

BREAST PROLIFERATION INDEX (BPI)**Explanation:**

Several reproductive hormones exert trophic effects on the breast tissue i.e. cellular division and differentiation. **Unchecked trophic stimulation can lead to undesired proliferation of the tissue.** Over time, breast cysts, hyperplasia and lesions are promoted. Estradiol (**E2**), Estrone (**E1**) and Estriol (**E3**) in descending order of potency exert proliferative influences on breast tissue. **Progesterone also exerts a proliferative influence with increasing concentration.** On the other hand, testosterone, in the normal to mildly hyper-physiologic range, **exerts a significant estrogen antagonizing and anti-proliferative effect which modulates and reduces estrogenic proliferative effects.**

Note:

Chronic exposure to high concentration of proliferative hormones is usually required to promote the initial proliferative stages of estrogen-sensitive lesions. However, the maintenance of the lesions **may not require high concentrations** of proliferative hormones. This phenomenon explains the difficulties and prolonged time required to reverse tissue proliferation that has already taken place.

What does the BPI Index mean?

The **BPI** is a graphical comparison of the proliferative and anti-proliferative hormone activity of the patient. The combined proliferative activity of the three estrogens plus the concentration-dependent contribution of **progesterone** is represented on the **horizontal graph axis (X-axis)**. The **testosterone** anti-proliferative activity is represented on the **vertical axis (Y-axis)**.

The **BPI** graphic grid has 8 distinct numbered zones with an explanatory key below the graph. The patient values of E1, E2, E3, progesterone and testosterone are used to calculate indices and plotted as a solid square that appears one of the numbered zones.

UTERINE PROLIFERATION INDEX (UPI)**Explanation:**

It is established that estrogens including Estradiol (**E2**), Estrone (**E1**) and Estriol (**E3**) in descending order of potency can **induce proliferative changes in the endometrium** at any age. Endometrial hyperplasia with rapid blood vessel formation is one of the major outcomes of estrogen hormone replacement therapy in postmenopausal women. On its own, the estrogen proliferative effect is additive and cumulative over time and is manifested clinically as breakthrough bleeding. Estrogens help organize and capacitate the endometrial cells to respond to progesterone-mediated functionalization with view of constructing an embryo-receptive lining.

Progesterone helps transform the rapidly growing cells into mature ones. It prevents the endometrium from rapidly outgrowing its developing blood supply. Progesterone inhibits uncontrolled endometrial cell growth that otherwise would lead to proliferative lesions.

What does the UPI Index mean?

The **UPI** is a graphical comparison of the correlation between the proliferative hormone activity (Measured Estrogenic Activity-EA) and the Anti-proliferative activity (Measured Progesterone levels). The EA takes into account the genomic and non-genomic proliferative activity of the three main estrogens. The EA is represented on the **horizontal axis (X-axis)**. The progesterone anti-proliferative activity is represented on the **vertical axis (Y-axis)**.

The **UPI** graphic grid has 8 distinct numbered zones with an explanatory key below the graph. The patient values of E1, E2, E3 and progesterone are used to calculate the indices and appear as a solid square in one of the numbered zones.

Why Choose Grid Analysis over Hormone Ratios?

Proper hormone balance is not achieved at all concentrations. It is only achieved within matched physiologic concentration ranges of the respective hormones. The use of arithmetic ratios of sex hormone concentrations for the purpose of reference range analysis, as used by other laboratories, is usually deceiving. The absolute concentrations of the hormones are extremely important and are not included in arithmetic ratio analysis.

For more accuracy in interpretation, a two dimensional **Grid Analysis Method** is used in this report. **The following example** will illustrate the inadequacy of the arithmetic ratio method. At high concentrations of the respective hormones (**Zone 3** in the **BPI**, and **Zone 1** in the **UPI**), you may have a perfect arithmetic ratio between the estrogens and testosterone which other labs consider normal. However, the following adaptive processes may come into play:

- I. At high hormone concentrations, receptor saturation takes place blocking the binding of hormone to receptors. This may lead to unpredictable or paradoxical effects.
- II. At high hormone concentrations there is receptor confusion, i.e. one hormone cross-reacts non-specifically with the receptors of another leading to unpredictable effects.
- III. At high concentrations certain hormones inhibit the synthesis of other antagonistic hormones, or promote the production of synergistic ones.