

# Ovarian and uterine development and hormonal feedback mechanism in a 46 XX Patient with CYP19A1 Deficiency under low dose Estrogen Replacement

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The authors have nothing to disclose.

## Background

Aromatase deficiency may result in a complete block of estrogen synthesis. In females, this results in virilisation at birth, ovarian cysts in prepuberty and lack of pubertal development but virilisation, thereafter.

## Objective and methods

We studied the impact of oral 17 $\beta$ -estradiol treatment on ovarian and uterine development, and on LH/FSH and inhibin B during the long-term follow-up of a girl harboring compound heterozygote point mutations in the *CYP19A1* gene (1).

## Results

At the beginning in early childhood low doses of oral 17 $\beta$ -estradiol (starting with 0.1mg daily) were given. In the follow-up doses were adequately increased (until 2.0 mg daily in late puberty) to ensure normal height velocity and bone age maturation. During prepuberty, this treatment resulted in normal uterine (Figure 1A) and almost normal development of ovarian volume (Figure 1B), as well as number and size of follicles (Figure 2). Only at the beginning of puberty we found a minimal increase of ovarian volume compared to literature, normalizing when gestagen replacement was added in late puberty. Regarding hormonal feedback mechanisms, inhibin B levels were in the upper normal range during childhood and puberty (Figure 4A). Low doses of estradiol did not suffice to achieve physiological gonadotropin levels in late prepuberty and puberty (Figure 4B). However, when estradiol doses were further increased in late puberty levels of both FSH and LH declined with estradiol levels within normal range (Figure 3).

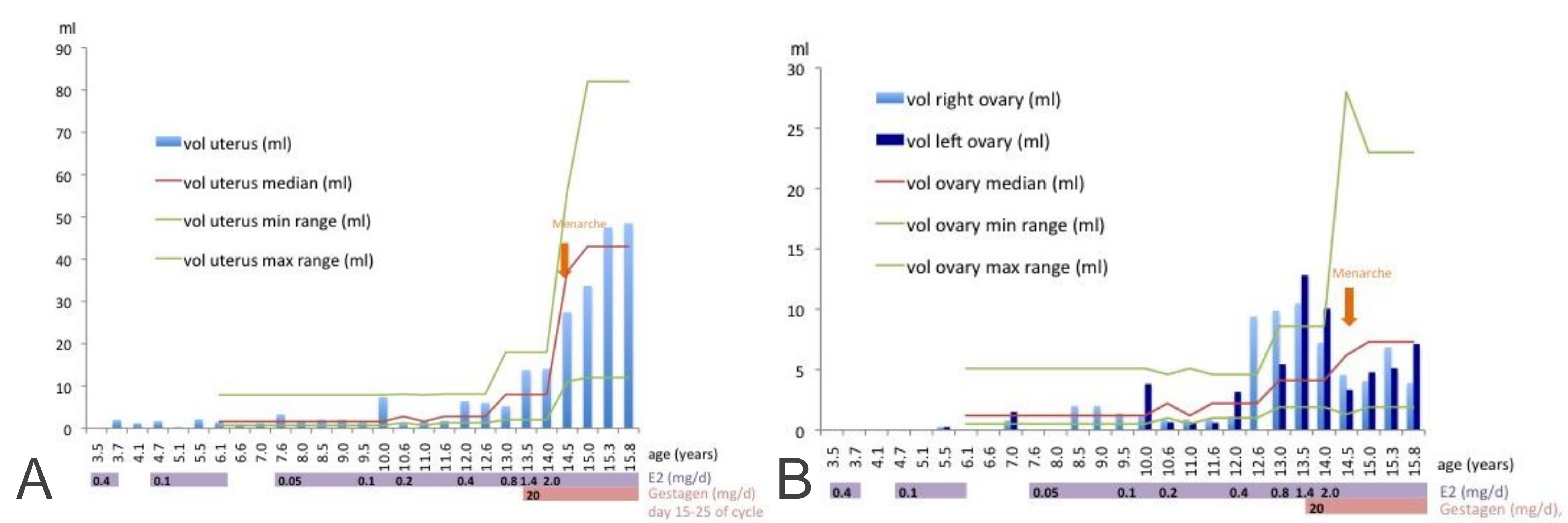
## Conclusion

This girl suffering from a complete aromatase deficiency provided a unique model of how ovarian and uterine development in relation to E2, LH, FSH and inhibin feedback may normally progress from infancy to adolescence. From this case, we may learn and extrapolate which doses of estradiol are required for normal ovarian and uterine development.

## References:

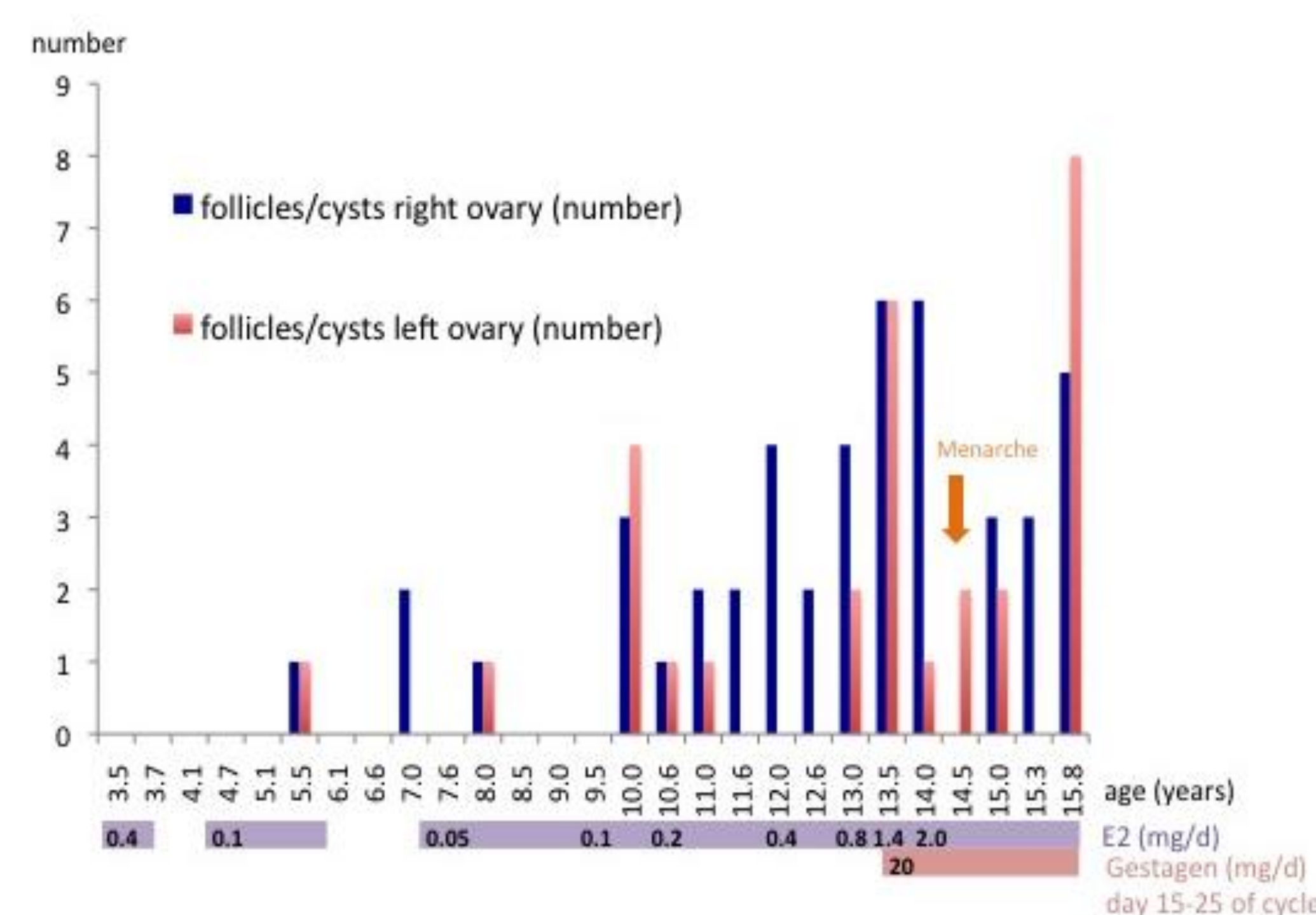
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Fig. 1: Ovarian and uterine development



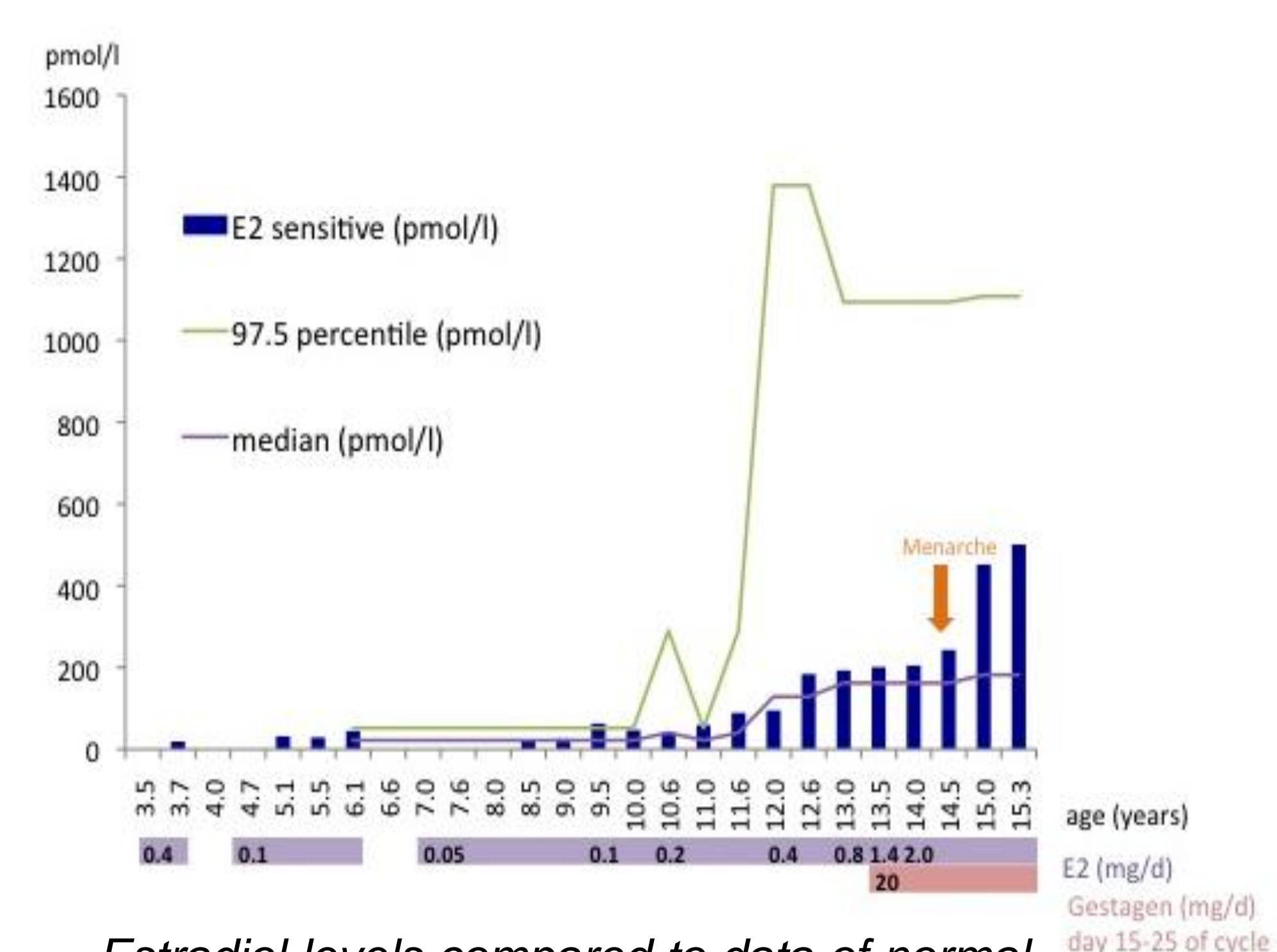
A) uterine volume (ml) and B) ovarian volume (ml) compared to data of normal healthy girls (2)

Fig. 2: Ovarian cysts / follicles



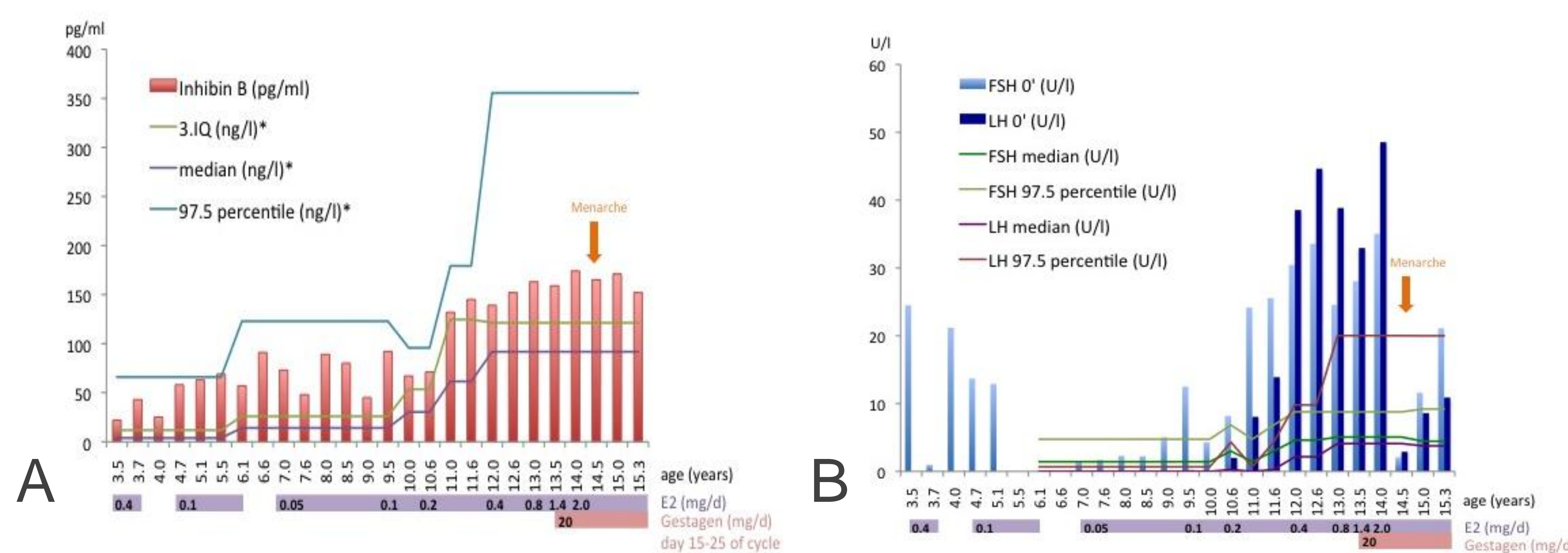
Number of ovarian follicles/cysts in our patient

Fig. 3: Estradiol levels



Estradiol levels compared to data of normal healthy girls (3)

Fig. 4: Hormonal feedback mechanism



Inhibin B levels (pg/ml) compared to data of normal healthy girls (4)

\*reference values adapted from Groome NP to Inhibin B Gen II assay

FSH and LH (U/l) levels compared to data of normal healthy girls (3)