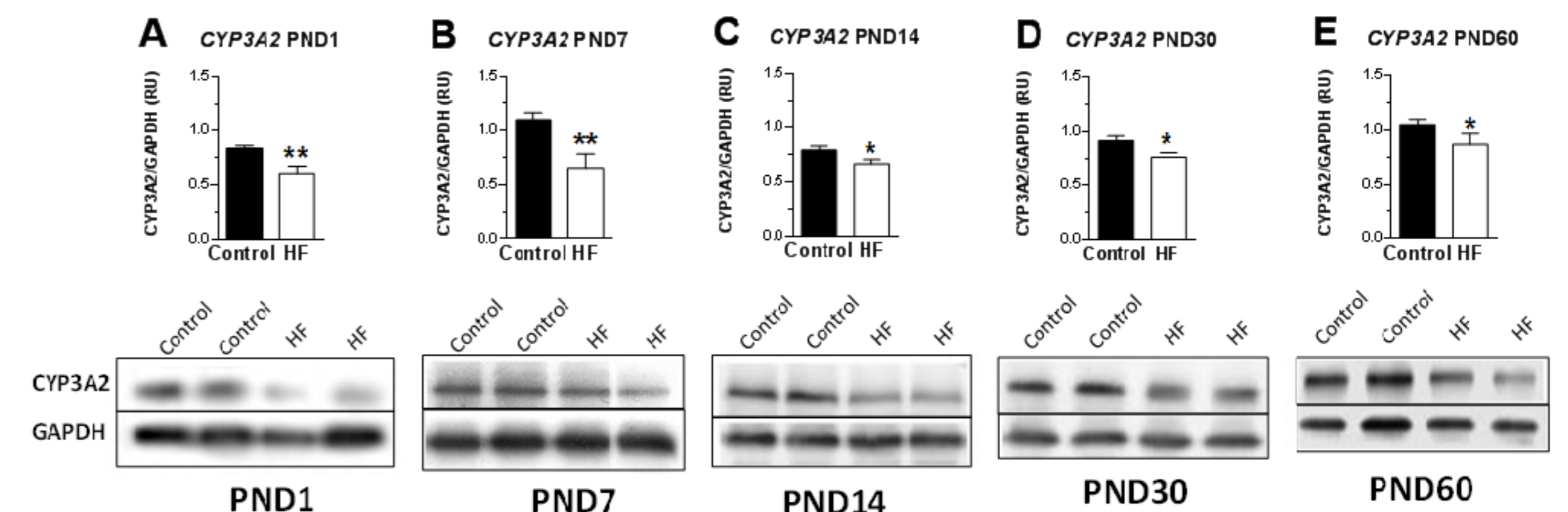


Figure 4.- The figure represents quantification of CYP3A2 by western blotting. Each sample was assessed 3 times in triplicate. Results are mean ± SEM of N=6 livers. Significance was obtained by a Student t-test. p<0,05 = *, p<0,01 = ** and p<0,001 = *** between control (black bars) vs HFD (white bars) in each age.

5 Change in hepatic CYP3A2 correlates with a increase in estradiol.

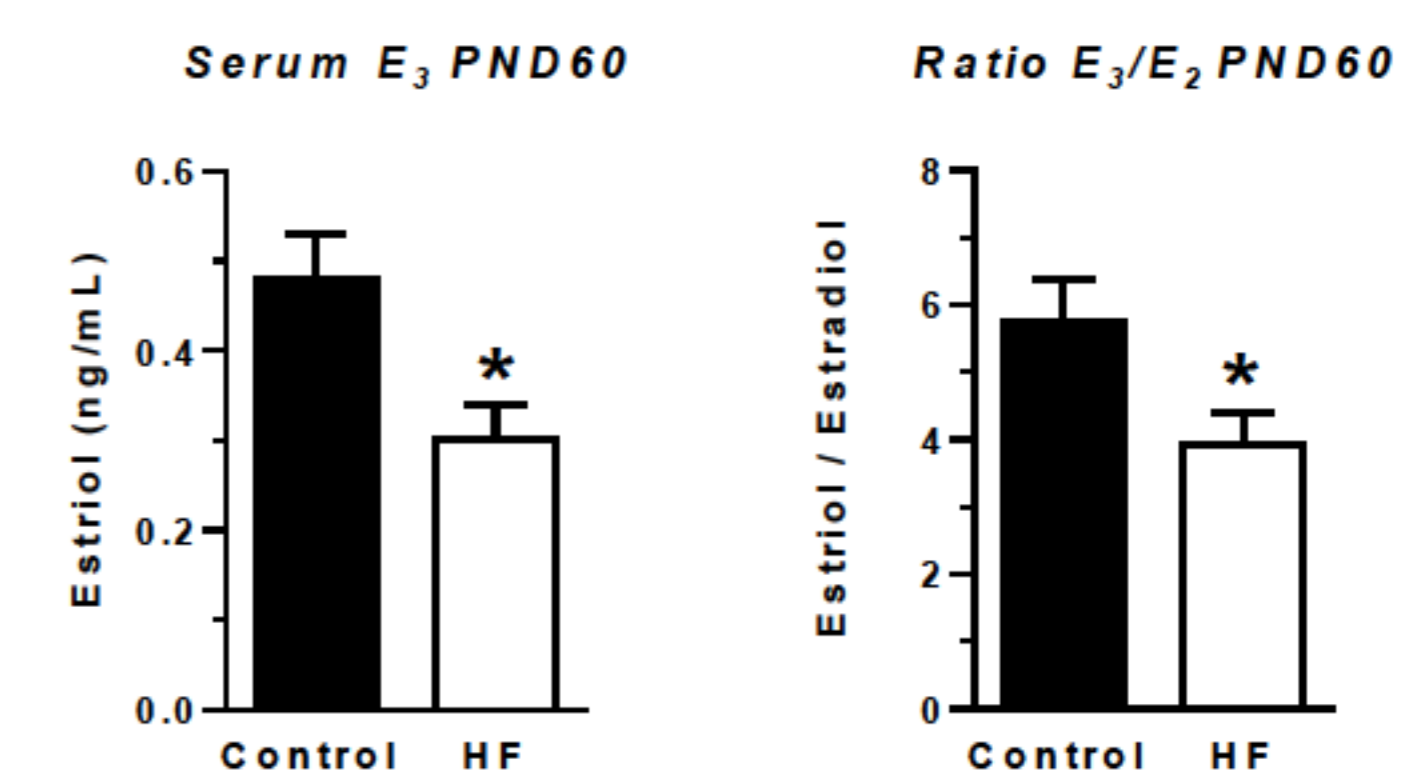


Figure 5.- A) E₂ at PND60, control, black bar (N=10) and HFD, white bar (N=6). All serum samples were measured in triplicate. B) The ratio E₃/E₂ was obtained by the division of each serum sample. Data are shown as mean ± SEM. Significance was obtained by a Student t-test. p<0,05 = * for control vs HFD.

Conclusion

We conclude that maternal obesity alters hepatic metabolism of estradiol in the offspring leading to increased levels of endogenous estradiol. In addition, the increase in estradiol levels during early postnatal development may be responsible of altered reproductive function in the offspring of obese mothers