1. PATIENT PRESENTATION
A 1 month old baby boy presented to a local district general hospital with failure to thrive (weight at birth = 3.1 kg, at 28 days = 2.9 kg). The infant was born following an unremarkable pregnancy with nil of note from the antenatal history.

Family History: The parents were non-consanguineous and of Eastern European origin. They had an 18 month old baby daughter who was healthy.

Clinical Observations: Upon clinical examination, the infant had a slightly low, but stable blood pressure for age (65/35 mmHg), but was otherwise normal.

2. INITIAL BIOCHEMICAL INVESTIGATIONS
- Plasma Na+: 125 mmol/L, K+: 6.1 mmol/L
- Spot urine Na+: <10 mmol/L
- Blood glucose: 3.5-4.2 mmol/L
- Random plasma cortisol: 152, 136 nmol/L

Following Na+ supplementation:
- Plasma Na+: 133 mmol/L
- Plasma K+: 6.3 mmol/L

A short synacthen stimulation test was performed (table 1). Based on these results congenital adrenal hyperplasia (CAH) remained a potential diagnosis and the infant was started on hydrocortisone treatment.

3. ADDITIONAL LABORATORY INVESTIGATIONS

Urine Steroid Profile (USP)
Prior to hydrocortisone treatment, a spot urine sample was taken for USP analysis (figure 1A). The USP did not indicate any variants of CAH but showed a normal sequence of steroids and low/absent product metabolites. Deficiencies in 18-hydroxylase and 11-hydroxylase activities also exist, but produce a different pattern of corticosterone metabolite excretion.

Plasma Aldosterone Concentration and Renin Activity
Radioimmunoassay measurement of plasma aldosterone showed a low-normal concentration of 1040 pmol/L (up to 5000 pmol/L in neonates) with a very raised renin activity of 185 nmol/L/h (neonatal range up to 25 nmol/L/h), which is supportive of an aldosterone synthase defect.

Aldosterone Synthase Whole Gene Sequencing
The CYP11B2 aldosterone synthase gene was sequenced and showed a c.554C>T substitution (p.Thr185Ile) in exon 3 (figure 3). This is a known pathological change associated with loss of 18-oxidation activity.

4. DISCUSSION
The investigation of a young infant presenting with hyponatraemia is challenging, further complicated by the need to obtain sufficient blood samples and prioritise informative tests. Where a steroid disorder is suspected, a USP has great utility since the specimen is easily accessible and the test can identify/exclude a variety of disorders including CAH (incidence ~ 1 in 18000 UK births) and aldosterone synthase defects (rare, unclear incidence). Where urgent samples are involved, analyses can be prioritised with a relatively rapid turnaround time. In this case, the USP diagnosis was made within 2 days of sample receipt, prompting fludrocortisone treatment and reduction of hydrocortisone.

References