Laboratory Testing for Transgender Individuals

Grace M. Kroner, Ph.D.

Clinical Chemistry Fellow
University of Utah / ARUP Laboratories

DOI: 10.15428/CCTC.2019.311480
Outline

• Terminology
• Laboratory Testing for Hormone Therapy
• Expected Changes to Reference Intervals and Laboratory Calculations
Terminology

- **Sex**: assigned at birth as male or female, usually based on the appearance of the external genitalia\(^2\)
- **Gender identity**: a person’s sense of being male, female, neither, or a combination of both\(^2\)

Uncopyrighted image from https://www.genderbread.org/resource/genderbread-person-v4-0
Terminology

- **Cisgender**: sex assigned at birth is *congruent* with gender identity
- **Transgender**: sex assigned at birth is *incongruent* with gender identity
- **Transwoman**: assigned male at birth (AMAB) but identifies as female
- **Transman**: assigned female at birth (AFAB) but identifies as male

Uncopyrighted image from https://www.genderbread.org/resource/genderbread-person-v4-0
Terminology

- **Gender dysphoria:**
  - Defined by the American Psychiatric Association in their Diagnostic and Statistical Manual of Mental Disorders (2013) as:
    - “Marked incongruence between one’s experienced/expressed gender and assigned gender” that is “associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning”
    - Lasts at least 6 months
    - Only affects some transgender or gender nonconforming people
  - Gender nonconformity is not a disorder
Guideline Resources

- Endocrine Society
- WPATH: World Professional Association for Transgender Health
Possible Treatment Options for Gender Dysphoria

- Social transition
  - Changes in gender expression in public, at work, etc.
  - Voice therapy
- **Hormone therapy (HT)**
  - Treatment with masculinizing or feminizing hormones/androgen blockers
- Surgery to change primary or secondary sex characteristics
Laboratory Testing for Hormone Therapy

- **Purpose**: monitor hormone concentrations during HT
  - Aim to maintain concentration within reference interval of the affirmed gender\(^1,2\)
- Test methods:
  - Immunoassay recommended for elevated concentrations
  - Mass spectrometry generally has improved performance at low concentrations
- Test timing depends on hormone formulation\(^1\)
Laboratory Testing for Hormone Therapy

• **Feminizing HT**
  • May include estrogens and anti-androgens
  • Measure estradiol, testosterone\(^1\)
  • Possibly measure SHBG (sex hormone binding globulin)

• **Masculinizing HT**
  • Includes various formulations of testosterone
  • Measure testosterone\(^1\)
    - Free testosterone measurement not routinely recommended
Laboratory Testing for Hormone Therapy

- **Purpose**: monitor potential risks of HT
- **Risks**:
  - **Feminizing and masculinizing HT**
    - Cardiovascular disease, diabetes
  - **Feminizing HT**
    - Thromboembolism, liver damage, prolactinoma
  - **Masculinizing HT**
    - Polycythemia
  - Relative risk of side effects depend on formulation
- **Other routine monitoring is also needed**\(^1,2\)
Laboratory Testing for Hormone Therapy

<table>
<thead>
<tr>
<th>HT Type</th>
<th>Tests to perform</th>
<th>Baseline</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feminizing HT</td>
<td>Estradiol</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Testosterone</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Prolactin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Electrolytes (K⁺)</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>*If on spironolactone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Masculinizing HT</td>
<td>Testosterone</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Hematocrit/</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>hemoglobin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Also perform lipid testing and diabetes screening as recommended by guidelines¹
Consistently altered by HT
• Reference intervals from transgender individuals on HT agree almost completely with cisgender reference intervals

Changes in Lipid Parameters

• Demonstrate variable response to HT

Changes in Lipid Parameters

- Baseline transwomen
- Transwomen
- Baseline transmen
- Transmen

Summary of Analyte Changes with HT$^{3-6,8-12}$

<table>
<thead>
<tr>
<th>HT</th>
<th>Inconsistent findings</th>
<th>Feminizing</th>
<th>Masculinizing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>SHBG</td>
<td>hematocrit, hemoglobin</td>
</tr>
<tr>
<td>Feminizing</td>
<td></td>
<td>hematocrit, hemoglobin</td>
<td>SHBG</td>
</tr>
<tr>
<td>Masculinizing</td>
<td></td>
<td>hematocrit, hemoglobin, creatinine</td>
<td></td>
</tr>
</tbody>
</table>

- Must consider HT duration/formulation and inter-individual variability
Take-Home Points

• Guidelines provide recommendations on testing for hormone concentrations and monitoring potential risks of HT

• Hematology parameters usually show consistent changes in individuals on HT

• Lipid panel analytes do not show predictable changes in individuals on HT
References

Disclosures/Potential Conflicts of Interest

Upon Pearl submission, the presenter completed the Clinical Chemistry disclosure form. Disclosures and/or potential conflicts of interest:

- **Employment or Leadership**: No disclosures
- **Consultant or Advisory Role**: No disclosures
- **Stock Ownership**: No disclosures
- **Honoraria**: No disclosures
- **Research Funding**: No disclosures
- **Expert Testimony**: No disclosures
- **Patents**: No disclosures
Thank you for participating in this *Clinical Chemistry* Trainee Council Pearl of Laboratory Medicine.

Find our upcoming Pearls and other Trainee Council information at [www.traineecouncil.org](http://www.traineecouncil.org)

Download the free *Clinical Chemistry* app on iTunes today for additional content!

Follow us: