Eastern
HEALTH

BRIEFING NOTE – ER/PR RECEPTORS

Background:

May 11, 2005: Dr. Joy McCarthy, Oncologist, contacted Dr. Don Cook, Chief of Laboratory Medicine, to retest a patient who previously tested negative for Estrogen (ER) and Progesterone Receptors (PR) in 2002. Using new technology for immunoperoxidase staining installed at the General Hospital Histology Lab in April of 2004, this woman's sample was retested and discovered to be positive for ER and PR.

Until April of 2004, the Dako testing technique was used in the laboratories. This technique required the manual boiling of tissue and measuring of minute mixtures of immunioperoxidase staining. The Dako test was implemented in 1997 to replace a bioassay method for ER/PR receptors.

The Ventana method (installed in April 2004) automates this process removing as much manipulation as possible. In addition, all re-agents used on the Ventana system are quality controlled by the company and arrive in the laboratory as "ready for use."

The Health Care Corporation of St. John's was one of the earliest laboratories to obtain the Ventana system and switch to an automated system.

When a breast cancer tumor is removed from the body, tests are used to determine if the cancer cells have estrogen or progesterone receptors. The more estrogen receptors present on those cells, the more likely that anti-estrogen therapy such as tamoxifen will work against a particular cancer. Breast cancer patients with high level hormone receptors have a slightly better prognosis than those without receptors.

Literature suggests about 50 – 85 per cent of breast cancers are estrogen–receptor–positive (or "ER-positive"), "positive" meaning that a significant number of cancer cells have receptors present. When a cancer shows few if any estrogen receptors (when it is "ER-negative"), anti-estrogen therapy is not as effective. But anti-estrogen therapy may also be useful in cases where progesterone receptors are present ("PR-positive"). Women whose cancers are PR-positive but ER-negative may still respond to anti-estrogen therapy. A high percentage of tumours with estrogen receptors may regress after hormonal manipulation whereas only a small number (about 5 per cent) of those that are negative respond.

May 17, 2005: Representatives from the Laboratory Program met with Drs. McCarthy and Kara Laing to discuss this new result and a decision was made to retest five more negative patients, who all retested positive. These patients were selected by the oncologists. It was decided to retest all negative results from 2002 to determine if these were isolated cases or symptomatic of a bigger issue. Specimens collected from 25 women, initially tested as negative in 2002, were retested. 16 of these came back positive. Testing on 33 more patients found 25 converted to positive. Twelve of these patients have been informed by their oncologists.

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June 13, 2005: Dr. Cook wrote to all Laboratory directors in the province to return all negative ER and PR specimens for the year 2002 for retesting on the new, more sensitive Ventana system.

July 14, 2005: The decision was made that all patients who were ER and PR negative from 1997-2004 would be retested, beginning with the 2002 patients, with testing to take place over the next number of weeks.

July 15, 2005: Dr. Cook spoke to four of the six provincial laboratory directors (two others were unreachable due to holidays) regarding sending specimens into St. John's for retesting. They said they will comply with the request as soon as possible.

July 18, 2005: Laboratory managers in St. John's began reviewing the statistical data for 2000-2004 to see if there are any inconsistencies in the findings of positive conversions or if this could just be a matter of the sensitivity of the Ventana system being more accurate with its findings.

July 20, 2005: Upon review of the statistical data is has been concluded that the positivity rates are, while on the low end of the scale, within acceptable range. Total positivity numbers for 2000 are 62 per cent; 2001 - 77 per cent; 2002 - 68 per cent; 2003 - 83 per cent and 2004/05 (after a full year with the Ventana system) - 90 per cent.

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Actions:

Considering the 50-85 per cent acceptable range in standard text books and Mount Sinai's standard of around 70-80 per cent, this also reconfirms that our numbers are legitimate. Regardless, the laboratory is still going ahead with retesting the specimens and officials will meet with the oncologists to see how they would like to proceed with informing patients of their conversion and possible change in treatment.

Extra resources have been identified within the HCCSJ lab to undertake identification and retesting. The list of patients will be double-checked with the names on the Cancer Registry to ensure none have been missed.

We do expect improved accuracy on retesting due to the sensitivity of the newer equipment.

As a precautionary measure and to back-up the validity of the new technology, the current testing standards (Ventana system) are being assessed by cross-referencing our results with another laboratory. (Mount Sinai)

A technology consultant from Mount Sinai will be reviewing our laboratory to assess the immunoperoxidase system. At that time we will ask the consultant his/her opinion of the past several years' results under the Dako methodology and for advice on the future direction of the immuno service.

HIROC have been contacted to determine if they are aware of any other issues with the Dako testing system and other hospitals are being contacted to see if there had been any inconsistencies reported with the DAKO system.

It is important to note that processes used by HCCSJ technicians were outlined in the Dako procedure manual. Also, as part of the protocol for testing, positive controls were conducted on the Dako system everyday, as part of the quality assurance process within the lab. The results were read and documented daily by a pathologist.

Eastern Health Vice President of Quality, Diagnostic and Medical Services Dr. Robert Williams has also asked that an investigation be conducted into the five-week stoppage of immunoperoxidase staining for ER/PR receptors in 2003 by Dr. Ejeckam.

Dr. Williams has also asked if we could repeat any of the negative tested specimens again on the "old" Dako system to confirm that it was indeed the system and not a lab error. Terry Gulliver, HCCSJ Laboratory Program Director says it is unlikely we would be able to obtain such a system at this time to retest on that method.