HOT SPOT

From the associate editor's desk

By Edward Chow

Hot Spot is entering its third year of publication. We received numerous requests to be on the mailing list, and have tripled our circulation.

Over the past two years we received enormous support from both our contributors and readers. This issue is dedicated to breast cancer. Dr. Kathleen Pritchard kindly writes an introduction about Dr. Maureen Trudeau, who has written three inserts on the management of breast cancer. Dr. Eva Grunfeld from Ottawa outlines the current study on follow-up for breast cancer. Dr. Charles Hayter discusses cancer treatment before medicare, and Dr. Mary Vachon looks at staff stress and suffering. Dr. Rebecca Wong's research corner discusses some of the research issues we are investigating. Please contact us if you would like a particular topic to appear in our newsletter. On behalf of the editorial board, we send you our sincere thanks and good wishes for the New Year.

Dr. Maureen Trudeau

By Dr. Kathleen Pritchard

Dr. Maureen Trudeau, who became head of medical oncology/hematology in January of 2000, has been a great addition to Toronto-Sunnybrook Regional Cancer Centre (T-SRCC), both in medical oncology and hematology and in the breast cancer program.

A 1981 graduate of the MD program of the University of Toronto, Dr. Trudeau previously received training in internal medicine and medical oncology in the University of Toronto system, and spent a year as a clinical research fellow at the Dana Farber Cancer Institute in Boston under the supervision of Dr. I. Craig Henderson, a well-known breast cancer investigator and trialist.

Dr. Trudeau is an extremely active collaborative researcher. She is a member of the Investigational New Drug Committee and Breast Cancer Site Group for the National Cancer Institute of Canada Clinical Trials Group (NCIC-CTG), where she has chaired the IND 68 Trial, a phase II study of taxotere in patients with metastatic breast cancer, and MA.15, a phase I/II study of docetaxel and epirubicin as first-line therapy for metastatic breast cancer. Dr. Trudeau's other research interests have involved prognostic factors in node-negative breast cancer using the Henrietta Banting Breast Centre Database, and a variety of clinical trials in prevention, adjuvant and metastatic breast cancer. She has also been funded by the Canadian Breast Cancer Research Initiative (CBCRI) for a study of quality of life and general health in long-term survivors of breast cancer. Dr. Trudeau has been a continuous holder of peer-reviewed grant support from the NCIC, the Ontario Ministry of Health and the CBCRI, and has published widely in a variety of prestigious journals. She is also an internationally known expert in the clinical care of women with breast cancer.

Dr. Kathleen Pritchard is Head of Clinical Epidemiology and Chair of Breast Site Group, T-SRCC.

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Staff stress and suffering

By Mary L.S. Vachon, RN, PhD

Staff working with critically ill and dying persons and their families can experience considerable stress that may be manifested physically, psychologically, or in one's behaviour.

A recent study of oncology staff in Ontario revealed that on the Maslach Burn-out Inventory, more than half of the oncologists and more than one-third of members of the allied health professions who responded experienced emotional exhaustion. Almost half the oncologists and more than half of the allied health professionals reported a low sense of personal accomplishment, and about a quarter of oncologists and four per cent of allied health professionals felt a sense of depersonalization. While previous work by the author and others has shown that organizational stressors often contribute more to stress than does work with dying persons, studies show that greater exposure to patient deaths was linked to higher reports of stress and burn-out in physicians and nurses.

A recent review of the literature shows the sources of stress and suffering in palliative care to be due to:

- Constant exposure to death and dying
- Identification with suffering individuals
- Feelings of inadequacy and/or helplessness
- Feeling out of control and that one is not providing good care or not able to provide a good death
- Being unable to provide the care one feels one should
- Multiple loss and grief.

Many years ago, Dr. Balfour Mount wrote of the impact of cumulative losses in oncology and palliative care. These losses may be conscious or unconscious and each rekindles the conscious or unconscious fires associated with earlier bereavements. The weight of these repeated losses may lead to a burden that is increasingly intolerable and often difficult to define. These losses may also trigger earlier unresolved losses from one's childhood. In **Surviving the Fall** (Yale University Press, 1998), Dr. Peter Selwyn wrote of how his unresolved grief from his father's suicide when he was a child led to his tendency to over-identify with and attempt to rescue his patients dying of AIDS and cancer. "Working through my own pain has been the key to enabling me to accompany others through theirs. With every loss we experience, and every struggle we survive, our lives become that much richer a source for empathy and connection with other people, as we all make our way along the human trail of living in the world. Recognizing death, accepting it, grieving our losses - these are the prerequisites of truly being able to be present with people who are facing life-threatening illness. Acknowledging and experiencing the pain allows the heart to open, enabling us to experience joy in a way that would otherwise not be possible."

Caregivers who do not work through their own earlier losses and learn to deal with the losses and deaths associated with their work in oncology and palliative care run the risk of developing burn-out, or the more recently described phenomenon of "*compassion fatigue*" (Figley, **Compassion Fatigue**, Bruner/Mazel 1995). Compassion fatigue is associated with exposure to the suffering of others leading to a vicarious experience of the fear, pain and suffering in the professional. Sometimes the professional can feel that s/he is losing him or herself to the clients being served. Professionals with a deep capacity to care for and with clients may be most susceptible to this mirroring effect.

The concept of the *"wounded healer"* (Nouen, **The Wounded Healer**, Doubleday, 1972) recognizes that it is from the recognized wounds of the caregiver that we can begin to heal others. Sulmasy, a physician, philosopher and Franciscan friar (**The Healer's Calling**, Paulist Press, 1997) notes that all health care professionals are wounded healers whose own suffering, pain, loneliness, fatigue and sacrifice can become the source of compassion in the healer's art. For this to happen, however, requires that the healer take the time to bind up one's own wounds before being able to reach out to another.

The **Talmud** asks how one might know the Messiah. "He is sitting among the poor covered with wounds. The others unbind all their wounds at the same time and then bind them up again. But he unbinds one at a time and binds it up again, saying to himself, 'perhaps I shall be needed: if so, I must always be ready so as not to delay for one moment' " (Nouen, 1972).

Caregivers can bind their own wounds through reflection, meditation, time in nature, exercise and self-care activities that replenish our own souls.

Mary Vachon, RN, PhD, is a psychotherapist in private practice. She can be reached at maryvachon@sympatico.ca.

Historical Vignette:
Cancer care before medicare

By Charles Hayter, MA, MD, FRCPC, Radiation Oncologist, T-SRCC

One of the issues that cancer patients today do not have to deal with is paying for treatment. However, it should not be forgotten that prior to the introduction of universal medicare in 1966, cancer patients often had to face additional anxiety about payment. In particular, radiotherapy could be very costly for patients.

In the early years of the twentieth century, radiotherapists charged by the hour for treatment. In Halifax, Dr. Ivan Mader charged 5c/hour for radium applications. Against the background of today's multi-million dollar hospital budgets, this rate seems trivial, but it was expensive for many patients.

During the depression of the 1930s, financial hardship became a pressing problem for many cancer patients and often led to reluctance to seek treatment.

In February of 1931, Ontario Premier George Henry received a letter from a woman suffering from cancer who had received three radium treatments but could not have any more because of lack of funds. She wrote: "If there is any chance of getting aid I would be certainly glad to get it as it is not very pleasant to be in such misery and not be able to get aid or even help myself."

In Saskatchewan, the situation was dire because of the failure of crops. The treatment of an impoverished young man with rectal cancer was delayed while hospitals, municipalities, and government wrangled over who should pay.

The memory of such situations led to appeals to make cancer treatment free. In 1944, the Province of Saskatchewan became the first jurisdiction in North America to provide cancer treatment free of charge to all citizens. After the passage of the Medical Care Act in 1966, cancer treatment became available to all Canadians regardless of income.

Pain and symptom management conference

Well over 300 health care professionals attended the seventh Annual Conference on the Science and Art of Pain and Symptom Management, November 17-18, 2000, at the Old Mill in Toronto. The program was jointly organized by the Interdepartmental Division of Oncology and the Division of Palliative Medicine of the Department of Family and Community Medicine at the University of Toronto, and the Rapid Response Radiotherapy Program at Toronto-Sunnybrook Regional Cancer Centre. The conference directors were Edward Chow (Department of Radiation Oncology) and Russell Goldman (Department of Family and Community Medicine). Larry Librach (Department of Family and Community Medicine) was the conference consultant.

Plenary sessions at the conference featured several faculty members: Larry Librach (Department of Family and Community Medicine), Linda Emanuel (Northwestern University Medical School), Sharon Watanabe (University of Alberta), Michelle Chaban (Department of Family and Community Medicine).

Topics included: "Predicting prognosis: How good are we?"; "What do dying patients care about?"; "How to set up regional palliative programs"; and "Caring for ourselves while looking after our patients".

The topics of the workshops included: "Management of dyspnea in terminally ill patients", "Management of pain and symptoms with palliative radiotherapy", "Latest advances in management of bone metastases", "Medical ethics: Case discussions", "Complex pain management", "Dealing with complex family situations", and "Management of epidural catheters in home or hospital setting".

Topics for the gastrointestinal malignancy session included: "Latest advances in GI surgery"; "Latest advances in pancreatic cancer"; "Latest advances in lower GI malignancies"; "Stomal care"; "Psychosocial perspective"; "Endoscopic intervention"; "Innovative approach in palliation"; and "Management of bowel obstruction".

Faculty participating in the debate session were: Jose Pereira (University of Alberta), and Sharon Watanabe (University of Alberta), vs. Larry Librach (Department of Family and Community Medicine), and Russell Goldman (Department of Family and Community Medicine). The topic was "Does this house believe opioid rotation is useful in palliative settings?"

The conference also featured a new workshop for radiation therapists with topics on: "What is s/he thinking? Approaching a palliative patient"; "Indications, dose fractionation, and other considerations"; and "Psychosocial issues and patient education".

The conference speakers' hand-outs are available at www.cme.utoronto.ca/AnnualCoursePalliativeCare/.

The eighth annual conference is planned for November 16 and 17, 2001, at the Old Mill in Toronto. The conference is aimed at medical and radiation oncologists, palliative care physicians, and other physicians and health care professionals with a specific interest in pain and symptom management. For course information, call 416-978-2719.

Follow-up for breast cancer

By Eva Grunfeld, MD, DPhil, CCFP

After a woman has completed her primary treatment for breast cancer, she requires regular check-ups with the goals of managing any side effects associated with the primary treatment, detecting and treating recurrence, detecting and treating new cancers that may develop in the opposite breast, and providing psychosocial support. It has been usual practice to have the check-ups at periodic intervals for five to 10 years after completing treatment, and for blood tests, x-rays, ultrasounds and mammograms to be performed at regular intervals. Usually the check-ups take place in specialist cancer or surgical clinics.

As the number of breast cancer survivors increases and the practice of regular check-ups affects more and more women, there has been an interest in better defining how best to conduct those check-ups. Some questions that have been asked by different research studies are: Is there a benefit in conducting blood tests and imaging tests at regular intervals so that, if the cancer does come back, it can be detected early? Do we know the best frequency for mammograms? Would there be any difference in outcome if the family doctor conducted the regular check-ups?

Two randomized controlled trials have shown that there is no benefit in routinely conducting blood tests and imaging tests, either in terms of patient survival or in terms of quality of life. These studies have been the basis of guidelines on follow-up, developed both in Canada and the US, that emphasize the importance of periodic check-ups for history and physical examination, but recommend *against* routine tests other than mammograms: rather, tests should be used to investigate any worrying signs or symptoms that may develop. These same guidelines do recommend annual mammograms for women who have had breast cancer. Dr. Larry Paszat, radiation oncologist at Toronto-Sunnybrook Regional Cancer Centre (T-SRCC), and others, are currently conducting research in Ontario to better define which women with breast cancer will benefit most from annual mammograms. A randomized controlled trial conducted in England found no difference in terms of delay in diagnosing recurrence or patient quality of life when the family doctor provided follow-up. We are currently conducting a larger trial throughout Ontario to help us better understand the role of the family doctor in follow-up.

Research Corner

Shared treatment decision-making

By Rebecca Wong, MBChB, FRCPC

Involving patients in shared treatment decision-making is rapidly being recognized as an essential aspect of quality patient care. Much research is ongoing to improve our understanding of the patterns of decision-making, the factors that affect the decisions that are made, identifying strategies to facilitate the process, and how improved decision-making can affect and improve the quality of care. The research efforts in this area within the RRRP are highlighted in this issue.

Dr. Szumacher headed a project addressing shared treatment decision-making for patients contemplating palliative radiotherapy for bone metastases. Patients with painful bony metastases are frequently recommended to receive either a single or a five-day course of radiotherapy. There exist 15 randomized studies addressing this area. Pertinent outcomes from these studies were incorporated into a decision board designed to facilitate shared decision-making around the choice between a single versus five fractions. The study was designed to determine the proportion of patients who would like to participate in shared decision-making, document the choice, and evaluate the factors that may affect the final decision. Forty patients participated in the study. Findings are currently being analyzed and will be presented at the upcoming International Congress in Radiation Oncology.

Dr. R. Wong conducted a study to determine the amount of palliative benefit that is necessary for patients to opt for a longer versus a shorter course of palliative radiotherapy. The choice of dose fractionation is a common dilemma when deciding on the optimal treatment to recommend in the palliative setting. In many situations (although by no means always), longer treatments are perceived to provide incremental benefits and are recommended. Especially in patients with relatively short life expectancies, the implications are not trivial. The clinical scenario which exemplifies this problem are patients with painful unresectable pelvic recurrences, who are faced with the choice between a shorter (five-day) and a longer (20-day) course of treatment for pain relief. This is the clinical context for this study. Using a decision aid to present a trade-off task, **the minimal clinically important effect size** for pain relief was ascertained. Fifty patients participated in this study. Pertinent findings from this study include the following: Patients on average required an over 2.3-fold increase in the duration of benefit (from three to seven months) before they would opt in favour of accepting the longer course of treatment. If the probability of benefit is increased from 50 to 80%, patients would opt for the longer treatment even if duration of benefit remained unaltered. Majority of patients placed greater importance on the probability of response rather than duration of response, although there exist definite subgroups of patients whose value systems are reversed.

These findings represent one of the first works in quantifying patient preferences in the palliative setting. Continual efforts in this area would allow us to better understand the issues that are most relevant to our patients living with advanced cancer.

Thank you...

During the past two years many individuals and sponsors were involved in making this publication possible. We received positive and encouraging feedback congratulating us on the quality of the information published in **Hot Spot**. Without the support of our sponsors and the contributing authors we would not have been able to continue publishing a quality newsletter. The editorial board wishes to thank all our sponsors and colleagues for their continued support.

The newsletter of the Rapid Response Radiotherapy Program of Toronto-Sunnybrook Regional Cancer Centre is published through the support of:

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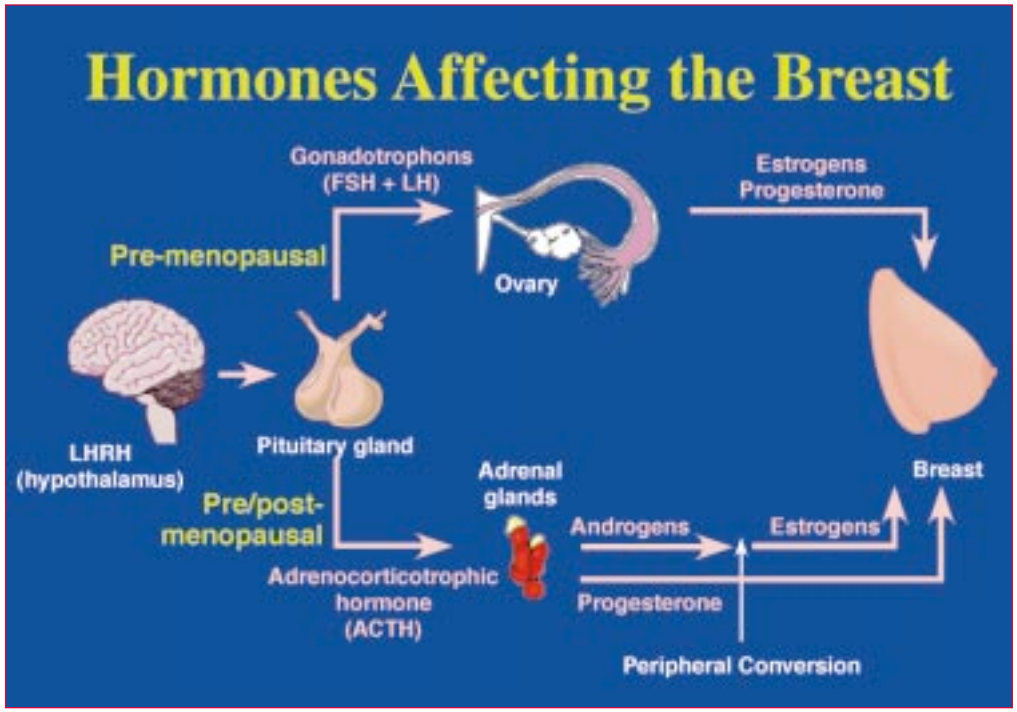
Hormones in Breast Cancer



Adjuvant Therapy

Facts about tamoxifen:

- Tamoxifen is only effective in hormonally sensitive tumours (estrogen or progesterone receptor positive)
- Tamoxifen for five years prolongs survival for pre- and post-menopausal women (26% improvement in survival)
- Tamoxifen treatment for five years is more effective than for two or three years
- Although five years is commonly used, the optimal duration of treatment is under investigation
- Tamoxifen reduces the risk of contralateral breast cancer (47% risk reduction)
- Tamoxifen reduces the risk of local recurrence after lumpectomy (tamoxifen + radiotherapy to the breast is superior to either alone)
- Tamoxifen plus chemotherapy is superior to either tamoxifen or chemotherapy alone in reducing recurrence of breast cancer and improving overall survival
- As chemo prevention, Tamoxifen reduces the risk of developing breast cancer in high risk women

Facts about oophorectomy:

- Oophorectomy is only effective in hormonally sensitive tumours in premenopausal women
- Oophorectomy/lutenizing hormone releasing hormone agonists (LHRHa) decrease the risk of contralateral breast cancer (40-50% risk reduction)
- Oophorectomy increases survival in premenopausal women (25% improvement in survival)

Areas of investigation in clinical trials:

- What is the role of chemotherapy plus LHRHa (Zoladex 3.6 mg) in premenopausal women?
- What is the role of tamoxifen combined with LHRHa (Zoladex) /oophorectomy in premenopausal women?
- What is the role of aromatase inhibitors (eg. Arimidex) either in combination, sequentially or instead of tamoxifen?

AstraZeneca

By Maureen Trudeau, MD, FRCPC,
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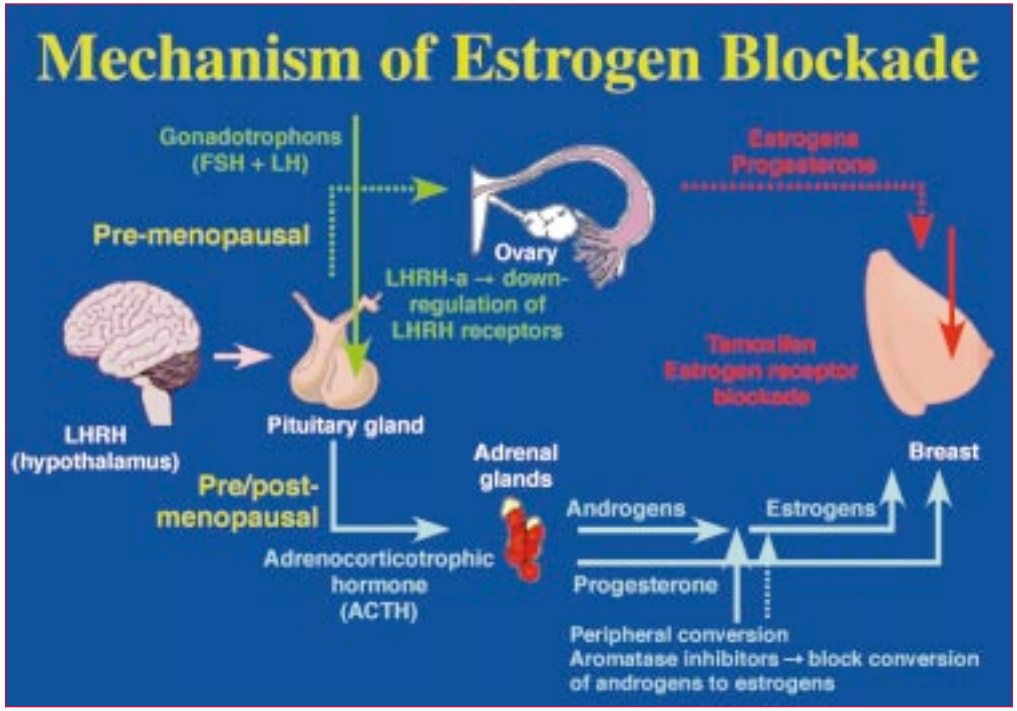
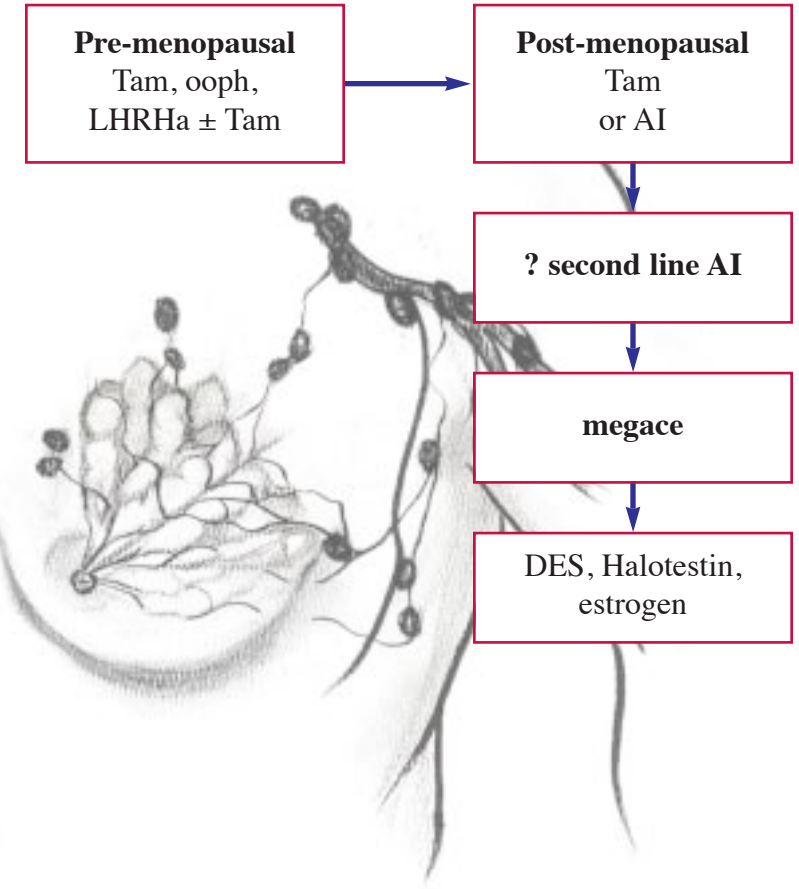
Metastatic Breast Cancer



Metastatic Breast Cancer Treatment Cascade



In Metastatic Disease:

- Hormones are used sequentially
- Aromatase Inhibitors (AI) are effective in post-menopausal women only
- AI's (Arimidex, letrozole) may be superior to tamoxifen in first line metastatic breast cancer
- Arimidex, letrozole are better in some aspects including decreased toxicity, (fewer DVT's) but no clear evidence yet of overall survival benefit
- AI's are superior to megace as second line therapy
- Another AI, exemestane, can be effective after failure of arimidex or letrozole
- A bisphosphonate should be given in addition to hormone therapy if ≥ one osteolytic bone lesion with reasonable life expectancy and renal function

Grace Tanouye, Japanese ink and charcoal, 2000

By Maureen Trudeau, MD, FRCPC, Head, Medical Oncology/Hematology, Toronto-Sunnybrook Regional Cancer Centre

Supported by an educational grant from AstraZeneca Canada Inc.

Supplement to **Hot Spot**, the newsletter of the **Rapid Response Radiotherapy Program** of Toronto-Sunnybrook Regional Cancer Centre - February 2001

Chemotherapy in metastatic breast cancer treatment

- Metastatic breast cancer is an incurable illness. The goals of therapy are to provide palliation, by controlling the disease and its symptoms, to improve quality of life and hopefully length of life
- Chemotherapy is usually given after hormones have been tried and failed in receptor positive disease
- Chemotherapy is usually not given in combination with hormones
- Very few studies have shown improved survival. Patients often receive multiple therapies in sequence
- High dose therapy with stem cell transplant has not been shown to provide benefits above that of standard therapies, and should be carried out in the context of a clinical trial

The decision about which treatment to use is dependent upon:

Tumour Characteristics:

- Sites
- Volume
- Rapidity of progression
- Time to recurrence from original diagnosis
- HER2 overexpression

Patient Characteristics:

- Her wishes
- Her performance status

Treatments Available:

- Toxicity
- Convenience of administration
- Previous treatment

Drugs may be used sequentially or in combination:

Combination:

- Increased response rates, increased toxicity

Sequential:

- Decreased response rates, decreased toxicity

- Duration of treatment depends on responsiveness of tumour, toxicity and patient wishes. Treatment over longer periods of time may translate into longer times of tumour control

Chemotherapy drugs commonly used in the treatment of metastatic breast cancer include:

- anthracyclines – adriamycin or epirubicin
- taxanes – Taxol (paclitaxel) or Taxotere (docetaxel)
- vinca alkaloids – Navelbine (vinorelbine)
- 5FU type drugs – Xeloda (capecitabine)
- Others – cyclophosphamide, methotrexate, cisplatinum, carboplatin

All may be used alone or in combination.

Studies are ongoing investigating the use of:

- vaccines
- angiogenesis inhibitors
- antisense molecules
- tyrosine kinase inhibitors
- farnysyl kinase inhibitors
- gene therapy
- cell cycle inhibitors

By Maureen Trudeau, MD, FRCPC, Head, Medical Oncology/Hematology, Toronto-Sunnybrook Regional Cancer Centre
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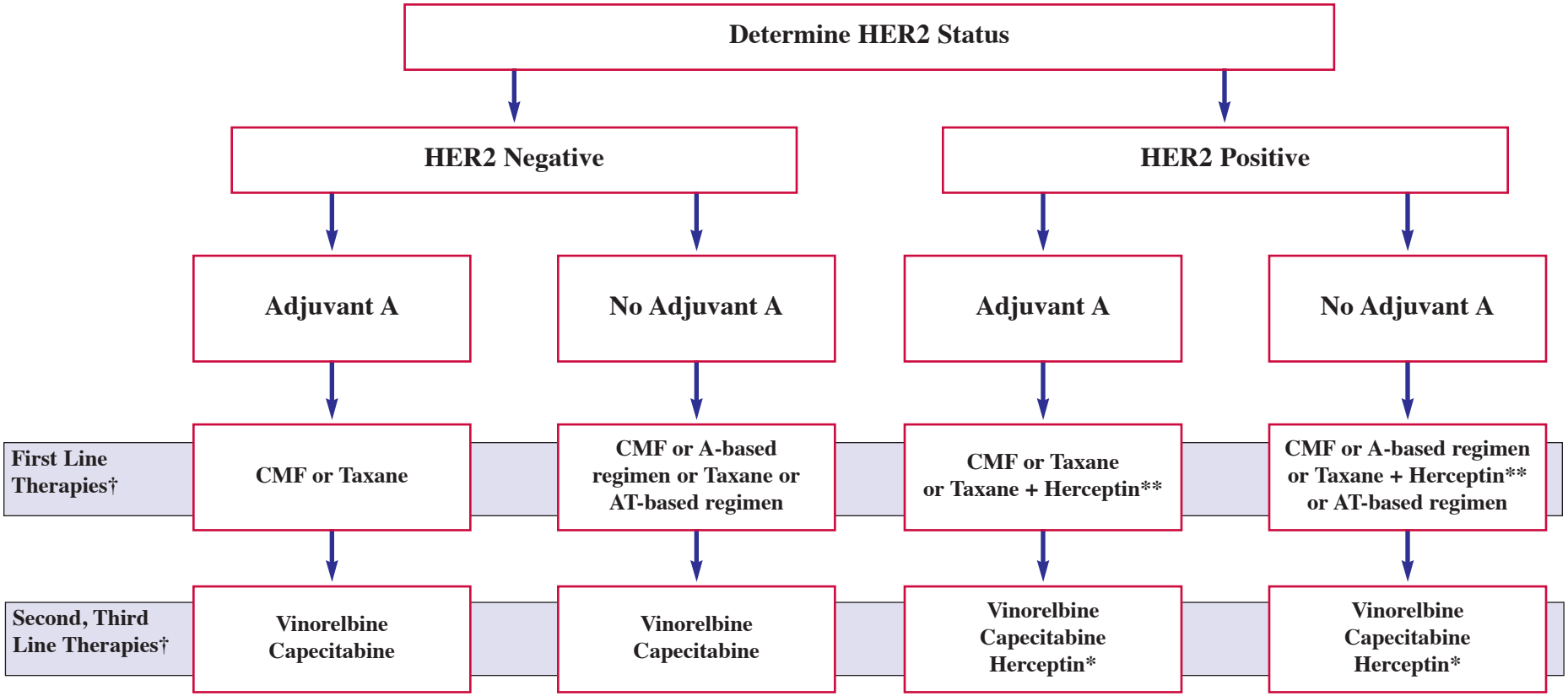
Treatment of Systemic Recurrence with Chemotherapy



A = anthracycline **T = taxane**

† Therapeutic regimens may be used sequentially at each level
* if T already used above
** Taxane = taxol as of March 2000 until safety and efficacy data is available for taxotere
• A bisphosphonate should be given in addition to chemotherapy if ≥ one osteolytic bone lesion with reasonable life expectancy and renal function

Always encourage participation in clinical trials - the patient will receive at least standard therapy, and maybe something better.

By Maureen Trudeau, MD, FRCPC, Head, Medical Oncology/Hematology, Toronto-Sunnybrook Regional Cancer Centre
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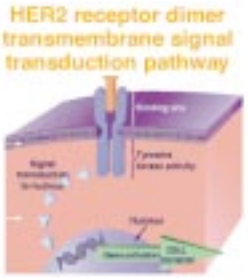
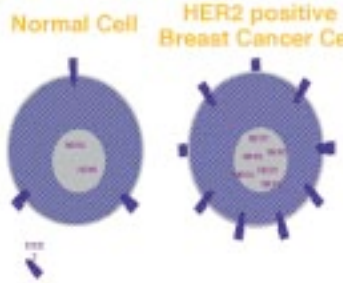
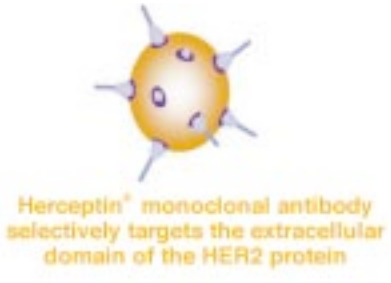
Herceptin® (trastuzumab)







- HER2 (also called HER-2/neu or c-erbB2) is a cellular tyrosine kinase transmembrane receptor responsible for triggering cell growth
- Overexpression is:
  - Prognostic of more aggressive disease
  - Prognostic of a poorer outcome in both node positive and node negative breast cancers
  - Detected in ≈ 25% of breast cancers (≈ 16% estrogen receptor positive)
  - Predictive of response to Herceptin (especially if highly overexpressed)
  - May indicate increased sensitivity to anthracyclines and decreased sensitivity to CMF (cyclophosphamide, methotrexate, fluorouracil) and Tamoxifen
- Testing is currently done by immunohistochemical staining methods (IHC)
  - If staining is strong (3+) then the test is considered positive
  - If staining is weak (0, 1+) then the test is considered negative
  - If staining is moderate (2+) then a confirmatory test is carried out using Fluorescent In Situ Hybridization (FISH) (detects gene amplification), and is either positive or negative.
- Herceptin (Trastuzumab) is an anti-HER2 monoclonal antibody that selectively targets the extracellular domain of the HER2 protein and stimulates antibody-dependent cell mediated cytotoxicity
- Use is now limited to patients with tumours 3+ by IHC or FISH+
- Currently Herceptin is administered intravenously once weekly, but every-three-week regimens are under investigation. It is generally well tolerated (sometimes with fever or chills on initial injection) but must be used with caution in patients with extensive lung disease.
- In the pivotol clinical trial comparing chemotherapy [either AC (adriamycin, cyclophosphamide) or T (taxol)] plus Herceptin versus that chemotherapy alone, significant improvements were noted with the addition of Herceptin (patients were included whose tumours were HER2 2+, HER2 3+). Response to treatment, duration of response, time to tumour progression and overall survival were all significantly better (25% or 4.5 months increase in overall survival). The survival benefit was greatest for women whose tumours were HER2 3+ (nine months). The side effect of cardiac dysfunction was seen particularly with AC, and use of concurrent anthracycline + Herceptin combinations are not recommended.
- **Recommendations for the use of Herceptin are as follows:**

For Metastatic Disease:*

- After anthracycline failure, Herceptin + Taxol may be given in combination. In the pivotol trial, because the survival benefit was seen with chemotherapy plus Herceptin, in spite of crossover by three quarters of the patients to Herceptin after chemotherapy, the combination is often offered first.
- After failure of two previous chemotherapies, (one of which may have been adjuvant therapy) Herceptin may be given as a single agent.
- Studies in combination with Taxanes ± platinum and other agents such as Navelbine are ongoing

For Adjuvant Therapy:

- Treatment is only recommended within the context of a clinical trial, eg chemotherapy with randomization to Herceptin or no Herceptin.

**** Current Cancer Care Ontario guidelines***

By Maureen Trudeau, MD, FRCPC, Head, Medical Oncology/Hematology, Toronto-Sunnybrook Regional Cancer Centre
Supported by an educational grant from Hoffmann LaRoche.

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