To the Editor: I greatly salute Ajlouni et al for their outstanding study on infantile and early childhood masturbation. I have three comments on their study:

First, it is well-known that in normal infants of both sexes pituitary gonadotropin secretion is higher during the first months of life than in the later prepubertal period. In addition, during infancy considerable gender differences can be observed in the secretion pattern of both gonadotropins. Plasma concentrations of luteinizing hormone (LH) are higher in boys than in girls until 6 months after birth, while plasma follicular stimulating hormone (FSH) is higher in girls than in boys during the first 2 years of life. The infants' gonads are stimulated by the increased endogenous gonadotropins and respond with elevated sex hormone production. Thus, a testosterone surge with peak values in the normal range of male adults occurs in healthy male infants during the first 6 months and elevated estradiol concentrations comparable to levels seen during advanced puberty can be observed in healthy female infants during the first 2 years of life. That physiological basis has led many panels of pediatricians, biochemists, endocrinologists, and statisticians to construct pediatric reference ranges for various hormones that are age, gender, and community-specific. American, German, and Spanish reference ranges are currently present to be applied in the clinical settings. According to my knowledge, no pediatric reference values are present in Jordan that are age and gender-specific. Relying upon other pediatric references to evaluate sex hormone profile in the studied infants and young children might make the conclusion made by Ajlouni et al questionable. Second, Ajlouni et al stated in their study that serum estradiol (E) was measured by a microparticle enzyme immunoassay. Some concerns exist regarding its sensitivity and specificity. Having an accurate and reliable E assay is of critical importance in epidemiologic studies, especially when measuring the very low E levels (<30 pg/mL), and for discerning the relatively small (usually less than 20%) case-control differences in E levels. Because E is metabolized to more than 100 metabolites in the body, some of which cross-react with E antibodies, direct radioimmunoassay (RIA) without purification steps lacks specificity for E and could substantially overestimate E levels. Although direct E RIA using commercial kits are simpler, less time consuming, and less expensive, and require less sample volume than conventional RIA with preceding purification steps, their lack of sensitivity and specificity makes them invalid for measuring circulating E levels in epidemiologic studies. Recently, the stable isotope dilution liquid chromatography-tandem mass spectrometry method has been found to be able to measure concurrently all 15 estrogens and estrogen metabolites (EM) in urine and serum with high sensitivity, specificity, accuracy, and precision (laboratory coefficients of variation (CV) ≤5% for nearly all EM). The assay requires only extraction, a single chemical derivatization, and less than 0.5 mL of serum or urine.

Third, despite the previous two limitations, the finding of significantly lower serum E levels in the studied case group is really interesting. If that is confirmed by extensive studies and I hope that it is, it could substantially support the emerging body of evidences that there is a role for hormones in emerging sex-linked behavior in early development.

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We agree with Professor Al-Mendalawi and thank him for his comments. We are aware of some pitfalls of the assay, but that was the best available at that time. We assure his and our reader that our interest in the subject will continue and we will collect more data and run the same samples published with the new collected ones and use the most updated essays available.

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