COBALT: EFFECTS ON ESTROGEN AND TESTOSTERONE METABOLISM

IODINE: EFFECTS ON ESTROGEN METABOLISM, FIBROCYSTIC DISEASE, AND BREAST CANCER

By Jonathan V. Wright, M.D. (N.D., Hon)
Relevant financial relationships in the past twelve months by presenter or spouse/partner:

- Employment: N/A
- Speakers Bureau: N/A
- Stock Shareholder: N/A
- Grant/Research Support: N/A
- Consultant: Meridian Valley Laboratory

Status of FDA devices used for the material being presented: NA/Non-Clinical

Status of off-label use of devices, drugs or other materials that constitute the subject of this presentation: NA/Non-Clinical

No other relevant financial relationships in the past twelve months by presenter or spouse/partner
COBALT AND ESTROGEN

BIO-IDENTICAL ESTROGEN TREATMENT FAILURE AND ESTROGEN HYPEREXCRETION:
Correction with Physiologic Dose Cobalt – Case Reports
Nearly all women who don’t respond to bio-identical estrogen replacement are found to be “hyperexcreting” their estrogens.

The combined urinary levels of E1+E2+E3 resulting from an “average effective treatment dose” are from 50% to 1800% higher.

As a result of estrogen hyperexcretion, apparently very little if any estrogen remains available to the brain and the rest of the body to quench menopausal symptoms.

As one woman put it: “It feels like my body is just getting rid of every bit of estrogen supplement I’m putting into it”.

©Jonathan V. Wright, MD, 2018
A small amount of clinical information accumulated so far indicates that in humans, cobalt normalizes estrogen hyper-excretion while relieving menopausal symptoms. Following is preliminary data from a few such cases observed at Tahoma Clinic.

A “typical normal response” case is outlined first for comparison purposes.
POPHYRINS

8-AMINO LEVULINIC ACID SYNTHETASE

(UP-REGULATED BY COBALT)

HEME PROTEINS INCL. CYTOCHROMES P450 & P488

HEME OXIDASE

(BILIVERDINI & BILIRUBIN)

(UP-REGULATED BY COBALT)
Typical Normal Response, 48 Year-Old Woman with Symptoms of Menopause

- Symptoms of “hot flashes”, night sweats, irritability, insomnia, and mood swings.
- Initial quantities of BHRT were prescribed on a 28 day cycle, including “triple estrogen” (2.5 milligrams on “days 1-25”), progesterone (25 milligrams on “days 12-25”), and DHEA (15 milligrams every day).
Typical Normal Response, 48 Year-Old Woman with Symptoms of Menopause

- [“Triple estrogen” (used in early 1980s) was a combination of estrone (10%), 17-β estradiol (10%), and estriol (80%).]
- Follow-up 24-hour urinary steroid test done in 60 days.
- She reported that nearly all the above noted symptoms were gone with the exception of occasional insomnia.
Typical 24-Hour Urine Test Response with Complete Symptom Relief

- Estrone: 33.7 micrograms
- Estradiol: 38.1 micrograms
- Estriol: 54.10 micrograms
- Total Estrogen: 125.90 micrograms

Micrograms per 24-hour Urine Collection
Example of Hyper-Excretion Prior to Cobalt Supplementation While Using Triple Estrogen:
2.5 mg on Days 1-25 (Progesterone 25 mg)

<table>
<thead>
<tr>
<th>Micrograms per 24-hour Urine Collection</th>
<th>Estrone</th>
<th>Estradiol</th>
<th>Estriol</th>
<th>Total Estrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>98.4</td>
<td>13.2</td>
<td>1,405.40</td>
<td>1,517.00</td>
</tr>
</tbody>
</table>
CASE 1: 49 year old woman with symptoms of hot flashes, insomnia, and anxiety

Initial 24-hr Urine Collection Results, No BHRT Suppl.

- Estrone: 12.30 mcgs/24 hrs
- Estradiol: 22.60 mcgs/24 hrs
- Estriol: 1.85 mcgs/24 hrs
- Total Estrogens: 36.75 mcgs/24 hrs

24-hr Urine Results after 1.25 mg daily Triple Estrogen {E1:E2:E3 10:10:80} Symptoms unabated.

- Estrone: 55.7 mcgs/24 hrs
- Estradiol: 53.6 mcgs/24 hrs
- Estriol: 808.8 mcgs/24 hrs
- Total Estrogens: 918.0 mcgs/24 hrs

☑️ Estrogens raised to 2.5 mg daily with no abatement of symptoms.
CASE 1 Continued
Results after Adding Cobalt Chloride

24-hr Urine Results after adding cobalt (400-500 mcgs daily). Symptoms relieved.

<table>
<thead>
<tr>
<th>Estrogen</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone</td>
<td>11.3 mcgs/24 hrs</td>
</tr>
<tr>
<td>Estradiol</td>
<td>50.4 mcgs/24 hrs</td>
</tr>
<tr>
<td>Estriol</td>
<td>41.7 mcgs/24 hrs</td>
</tr>
<tr>
<td>Total Estrogens</td>
<td>103.4 mcgs/24 hrs</td>
</tr>
</tbody>
</table>
CASE 2: 63 year old woman with symptoms of night sweats, insomnia, memory and concentration difficulties.

<table>
<thead>
<tr>
<th></th>
<th>Estrone</th>
<th>Estradiol</th>
<th>Estriol</th>
<th>Total Estrogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-hr Urine Results after 3 years of bio-identical hormone replacement therapy. Symptoms slightly lessened.</td>
<td>98.4 mcgs/24 hrs</td>
<td>13.2 mcgs/24 hrs</td>
<td>1405.4 mcgs/24 hrs</td>
<td>1517.0 mcgs/24 hrs</td>
</tr>
<tr>
<td>24-hr Urine Results after adding cobalt supplementation. Hormone dose unchanged. Symptoms relieved.</td>
<td>8.8 mcgs/24 hrs</td>
<td>95.6 mcgs/24 hrs</td>
<td>32.2 mcgs/24 hrs</td>
<td>136.5 mcgs/24 hrs</td>
</tr>
</tbody>
</table>
CASE 3: 52 year old woman with symptoms of hypothyroidism and multiple menopause symptoms.

<table>
<thead>
<tr>
<th></th>
<th>Estrone</th>
<th>Estradiol</th>
<th>Estriol</th>
<th>Total Estrogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone</td>
<td>396.9 mcgs/24 hrs</td>
<td>101.3 mcgs/24 hrs</td>
<td>1405.4 mcgs/24 hrs</td>
<td>1903.5 mcgs/24 hrs</td>
</tr>
<tr>
<td>Estradiol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estriol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Estrogens</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

24-Hr Urine results after using Bi-Estrogen (estriol 1 mg, estradiol 250 mg). Symptoms unchanged.

24-hr Urine results after adding 500 mcg cobalt daily. Symptoms relieved.

<table>
<thead>
<tr>
<th></th>
<th>Estrone</th>
<th>Estradiol</th>
<th>Estriol</th>
<th>Total Estrogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone</td>
<td>212.8 mcgs/24 hrs</td>
<td>73.3 mcgs/24 hrs</td>
<td>25.9 mcgs/24 hrs</td>
<td>311.9 mcgs/24 hrs</td>
</tr>
<tr>
<td>Estradiol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estriol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Estrogens</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Many more details on ppts #27-30
Liquid Cobalt Chloride

- Experience has shown that liquid cobalt chloride (250 mcg/drop) is effective for this problem. It’s available to practitioners only.
- Cobalt supplement can often be discontinued once the cytochrome enzymes have been “down-regulated” to an apparent normal level of activity.
  ✓ If symptoms return, laboratory evaluation can easily detect “recurrent hyperexcretion (and apparent “re-current cytochrome p450 up-regulation) and cobalt can be temporarily re-recommended.
From the Previous Data, it Seems Reasonable to Infer:

- A small minority of women have “upregulated” estrogen-metabolizing enzymes, likely including cytochrome p450s.
- Ionic cobalt “downregulates” these enzymes and “normalizes” the “upregulated enzymes”. In doing so, ionic cobalt enables normalization of bio-identical hormone metabolism, with coincidental symptom relief.
COBALT AND TESTOSTERONE

Bio-Identical Testosterone Hyperexcretion: Correction with Physiologic Dose Cobalt

CASE REPORTS
Testosterone Detail:

- **Materials used:**
  - Compounded bio-identical testosterone transdermal cream formula
  - 50-80 mg for men

- **Application:**
  - Mucosal application site
  - No rotation schedule
Hyperexcretion of Testosterone

- Suspect testosterone hyperexcretion when 24-hr urine test results are high-normal or high, but patient indicates no benefits of treatment.
  - Order serum tests of free and total testosterone ...suspect hyperexcretion if serum results are low.
- Cases following exemplify these anomalies.
Case 1: Starting Treatment Dose

- Patient started testosterone:
  - 75 mg/day
  - Transdermal application
  - In February 2005
## Case 1, 75 mg Testosterone Daily

### June ‘05 Serum Results

<table>
<thead>
<tr>
<th>Component</th>
<th>Result Values</th>
<th>Ref. Ranges</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Total Testosterone</td>
<td>179</td>
<td>119-1104</td>
<td>NG/DL</td>
</tr>
<tr>
<td>Serum Free Testosterone</td>
<td>25.2</td>
<td>11-141</td>
<td>PG/ML</td>
</tr>
</tbody>
</table>
Case 1, 75 mg Testosterone Daily

June ‘05 24-Hr Urine Results:

<table>
<thead>
<tr>
<th>Component</th>
<th>Excreted in ug/24 hr.</th>
<th>Normal Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone</td>
<td>282.30</td>
<td>20-200</td>
</tr>
</tbody>
</table>
Case 1, Cobalt Corrects Testosterone Hyperexcretion

- Patient started cobalt chloride.
  - 250 mcg per drop, 3 drops daily
### January ‘06 Serum Results:

<table>
<thead>
<tr>
<th>Component</th>
<th>Result Values</th>
<th>Ref. Ranges</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Total Testosterone</td>
<td>633</td>
<td>250-1100</td>
<td>NG/DL</td>
</tr>
<tr>
<td>Serum Free Testosterone</td>
<td>119.2</td>
<td>35.0-155.0</td>
<td>PG/ML</td>
</tr>
</tbody>
</table>
Case 1, 75 mg T Daily, Using 3 Drops of Cobalt Chloride

Feb. ‘06 24-Hr Urine Results:

<table>
<thead>
<tr>
<th>Component</th>
<th>Excreted in ug/24 hr.</th>
<th>Normal Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone</td>
<td>195.5</td>
<td>20-200</td>
</tr>
</tbody>
</table>

©Jonathan V. Wright, MD, 2018
“Recent studies have established that metal ions directly regulate cellular content of heme, and thus of heme proteins by controlling production of delta-aminolevulinate synthetase and heme oxygenase, the rate-limiting enzymes for heme synthesis and degradation, respectively.”

Mechanism of Cobalt Action on Estrogen (and other steroid) Hyperexcretion

- While not mentioning estrogen or other steroid metabolism specifically, Maines’ & Kappas’ research reported that cobalt (an essential-to-life mineral) is the most active ALA synthase inhibitor and heme oxygenase stimulator, thus reducing excess cytochrome activity.

✓ (For further information, see Wright JV, Ann NY Acad Sci 2005;1057:506-524)
POPHYRINS

8-AMINO LEVULINIC ACID SYNTHETASE (DOWN-REGULATED BY COBALT)

HEME PROTEINS INCL. CYTOCHROMES P450 & P488

HEME OXIDASE (UP-REGULATED BY COBALT)

BILIVERDIN & BILIRUBIN
Mechanism of Cobalt Action on Estrogen (and other steroid) Hyperexcretion

- As estrogens and other steroids are metabolized by cytochromes, trials of dietary dose cobalt in individuals with steroid hyperexcretion are uniformly successful in normalizing steroid hyperexcretion and enabling steroid retention and activity.

✓ (For further information, see Wright JV, Ann NY Acad Sci 2005;1057:506-524)
COBALT AND CORTISOL

HYPEREXCRETION OF CORTISOL: Correction with Physiologic Dose Cobalt

CASE REPORTS
50-year-old female patient with multiple symptoms of adrenal fatigue.

“Unable to function” with less than 140 mg Cortef daily.

Serum Cortisol below median.

Dosage reduction tried several times with no success.
Cortisol Hyperexcretion, 50 Year Old Woman, Pre-treatment Results
24-hr Urine Results May 22, 2006

<table>
<thead>
<tr>
<th>Steroid</th>
<th>Excreted ug/24hrs</th>
<th>Ref. Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisone</td>
<td>289</td>
<td>31-209</td>
</tr>
<tr>
<td>Cortisol</td>
<td>255</td>
<td>30-170</td>
</tr>
<tr>
<td>Tetrahydrocortisone</td>
<td>9087</td>
<td>1700-4200</td>
</tr>
<tr>
<td>Allo-Tetrahydrocortisone</td>
<td>8053</td>
<td>400-2100</td>
</tr>
<tr>
<td>Tetrahydrocortisol</td>
<td>6108</td>
<td>900-2600</td>
</tr>
</tbody>
</table>
Cortisol Hyperexcretion, 50 Year-Old Woman, Treatment History:

- Patient started 6 drops cobalt chloride daily (1500 mcg.) on July 7.
  - Patient taking 140 mg Cortef.
- Decreased cobalt on Aug. 4 to 3 drops daily.
- Patient continued to decrease Cortef dose down to 0-5 mg.
  - Patient no longer fatigued.
Cortisol Hyperexcretion, 50 Year-Old Woman, Treatment History:

- October 1st, started feeling worse and increased Cortef dose to 7.5-10 mg.
  - Increased cobalt on Oct. 10th to 5 drops.
- October 21st, significant improvement in fatigue and alertness.
  - Able to decrease Cortef back down to 0-5 mg.
- See next slide for supplementation in chart format.
Cortisol Hyper-Excretion
50 Year-Old Patient
Chart of Supplementation:

<table>
<thead>
<tr>
<th>Date</th>
<th>Dose Cortef</th>
<th>Cobalt Drops</th>
</tr>
</thead>
<tbody>
<tr>
<td>July 7</td>
<td>140 mg</td>
<td>6</td>
</tr>
<tr>
<td>Aug 4</td>
<td>20-35 mg</td>
<td>3</td>
</tr>
<tr>
<td>Btwn Aug. &amp; Oct.</td>
<td>0-5 mg</td>
<td>3</td>
</tr>
<tr>
<td>Oct. 10</td>
<td>7.5-10 mg</td>
<td>5</td>
</tr>
<tr>
<td>Oct. 21</td>
<td>0-5 mg</td>
<td>5</td>
</tr>
</tbody>
</table>
Cortisol Hyper-Excretion

50 Year-Old Woman

Follow-Up 24-Hr Urine Results in November

<table>
<thead>
<tr>
<th>Steroid</th>
<th>Excreted ug/24 hrs.</th>
<th>Ref. Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisone</td>
<td>75</td>
<td>31-209</td>
</tr>
<tr>
<td>Cortisol</td>
<td>116</td>
<td>30-170</td>
</tr>
<tr>
<td>Tetrahydrocortisone</td>
<td>1728</td>
<td>1700-4200</td>
</tr>
<tr>
<td>Allo-Tetrahydrocortisone</td>
<td>1643</td>
<td>400-2100</td>
</tr>
<tr>
<td>Tetrahydrocortisol</td>
<td>1462</td>
<td>900-2600</td>
</tr>
</tbody>
</table>
Another Action of Cobalt: Inhibition of Glutathione Reductase

“Effects of Co(+2), Mg(+2) [and other minerals] ... on the enzymatic activity of glutathione reductase (GR) were investigated. Following enzyme isolation, inhibitory effects...were analyzed. Cobalt was the most powerful inhibitor.... Magnesium exhibited activatory effect on the enzyme.”
Another Action of Cobalt, Inhibition of Glutathione Reductase

Hyperexcretion and Other BHRT Information

IODINE

Cures Fibrocystic Breast Disease
Stimulates Estriol Synthesis
Kills Breast and Other Cancer Cells
Curing Fibrocystic Breasts
(John Myers, MD)...in one “ppt”!

- Swab vagina/cervix with “di-atomic” iodine (I-I): Lugol’s works also, but not SSKI
- Within the next 2-5 minutes inject Magnesium sulfate 3 grams; pyridoxine 300 milligrams
- Repeat at variable intervals, according to severity until fibrocystic breast disease is gone.
- Learned from John Myers MD in 1976, 100% effective for hundreds of women!
While treating over 200 women with the Myers method, a significant minority with EQ < 1.0 before treatment were observed.

After treatment, re-testing showed significant improvement.

In almost all cases, EQ rose to notably more than > 1.0.
Henry Lemon’s Urinary Estrogen Quotient:

\[ EQ = \frac{E3}{E2 + E1} \]
Estrogen Quotient

- In a group of women surgically treated for breast cancer, those with an EQ > 1.0 had a significantly longer post-surgical survival than those with an EQ < 1.0.

Iodine, Stimulating Estriol:

First reported observation:

- Pathway in women stimulated by iodine (and iodide)

Wright JV. *Bio-identical Steroid Hormone Replacement from 23 years of Clinical and Laboratory Practice*. Ann NY Acad Sci 2005; 1057:506-524
INADEQUATE E1 ⇔ E3 METABOLISM
(Low “Estrogen Quotient”)
Correction with Iodine, Iodide: 4 Cases
Case 1: Fibrocystic Breast Disease, Urinary Estrogens

1984 October, on Lugol's iodine, 6 drops daily

<table>
<thead>
<tr>
<th>Estrone</th>
<th>40 mcg/24 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>4 mcg/24 hrs</td>
</tr>
<tr>
<td>Estriol</td>
<td>44 mcg/24 hrs</td>
</tr>
<tr>
<td>Estrogen Quotient</td>
<td>1.0</td>
</tr>
</tbody>
</table>

1987 March
Still using Lugol’s
Thyroid tests remain normal

<table>
<thead>
<tr>
<th>Estrone</th>
<th>15 mcg/24 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>2 mcg/24 hrs</td>
</tr>
<tr>
<td>Estriol</td>
<td>76 mcg/24 hrs</td>
</tr>
<tr>
<td>Estrogen Quotient</td>
<td>4.47</td>
</tr>
</tbody>
</table>
Case 1: Fibrocystic Breast Disease, Urinary Estrogens, Continued

### 1989 September, off Lugol’s again
Start SSKI 6 drops daily

<table>
<thead>
<tr>
<th>Estrogen</th>
<th>19.2 mcg/24 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone</td>
<td></td>
</tr>
<tr>
<td>Estradiol</td>
<td>9.6 mcg/24 hrs</td>
</tr>
<tr>
<td>Estriol</td>
<td>11.5 mcg/24 hrs</td>
</tr>
<tr>
<td>Estrogen Quotient</td>
<td>0.4</td>
</tr>
</tbody>
</table>

### 1992 February
On SSKI 6 drops daily

<table>
<thead>
<tr>
<th>Estrogen</th>
<th>2 mcg/24 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone</td>
<td></td>
</tr>
<tr>
<td>Estradiol</td>
<td>1 mcg/24 hrs</td>
</tr>
<tr>
<td>Estriol</td>
<td>9 mcg/24 hrs</td>
</tr>
<tr>
<td>Estrogen Quotient</td>
<td>3.0</td>
</tr>
</tbody>
</table>

©Jonathan V. Wright, MD, 2018
CASE 2: Post Menopausal, Family History of Estrogen-Related Cancer; no BHRT

### Initial 24-hr Urinary Estrogen Results (August 1985)

<table>
<thead>
<tr>
<th>Estrogen</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone</td>
<td>3 mcg./24 hrs</td>
</tr>
<tr>
<td>Estradiol</td>
<td>16 mcg/24 hrs</td>
</tr>
<tr>
<td>Estriol</td>
<td>1 mcg/24 hrs</td>
</tr>
<tr>
<td>Estrogen Quotient</td>
<td>0.05</td>
</tr>
</tbody>
</table>

### Urinary estrogens after 8 drops (= 50 mgs iodine/iodide) Lugol’s iodine daily (December 1985)

<table>
<thead>
<tr>
<th>Estrogen</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone</td>
<td>8 mcg./24 hrs</td>
</tr>
<tr>
<td>Estradiol</td>
<td>1 mcg./24 hrs</td>
</tr>
<tr>
<td>Estriol</td>
<td>14 mcg/24 hrs</td>
</tr>
<tr>
<td>Estrogen Quotient</td>
<td>1.55</td>
</tr>
</tbody>
</table>
CASE 3: Post Menopausal, Family History of Estrogen-Related Cancer. No BHRT...

March 1993 - Initial 24-hr urinary estrogen results

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone</td>
<td>10 mcg./24 hours</td>
</tr>
<tr>
<td>Estradiol</td>
<td>5 mcg./24 hours</td>
</tr>
<tr>
<td>Estriol</td>
<td>15 mcg./24 hours</td>
</tr>
<tr>
<td>Estrogen Quotient</td>
<td>1.0</td>
</tr>
</tbody>
</table>

September 1993 - Follow-up 24-hr urinary estrogen results after one month using Lugol’s Iodine, 8 drops daily.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone</td>
<td>20 mcg./24 hours</td>
</tr>
<tr>
<td>Estradiol</td>
<td>13 mcg./24 hours</td>
</tr>
<tr>
<td>Estriol</td>
<td>46 mcg./24 hours</td>
</tr>
<tr>
<td>Estrogen Quotient</td>
<td>1.39</td>
</tr>
</tbody>
</table>
Case 4: Fibrocystic Breast Disease, 2+ Fibrocystic Changes Bi-laterally

March 1984 - Initial 24-hr urinary estrogen results after 3 months using Myers iodine.

<table>
<thead>
<tr>
<th></th>
<th>Estrone</th>
<th>Estradiol</th>
<th>Estriol</th>
<th>Estrogen Quotient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone</td>
<td>13 mcg/24 hrs</td>
<td>11 mcg/24 hrs</td>
<td>45 mcg/24 hrs</td>
<td>0.67</td>
</tr>
</tbody>
</table>

April '85 urinary estrogens after switching to Iodo-niacin, 1 tablet daily

<table>
<thead>
<tr>
<th></th>
<th>Estrone</th>
<th>Estradiol</th>
<th>Estriol</th>
<th>Estrogen Quotient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone</td>
<td>13 mcg/24 hrs</td>
<td>2 mcg/24 hrs</td>
<td>10 mcg/24 hrs</td>
<td>0.67</td>
</tr>
</tbody>
</table>

©Jonathan V. Wright, MD, 2018
Case 4: Fibrocystic Breast Disease, 2+ Fibrocystic Changes Bi-laterally

November ‘86 urinary estrogens after increasing to 2 tablets 3 times daily.

<table>
<thead>
<tr>
<th>Estrogen</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone</td>
<td>14 mcg/24 hours</td>
</tr>
<tr>
<td>Estradiol</td>
<td>3 mcg/24 hours</td>
</tr>
<tr>
<td>Estriol</td>
<td>33 mcg/24 hours</td>
</tr>
<tr>
<td>Estrogen Quotient</td>
<td>1.94</td>
</tr>
</tbody>
</table>
Iodine (not Iodide) and Cancer

- Iodine (and iodide) indirectly protects against breast cancer by stimulating estriol synthesis.
- Lack of iodine pre-disposes to precancerous changes.
- Iodine (but not iodide) inhibits neoplastic changes in breast cells and also combines to form iodolactones which kill breast cancer cells.
Breast tissue treated with an iodine blocking agent showed atypia and pleomorphism proportionate to the degree of iodine blockade.

Changes were greatest in thyroxine-treated euthyroid breasts, demonstrating that iodine itself is necessary for normal breast tissue maintenance.

“Iodine deficient breast tissue in rodents and humans demonstrates atypia, dyplasia, and neoplasia, and is more susceptible to carcinogen action which promotes lesions early and in large numbers.”

Iodine Kills Many Breast Cancer Cells

- Iodine induced apoptosis in human breast cancer cell lines MCF-7, MDA-MB-453, ZR-75-1, and T-47D, but not MDA-MB-231.
- Iodine inhibited but did not kill human peripheral blood mono-nuclear cells.
- Iodine treatment activates a caspase-independent and mitochondria-mediated apoptotic pathway.

Iodine Kills Many Breast Cancer Cells

- Non-radiolabeled I(2) and 6-iodo-5-hydroxy-8,11,14-eicosatrienoic acid (6-iodolactone, an iodinated arachidonic acid), **but not KI**, significantly inhibited proliferation of MCF-7 cells.

- In mammary cancer cells, I(2) is taken up by a facilitated diffusion system and then covalently bound to lipids or proteins that, in turn, inhibit proliferation

Iodine Kills Many Breast Cancer Cells

- In animal and human studies, molecular iodine \([I(2)]\) supplementation exerts a suppressive effect on the development and size of neoplasias.

- Iodine is bound into antiproliferative iodolipids termed iodolactones. \(I(2)\) should be considered as an adjuvant in breast cancer therapy.

Aranda N, Sosa et al. *Uptake and antitumoral effects of iodine and 6-iodolactone in differentiated and undifferentiated human prostate cancer cell lines.* Prostate 2012

“Normal and cancerous prostate cells can take up iodine, and depending on the chemical form, it exerts antiproliferative and apoptotic effects both in vitro and in vivo...”
“Twelve human cancer cell lines...one non-malignant cell line...investigated [for] potential antiproliferative/cytotoxic activity of molecular iodine and iodolactones. Except...colon carcinoma cells....growth of all cancer cell lines decreased....in the presence of 10 microM molecular iodine [I(2)] for at least two days. Delta-iodolactone (5 microM) ...[had] a similar effect.”
...neuroblastoma cells...most susceptible to both iodine compounds (total inhibition), followed by MCF-7 mammary carcinoma cells (60%...77.7% inhibition...I(2)...IL)...HS24 lung carcinoma cells (36.3%...40.3% inhibition)...normal mammary epithelial cells...much less affected.
Iodine v Cancer: Safety

Other Thoughts about Breast Cancer Therapy: CBD

- “CBD enhances...the activation of the intrinsic apoptotic pathway in breast cancer cells”
  ✓ Prasad A et al. Cannabidiol induces programmed cell death in breast cancer cells by coordinating the cross-talk between apoptosis and autophagy. Mol Cancer Ther 2011;July 10(7):1161-72
Other Thoughts about Breast Cancer Therapy: MSM

“Methylsulfone introduced structural order, with cancer cell tissue taking on the morphology of normal in vivo breast tissue; this structural order was sustainable over long-term culture....Methyl sulfone re-introduced a normal structural phenotype to human breast cancer tissues.”

BHRT TEST OPTIONS

PROS AND CONS EXPLORED
BHRT Lab Test Review

- Lab Test Review
  - Saliva
  - Serum
  - 24 Hour Urine Collection
  - 24 Hour Urine 4-Point Test
Testing, Saliva

- **Pro**—Measures free estrone, estradiol, estriol progesterone, testosterone, cortisol, and DHEA-S
- **Pro**—Easy collection procedure
- **Pro**—Diurnal pattern of cortisol measured
- **Pro**—*Endogenous* hormones accurately measured
- **Con**—*Exogenous* hormones not accurately measured
- **Con**—“2/16” ratio, 2-methoxyestradiol, 4-OH estrogen, cortisol metabolites, testosterone metabolites, aldosterone, HGH, melatonin, 6-sulfatoxymelatonin, oxytocin, nitrate not measured
“Saliva progesterone levels were very high and variable in the progesterone cream groups compared to the placebo group and presented a paradox to the usual relationship observed between plasma and saliva progesterone in premenopausal women.”

Pro - Direct assessment of circulating hormones.

Pro - Relatively accurate for men or women on or off bio-identical hormone replacement therapy.

Pro - Well established reference ranges, but reference ranges are quite broad.

Pro - Testosterone Metabolites measured.
Testing, Serum

- **Con** - Estriol “half-life” in serum 3 to 64 minutes; measurement not useful.
- **Con** - Free estrone, estradiol, estrone and free progesterone are rarely if ever measured; however free testosterone is often measured.
- **Con** - One time blood draw within 24 hours; comparability of testing problematic, because half-life of topical exogenous hormones is 3-4 hours.
Testing, Urine (24-Hour)

- **Pro** - Measures estrone, estradiol, estriol, EQ, “2/16” OH ratio, 2-methoxyestradiol, 4-OH estrone, pregnanediol (progesterone surrogate) DHEA, Testosterone, androsterone, etiocholanolone, 5α-5β-androstanediol, free and conjugated cortisol/cortisone, cortisol metabolites (α-THF, β-THF, β-THE), 11β-OH androsterone and etiocholanolone, aldosterone.
Testing, Urine (24-Hour)

- **Pro** - Also measures melatonin, 6-sulfa-toxymelatonin HGH, oxytocin, nitrates, sodium/potassium ratio, free T3, free T4.
- **Pro** - Accurate for endogenous hormones and exogenous BHRT.
- **Pro** - Test comparisons accurate; no “timing” issues.
Testing, Urine (24-Hour)

- **Con** - 24-hour urine test completion more cumbersome than saliva, single blood test or 4-point dried urine collections.

- **Con** - Testosterone Metabolites not presently tested.
Testing, Urine (4-Point Dried)

- **Pro** - Measures estrone, estradiol, estriol, EQ, “2/16” OH ratio, 4-OH estrone, pregnanediols (progesterone surrogates) DHEA-S, testosterone, androsterone, etiocholanolone, 5a-5b-androstanediol, epi-testosterone, free cortisol, free cortisone, cortisol metabolites (a-THF, b-THF, b-THE), 6-sulfatoxy-melatonin.

- **Pro** - Less work to collect and mail.

- **Pro** - Diurnal pattern of cortisol.
Testing, Urine (4-Point Dried)

- **Con** - Conjugated cortisol and cortisone *not measured*; these are important components of total cortisol/cortisone excretion.
- **Con** – 2-methoxyestradiol often *not measured*
- **Con** - HGH, oxytocin, melatonin, free T3, free T4, nitrate, sodium/potassium ratio *not measured.*
Testing, Urine (4-Point Dried)

- **Con** - Timing of hormone application and collection of 4 urine specimens must be exactly the same for accurate comparison of initial and repeat tests.

- **Con** - Testosterone Metabolites not presently tested.
“BONUS” INFO TO INVESTIGATE AS TIME ALLOWS!

The Real Origin of Bio-Identical Hormone Replacement Therapy
Proto-Endocrinology
1025 AD - 1833 AD:

- Describes in detail therapeutic preparations and uses of hormones from urine (ch’hiu shih).
- Many processes used saponin precipitation, which separates steroids from other solutes.

Excellent, remarkably complete 4-page summary of Needham and Lu’s material to be found in: Temple, Robert, *The Genius of China*, pages 127-130.

As of 7th September 2018
388 copies available,
$1 and up (plus shipping)
@ www.usedbooksearch.co.uk

Aranda N, Sosa et al. *Uptake and antitumoral effects of iodine and 6-iodolactone in differentiated and undifferentiated human prostate cancer cell lines.* Prostate 2012


Anguiano, B, Garci´a-Solís B, et al. *Uptake and Gene Expression with Antitumoral Doses of Iodine in Thyroid and Mammary Gland: Evidence That Chronic Administration Has No Harmful Effects Thyroid* 2007:17(9)


- Prasad A et al. *Cannabidiol induces programmed cell death in breast cancer cells by coordinating the cross-talk between apoptosis and autophagy.* Mol Cancer Ther 2011;July 10(7):1161-72


THE END

Thank You For Attending!