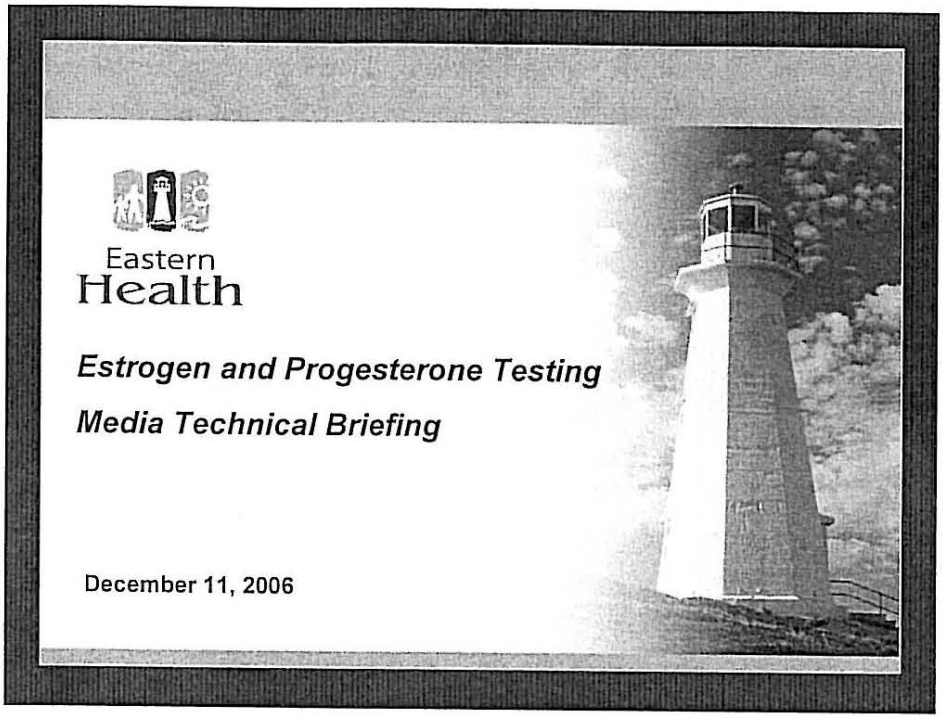
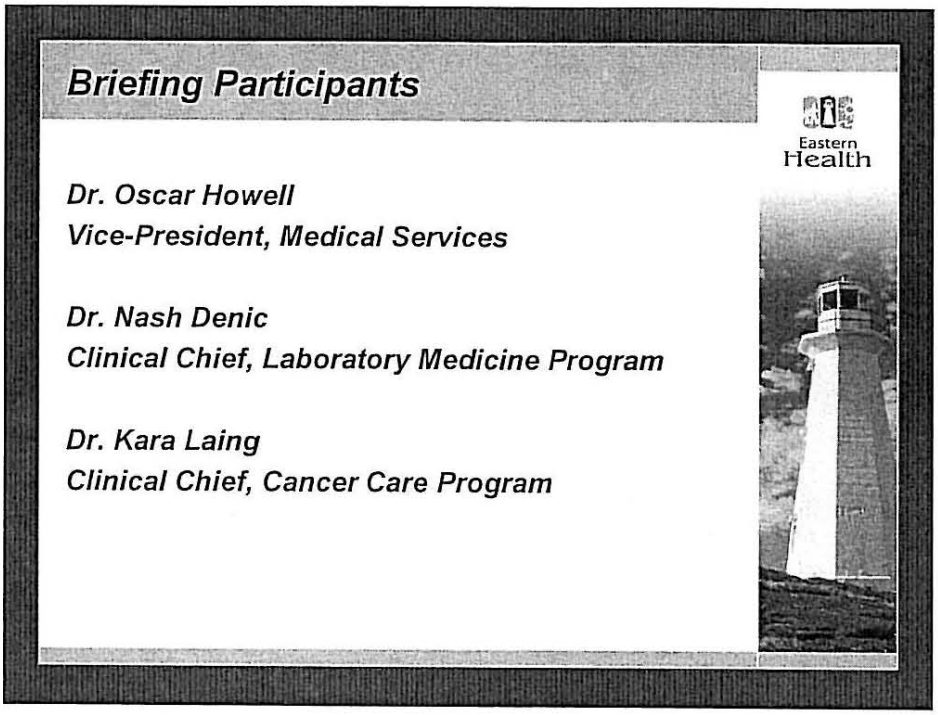


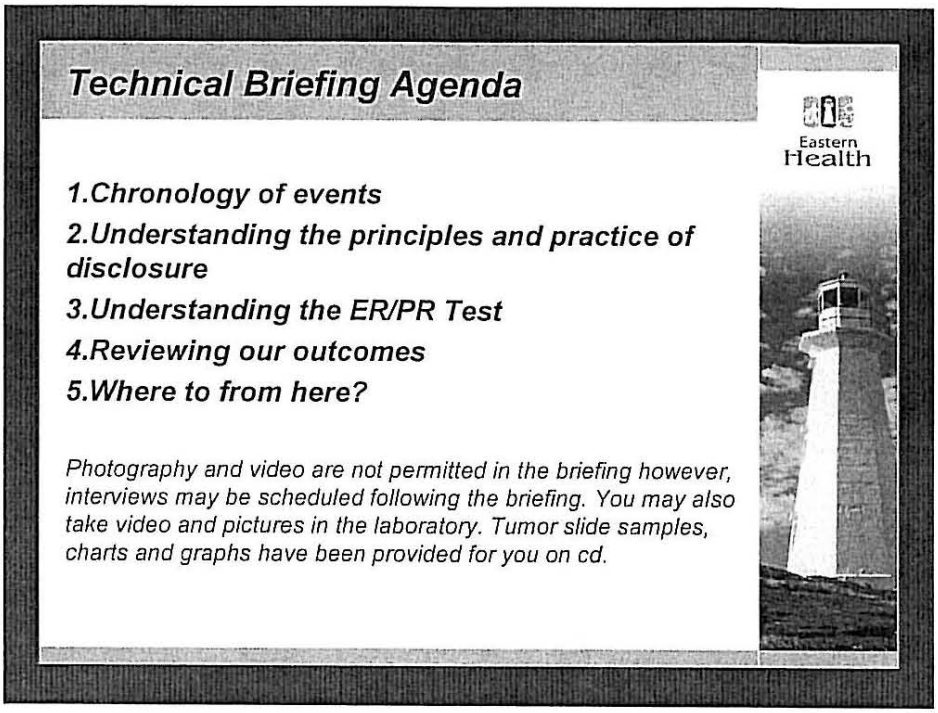
OSCAR

- As you are aware, the organization is facing a class action lawsuit related to the ER/PR testing review. Because of this, we are unable to address some of the circumstances around this case.
- Normally, we would not speak publicly when an issue is before the courts; in this case, we feel we have an obligation to assure the public that we take this matter very seriously and that, despite the length of the review, we have been working diligently to move this process as quickly as possible.
- Our first priority has always been to our patients. The reason for the review in the first place was that we became aware of a potential to improve the care we provide to our patients by offering them a possible treatment opportunity.
- To date, this has been our focus.
- We also hope that, by talking to you today we can assure the public that they can have faith in the expertise, dedication and commitment of our staff and physicians to providing quality care, especially through our laboratory.

- *Encourage reporters to ask questions as you go along rather than leave them to the end. Session will end with a tour of laboratory for those who want it.*


Briefing Participants
Eastern Health
Dr. Oscar Howell
Vice-President, Medical Services
Dr. Nash Denic
Clinical Chief, Laboratory Medicine Program
Dr. Kara Laing
Clinical Chief, Cancer Care Program

OSCAR



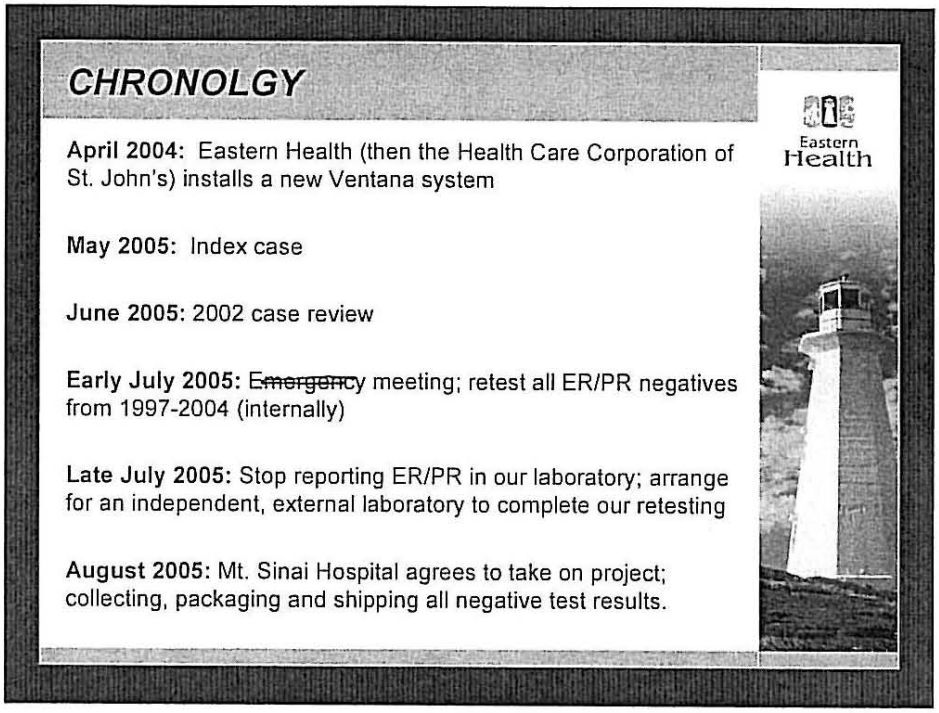
OSCAR:

Go over agenda.

Start with a little background on ER/PR testing (more to follow from Dr. Laing)

When a breast cancer tumor is removed from the body, tests are used to determine if the cancer cells have estrogen and progesterone (ER/PR) receptors.

Oncologists have always relied on the level of ER/PR positivity to determine whether patients can have hormonal therapy, such as tamoxifen. However, a major change in practice has occurred in the last ~~five~~ seven years. At one time, patients with an ER/PR positivity rate of lower than 30% were not considered suitable. However, recent research and best practices from across Canada and the United States have reduced that rate to less than 10%. In fact, because of the benefits of this drug, some physicians will consider tamoxifen for patients with 1% positivity.



OSCAR:

In 2004 Eastern Health introduced a new technology to our laboratory called the Ventana System, a semi-automated process to reduce the human manipulation of tumor samples. We will discuss the Ventana in greater detail later.

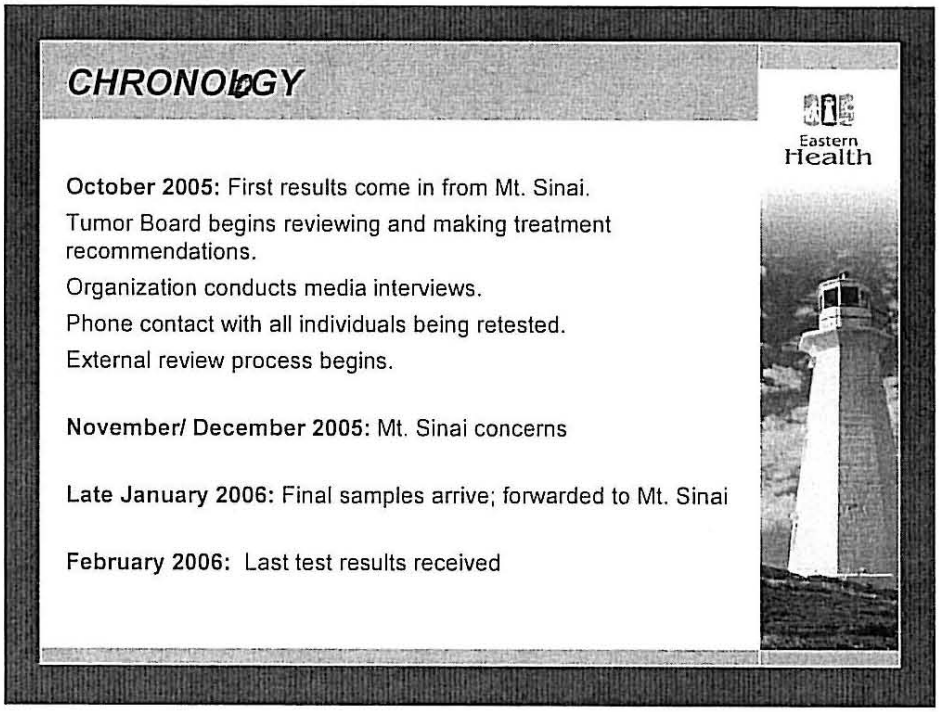
About one year later, on May 11th, one of our oncologists contacted the pathology lab, requesting the retest of a patient who previously tested negative for Estrogen and Progesterone Receptors in 2002. *(Why?: Other clinical factors indicated that this individual should probably be ER/PR positive – not negative)*

Using the Ventana this individuals' sample was retested and converted to ER/PR positive.

The next week, representatives from the Laboratory Program met with oncologists to discuss this new result and a decision was made to retest five more negative patients selected by the oncologists who they suspected may be positive, and all 5 converted.

A review of negative results from 2002 began to determine if this was a few isolated cases or a bigger issue. A significant number converted, but we were unable to determine why. So on July 14th the decision was that all patients who were negative from 1997-2005 would be retested.

Initially, we planned to conduct the review internally, but we made the decision in late July to approach an independent laboratory to conduct the retesting. *(Why?: This way, we could compare our results with another laboratory)* and Mt. Sinai, considered to be a "gold standard" laboratory in Canada, was contacted.



OSCAR:

In the next two months, we began the extensive process of collecting, reviewing, packaging and sending all negative ER/PR tests for this seven year period. We also suspended testing in our own laboratory so that we could conduct a quality review.

From that point until today, all our ER/PR tests have been going to Mt. Sinai.

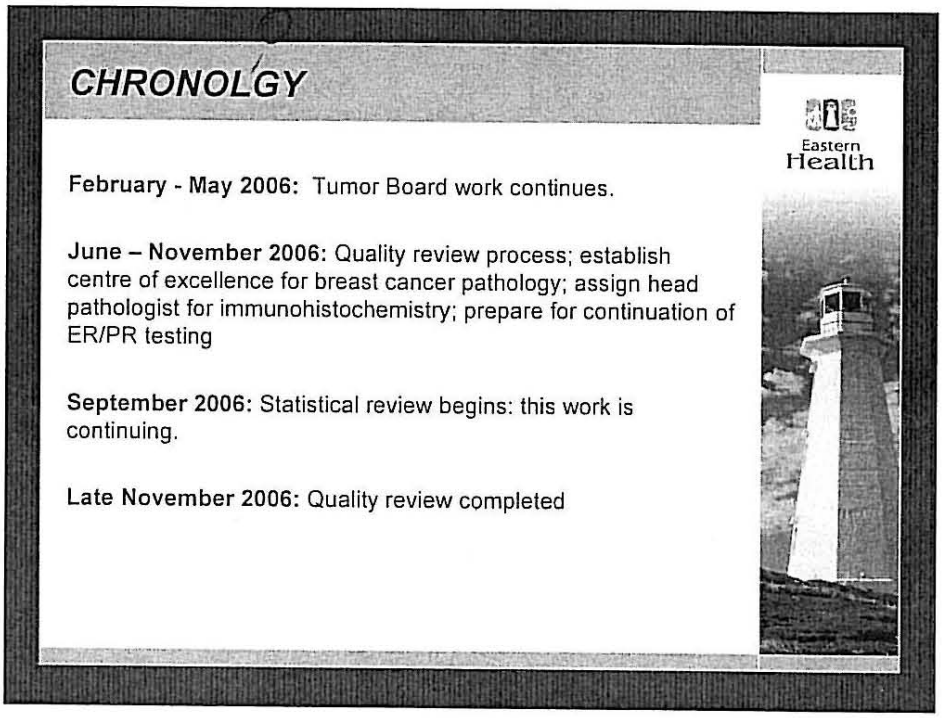
By October, we began to receive the first results from Mt. Sinai. Eastern Health established a Tumor Board to review all of the test results. This panel of experts continued to meet every week for the next eight months as the results flowed in.

Originally we believed that results would be returned to us much quicker than they actually were. It was our intention to wait for the results so that we could disclose actual information to our patients instead of having to tell them that they may or may not be impacted by this review; that we didn't know what this would mean for them; and to unnecessarily raise alarm for individuals who may not affected.

Unfortunately, we experienced unanticipated delays in getting results back as Mt. Sinai was experiencing workload and human resource issues. Disclosures had already begun and the issue became public in October. We conducted numerous media interviews, purchased advertising, and contacted all patients directly by telephone to tell them about the review.

Since that point, we have had thousands of phone calls with individuals and we have kept open the lines of communications for any individual or their family members who have questions and concerns.

By late February most of the test results were received.



OSCAR:

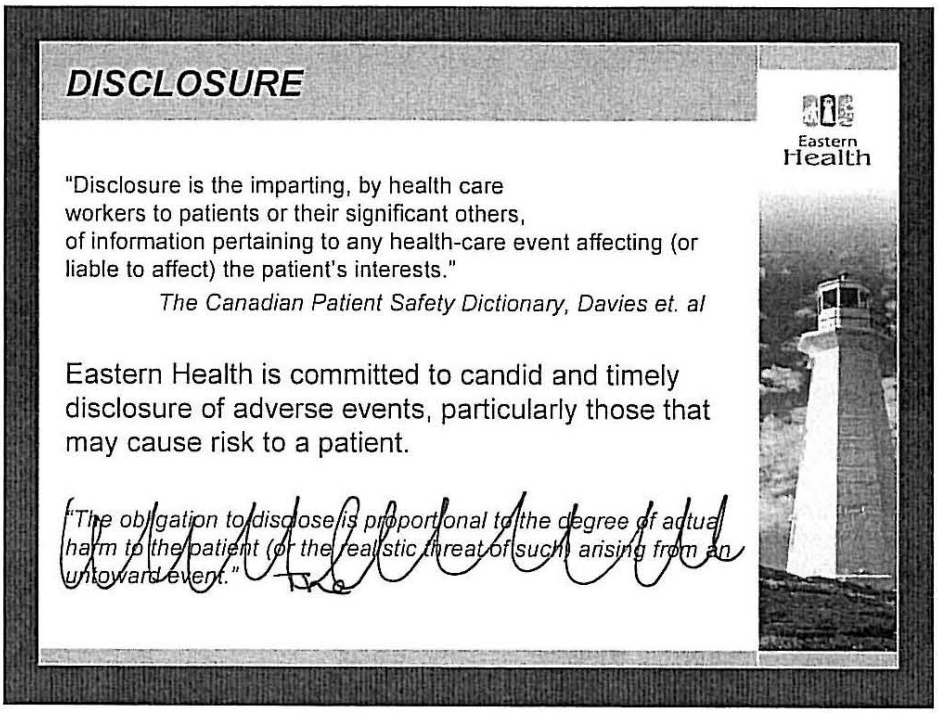
Throughout the Spring and into the Summer we focused on reviewing each individual case and making recommendations where necessary; and on contacting patients by phone or in person.

We also conducted an external review of the laboratory and spent a significant amount of time implementing the results of the quality review.

Quality review materials are kept confidential. The reason for this is that the courts and the legislature recognize that quality review in the health care sector is vital. In order to encourage staff and external reviewers to express their opinions freely, there must be protection from disclosure beyond the quality review.

This protection from disclosure is recognized in the Evidence Act, which provides that quality assurance material is not to be disclosed within a legal proceeding. It is also recognized in the Access to Information and Privacy Act, which provides that opinions or recommendations made to an agency do not have to be disclosed. However, it is important to note that there is no protection from disclosure for facts uncovered or disclosed during quality review investigations.

We will not be talking about these facts today, as this is a matter that is before the courts.



OSCAR:

-Draw a distinction between public and patient disclosure.

-At Eastern Health, we are committed to disclosure to those individuals directly impacted by any event that may affect that person's health or interests. But we are also committed **and in fact legislated** to protect patient confidentiality.

For most organizations, disclosure policies include:

•Investigation and notification of patient by phone; and

•Face-to-face meetings to provide details, express regret, discuss corrective action, and offer restitution.

Policies outline:

•How to provide the information in a complete, sympathetic and direct manner, describing what improvements have been made to the system; and

•Who will disclose the information, typically the involved clinicians and chief of staff with assistance of lawyers and quality or risk management support.

-Our policy around disclosure includes a process for conducting those disclosures:

DISCLOSURE

Eastern Health

Our Policy States:

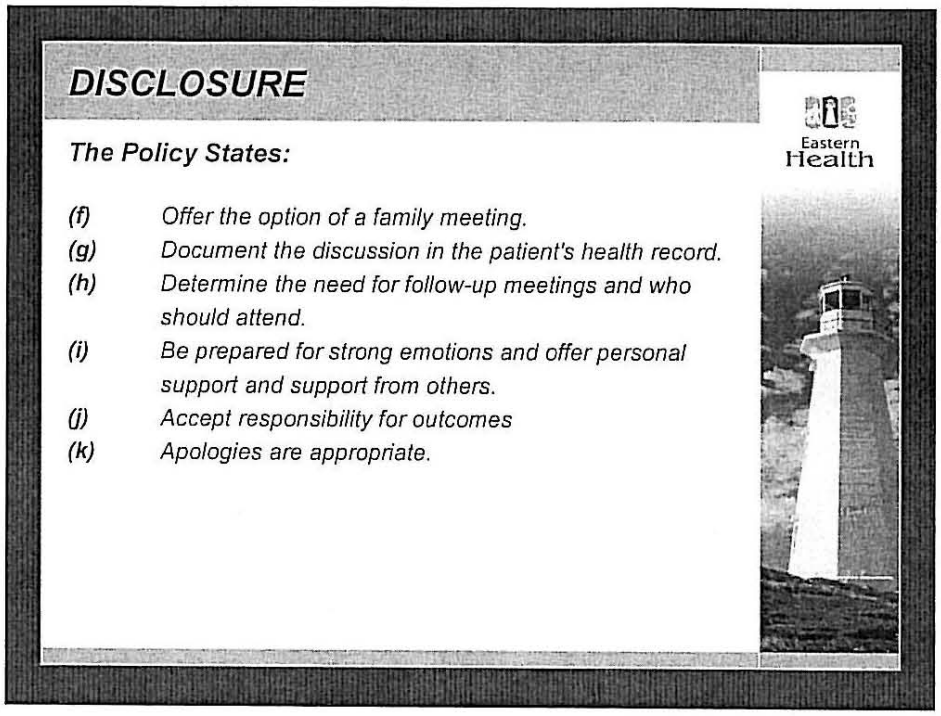
(a) *Concentrate on what happened and the possible consequences. Avoid too much detail and technical language.*

(b) *Remain factual.*

(c) *Take the lead in disclosure*

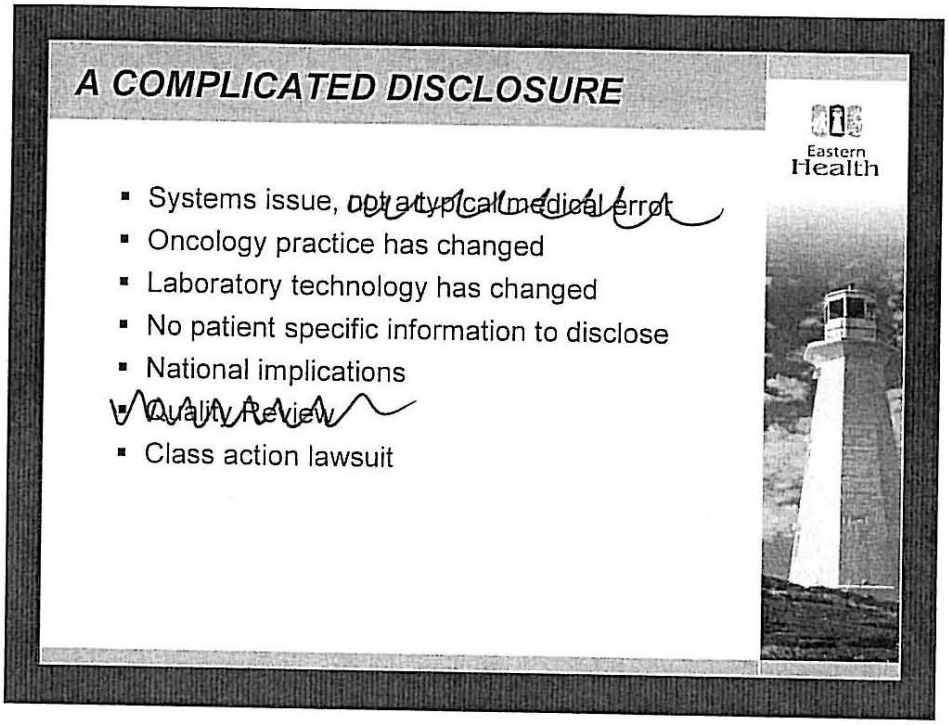
(d) *Outline a plan of care to rectify the harm and prevent recurrence for this patient and others.*

(e) *Offer to obtain second opinions where appropriate.*



OSCAR:

This would be the process that we used with all patients affected by ER/PR restesting that we contacted ourselves.



OSCAR:

The ER/PR case falls into the category of a complicated disclosure:

•this is a systems issue, rather than a typical "medical error" (no one individual is responsible; who contacts the patients if their physician is no longer with us?; and **we still have not yet determined that an error has even occurred**)

•Oncology practice has changed; (in 1997, oncologists consider 30% and under to be a negative result. Over time this has amount decreased to today when even the lowest expressors are considered as possible candidates for hormonal therapy – more on this later from Dr. Laing)

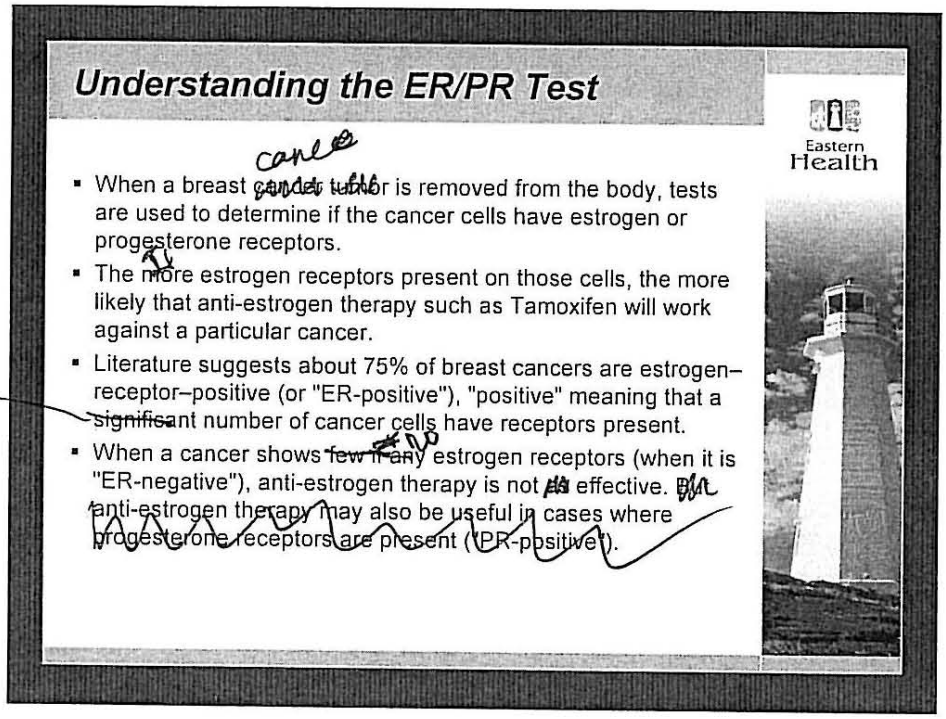
•Laboratory technology has changed (our processes have become more automated, our antibodies have become more ~~precise~~ sensitive – more on this from Dr. Denic later)

•The situation was unfolding daily: it was unclear what we were going to discover. The scope of the issue changed several times over the initial couple of months.

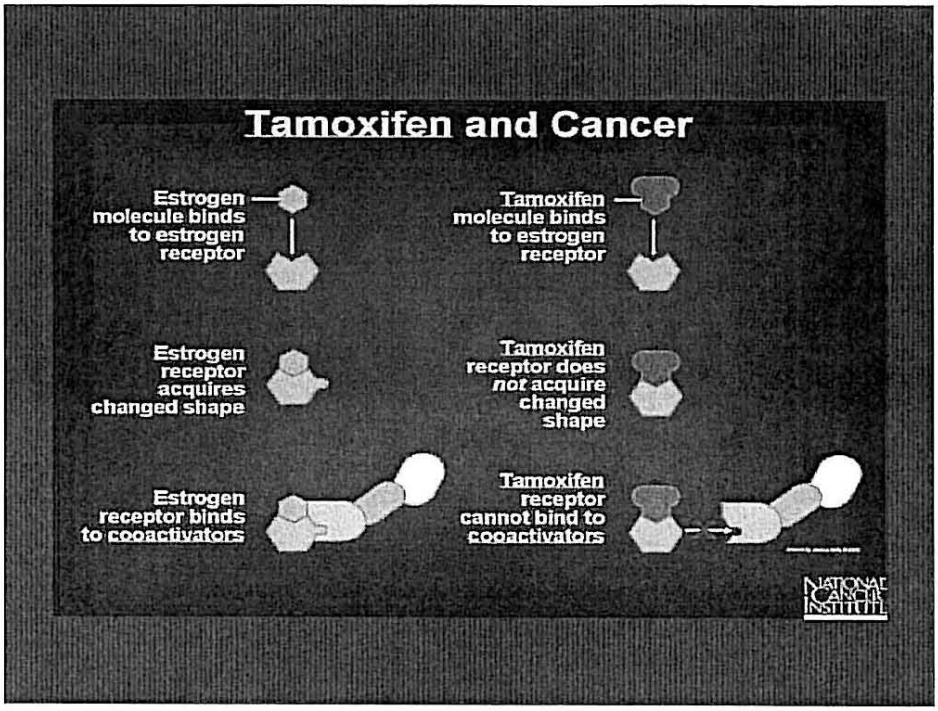
•Initially we had **no specific information** to disclose, only that there **appeared to be** an issue.

•There are potential national implications for this issue; if we have experienced this problem, have other laboratories also experienced it?

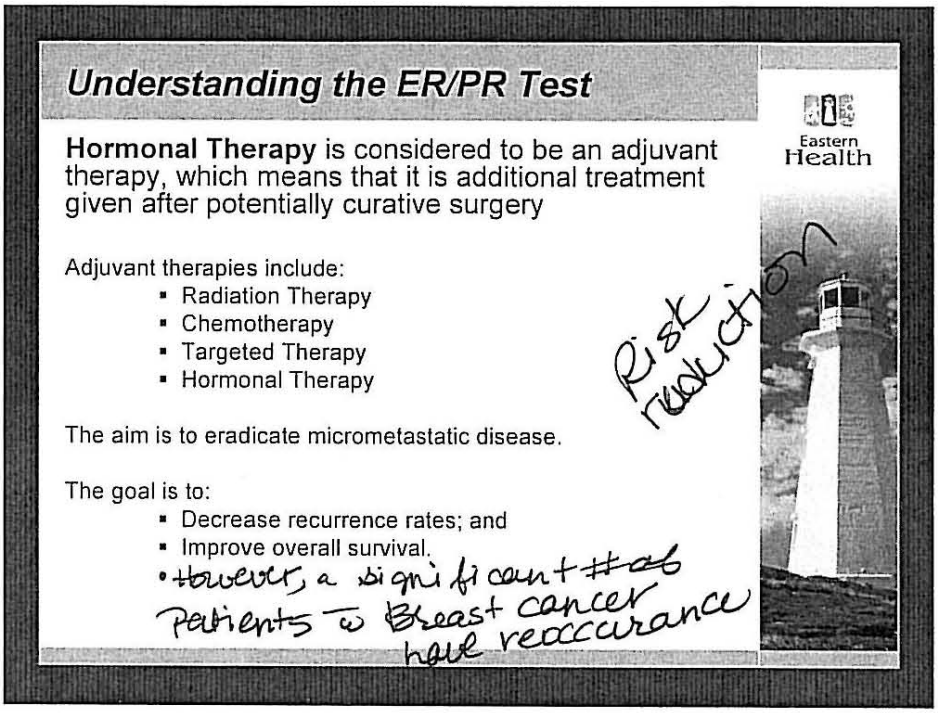
•The potential for a class action lawsuit was always great and when one was filed it changed the way we could talk about the issue in the public realm.


Understanding the ER/PR Test
Eastern Health
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.
Literature suggests about 75% 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").

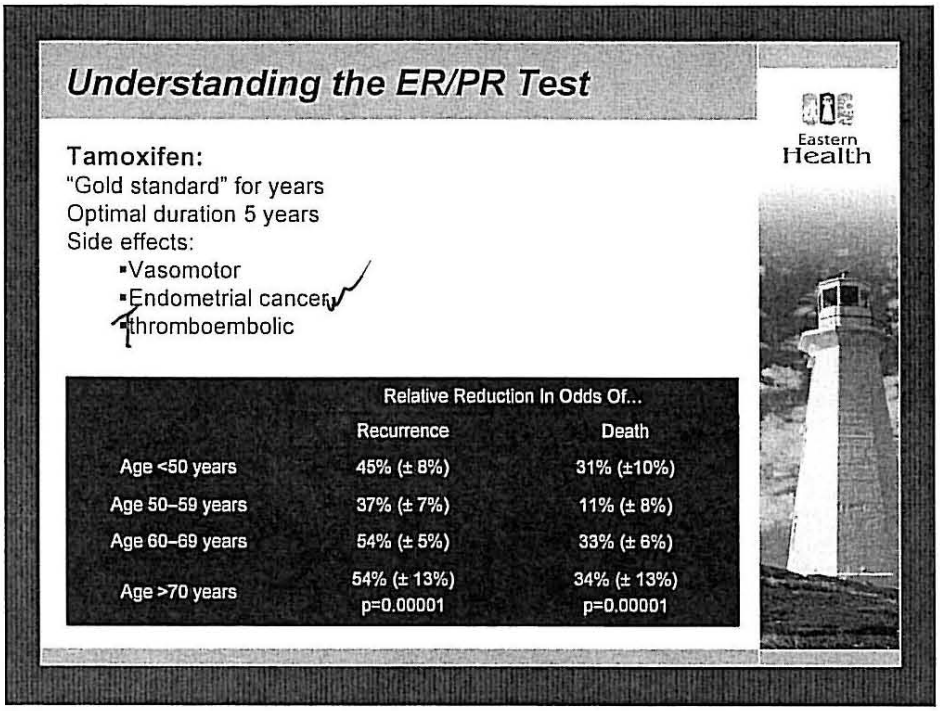
KARA


Tamoxifen and Cancer
Estrogen molecule binds to estrogen receptor
Tamoxifen molecule binds to estrogen receptor
Estrogen receptor acquires changed shape
Tamoxifen receptor does not acquire changed shape
Estrogen receptor binds to coactivators
Tamoxifen receptor cannot bind to coactivators
NATIONAL CANCER INSTITUTE

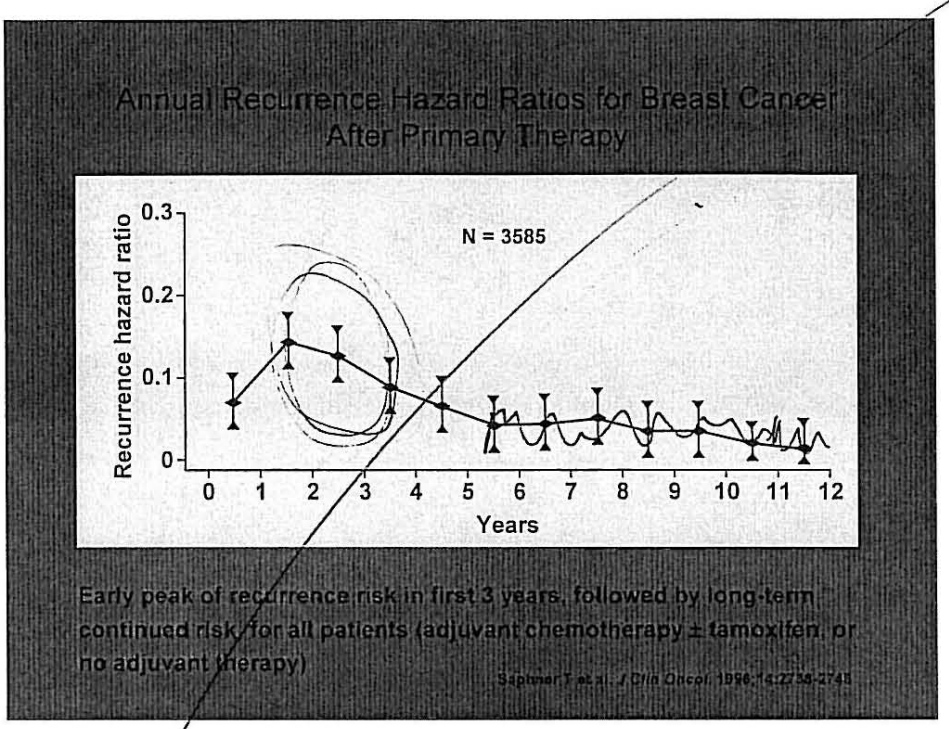
KARA


Understanding the ER/PR Test
Eastern Health
Hormonal Therapy is considered to be an adjuvant therapy, which means that it is additional treatment given after potentially curative surgery
Adjuvant therapies include:
Radiation Therapy
Chemotherapy
Targeted Therapy
Hormonal Therapy
The aim is to eradicate micrometastatic disease.
The goal is to:
Decrease recurrence rates; and
Improve overall survival.
Risk reduction
however, a significant # of patients w Breast cancer have reoccurance

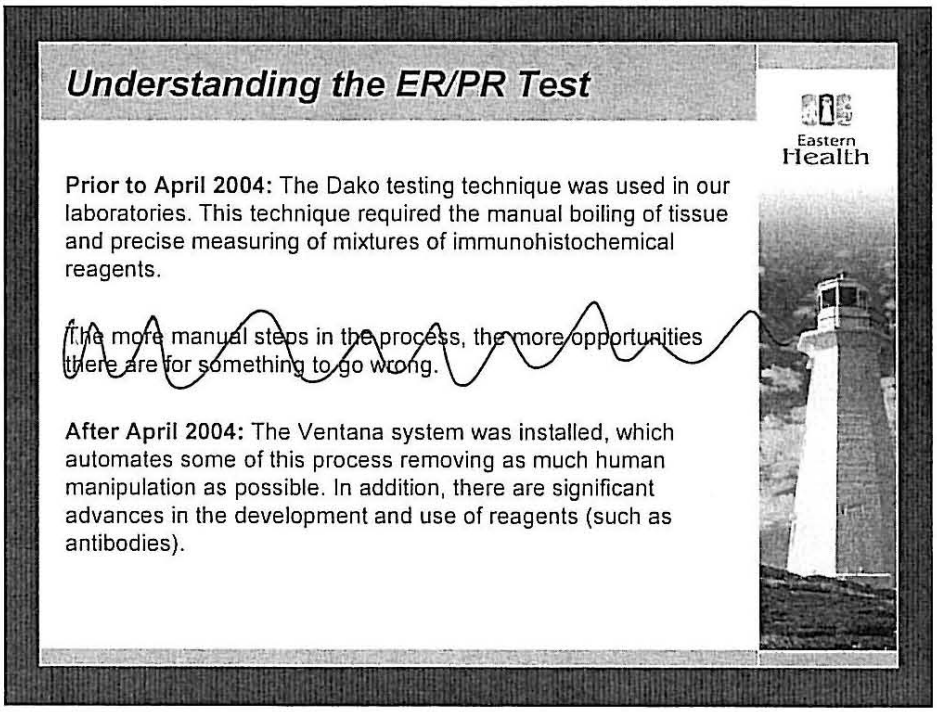
KARA


Understanding the ER/PR Test
Eastern Health
Tamoxifen:
"Gold standard" for years
Optimal duration 5 years
Side effects:
▪Vasomotor
▪Endometrial cancer
▪thromboembolic
Relative Reduction In Odds Of...
Recurrence
Death
Age <50 years
45% (± 8%)
31% (±10%)
Age 50–59 years
37% (± 7%)
11% (± 8%)
Age 60–69 years
54% (± 5%)
33% (± 6%)
Age >70 years
54% (± 13%) p=0.00001
34% (± 13%) p=0.00001

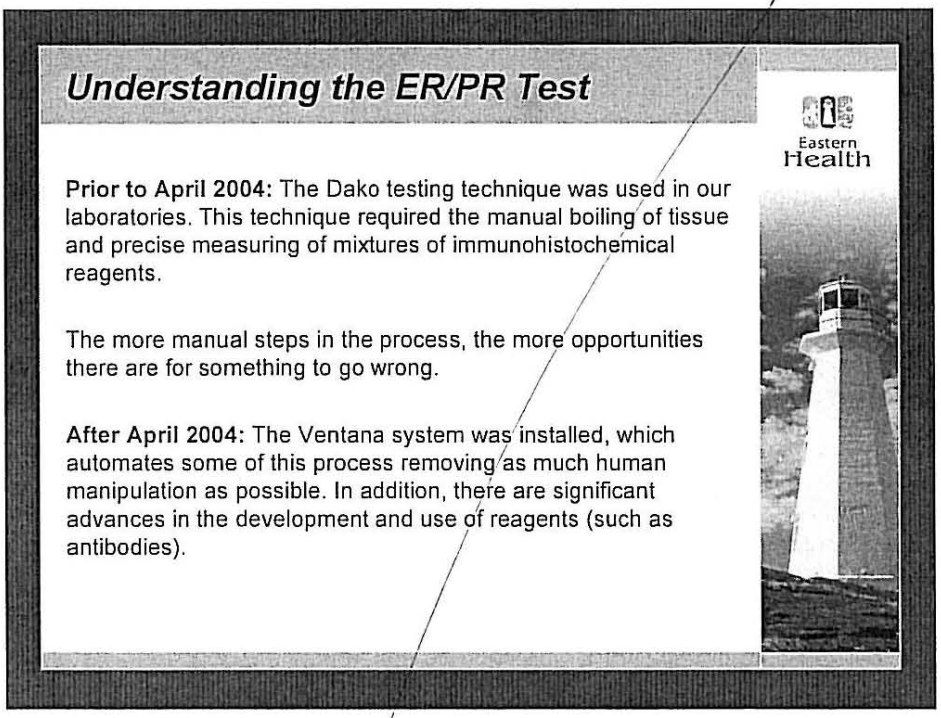
KARA


Annual Recurrence Hazard Ratios for Breast Cancer After Primary Therapy
Recurrence hazard ratio
0.3
0.2
0.1
0
N = 3585
0 1 2 3 4 5 6 7 8 9 10 11 12
Years
Early peak of recurrence risk in first 3 years, followed by long-term continued risk for all patients (adjuvant chemotherapy ± tamoxifen, or no adjuvant therapy)
Saphner T et al. J Clin Oncol 1996;14:2738-2746

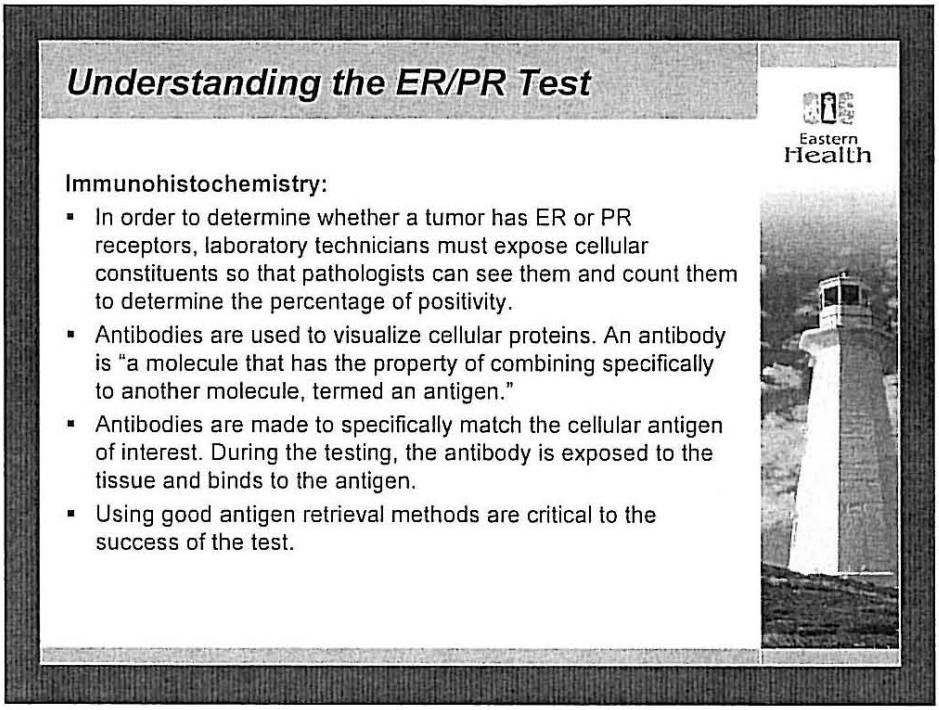
KARA


Understanding the ER/PR Test
Eastern Health
Prior to April 2004: The Dako testing technique was used in our laboratories. This technique required the manual boiling of tissue and precise measuring of mixtures of immunohistochemical reagents.
The more manual steps in the process, the more opportunities there are for something to go wrong.
After April 2004: The Ventana system was installed, which automates some of this process removing as much human manipulation as possible. In addition, there are significant advances in the development and use of reagents (such as antibodies).

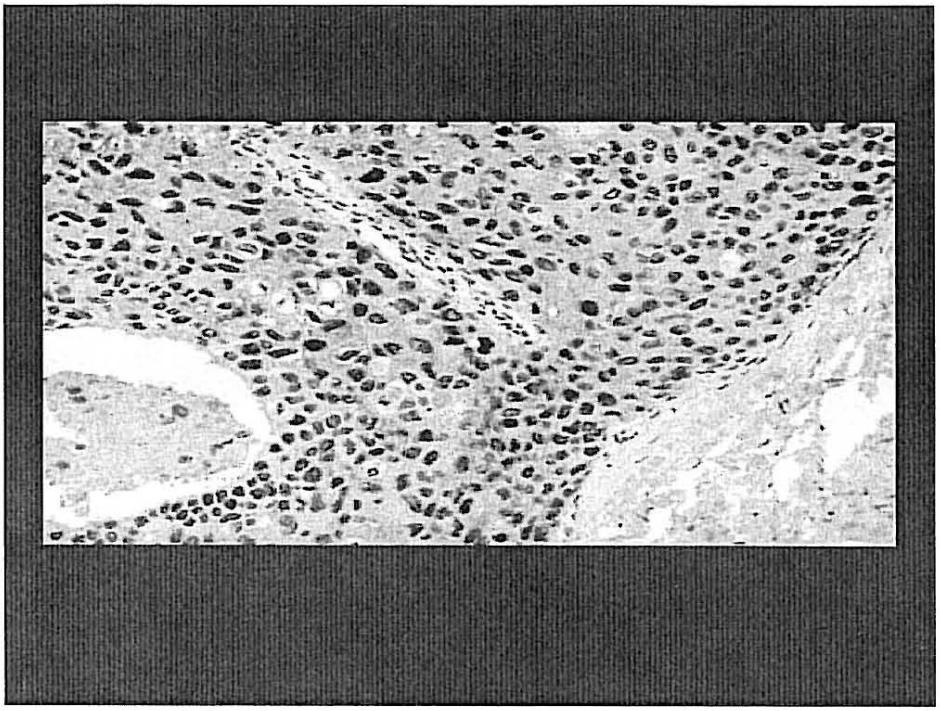
NASH


Understanding the ER/PR Test
Eastern Health
Prior to April 2004: The Dako testing technique was used in our laboratories. This technique required the manual boiling of tissue and precise measuring of mixtures of immunohistochemical reagents.
The more manual steps in the process, the more opportunities there are for something to go wrong.
After April 2004: The Ventana system was installed, which automates some of this process removing as much human manipulation as possible. In addition, there are significant advances in the development and use of reagents (such as antibodies).

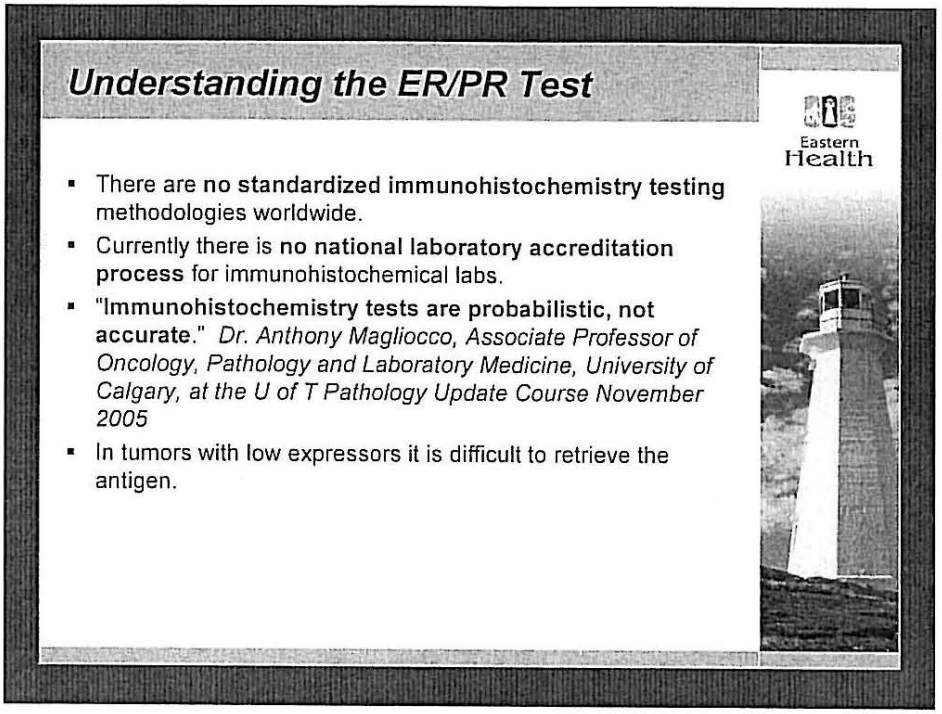
NASH


Understanding the ER/PR Test
Eastern Health
Immunohistochemistry:
In order to determine whether a tumor has ER or PR receptors, laboratory technicians must expose cellular constituents so that pathologists can see them and count them to determine the percentage of positivity.
Antibodies are used to visualize cellular proteins. An antibody is "a molecule that has the property of combining specifically to another molecule, termed an antigen."
Antibodies are made to specifically match the cellular antigen of interest. During the testing, the antibody is exposed to the tissue and binds to the antigen.
Using good antigen retrieval methods are critical to the success of the test.

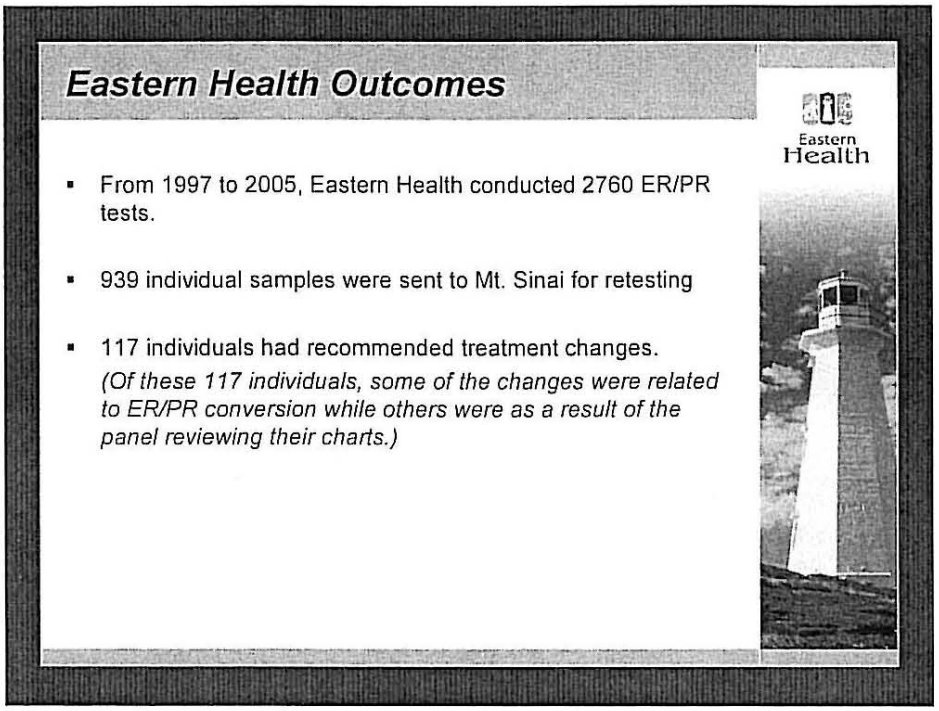
NASH



NASH


Understanding the ER/PR Test
Eastern Health
There are no standardized immunohistochemistry testing methodologies worldwide.
Currently there is no national laboratory accreditation process for immunohistochemical labs.
"Immunohistochemistry tests are probabilistic, not accurate." Dr. Anthony Magliocco, Associate Professor of Oncology, Pathology and Laboratory Medicine, University of Calgary, at the U of T Pathology Update Course November 2005
In tumors with low expressors it is difficult to retrieve the antigen.

NASH



OSCAR

It is important to note that our first priority was not to conduct a research project but to concentrate on assessing each patient's file and ensuring that they had every treatment opportunity available to them.

False neg. rate

If asked about ~~rate of error~~:

We do not intend to establish a "rate of error." Up to this point, our focus has been on making treatment changes, where appropriate, and 117 individuals have experienced treatment changes.

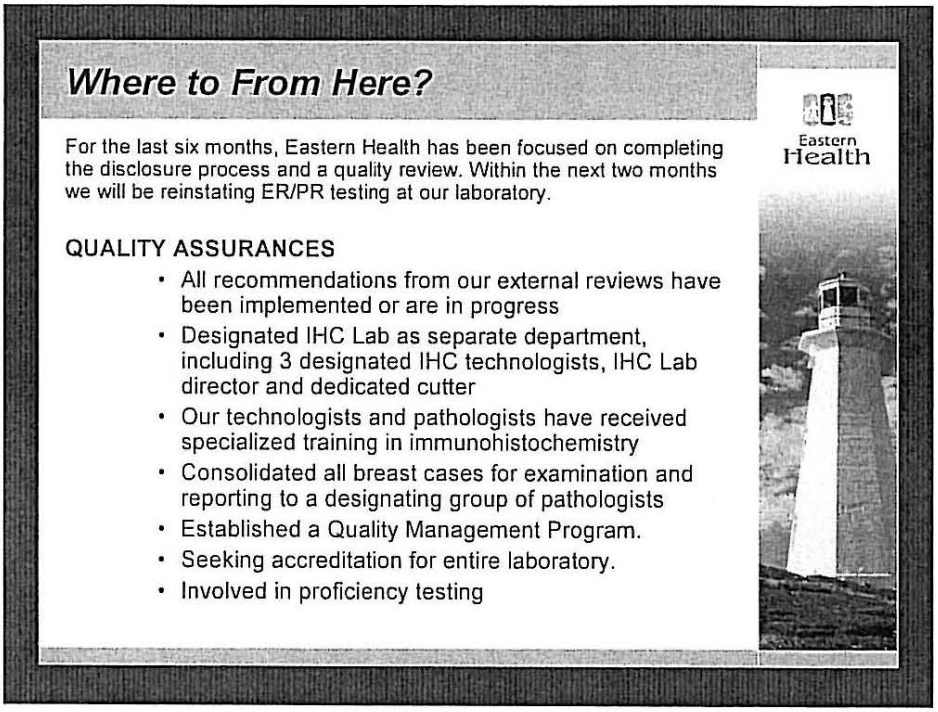
Some of these changes are because of a conversion in their ER/PR test result from negative to positive; some because the definition of "negative" has changed; some because of where they are today with their disease – there are multiple factors involved.

Now that legal proceedings have been initiated, we will have to allow the legal process to determine if in fact error has occurred.

If pressed on rate of conversion:

The number of conversions is not what the process is about or what we are reporting. For one thing, this would be material to our quality review, but moreover, this can easily become a numbers game. Individuals may have had minor changes in their "percentage" that have not impacted upon the treatment they need to receive. Some people tested "negative" in the past but were given hormonal therapy anyway because of other clinical factors.

From day one, we have been focused on who may be impacted in terms of potentially positive treatments. That was and continues to be our focus, and that is 117 of those tested in this period.



NASH

(Dr. Denic to take reporters to laboratory for a tour)