

# The urinary steroid signature of premature adrenarche

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## Conclusions

Girls with premature adrenarche produce more androgens than healthy girls of the same age. The urinary steroid signature of adrenarche includes steroid metabolites of alternate pathways, which shows differences in premature adrenarche. Future studies should assess whether the steroid signature of adrenarche is just appearing earlier in girls with premature adrenarche or earlier and different compared to adrenarche at normal timing.

## Background:

Adrenarche describes the developmental event of the human adrenal cortex when the zona reticularis increases the synthesis of C19 steroids (DHEA/-S) markedly at around 6-8 years of age. Early appearance of this event is called premature adrenarche (PA) and has been associated with adverse outcomes including polycystic ovary syndrome and metabolic syndrome. Recently novel biosynthetic pathways of androgen production have been revealed, but their role in health and disease remains largely unsolved.

## Participants and Methods

39 steroid metabolites comprising progesterones, corticosterones, aldosterone, androgens, estrogens and glucocorticoids were measured in the urine by gas chromatography mass spectrometry in 23 girls with premature adrenarche (age range 3.9-8.4 years) and 22 healthy, age-matched controls (4.3-8.5 years). Groups were compared using Mann-Whitney test and Bonferroni correction applied to account for multiple testing.

## Aim

To characterise the urinary steroid metabolome of girls with premature adrenarche in comparison to healthy controls with a special focus on metabolites originating of novel, alternate androgen pathways.

## Results

### 1 Baseline characteristics

	PA (N=23)		Controls (N=22)		p-value
	Median	SD	Median	SD	
Age at consultation (years)	7.0	1.1	6.5	1.1	0.281
Weight (kg)	26.2	4.5	21.5	3.4	0.000
Weight (SDS)	0.9	1.6	0.3	1.0	0.019
Height (cm)	125.3	8.0	120.2	7.2	0.056
Height (SDS)	1.0	1.2	0.4	1.0	0.137
BMI (kg/m <sup>2</sup> )	17.2	2.0	15.0	1.3	0.000
BMI (SDS)	0.9	1.0	-0.3	0.8	0.001
Gestational age (weeks)	40.0	2.1	39.7	1.3	0.693
Birth weight (kg)	3.0	0.7	3.3	0.5	0.301
Systolic	99.0	9.9	98.0	6.5	0.762
Diastolic	65.5	7.3	68.0	8.0	0.918

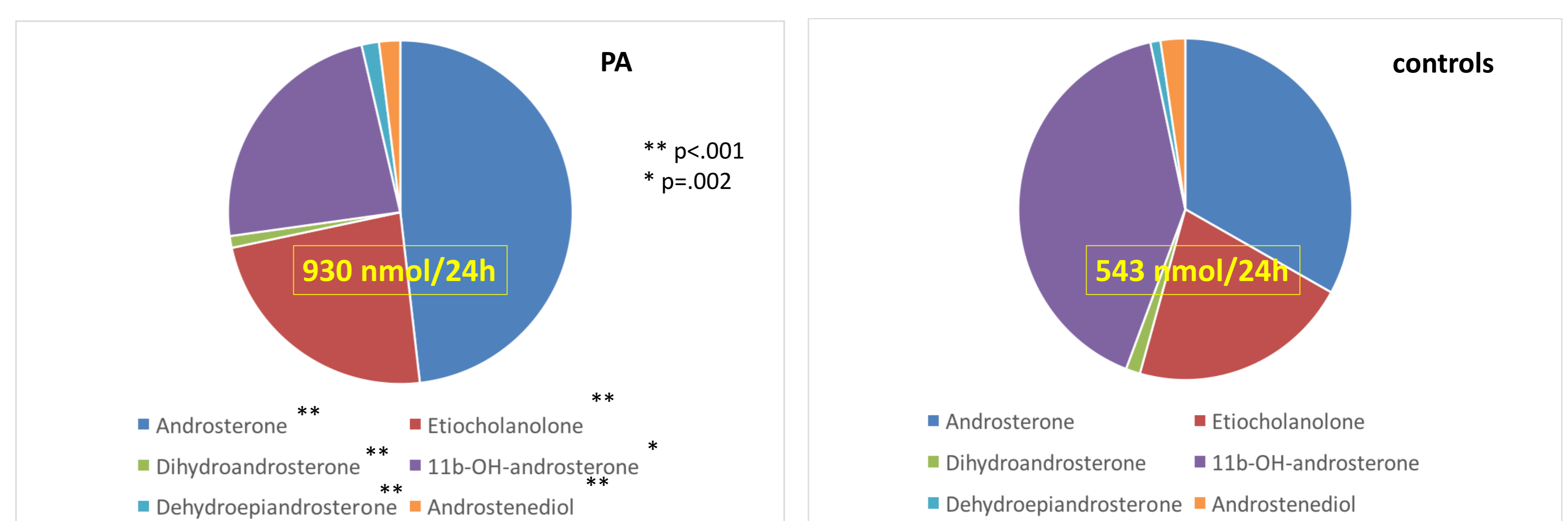
### 4 Steroid hormone enzyme activities by selected steroid hormone metabolite ratios

	PA		Controls		p-value
	Median	SD	Median	SD	
21-hydroxylase deficiency					
17HP/(THE+THFs)	0.008	0.003	0.006	0.009	0.063
PT/(THE+THFs)	0.045	0.021	0.032	0.029	0.054
100*PTONE/(THE+THFs)	0.167	0.441	0.325	0.560	0.023
17-hydroxylase deficiency					
(THA+THBs)/(THE+THFs)	0.099	0.044	0.104	0.052	0.666
(THA+THBs)/(AN+ET)	0.562	1.974	1.120	3.188	0.0032
100*THDOC/(THE+THFs)	0.116	0.075	0.121	0.067	0.525
11-hydroxylase deficiency					
100*THS/(THE+THFs)	1.315	0.772	1.658	0.667	0.033
100*THDOC/(THE+THFs)	0.116	0.075	0.121	0.067	0.525
3β-HSD deficiency/ Hyperaldosteronism					
DHEA/(THE+THFs)	0.004	0.207	0.002	0.002	0.001
5-PT/(THE+THFs)	0.012	0.020	0.002	0.005	0.0034
Glucocorticoid remediable aldosteronism					
18-OH-F	91.272	77.160	75.871	47.351	0.231
18-OH-F/Cortisolmetab.	0.023	0.017	0.020	0.018	0.981
Pseudohypoaldosteronism					
100*THALDO/(THE+THFs)	0.377	0.423	0.518	0.230	0.525
Glucocorticoid metabolic disorder					
Total cortisol metabolites	4029.238	2253.461	2814.788	801.144	0.0032
11β-HSD deficiency					
Cortisol to cortisone	0.548	0.208	0.579	0.333	0.364
(THFs)/THE	0.672	0.354	0.736	0.331	0.440
(F+E)/(THE+THFs)	0.047	0.024	0.048	0.031	0.716
5-alpha reductase deficiency					
THF/5aTHF	0.658	0.469	0.605	0.217	0.820

### 2 Urinary steroid excretion (nmol/24 h)

	PA				Controls				p-value*
	Median	SD	min	max	Median	SD	min	max	
Progesterone metabolites (sum)	181	237	78	955	115	64	48	270	0.0014
Corticosterone metabolites (sum)	250	243	95	1244	183	112	58	448	0.010
Aldosterone metabolites									
TH-Aldosterone	13	9	3	32	10	4	2	17	0.117
Androgene metabolites (sum)	930	4191	391	20068	543	206	149	972	<0.001
Estrogen metabolites (sum)	1	3	0	13	1	1	0	3	0.318
11-Deoxycortisol metabolites									
TH-11-deoxycortisol	40	29	5	119	33	13	15	56	0.482
Cortisol metabolites (sum)	4880	2534	2605	11268	3274	862	2286	5433	0.007

### 3 Urinary androgen metabolite excretion (% of total androgens)



## Summary

