6 month-old female with abnormal TFTs

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University of Chicago Medical Center
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Chief complaint

- 6 month-old female admitted for pneumonia. Endocrine service was consulted for hyperphosphatemia and abnormal TFTs.
History of present illness

- **11/11/15:** fever 104°F, increased O2 requirement, WOB
  - ED: NS boluses, CXR w/ RUL opacity
  - CMP: Na 162, K 6.4, Ca 11.4, phos 7.5, mag 2.8, AP 273
  - TSH 4.43
  - Blood & urine cx neg
  - Broad-spectrum abx
  - PICU: HFNC -> 0.5 L NC
- **11/14:** Endocrine consulted
  - 11/13 FT4 0.56
Medical history

- **PMH:**
  - Born at 25 wks, CGA 2 mos
  - GT dependence, GERD
  - 9/2-10/9/14: hosp for GBS sepsis, inferior cerebellar hemorrhage, subdural hematoma, acute DVTs, PFO w/ bidirectional shunt; 9/2-7 HC + wean, 9/18-19 dexamethasone x4 doses
  - 10/31-11/6/14: hosp for hypoxia, resp distress

- **Medications:**
  - Lovenox, lasix, phenobarbital, bacitracin, Fe sulfate, clindamycin

- **DH:**
  - Tracks, grasps objects.

- **FMH:**
  - Mother: “thyroid condition”, asthma, 2 premature infant deaths d/t congenital heart disease
  - Brother healthy

- **SH:**
  - Lives w/ mother and brother
  - No daycare

- **PSH:** GT placement
- **Allergies:** NKDA
Review of systems

- Constitutional: neg for appetite change, weight loss, fatigue, + fever
- HENT: neg for congestion, rhinorrhea
- Eyes: neg for visual disturbance
- Resp: + cough, SOB, tachypnea, resp distress
- CV: neg for HTN, hypotension, arrhythmia
- GI: neg for abd pain, diarrhea, constipation, + vomiting
- Endocrine: neg for hypoglycemia, cold/heat intolerance, + hypernatremia, hyperphosphatemia
- GU: neg for polyuria
- Musc: neg for arthralgias
- Skin: neg for rash, color change
- Neuro: neg for headache, lightheadedness
- Heme: + DVTs
- Psych/Beh: neg for agitation
Physical exam

- T 36.2°C, HR 146, BP 65/33, RR 29, SpO2 99% (0.4 L NC), Wt 5.939 kg (~3%), L 54.5 cm (0%), BSA 0.3 m²
- Constitutional: active, no distress
- HEENT: AFSOF, PERRL, NC in place, moist mucous membranes, no midline defect
- Neck: supple, no adenopathy, thyroid nonpalpable
- CV: RRR, no murmur, 2+ pulses, 2sec CR
- Resp: nl air entry, no retractions, no w/r/c
- GI: S/NT/ND, no HSM
- GU: Tanner 1 breasts, AH, PH
- Musc: nl ROM, no edema or tenderness
- Neuro: alert, nl muscle tone, 2+ DTRs
- Skin: warm, no rash or acanthosis
## Labs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>RR (Harriet Lane/Esoterix)</th>
<th>11/11</th>
<th>11/12</th>
<th>11/13</th>
<th>11/14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phos</td>
<td>4-6.5 mg/dL</td>
<td>7.5 → 5.7</td>
<td>5.6</td>
<td>5.7</td>
<td>5.5</td>
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<tr>
<td>Ca</td>
<td>9-11 mg/dL</td>
<td>11.4 (corr 10.76) → 9.9</td>
<td>9.3</td>
<td>9.8</td>
<td>10.7</td>
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<tr>
<td>AP</td>
<td>150-420 U/L</td>
<td>273</td>
<td>196</td>
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<tr>
<td>PTH</td>
<td>10-65 pg/mL</td>
<td>43</td>
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<tr>
<td>Vit D 25-OH</td>
<td>32-100 ng/mL</td>
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<tr>
<td>Na</td>
<td>130-145 mEq/L</td>
<td>162 → 156</td>
<td>149</td>
<td>150</td>
<td>146</td>
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<tr>
<td>TSH</td>
<td>0.9-7.7 uU/mL</td>
<td>4.43</td>
<td></td>
<td></td>
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<tr>
<td>FT4</td>
<td>0.48-2.34 ng/dL</td>
<td>0.56</td>
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</table>

• **Next steps?**
### More labs...

<table>
<thead>
<tr>
<th></th>
<th>RR (Esoterix)</th>
<th>11/11</th>
<th>11/13</th>
<th>11/14</th>
<th>11/15 1522</th>
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<tbody>
<tr>
<td>FT4</td>
<td>0.48-2.34 ng/dL</td>
<td>0.45</td>
<td>0.56</td>
<td>0.59</td>
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<tr>
<td></td>
<td>0.9-2.3 ng/dL (UpToDate)</td>
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<tr>
<td>TSH</td>
<td>0.9-7.7 uU/mL</td>
<td>4.43</td>
<td></td>
<td>3.48</td>
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<tr>
<td>T4</td>
<td>6.1-14.9 ug/dL</td>
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<td></td>
<td>4.3</td>
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<tr>
<td>T3</td>
<td>85-250 ng/dL</td>
<td>149</td>
<td>137</td>
<td>118</td>
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<tr>
<td>FT3</td>
<td>1.6-6.4 pg/mL</td>
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<td>2.66</td>
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<tr>
<td>RT3</td>
<td>12-74 ng/dL</td>
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<td>251 pg/mL</td>
<td>284 pg/mL</td>
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<tr>
<td>Cortisol</td>
<td>2.8-23 ug/dL</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.4</td>
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<tr>
<td>DHEA-S</td>
<td>&lt;49 ug/dL</td>
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<td></td>
<td>&lt;15</td>
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</table>

- **UOP 2.7-3.8 cc/kg/hr**
Recommendations/Discharge

- Start HC 1.25 mg TID (~12.5 mg/m²/d) on 11/16
  - Continue for 2 wks, taper for 2 wks, then off
  - Stress dose steroid instructions
- Start LT4 37.5 mcg (6.8 mcg/kg/day) on 11/17
- 11/16 FT4 by dialysis 2.3 ng/dL (RR 0.81-2.12)
- Discharged to LaRabida
  - Obtain remaining hypopituitarism labs at future date
  - Consider MRI w/ pituitary cuts
  - Follow up TBD
1. Length of steroid replacement prior to thyroxine therapy in combined AI and hypothyroidism?
Late-Onset Circulatory Dysfunction After Thyroid Hormone Treatment in an Extremely Low Birth Weight Infant

Hideaki Yagasaki¹, Kisho Kobayashi², Atsushi Nemoto¹, Atsushi Naito¹, Kanji Sugita², and Kenji Ohyama²

- 15 day-old F with LCD
- Born at 25 1/7 wks, BW 672 gm, Apgars 5/7
- RDS, PDA, slow weight gain
- DOL 14: FT₃ 1.65 pg/mL, FT₄ 0.19 ng/dL, TSH 26.3 uIU/mL
  - Started LT₄ 5 mcg/day
- DOL 15: Na 129, BP 45/24, oliguria, edema
  - Cortisol 2 ug/dL, ACTH 51.9 pg/mL
  - Started HC 1 mg BID

Clinical course

![Graph showing body weight progression and hormone levels over days]

<table>
<thead>
<tr>
<th>Day</th>
<th>Onset of LCD</th>
<th>Extubation</th>
<th>CRH test</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>25</td>
<td>42</td>
<td>116</td>
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</table>

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Day 14</th>
<th>Day 25</th>
<th>Day 42</th>
<th>Day 116</th>
<th>Day 147</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH (μIU/ml)</td>
<td>26.36</td>
<td>2.56</td>
<td>0.67</td>
<td>3.38</td>
<td>2.58</td>
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<tr>
<td>fT3 (ng/ml)</td>
<td>1.65</td>
<td>1.41</td>
<td>1.89</td>
<td>2.68</td>
<td>3.68</td>
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<tr>
<td>fT4 (pg/ml)</td>
<td>0.19</td>
<td>0.33</td>
<td>0.96</td>
<td>0.91</td>
<td>1.28</td>
</tr>
</tbody>
</table>

70 infants <30 wks GA
Late-onset refractory hypotension correlates with younger GA and LT4 therapy
Central hypothyroidism

Figure 2 Proposed algorithm for the diagnosis and confirmation of central hypothyroidism. Abbreviations: GH, growth hormone; LAH, lymphocytic adenohypophysitis; SAH, subarachnoid hemorrhage; SOL, space-occupying lesions; TBI, traumatic brain injury.

Combined central AI and hypothyroidism

Figure 3 Proposed algorithm for the treatment of central hypothyroidism.
2. Effect of heparin on FT4 by dialysis?
Extremely Low Doses of Heparin Release Lipase Activity into the Plasma and Can Thereby Cause Artifactual Elevations in the Serum-Free Thyroxine Concentration as Measured by Equilibrium Dialysis

- Heparin → release of lipase → acts on TG → release of FFA → block binding of T_4 to TBG → ↑ FT_4
- TG must be >180 mg/dL
- Subject 1:
  - preheparin and postheparin samples
  - added TG
  - added protamine and hepatic TG lipase antibody

Jaume et al. Thyroid 1996.
Abnormal serum free thyroid hormone levels due to heparin administration

K. LAJI, B. RHIDHA, R. JOHN¹, J. LAZARUS and J.S. DAVIES

- 4 adult patients on IV or SC heparin for DVT ppx
- TFTs evaluated by Bayer ACS-180 and Delfia assays

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Thyroid function test results using the ACS-180 assay and the Delfia assay during treatment with heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient 1</td>
</tr>
<tr>
<td><strong>ACS-180 results</strong></td>
<td></td>
</tr>
<tr>
<td>Free T4 (pmol/l)</td>
<td>34.7</td>
</tr>
<tr>
<td>TSH (mU/l)</td>
<td>0.94</td>
</tr>
<tr>
<td>Free T3 (pmol/l)</td>
<td>5.4</td>
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<tr>
<td><strong>Delfia assay results</strong></td>
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<tr>
<td>Free T4 (pmol/l)</td>
<td>79.0</td>
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<tr>
<td>TSH (mU/l)</td>
<td>3.75</td>
</tr>
<tr>
<td>Free T3 (pmol/l)</td>
<td>10.7</td>
</tr>
</tbody>
</table>

1/12-16/15:
- Admitted for bronchiolitis
- FT4 1.34, TSH 0.03, T3 137, T4 9.5, RT3 493 pg/mL → continue LT4 37.5 mcg/day
- Cortisol <0.4, DHEA-S <15: started on stress dose HC
- Na 156 → 144 as IVF weaned

2/11/15:
- F/u in endo clinic
- Preprandial dexis in low 100s, Na 140
- FT4 1.46, TSH 0.02, T3 132, T4 9.5 → continue LT4
- IGF-1 <25 (RR 15-179), IGF-BP3 1.6 (1.0-2.3) → risk of GHD
- On HC 2.5 mg TID (~21 mg/m2/day) → wean restarted
- Stress dose steroid instructions provided

5/18/15: next follow up in endo clinic
Conclusions

- Ruling out adrenal insufficiency should be considered prior to initiation of thyroxine replacement in children.
- Patients should receive at least 1 week of glucocorticoid therapy prior to LT4 initiation in the setting of combined hypothyroidism and AI. Caution against precipitating adrenal crisis has to be balanced against the potential loss of IQ points and lower cognitive function with each week that LT4 replacement is delayed.
- Heparin, through a mechanism of increased release of FFA and TBG displacement, may artifactualy raise FT4 and/or FT3.
References

- Jaume JC et al. Extremely low doses of heparin release lipase activity into the plasma and can thereby cause artifactual elevations in the serum-free thyroxine concentration as measured by equilibrium dialysis. Thyroid 1996;6(2):79-83.
- Laji K et al. Abnormal serum free thyroid hormone levels due to heparin administration. Q J Med 2001;94:471-3.