



Estimation of reference curves for the urinary steroid metabolome in the first year of life in healthy children: Tracing the complexity of human postnatal steroidogenesis



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ABSTRACT

Context: Complex steroid disorders such as P450 oxidoreductase deficiency or apparent cortisone reductase deficiency may be recognized by steroid profiling using chromatographic mass spectrometric methods. These methods are highly specific and sensitive, and provide a complete spectrum of steroid metabolites in a single measurement of one sample which makes them superior to immunoassays. The steroid metabolome during the fetal-neonatal transition is characterized by (a) the metabolites of the fetal-placental unit at birth, (b) the fetal adrenal androgens until its involution 3–6 months postnatally, and (c) the steroid metabolites produced by the developing endocrine organs. All these developmental events change the steroid metabolome in an age- and sex-dependent manner during the first year of life. **Objective:** The aim of this study was to provide normative values for the urinary steroid metabolome of healthy newborns at short time intervals in the first year of life.

Methods: We conducted a prospective, longitudinal study to measure 67 urinary steroid metabolites in 21 male and 22 female term healthy newborn infants at 13 time-points from week 1 to week 49 of life. Urine samples were collected from newborn infants before discharge from hospital and from healthy infants at home. Steroid metabolites were measured by gas chromatography-mass spectrometry (GC-MS) and steroid concentrations corrected for urinary creatinine excretion were calculated.

Results: 61 steroids showed age and 15 steroids sex specificity. Highest urinary steroid concentrations were found in both sexes for progesterone derivatives, in particular 20 α -DH-5 α -DH-progesterone, and for highly polar 6 α -hydroxylated glucocorticoids. The steroids peaked at week 3 and decreased by ~80% at week 25 in both sexes. The decline of progestins, androgens and estrogens was more pronounced than of glucocorticoids whereas the excretion of corticosterone and its metabolites and of mineralocorticoids remained constant during the first year of life.

Conclusion: The urinary steroid profile changes dramatically during the first year of life and correlates with the physiologic developmental changes during the fetal-neonatal transition. Thus detailed normative data during this time period permit the use of steroid profiling as a powerful diagnostic tool.

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1. Introduction

Steroid hormones regulate various biological processes including salt balance, sexual development, reproductive function, and immune and stress responses. Because the secretion of each steroid hormone may vary with age and sex, especially in the newborn period during adjustment to extra-uterine life and fetal adrenal involution, detailed normative data are needed for effective quantitative assessment of steroids.

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Table 1

Steroid metabolites measured in this study and their molar mass. The nomenclature of the systematic names follows the recommendations published by the IUPAC commission on the Nomenclature of Organic Chemistry in 1969 [32], amended by the IUPAC–IUB Commission on Biochemical Nomenclature in 1971 [33] and again revised in 1989 [34]. OH: hydroxy, DH: dihydro, TH: tetrahydro.

Trivial name	Systematic name	Molar mass
Progesterones		
progesterone	4-pregnene-3,20-dione	314.5
6 α -OH-progesterone	6 α -hydroxy-4-pregnene-3,20-dione	330.5
6 β -OH-progesterone	6 β -hydroxy-4-pregnene-3,20-dione	330.5
11 α -OH-progesterone	11 α -hydroxy-4-pregnene-3,20-dione	330.5
11 β -OH-progesterone	11 β -hydroxy-4-pregnene-3,20-dione	330.5
11-keto-progesterone	4-pregnene-3,11,20-trione	328.5
17 α -OH-progesterone	17 α -hydroxy-4-pregnene-3,20-dione	330.5
17-OH-pregnanolone	3 β ,17-dihydroxy-5-pregnen-20-one	334.5
pregnanetriol	5 β -pregnane-3 α ,17 α ,20 α -triol	336.5
pregnenetriol	5-pregnene-3 β ,17 α ,20 α -triol	334.5
pregnanetriolone	3 α ,17 α ,20 α -trihydroxy-5 β -pregnan-11-one	350.5
5 α -DH-progesterone	5 α -pregnane-3,20-dione	316.5
3 α 5 α -TH-progesterone/allopregnanolone	3 α -hydroxy-5 α -pregnan-20-one	318.5
3 β 5 α -TH-progesterone/isopregnanolone	3 β -hydroxy-5 α -pregnan-20-one	318.5
5 β -DH-progesterone	5 β -pregnane-3,20-dione	316.5
3 α 5 β -TH-progesterone/epipregnanolone	3 α -hydroxy-5 β -pregnan-20-one	318.5
6 α -OH-3 α 5 β -TH-progesterone	3 α ,6 α -dihydroxy-5 β -pregnan-20-one	334.5
3 β 5 β -TH-progesterone/pregnanolone	3 β -hydroxy-5 β -pregnan-20-one	318.5
20 α -DH-progesterone	20 α -hydroxy-4-pregnen-3-one	316.5
17 α -OH-20 α -DH-progesterone	17 α ,20 α -dihydroxy-4-pregnene-3,20-dione	332.5
20 α -DH-5 α -DH-progesterone	20 α -hydroxy-5 α -pregnan-3-one	318.5
20 α -DH-3 α 5 α -TH-progesterone/allopregnanediol	5 α -pregnane-3 α ,20 α -diol	320.5
20 α -DH-3 β 5 α -TH-progesterone	5 α -pregnane-3 β ,20 α -diol	320.5
20 α -DH-3 α 5 β -TH-progesterone/pregnanediol	5 β -pregnane-3 α ,20 α -diol	316.5
20 α -DH-3 β 5 β -TH-progesterone	5 β -pregnane-3 β ,20 α -diol	320.5
20 β -DH-progesterone	20 β -hydroxy-4-pregnen-3-one	316.5
Androgens		
dehydroepiandrosterone	3 β -hydroxy-5-androsten-17-one	288.4
16 α -OH-dehydroepiandrosterone	3 β ,16 α -dihydroxy-5-androsten-17-one	304.4
androstenediol	5-androstene-3 β ,17 β -diol	290.4
testosterone	17 β -hydroxy-4-androsten-3-one	288.4
5 α -DH-testosterone	17 β -hydroxy-5 α -androstan-3-one	290.4
androstenediol/dihydroandrosterone	5 α -androstane-3 α ,17 β -diol	292.4
androsterone	3 α -hydroxy-5 α -androstan-17-one	290.4
5-androstenetriol	5-androstene-3 β ,16 α ,17 β -triol	306.4
11 β -OH-androsterone	3 α ,11 β -dihydroxy-5 α -androstan-17-one	306.4
etiocholanolone	3 α -Hydroxy-5 β -androstan-17-one	290.4
Estrogens		
17 β -estradiol	1,3,5(10)-estratriene-3,17 β -diol	272.4
estriol	1,3,5(10)-estratriene-3,16 α ,17 β -triol	288.4
Corticosterones		
11-deoxycorticosterone	21-hydroxy-pregnene-3,20-dione	330.5
11-deoxy-TH-corticosterone	3 α ,21-dihydroxy-5 β -pregnan-20-one	334.5
11-dehydro-TH-corticosterone	3 α ,21-dihydroxy-5 β -pregnane-11,20-dione	348.5
18-OH-11-dehydro-TH-corticosterone	3 α ,18,21-trihydroxy-5 β -pregnane-11,20-dione	364.5
TH-corticosterone	3 α ,11 β ,21-trihydroxy-5 β -pregnan-20-one	350.5
allo-TH-corticosterone	3 α ,11 β ,21-trihydroxy-5 α -pregnan-20-one	350.5
Mineralocorticoids		
TH-aldosterone	11 β ,18-epoxy-3 α ,18,21-trihydroxy-5 β -pregnan-20-one	364.5
TH-11-deoxycortisol	3 α ,17,21-trihydroxy-5 β -pregnan-20-one	350.5
Glucocorticoids		
cortisol	11 β ,17,21-trihydroxy-4-pregnene-3,20-dione	362.5
6 β -OH-cortisol	6 β ,11 β ,17 α ,21-tetrahydroxy-4-pregnene-3,20-dione	378.5
18-OH-cortisol	11,17,18,21-tetrahydroxy-4-pregnene-3,20-dione	378.5
20 α -DH-cortisol	11 β ,17,20 α ,21-tetrahydroxy-4-pregnen-3-one	364.5
TH-cortisol	3 α ,11 β ,17,21-tetrahydroxy-5 β -pregnan-20-one	366.5
α -cortol	5 β -pregnane-3 α ,11 β ,17 α ,20 α ,21-pentol	368.5
β -cortol	5 β -pregnane-3 α ,11 β ,17 α ,20 β ,21-pentol	368.5
11 β -OH-etiocholanolone	3 α ,11 β -dihydroxy-5 β -androstan-17-one	306.4
allo-TH-cortisol	3 α ,11 β ,17,21-tetrahydroxy-5 α -pregnan-20-one	366.5
cortisone	17,21-dihydroxy-4-pregnene-3,11,20-trione	360.5
20 α -DH-cortisone	17 α ,20 α ,21-trihydroxy-4-pregnene-3,11-dione	362.5
20 β -DH-cortisone	17 α ,20 β ,21-trihydroxy-4-pregnene-3,11-dione	362.5
TH-cortisone	3 α ,17,21-trihydroxy-5 β -pregnan-11,20-dione	364.5
1 β -OH-TH-cortisone	1 β ,3 α ,17,21-tetrahydroxy-5 β -pregnan-11,20-dione	380.5
6 α -OH-TH-cortisone	3 α ,6,17,21-tetrahydroxy-5 β -pregnan-11,20-dione	396.5
α -cortolone	3 α ,17 α ,20 α ,21-tetrahydroxy-5 β -pregnane-11-one	366.5
6 α -OH- α -cortolone	3 α ,6 α ,17 α ,20 α ,21-pentahydroxy-5 β -pregnane-11-one	382.5

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