

# RAPID CLEARANCE OF HYDROCORTISONE AS A CAUSE OF POOR CONTROL OF CAH DETECTED BY 24 HOUR PROFILING OF HYDROCORTISONE CONCENTRATIONS

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## INTRODUCTION

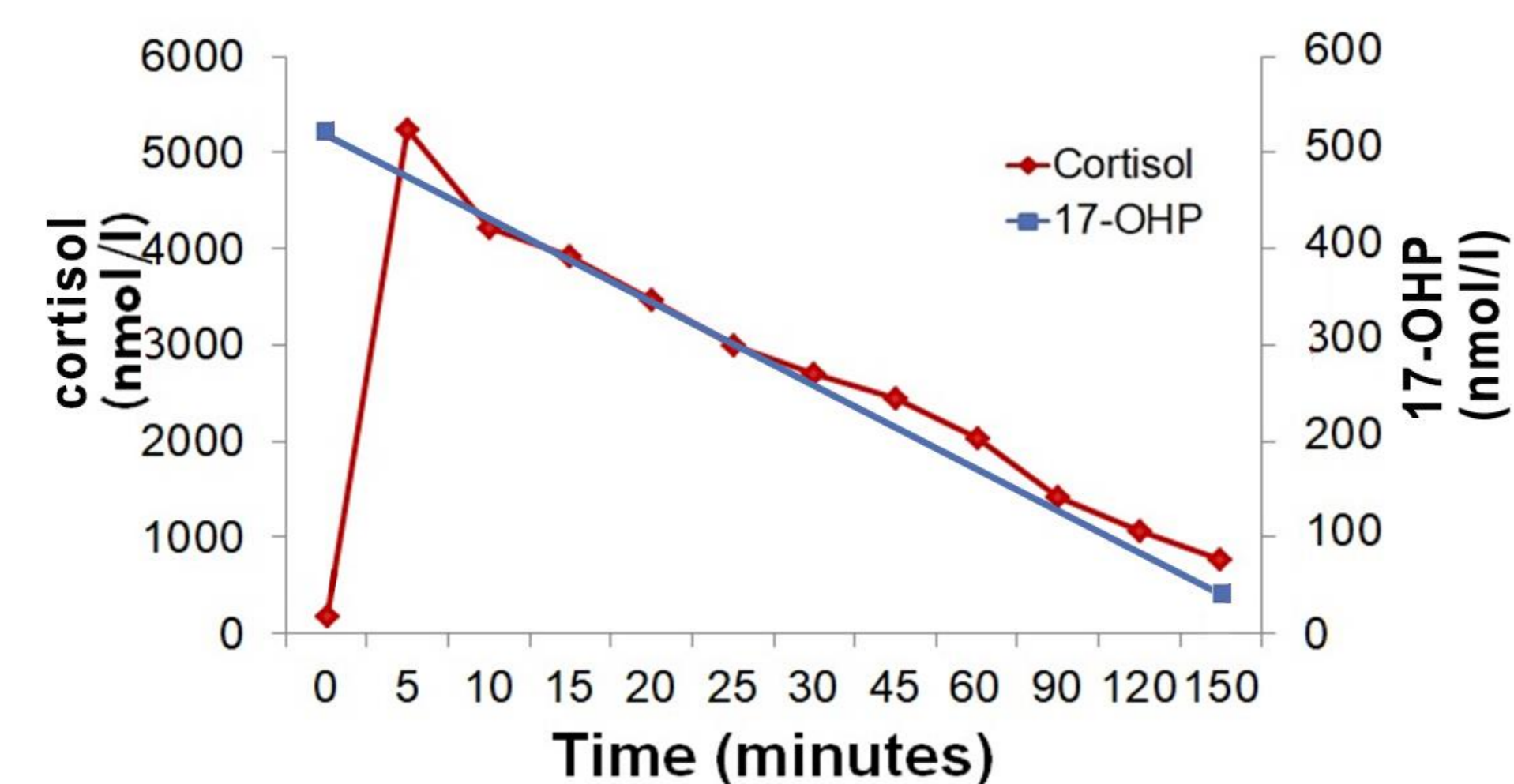
- Hydrocortisone (HC) has a short half-life and individualisation of treatment is required for optimal treatment of CAH, balancing between under- and overtreatment.
- 24 hour profiling of HC concentrations has shown large inter-individual variation in clearance of HC and therefore has been used to individualise treatment.
- We present a rare case of a severely virilised girl with CAH (due to 21 hydroxylase deficiency) and chronic bowel dysfunction, in whom high doses of steroids failed to suppress androgen production, thought to be due to malabsorption. Investigations showed fast clearance of HC, and 24 hour profiling allowed for dose adjustment and improved disease control.

## CLINICAL CASE

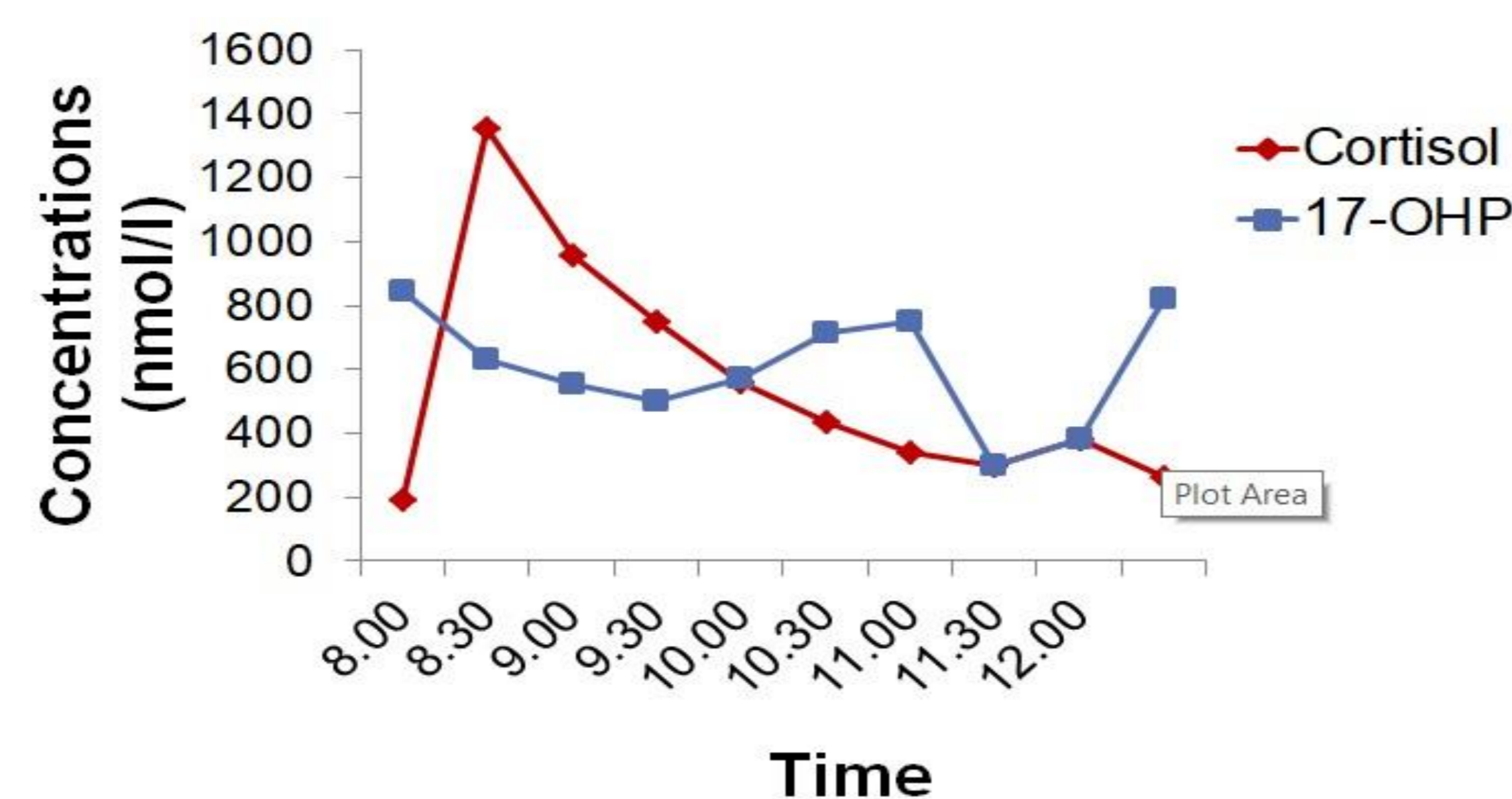
### Background

A 7.5year old girl with **21-hydroxylase deficiency, Prader Stage V virilisation and enlarged adrenal glands** was referred to our clinic for assessment for continuous subcutaneous HC pump treatment. Poor control of CAH was thought due malabsorption due to a **complex bowel condition**. Despite 8-hourly HC doses totalling **116mg/m2/d** pre dose, saliva 17-OHP concentrations were as high as 1600 and 800 nmol/l.

### Initial investigations



**Figure 1.** HC clearance study using 15 mg HC IV showed that HC was cleared quickly (t<sub>1/2</sub> 57 minutes compared to usual 80 minutes) but the HC was able to suppress the 17-OHP concentration from 537nmol/l at 0 minutes to 54nmol/l at 150 minutes.



**Figure 2.** HC clearance study using 15 mg HC orally showed high HC concentration and thus some absorption but only little 17-OHP suppression despite high HC concentrations.

Time (min)	10.00	11.00	12.00	13.00	14.00	15.00	16.00	17.00	18.00	19.00	20.00	21.00	22.00	23.00	24.00	01.00	02.00	03.00	04.00	05.00	06.00	07.00	
Assays																							
Cortisol (nmol/l)	395	411	348	278	252	1439	712	286	290	216	219	?	739	256	222	170	176	?	164	161	170	195	
17 OHP (nmol/L)	98.2	504.4	440.2	626.0	577.3	427.8	182.2	91.8	232.7	242.0	337.4	233.4	489.0	160.9	608.0	?	365.8	777.4	645.3	733.5	817.8	961.5	
Androstenedione (nmol/l)					39.1								37.6										
Hydrocortisone Dose					30mg								20mg								58		

**Figure 3.** 24h cortisol profile on her usual HC treatment showed that some hydrocortisone is absorbed as she could achieve cortisol levels up to 1439 nmol dropping to approximately 200nmol/l prior to her next dose. However 17OHP, androstenedione and ACTH concentrations (8am ACTH:400ng/l) were persistently very high with 17OHP only showing a small temporary reduction when very high HC concentrations were achieved, suggesting that the adrenal glands are not appropriately responding to the HC.

**Imaging :** abdominal USS confirmed that both adrenal glands were enlarged.

**Impression following the investigations:** Adrenal hyperplasia with autonomous adrenal androgen production

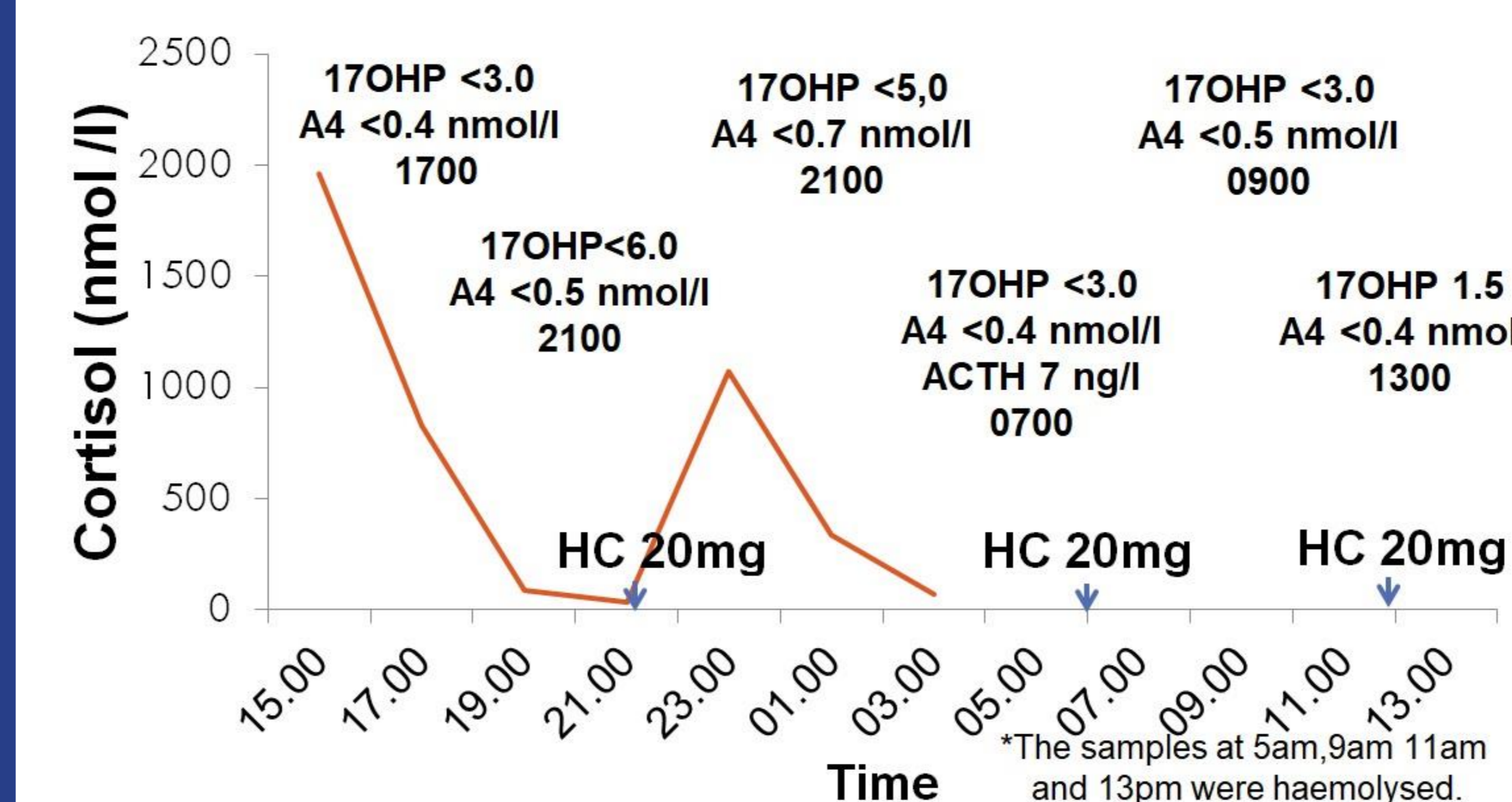
- Management plan:**
- oral dexamethasone in order to suppress the adrenal androgen production, and ACTH production and normalise adrenal size.
  - close follow up with regular cortisol profiles.

## CORTISOL PROFILES

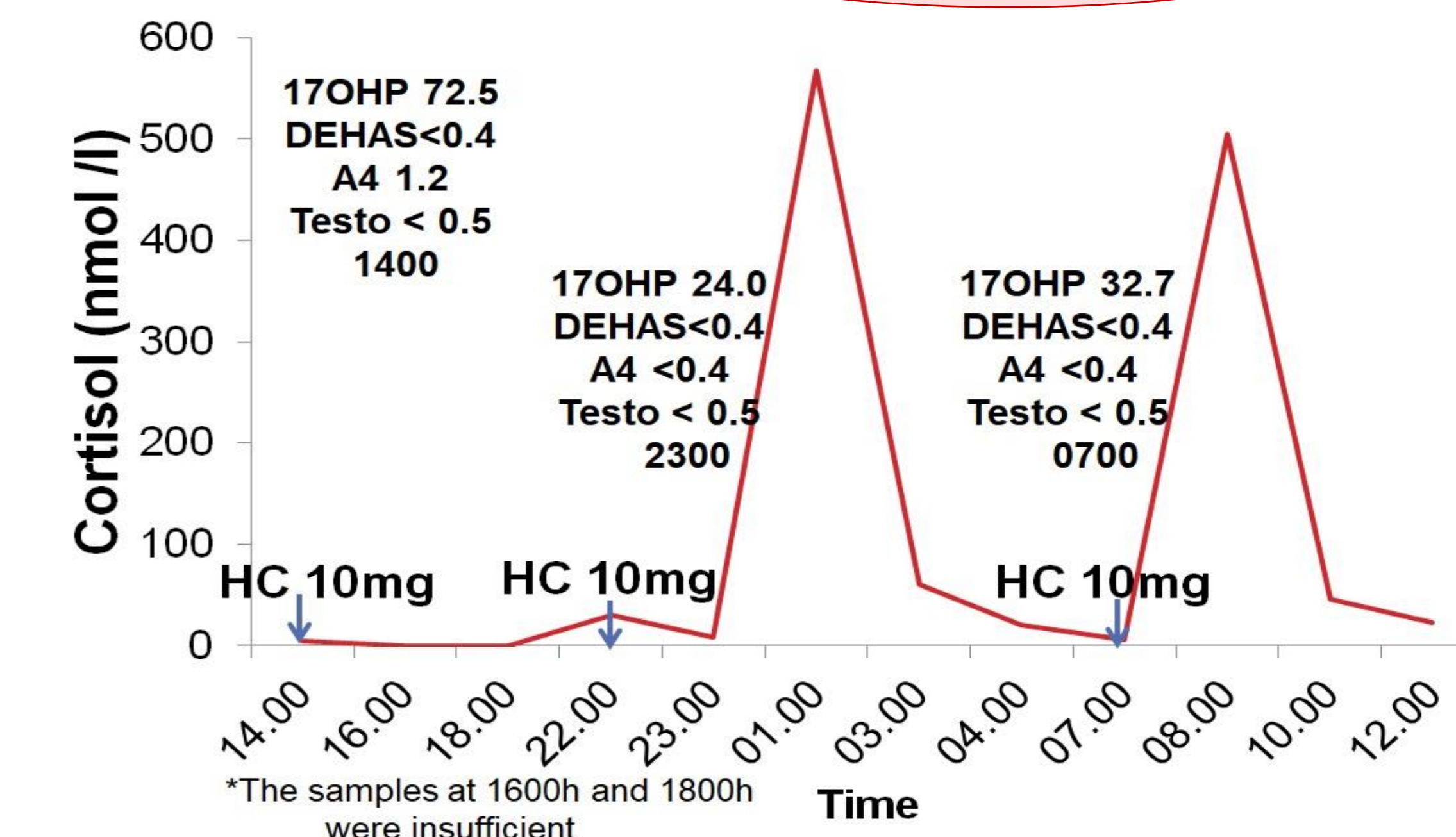
Time	1200	1400	1700	1800	0000	0200	0400	0600	0800	1000	1100
17OHP	<17.0	<12.0	<7.0	<6.0	<18.0	<21.0	insuff	<17.0	<6.0	<14.0	<16.0
A4	<0.7	2.2	1.3	0.9	4.0	interf	insuff	interf	1.2	0.8	interf
ACTH									9		
Dex				0.5mg					0.5mg		

**Table 1.** 24h cortisol profile on twice daily Dexamethasone 0.5mg – twice daily dose required in order to suppress the androgens and the ACTH.

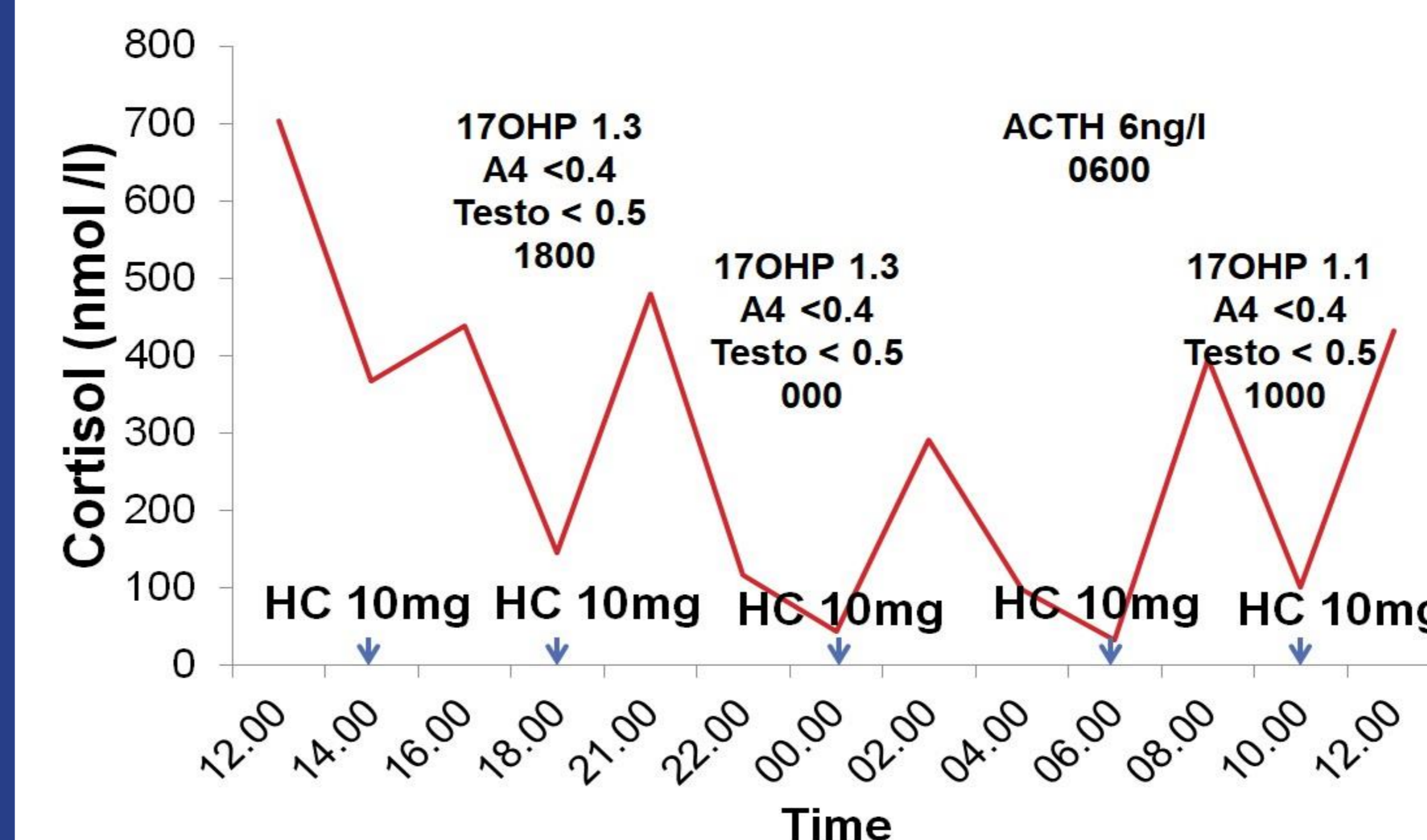
Once the androgens were suppressed and adrenal size normalised, she was switched back to her HC dose.



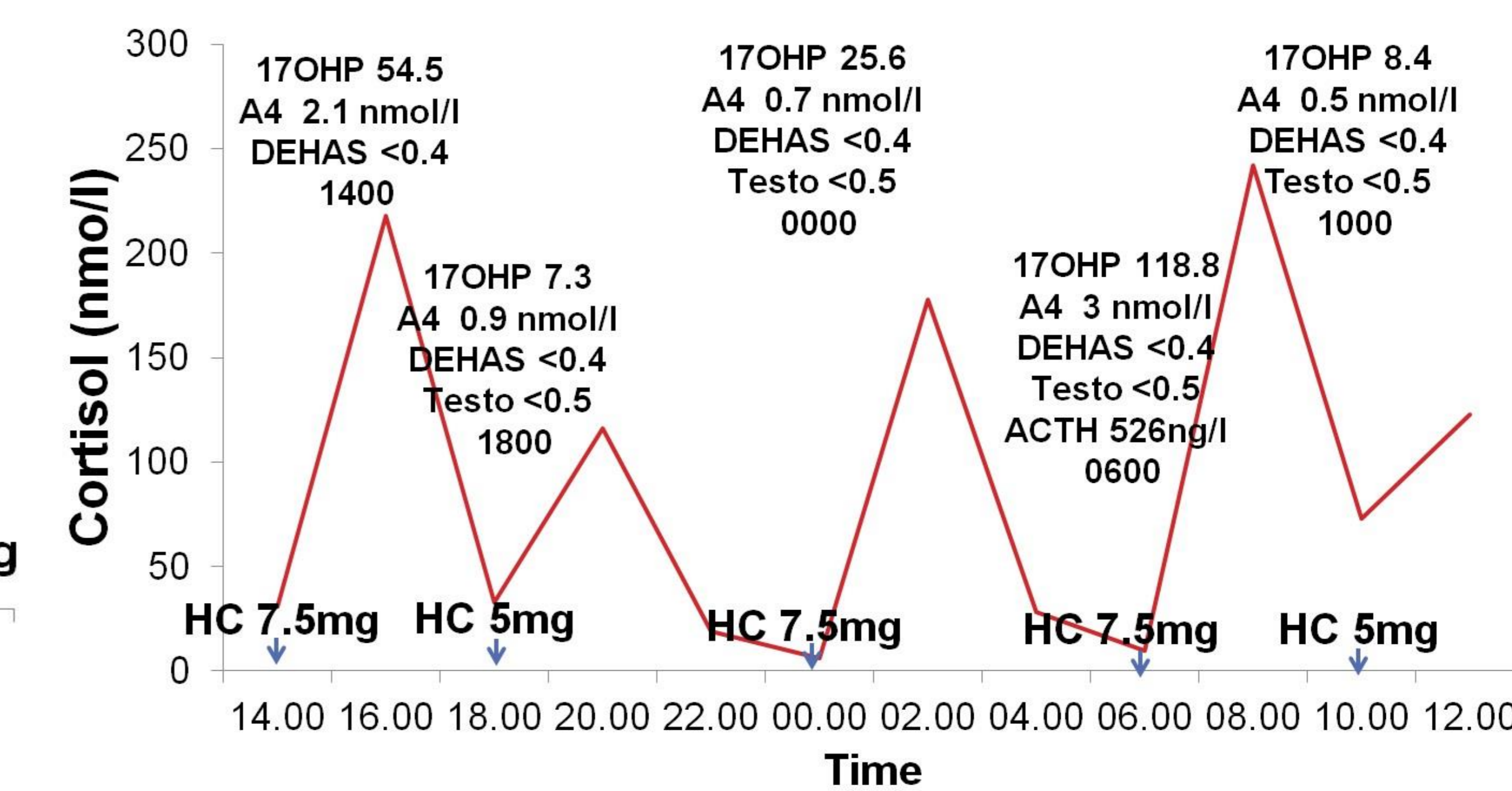
**Figure 4.** 24h cortisol profile on reduced HC dose of 20 mg 3x/day (TDS) (70mg/m2/d) showed ongoing androgen and ACTH suppression → HC was reduced further to 10 mg TDS (32mg/m2/d).



**Figure 5.** 24h cortisol profile on 10 mg HC TDS (32mg/m2/d) showed ongoing androgen suppression, however the 17-OHP increased and the cortisol concentrations dropped quickly, in line with fast HC clearance → HC frequency was increased to 5x/day, 10 mg (total dose 52mg/m2/d).



**Figure 6.** 24h cortisol profile on HC 10 mg 5x/day (52mg/m2/d) showed appropriate cortisol concentrations, but over-suppression of 17OHP, testosterone and androstenedione concentration → HC was reduced to 7.5mg 5x/day (total 39mg/m2/d).



**Figure 7.** HC was further reduced to 34mg/m2/d and the 24cortisol profile showed ongoing androgen suppression but increased morning 17-OHP and high ACTH, therefore the midnight HC dose was increased to 10mg (total 37mg/m2/d).

## CONCLUSION

- In this patient with poorly controlled CAH, in depth investigations revealed rapid clearance of hydrocortisone and autonomous adrenal androgen production. Dexamethasone treatment followed by careful adjustment of HC treatment improved control of CA.
- 24 hour hydrocortisone profiling is a useful tool to find optimal HC dose and frequency. Individualised treatment with frequent dosing of hydrocortisone can improve control of CAH.