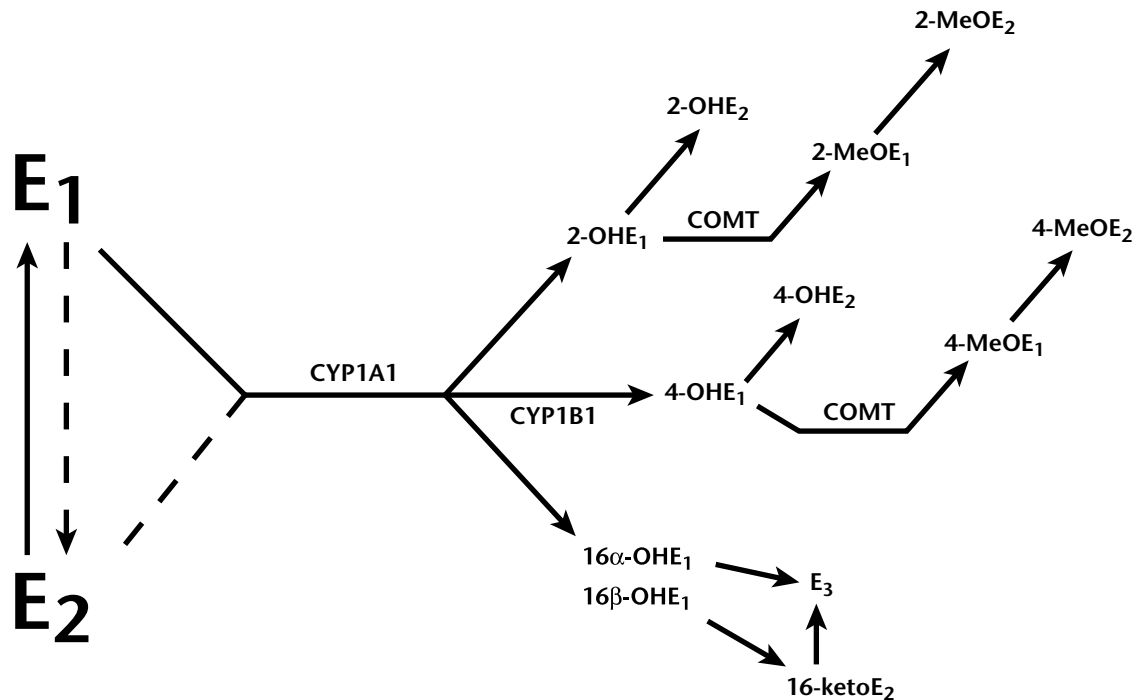


Spotlight on Estrogen and Lowering Breast Cancer Risk  
 Metamatrix Teleconference Series  
 10/05/07 1pm EST  
 Presented by  
 Dr. Kara Fitzgerald and Cass Nelson-Dooley, MS

- 2007 statistics on breast cancer risk and incidence
- Risks associated with the development of breast and other estrogen-sensitive cancers
- Risk reduction- interventions and prevention
- Laboratory evaluation for risk reduction
- Estronex Test (2 hydroxyestrogens:16 hydroxyestrone )
  - What is it?
  - Basics in estrogen metabolism (see figure below)
  - Research behind modulation of estrogen metabolism
  - Factors that modify 2OHE
  - Factors that modify 16OHE1
  - Phase II Methylation, sulfation and glucuronidation
  - 2:16 ratio in men
  - Specimen collection, preparation, timing
  - Case studies & questions



## Case 1. Series of Estronex Tests to Decrease Breast Cancer Risk

### Summary:

A series of 5 tests over a year show how a 31-year-old woman can detect her estrogen metabolic status and make dietary modifications to reduce cancer risk.

### History:

A healthy 31 year-old female, Jen, presents for evaluation of estrogen metabolism to rule out a risk factor for breast cancer. Patient is currently on OCP, nutritional supplementation, including multiple vitamins and minerals, B complex, essential fatty acids (EFA) and vitamin E. She has no history of breast cancer in the family.

### Description of Results:

Jen's baseline ratio was significantly low, at which point she started on a DIM supplement 75 mg BID, increased cruciferous vegetables, flax, soy, and EFA consumption and retested after 4 months.

Repeat testing showed a lowered ratio. It was recommended that she increase the DIM to 150 mg BID and retest in 3 months. At this time the ratio improved to low normal. The patient then switched to a different formulation of DIM (100 mg) complexed with Vit C, E, B6, B12, Folate, NAC, Bioflavonoids, and Calcium-d-glucarate, BID.

Repeat testing 2 months later showed minimal increase in Jen's 2/16 ratio. However, after another 2 months of following the same regimen her ratio improved more significantly.

### Recommendations:

Continue DIM at current dose and repeat test in 6 months to determine whether dose reduction would be appropriate. Continue to include flax seed, EFAs, and soy foods.

### Other Comments:

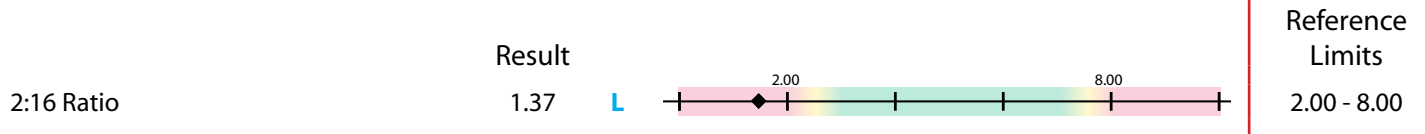
It appears in this case that time and formulation of DIM may have an impact on effectiveness of supplementation. DIM in combination with other hormonally supportive and cancer protective nutrients may have a more positive and profound effect on estrogen metabolism.

Lab Data

Figure 1

**0142 Estronex™ - 2/16 OH Estrogen Ratio in Urine**

Methodology: Enzyme Immunoassay, Colormetric Assay



	Result	Normal Limits		
		Pre-Menopausal	Post-Menopausal without hormone therapy	Post-Menopausal with hormone therapy
2-Hydroxyestrogens (2OHE)	8.6	3 - 40	2 - 10	10 - 75
16-Hydroxyestrone (16OHE1)	6.3	3 - 30	2 - 8	5 - 25

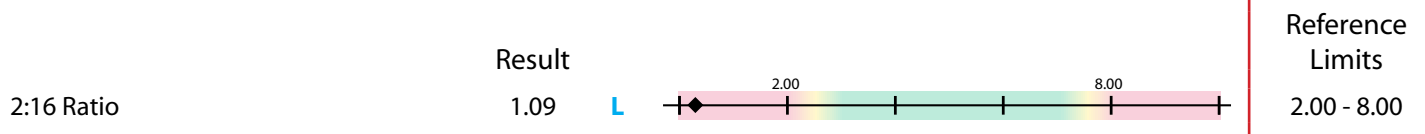
Creatinine = 71 mg/dl



Figure 2

**0142 Estronex™ - 2/16 OH Estrogen Ratio in Urine**

Methodology: Enzyme Immunoassay, Colormetric Assay



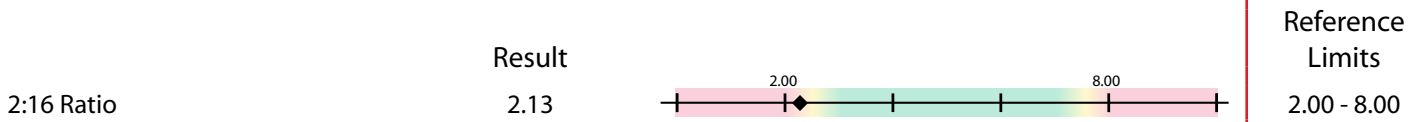
	Result	Normal Limits		
		Pre-Menopausal	Post-Menopausal without hormone therapy	Post-Menopausal with hormone therapy
2-Hydroxyestrogens (2OHE)	10.3	3 - 40	2 - 10	10 - 75
16-Hydroxyestrone (16OHE1)	9.5	3 - 30	2 - 8	5 - 25

Creatinine = 41 mg/dl

Figure 3

**0142 Estronex™ - 2/16 OH Estrogen Ratio in Urine**

Methodology: Enzyme Immunoassay, Colormetric Assay



	Result	Normal Limits		
		Pre-Menopausal	Post-Menopausal without hormone therapy	Post-Menopausal with hormone therapy
2-Hydroxyestrogens (2OHE)	11.5	3 - 40	2 - 10	10 - 75
16-Hydroxyestrone (16OHE1)	5.4	3 - 30	2 - 8	5 - 25

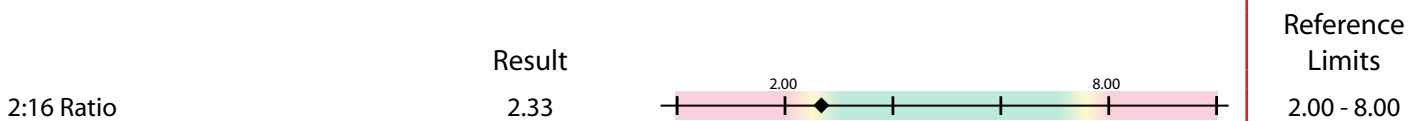
Creatinine = 50 mg/dl



Figure 4

**0142 Estronex™ - 2/16 OH Estrogen Ratio in Urine**

Methodology: Enzyme Immunoassay, Colormetric Assay



	Result	Normal Limits		
		Pre-Menopausal	Post-Menopausal without hormone therapy	Post-Menopausal with hormone therapy
2-Hydroxyestrogens (2OHE)	13.1	3 - 40	2 - 10	10 - 75
16-Hydroxyestrone (16OHE1)	5.6	3 - 30	2 - 8	5 - 25

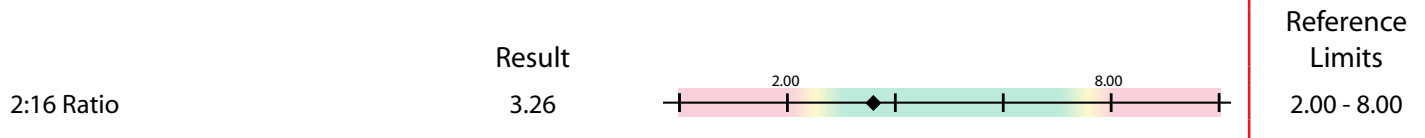
Creatinine = 52 mg/dl



Figure 5

**0142 Estronex™ - 2/16 OH Estrogen Ratio in Urine**

Methodology: Enzyme Immunoassay, Colormetric Assay



	Result	Normal Limits		
		Pre-Menopausal	Post-Menopausal without hormone therapy	Post-Menopausal with hormone therapy
2-Hydroxyestrogens (2OHE)	37.7	3 - 40	2 - 10	10 - 75
16-Hydroxyestrone (16OHE1)	11.5	3 - 30	2 - 8	5 - 25

Creatinine = 30 mg/dl



## Case 2. Estronex Tests with Breast Cancer Treatment, Letrozole

Pam, a 60-year-old female, was diagnosed with breast cancer in August 2004. She underwent lumpectomy and radiation. She was started on letrozole (Femara) February 2005 and was on Femara throughout testing. Femara is a competitive inhibitor of the aromatase enzyme system, the enzyme responsible for conversion of androgens to estrogens. Letrozole is used to reduce estrogen biosynthesis in all tissues and in the tumor itself. Letrozole lowers serum estrone, estradiol, and estrone sulfate.

Test Results: The first Estronex Profile shows that Pam has a low total estrogen and low 2:16 ratio. This fits with aromatase inhibition. Pam's follow-up results 4 months later show a high total estrogen, a high 2:16 ratio, and her 2OHE is very high for the post-menopausal without hormone therapy category. Her third Estronex test showed a decreased 2OHE, but it was still elevated for its respective range. The 2:16 ratio is high.

Treatment: After 2nd test, the clinician treated her with flax, DIM, fish oil, cruciferous vegetables, and vitamin D.

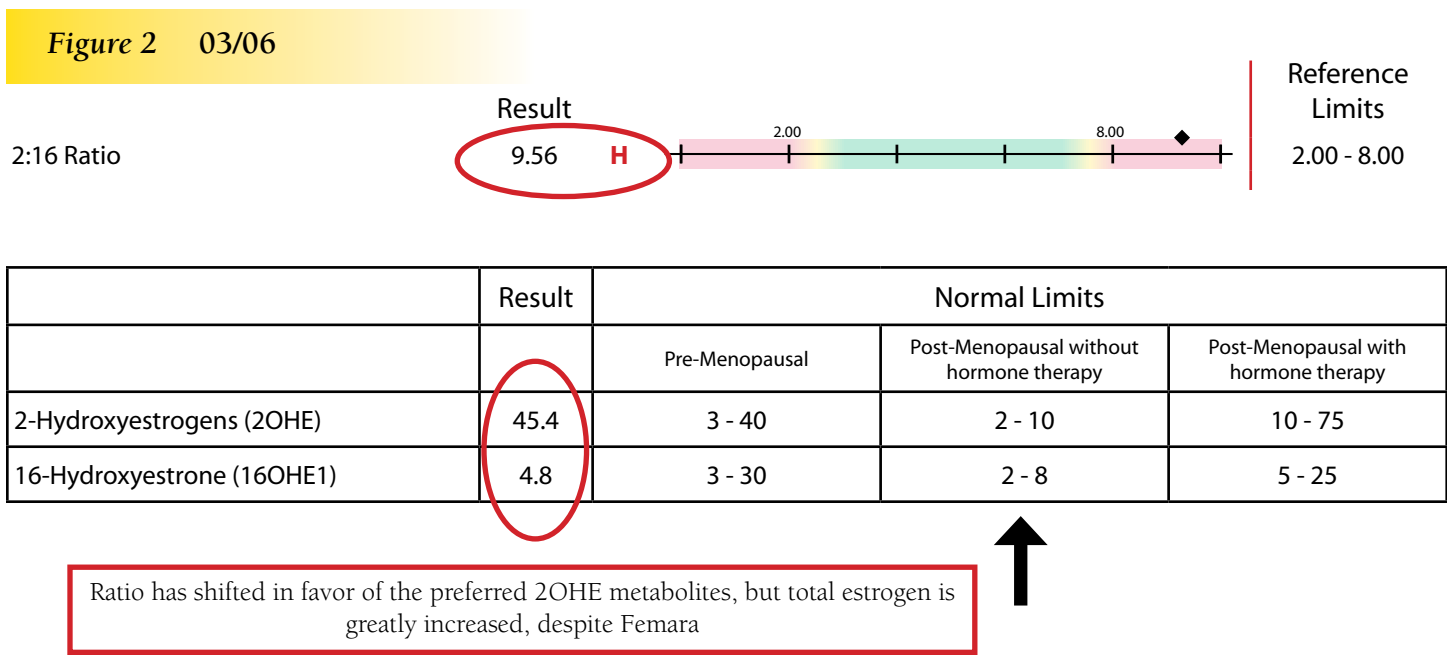
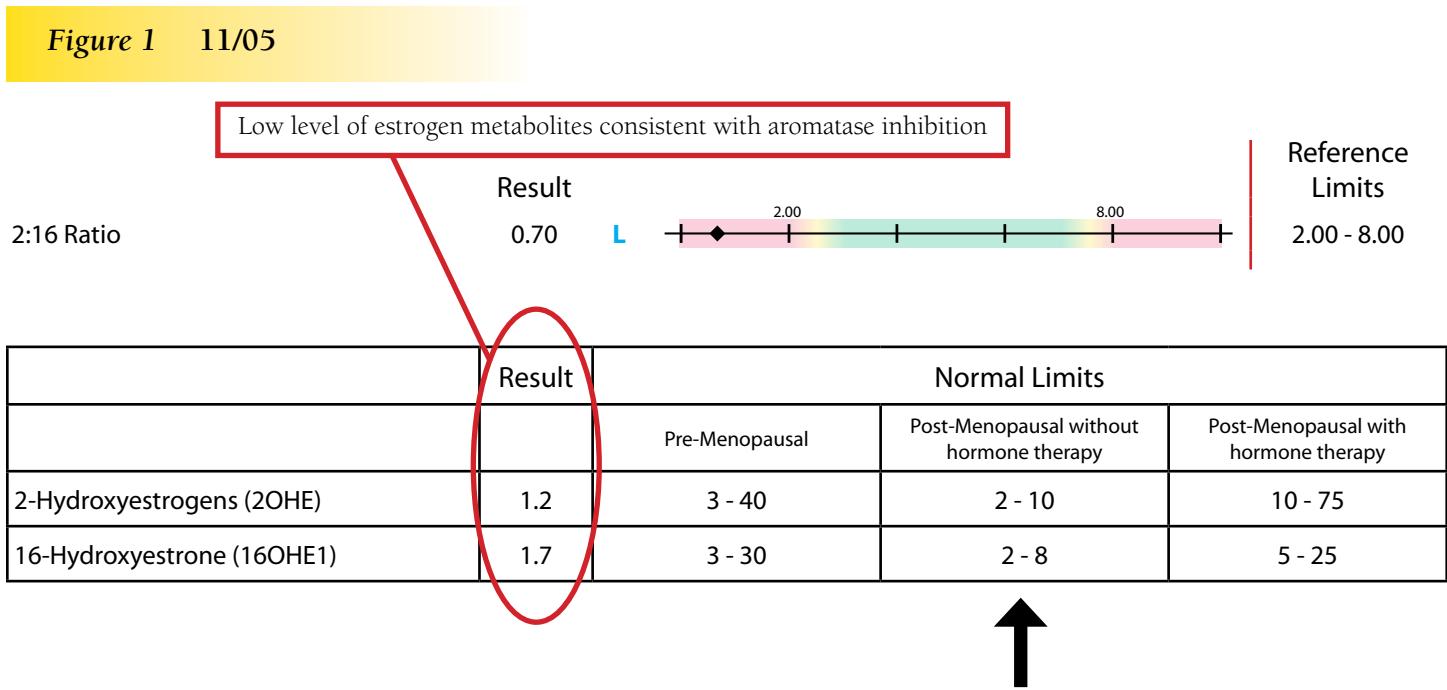
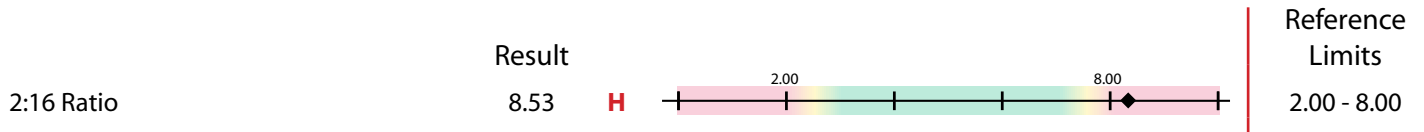


Figure 3 07/06



	Result	Normal Limits		
		Pre-Menopausal	Post-Menopausal without hormone therapy	Post-Menopausal with hormone therapy
2-Hydroxyestrogens (2OHE)	21.6	3 - 40	2 - 10	10 - 75
16-Hydroxyestrone (16OHE1)	2.5	3 - 30	2 - 8	5 - 25

Ratio is improved, but total urinary estrogen metabolites continue to be elevated.

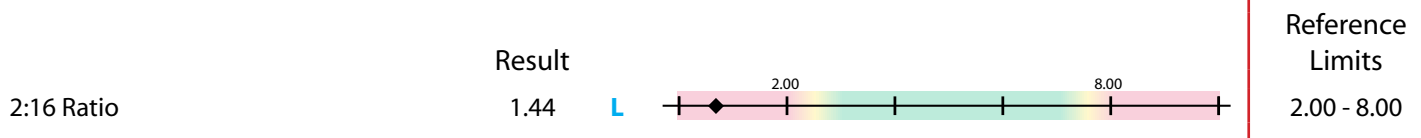


### Case 3. Peri-menopausal Female with Family History of Cancer

Carla is a peri-menopausal, 53-year-old female and has a family history of cancer. She has menorrhagia and had a small fibroid for 5-10 years. Three months ago she found a lump in her left breast and was diagnosed with infiltrating ductal carcinoma at which time she had a partial mastectomy. She completed 20 radiation treatments and started Tamoxifen 20 mg/d after collecting urine for the Estronex test. Tamoxifen shows antiestrogenic properties and may compete with estrogen for binding sites in tissues. She took DIM (100-200 mg/d) regularly for 3 years to help with menorrhagia. She took it sporadically during the last year and switched to I3C (300 mg/d) after this test. She eats a diet high in vegetables and fruits with mainly fish and free range chicken. Other supplements: Spirulina, barley grass, whey protein shakes, fish oil, flaxseed fiber, green tea, ginkgo, hawthorne, and garlic.

#### 0142 Estronex™ - 2/16 OH Estrogen Ratio in Urine

Methodology: Enzyme Immunoassay, Colormetric Assay



	Result	Normal Limits		
		Pre-Menopausal	Post-Menopausal without hormone therapy	Post-Menopausal with hormone therapy
2-Hydroxyestrogens (2OHE)	87.8	3 - 40	2 - 10	10 - 75
16-Hydroxyestrone (16OHE1)	60.8	3 - 30	2 - 8	5 - 25

Creatinine = 55 mg/dl



Family: Her mother had pre-menopausal breast cancer, her sister had post-menopausal breast cancer, and her aunt and grandmother on her mother's side had breast cancer. Three of her sisters had hysterectomies as well as her mother for heavy bleeding and fibroids.

Test Results: The patient is peri-menopausal and her 2OHE and 16OHE1 are higher than their respective ranges. The high estrogen output may reveal an origin of the familial occurrence of breast cancer. Further, her 2OHE is only 1.44 times greater than her 16OHE1. The goal is to have 2OHE 2-8 times greater than 16OHE1.

Treatment: The patient's 2:16 ratio is low and further treatments are indicated to increase 2OHE and decrease 16OHE1 especially because risk of breast cancer recurrence can be significantly lowered by achieving a higher 2:16 ratio. Treatment interventions include cruciferous vegetables, I3C or DIM, soy isoflavones, flax seeds, and omega 3 fatty acids. Because the individual estrogen metabolites are so high for her category, she should do intensive gut and liver support so that she can effectively clear estrogen. She is on a good protocol (fish, fish oil, no grain-fed beef) and may want to increase fish oil further with antioxidants (based on fatty acid test results, preferably).

Other testing to consider: full urine hormone panel, dysbiosis and liver function tests, frequent follow-up Estronex profiles, fatty acids, and toxic elements.