

**September 2018**

### **Accuracy of Serum Estradiol Levels in Era of Aromatase Inhibitor Adjuvant Therapy**

Accurate measurement of serum estradiol in the era of aromatase inhibitor therapy can be challenging. Hormonal suppression in estrogen or progesterone receptor (ER or PR) positive breast cancer has been associated with significant benefits including decreased local and distant recurrences, lower risk of contralateral breast cancer, and improved breast cancer specific mortality. Adjuvant therapy with hormone suppressing drugs is therefore standard of care in patient with ER/PR positive breast cancer. Drugs such as tamoxifen were developed in 1970s and classified as selective estrogen receptor modulators (SERM) because of tissue specific ER activity. For example, in breast tissue tamoxifen acts as an ER antagonist, whereas in bones it stimulates ER as agonist. Similar ER agonistic activity in uterine tissue is reported to cause hyperplasia and increased polyp production, resulting in high risk of uterine cancer in patients receiving tamoxifen therapy.

The second class of drugs used as adjuvant therapy in ER/PR positive breast cancer are aromatase inhibitors (AI). In post menopausal women, the primary source of estrogen is adipose tissue, where the enzyme aromatase converts testosterone and androstenedione into estradiol (E2) and the weaker estrogen, estrone, respectively. AIs have been shown to reduce 5-year relapse rates with improved side effect profiles as compared to tamoxifen. The third generation AIs suppress aromatase activity by 90-99%, resulting in decreased circulating estrogen levels of 1% to 10% compared to pretreatment levels. Periodic

evaluation of serum estrogen/estradiol levels may be necessary for optimal care.

Historically, the quantitative methods used for measurement of serum estradiol have included bioassay, mass spectrometry (MS), UV absorbance, and immunoassays, of which only MS and immunoassays were considered to have the attributes necessary for clinical application. MS based methods for measurement of estradiol, although considered "gold standard" are very complex and have a low throughput for routine clinical use. Earlier immunoassays were similarly complex and consisted of extraction of serum. Newer immunological methods are "direct" and do not require a prior extraction step resulting in greater automation and high throughput.

Currently, for hospital settings, 28 different immunoassay platforms offered by eight companies are available for serum estradiol testing. While these tests are cost effective and less labor intensive, the sensitivity at lower serum estradiol concentrations is poor, for example, in elderly or post-menopausal women where the serum estradiol levels are commonly below 5pg/mL. Secondly, the removal of an extraction step prior to analysis has resulted in decreased test specificity, which is one of the main contributing factors to falsely high levels in breast cancer patients treated with AIs. Mechanistically, these drugs result in formation of estradiol metabolites that potentially cross-react with the antibodies present in the assay causing falsely high serum estradiol levels.

At Saint Luke's Hospital, the serum estradiol test offered is an immunoassay with appropriate reference ranges depending on the phase of menstrual cycle and menopausal

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status. It is available Monday through Sunday and the specimen requirement is 2 mL serum or plasma (plain red top, serum gel tube, or green top tube). For accurate determination of serum estradiol in patients on AI adjuvant therapy, send out testing to a reference laboratory using MS based methods is preferred. The test can be requested through EPIC by completing the “MISC LABORATORY TESTING” requisition.

Saint Luke’s Laboratories offer a variety of test options for detection of influenza and RSV. Rapid antigen testing is performed by all testing sites. The major disadvantage of rapid antigen testing is low sensitivity of 60-80%. Sensitivity of rapid influenza antigen tests is variable from season to season, depending on the predominant strain. Likewise, RSV antigen testing has poor sensitivity in adults, compared to children.

### **Respiratory Season 2018-19**

The Center for Disease Control and Prevention (CDC) classified the winter of 2017-18 as a high-severity, influenza A type H3N2-predominant season. Likewise, reported influenza-like illnesses were at or above baseline for nineteen weeks, resulting in one of the longest flu seasons in recent years. During the winter months, multiple non-influenza respiratory viruses were circulating as well. A tally of results from respiratory virus panels performed by Saint Luke’s Microbiology from January 1 through March 31, 2018 show that RSV (respiratory syncytial virus) detection was frequent, and the second most common virus detected after influenza. The majority of RSV infections occurred in elderly patients. Coronavirus and human metapneumovirus were third & fourth most common, respectively.

New this season, a combination influenza A/B PCR is now available on-site at Saint Luke’s East, Saint Luke’s North, and Saint Luke’s South as well as through the central Microbiology laboratory at Saint Luke’s Hospital. RSV PCR testing is available at these test sites as well, and can be ordered separately from, or in combination with Flu PCR. Inpatients with negative rapid influenza antigen test results should have Flu PCR testing performed prior to discontinuing appropriate isolation precautions. Combination testing for influenza and RSV should be considered for either children or elderly patients.

A multi-organism respiratory PCR panel is performed by Saint Luke’s Microbiology as well on both upper and lower respiratory specimens. Optimal utilization of the multi-organism panel is for severely ill, immunocompromised, or transplant patients.

<b>Test Name</b>	<b>Detects</b>	<b>Specimen types</b>	<b>Transport</b>
Flu AB Ag	Influenza A & B	NP/nasal swab Nasal wash	Flocked swab in UTM or M6 Flocked swab in saline Eswab in Amies
Flu PCR	Influenza A & B	NP/nasal swab	Flocked swab in UTM
Flu RSV PCR	Influenza A, B, & RSV	NP/nasal swab	Flocked swab in UTM
Respiratory Panel PCR	7 respiratory viruses, Bordetella, Mycoplasma, Chlamydomphila	NP/nasal swab Nasal wash Bronchoscopy wash/lavage	Flocked swab in UTM or M6

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