

Laboratory evaluation of estrogen metabolism - Estrogen Metabolism

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Higher levels of [estradiol \(E2\)](#), and especially [estrone \(E1\)](#), in serum and urine have been consistently associated with a moderately elevated risk of [breast cancer](#). There is some evidence that higher levels of [estriol \(E3\)](#) are associated with a reduced risk of breast cancer. Higher values for the estrogen quotient (E3/E1 E2) have been associated with a reduced risk of breast cancer in some, but not all studies. Many women are seeking alternatives to HRT comprised of conjugated equine estrogens. Popular alternatives include [estriol](#) alone or in combination with other natural estrogens. Thus further research on the roles of [estriol](#) and the estrogen quotient in assessing breast cancer risk are urgently needed.

Laboratory monitoring of HRT has provided a number of useful insights, which may help healthcare practitioners to individualize dosing to achieve the minimum [estrogen](#) exposure consistent with symptom relief.

Recommended estrogen doses for HRT have been reduced dramatically during the last decade.

Studies of [estrogen metabolites](#) show that some are highly toxic, mutagenic, and procarcinogenic; others strongly stimulate cell proliferation, still others are only weakly estrogenic, and some even have anticancer activity.

The 2/16 estrogen metabolite ratio test has a compelling rationale and very promising preliminary data. This test gives a ratio of "good" to "bad" estrogens in urine. Higher values are associated with a reduced risk of breast cancer in premenopausal Caucasian women. However, data from studies of post-menopausal women do not show the same pattern. The 2/16 estrogen metabolite ratio varies from one ethnic group to another, and some lower-risk groups actually have lower, rather than the expected higher ratios, when compared to high-risk groups.

The area of greatest current research interest concerns toxic and mutagenic 4-hydroxyestrogen metabolites, which are produced by the enzyme CYP1B1. Women with the high activity polymorphism for CYP1B1, who produce excessive 4-hydroxyestrogens, are at increased risk for several [estrogen-related cancers](#). Studies of malignant tissues also demonstrate excess 4-hydroxyestrogens. Laboratory studies suggest that the toxicity of 4-hydroxyestrogens can be mitigated to some extent by antioxidant supplementation. Tests for CYP1B1 polymorphisms are not currently routinely available, but may provide a valuable screen for persons at high risk for estrogen-related cancers.

Estrogen-related cancers are thought to result from multiple genetic and environmental factors. Thus all of the tests discussed are probabilistic in nature. They provide information on relative risks, but cannot give "yes or no" answers. In the future, use of several of the tests discussed in this review in combination may improve our ability to estimate cancer risk.

Table 1 - Influence of Route of Administration on Urinary Estrogen Profiles

Transdermal

	Premenopausal Normal range (Luteal phase)	Patient 1 TriEst cream 2.5 mg/day	Patient 2 TriEst cream 5mg/day
Estrone	3-52	33	30
Estradiol	1-27	17	23
Estriol	9-60	165	366
Estrogen Quotient	>1.0 desirable	33	7

Oral

	Patient 3 TriEst oral 3 mg/day	Patient 4 TriEst oral 2.5 mg/day
Estrone	88	81
Estradiol	37	24
Estriol	1264	935
Estrogen Quotient	10.2	8.9

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