PHYSIOLOGIC DOSING OF HORMONES IN FEMALES AND LABORATORY FINDINGS

Paul Savage MD, FACEP, FAARM
Objectives

1. Explain physiologic dosing of female hormones with regards to menopause.

2. Correct misinformation about laboratory testing in regards to treatment modality.

3. Define evidence-based clinical algorithms for female BHT.
Daily Serum Levels of Hormones in Women

- Testosterone Peak Serum: 55 pg/ml
- Estradiol Peak Serum: 160 pg/ml
- Progesterone Peak Serum 12 ng/ml
# Daily Endogenous Production of Hormones in Women

<table>
<thead>
<tr>
<th>Steroids</th>
<th>Follicular</th>
<th>Luteal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progesterone</td>
<td>1mg/day</td>
<td>25mgs/day</td>
</tr>
<tr>
<td>DHEA</td>
<td>7mgs/day</td>
<td>7mgs/day</td>
</tr>
<tr>
<td>Testosterone</td>
<td>0.144mgs/day</td>
<td>0.126mgs/day</td>
</tr>
<tr>
<td>Estradiol</td>
<td>0.036mgs/day</td>
<td>0.25mgs/day</td>
</tr>
</tbody>
</table>

The Power2Practice Study/Chart Review

Purpose
Determine range of Various Lab Values for asymptomatic women on BHT

Inclusion
Female
One year without periods or TAHBSO
On Bioidentical Hormone Therapy
Asymptomatic (MRS <4)

Study
2008-2013
598 Patient Visits
1914 lab values

Average Age
55.3

Methods
LabCorp - Serum
ZRT - Saliva
ZRT – Capillary Blood Spot
Rhein Labs - Urine

Pharmacy
Diplomat Compounding Pharmacy

Unpublished Data
The Power2Practice Study/Chart Review

Dosing Methods Evaluated

• Patches
  – Estradiol patch
• Topical Creams
  – Estradiol Cream
  – Testosterone Cream
  – Progesterone Cream
• Oral
  – Progesterone SR
  – DHEA
• Pellets
  – Testosterone
Estradiol Patch

**Serum E2**
- Baseline E2
- E2 Patch
- E2 Patch 0.05mgS
- E2 Patch 0.075-1.0mgS

42-289 pg/mL

**Blood Spot E2**
- Baseline E2
- E2 Patch
- E2 Patch 0.05mgS
- E2 Patch 0.075-1.0mgS

43-180 pg/mL

**Saliva E2**
- Baseline E2
- E2 Patch
- E2 Patch 0.05mgS
- E2 Patch 0.075-1.0mgS

1.3-3.3 pg/mL

**Urine E2**
- Baseline E2
- E2 Patch
- E2 Patch 0.05mgS
- E2 Patch 0.075-1.0mgS

2-5 µg/24hrs

Physiologic Level
**Estradiol Patch**

<table>
<thead>
<tr>
<th>Estradiol Patch</th>
<th>Contains</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.025mgs/day of estradiol</td>
<td>0.39mgs of estradiol (0.11mgs/day)</td>
</tr>
<tr>
<td>0.0375mgs/day of estradiol</td>
<td>0.585mgs of estradiol (0.17mgs/day)</td>
</tr>
<tr>
<td>0.05mgs/day of estradiol</td>
<td>0.78mgs of estradiol (0.22mgs/day)</td>
</tr>
<tr>
<td>0.075mgs/day of estradiol</td>
<td>1.17mgs of estradiol (0.33mgs/day)</td>
</tr>
<tr>
<td>0.1mgs/day of estradiol</td>
<td>1.56mgs of estradiol (0.44mgs/day)</td>
</tr>
</tbody>
</table>

**Daily Endogenous Production of Estradiol**

<table>
<thead>
<tr>
<th>Steroids</th>
<th>Follicular</th>
<th>Luteal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>0.036mgs/day</td>
<td>0.25mgs/day</td>
</tr>
</tbody>
</table>
Dr. Paul’s Pearls

• Estradiol patch works well for treatment of estradiol deficiency symptoms.
• Estradiol patch dosing effective range is 0.025-0.1mgs patch twice weekly.
• Estradiol patch can be monitored by all methods of testing.
Estradiol Cream Topical

Serum E2

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline E2</th>
<th>E2 Cream 0.125mgs</th>
<th>E2 Cream 0.25mgs</th>
<th>E2 Cream 0.5-0.75mgs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>42-289 pg/mL</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Blood Spot E2

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline E2</th>
<th>E2 Cream 0.125mgs</th>
<th>E2 Cream 0.25mgs</th>
<th>E2 Cream 0.5-0.75mgs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>43-180 pg/mL</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Saliva E2

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline E2</th>
<th>E2 Cream 0.125mgs</th>
<th>E2 Cream 0.25mgs</th>
<th>E2 Cream 0.5-0.75mgs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>1.3-3.3 pg/mL</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Urine E2

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline E2</th>
<th>E2 Cream 0.125mgs</th>
<th>E2 Cream 0.25mgs</th>
<th>E2 Cream 0.5-0.75mgs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>2-5 µg/24hrs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Urinary Levels of Estradiol

GC/MS/MS Testing of Urinary Estradiol in Premenopausal Women at Different Phases of the Menstrual Cycle and on Hormonal Contraceptives, and in Postmenopausal Women Supplementing with Topical, Vaginal, and Oral Estrogens

Estradiol (median)

- **E2 Oral**: Median 6.70 (2.62-12.43) N=7
- **E2 Patch**: Median 0.63 (0.33-1.42) N=27
- **E2 Cream**: Median 0.74 (0.37-1.19) N=173
Dr. Paul’s Pearls

• Estradiol cream topical works well for treatment of estradiol deficiency symptoms.
• Estradiol cream topical dosing effective range is 0.25-0.5mgs applied daily.
• Estradiol cream topical can be only monitored by Blood Spot or Saliva Testing:
  – Not monitored well with Serum or Urine
Progesterone Oral

Serum PG

- Baseline PG
- PG Oral 100-150mgs
- PG Oral 200-250mgs
1.7-27.0 ng/mL

Blood Spot PG

- Baseline PG
- PG Oral 100-150mgs
- PG Oral 200-250mgs
3.3-22.5 ng/mL

Saliva PG

- Baseline PG
- PG Oral 100-150mgs
- PG Oral 200-250mgs
30-300 pg/mL

Urine Preg

- Baseline PG
- PG Oral 100-150mgs
- PG Oral 200-250mgs
100-3287 µg/24hrs

Physiologic Level
Dr. Paul’s Pearls

• Progesterone orally works well for treatment of progesterone deficiency symptoms.
• Progesterone orally dosing effective range is 100-250mgs daily.
• Progesterone orally can be monitored by all methods of testing:
  – Adjusting range for Urine to 5000-30,000 µg/24hrs
Progesterone Cream Topical

Serum PG

1.7-27.0 ng/mL

Baseline PG  PG Cream TD  PG Cream TD  PG Cream TD
20-40mgs  50-75mgs  100 mgs

Blood Spot PG

3.3-22.5 ng/mL

Baseline PG  PG Cream TD  PG Cream TD  PG Cream TD
20-40mgs  50-75mgs  100 mgs

Saliva PG

300-3000 pg/mL

Baseline PG  PG Cream TD  PG Cream TD  PG Cream TD
20-40mgs  50-75mgs  100 mgs

Urine Preg

100-3287 µg/24hrs

Baseline PG  PG Cream TD  PG Cream TD  PG Cream TD
20-40mgs  50-75mgs  100 mgs
Urinary Levels of Progesterone

**Pregnanediol (median)**

<table>
<thead>
<tr>
<th>Group</th>
<th>Level (µg/mg creatinine)</th>
<th>Median (20-80% Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicular Females</td>
<td>152 (92-346)</td>
<td>N=24</td>
</tr>
<tr>
<td>Luteal 36-45 y/o</td>
<td>1324 (849-1932)</td>
<td>N=37</td>
</tr>
<tr>
<td>Postmenopausal /...</td>
<td>81 (42-171)</td>
<td>N=97</td>
</tr>
<tr>
<td>BC Pills</td>
<td>209 (121-2876)</td>
<td>N=7</td>
</tr>
<tr>
<td>Topical Pg Supp</td>
<td>170 (85-403)</td>
<td>N=262</td>
</tr>
<tr>
<td>Vaginal Pg Supp</td>
<td>400 (180-588)</td>
<td>N=6</td>
</tr>
<tr>
<td>Oral Pg Supp</td>
<td>3930 (1965-7377)</td>
<td>N=121</td>
</tr>
</tbody>
</table>

**GC/MS/MS** Testing of Urinary Pregnanediol in Premenopausal Women at Different Phases of the Menstrual Cycle and on Hormonal Contraceptives, and in Postmenopausal Women Supplementing with Topical, Vaginal, and Oral Progesterone
Dr. Paul’s Pearls

• Progesterone cream topical works well for treatment of progesterone deficiency symptoms.
• Progesterone cream topical dosing effective range is 20-50mgs applied daily.
• Progesterone cream topical can be only monitored by Blood Spot or Saliva Testing:
  – Adjusting range for Saliva to 300-3000 pg/mL
  – Not monitored well with Serum or Urine
Testosterone Cream Topical

Serum Test

Blood Spot Test

Saliva Test

Urine Test

Physiologic Level
Testosterone cream topical works well for treatment of testosterone deficiency symptoms.

Testosterone cream topical dosing effective range is 0.5-1.5mgs applied daily.

Testosterone cream topical can be only monitored by Serum, Blood Spot or Saliva Testing.

– Not monitored well with Urine
Testosterone Pellet – 90 days

Serum Test

- Baseline Testosterone
- Tespel 75mgs
- Tespel 100mgs
- Tespel 125mgs
- Tespel 150mgs

Saliva Test

- Baseline Testosterone
- Tespel 75mgs
- Tespel 100mgs
- Tespel 125mgs
- Tespel 150mgs

Blood Spot Test

- Baseline Testosterone
- Tespel 75mgs
- Tespel 100mgs
- Tespel 125mgs
- Tespel 150mgs

Physiologic Level

Urine Testing Data Not Sufficient
Urinary Levels of Testosterone

Testing of Urinary Testosterone in Premenopausal Women at Different Phases of the Menstrual Cycle and on Hormonal Contraceptives, and in Postmenopausal Women Supplementing with Troche, SC-Pellets, Vaginal, and Topical Testosterone

Testosterone (median)  
Females Only

<table>
<thead>
<tr>
<th>Condition</th>
<th>Median (Range) N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicular Females</td>
<td>1.9 (0.4-2.8) N=24</td>
</tr>
<tr>
<td>Luteal Females</td>
<td>2.3 (0.7-3.8) N=75</td>
</tr>
<tr>
<td>Postmenopausal /...</td>
<td>1.2 (0.5-2.3) N=96</td>
</tr>
<tr>
<td>BC Pills</td>
<td>1.3 (0.6-2.4) N=7</td>
</tr>
<tr>
<td>Females - Troche Ts</td>
<td>1.1 (0.7-2.6) N=20</td>
</tr>
<tr>
<td>Females - Pellet Ts</td>
<td>3.8 (0.8-9.1) N=54</td>
</tr>
<tr>
<td>Females - Vaginal...</td>
<td>2.2 (1.0-4.8) N=90</td>
</tr>
<tr>
<td>Females - Topical...</td>
<td>1.9 (1.1-4.2) N=226</td>
</tr>
</tbody>
</table>
Dr. Paul’s Pearls

• Testosterone pellets works well for treatment of testosterone deficiency symptoms.
• Testosterone pellets dosing effective range is 75-125mgs implanted q4-6mo.
• Testosterone pellets can be monitored by all methods of testing:
  – Adjusting range for serum to 20-130 ng/dL at 90 days
DHEA Oral

Serum DHEAS

Baseline DHEA  
DHEA Oral 5-7.5mgs  
DHEA Oral 10-15mgs

Blood Spot DHEAS

Baseline DHEA  
DHEA Oral 5-7.5mgs  
DHEA Oral 10-15mgs

Saliva DHEA-S

Baseline DHEA  
DHEA Oral 5-7.5mgs  
DHEA Oral 10-15mgs

Urine DHEA (S)

Baseline DHEA  
DHEA Oral 5-7.5mgs  
DHEA Oral 10-15mgs

Physiologic Level
Dr. Paul’s Pearls

- DHEA oral works well for treatment of DHEA deficiency symptoms.
- DHEA oral dosing effective range is 5-15mgs daily.
- DHEA oral can be monitored by all methods of testing.
DHEA Cream Topical

Serum DHEAS

35-256 µg/dL

Blood Spot DHEAS

40-290 µg/dL

Saliva DHEA-S

2-23 ng/mL

Urine DHEA (S)

20-1139 µg/24hrs
Dr. Paul’s Pearls

• DHEA cream topical works well for treatment of DHEA deficiency symptoms.
• DHEA cream topical dosing effective range is 5-15mgs daily.
• DHEA cream topical CANNOT be monitored well by any method of testing.
• DHEA Cream Topical measurement is misleading because what most labs are measuring is DHEAS.
  – DHEA given topically will not increase DHEAS, which is why Blood Spot DHEAS does not go up.
  – Urine actually measures DHEA, but they are really measuring DHEA and DHEAS because the DHEAS is desulfated by digestion and then measured as DHEA.
  – SO, careful about the interpretation-its tricky.
Guide to Steroid Testing on Hormone Therapy

<table>
<thead>
<tr>
<th>Lab Testing</th>
<th>Baseline (no BHT)</th>
<th>Oral</th>
<th>Topical/Vaginal</th>
<th>Troche/Sublingual</th>
<th>Patches</th>
<th>Pellets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Blood Spot</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Saliva</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes¹</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Urine</td>
<td>Yes</td>
<td>Yes²</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

1. Progesterone Saliva levels must be adjusted to 200-3000 pg/mL
2. Progesterone Urine levels must be adjusted to 5000-30,000 µg/24hrs
## Therapeutic Dosing of Hormones in Women

<table>
<thead>
<tr>
<th>Steroids</th>
<th>Oral</th>
<th>Topical</th>
<th>Patch</th>
<th>Pellet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progesterone</td>
<td>50-250mgs daily</td>
<td>20-50mgs daily</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>DHEA</td>
<td>5-15mgs daily</td>
<td>5-15mgs daily</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Testosterone</td>
<td>1-2mgs daily</td>
<td>0.5-1.5mgs daily</td>
<td>*</td>
<td>75-125mgs q4-6mo</td>
</tr>
<tr>
<td>Estradiol</td>
<td>*</td>
<td>0.25-0.75mgs daily</td>
<td>0.025-0.1mg s twice weekly</td>
<td>*</td>
</tr>
</tbody>
</table>

**Dr. Paul’s Pearls:**
1. Treat symptoms, not numbers
2. Baseline testing: Every method works
3. Treatment with Oral, Patches, and Pellets: Every method works
4. Treatment with Topical Creams: Only Blood Spot and Saliva work
# Therapeutic Dosing Methods of Hormones in Women

<table>
<thead>
<tr>
<th>Steroid</th>
<th>Oral</th>
<th>Topical/Vaginal</th>
<th>Patches</th>
<th>Pellets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progesterone</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>DHEA</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Testosterone</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Estradiol</td>
<td>Yes*</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Steroid</th>
<th>Serum</th>
<th>Capillary Blood Spot</th>
<th>Saliva</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol Patches</td>
<td>42-289 pg/mL</td>
<td>43-180 pg/mL</td>
<td>1.3-3.3 pg/mL</td>
<td>2-5 µg/24hrs</td>
</tr>
<tr>
<td>Estradiol Cream</td>
<td>*</td>
<td>43-180 pg/mL</td>
<td>1.3-3.3 pg/mL</td>
<td>*</td>
</tr>
<tr>
<td>Progesterone Oral</td>
<td>1.7-27 ng/mL</td>
<td>3.3-22.5 ng/mL</td>
<td>30-300 pg/mL</td>
<td>5000-30,000 µg/24hrs¹</td>
</tr>
<tr>
<td>Progesterone Cream</td>
<td>*</td>
<td>3.3-22.5 ng/mL</td>
<td>300-3000 pg/mL²</td>
<td>*</td>
</tr>
<tr>
<td>Testosterone Cream</td>
<td>10-55 ng/dL</td>
<td>20-130 ng/dL</td>
<td>16-55 pg/mL</td>
<td>4-18 µg/24hrs</td>
</tr>
<tr>
<td>Testosterone Pellets</td>
<td>20-130 ng/dL³</td>
<td>20-130 ng/dL</td>
<td>16-55 pg/mL</td>
<td>?</td>
</tr>
<tr>
<td>DHEA Oral</td>
<td>35-256 µg/dL</td>
<td>40-290 µg/dL</td>
<td>2-23 ng/mL</td>
<td>20-1139 µg/24hrs</td>
</tr>
<tr>
<td>DHEA Cream</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

* = Not well measured by test  
? = Not studied  
1 = Higher value  
2 = Higher value  
3 = Higher value
Dr. Paul’s Final Pearls

• Treat *symptoms*, not numbers
• Therapy with Oral, Topical Creams, Patches, and Pellets
  – Every treatment method works to eliminate symptoms
• Lab baseline testing
  – Every method works
• Lab monitoring of therapy
  – Treatment with Oral, Patches and Pellets
    • Every lab works
  – Treatment with Topical Creams
    • Blood Spot and Saliva work best
Thank You

Paul Savage MD, FACEP, FFARM