Introduction

A diagnosis of breast cancer can be an incredibly frightening time in a woman’s life and in the lives of her family members. How, or why, has this happened to me? What will happen to me? Can I expect to live? What will my life be like after this? Questions such as these are inevitable and must be addressed. The process of coping begins with answering them. Survivors of breast cancer often find that they feel more in control of their care, their lives, and their future when sufficient and accurate information is made available to them. The disease and its treatment become less of a “dark tunnel” and become something more measurable and within their grasp.

Since its first publication several years ago, Breast Cancer and You has been read by thousands of women and healthcare providers and has often been the starting point for initial discussions between newly diagnosed patients and their oncologists regarding the choice, side effects, and outcomes of various treatments. Over the past decade, there have been immense advances in the state of our knowledge about breast cancer, and treatment decisions have increasingly become more individualized. The differences between the various types and stages of breast cancer and the individual ways in which treatment might be approached are particular strengths of this edition of Breast Cancer and You. It is our collective hope that you will benefit from the up-to-date information in your effort to progress from patient to survivor!

**Dr. Shailendra Verma**

*Medical Oncologist*

Ottawa Regional Cancer Centre
Physicians who contributed their time and expertise:

Fourth Edition

Chief Editor
Katia Tonkin
Medical Oncologist
Edmonton, AB

Nadia Califaretti
Medical Oncologist
Kitchener, ON

Stephen Chia
Medical Oncologist
Vancouver, BC

Mark Clemons
Medical Oncologist
Toronto, ON

Daniel Rayson
Medical Oncologist
Halifax, NS

Sandy Sehdev
Medical Oncologist
Brampton, ON

Shailendra Verma
Medical Oncologist
Ottawa, ON

Third Edition

Chief Editor
Katia Tonkin
Medical Oncologist

Nadia Califaretti
Medical Oncologist

Mark Clemons
Medical Oncologist

Ginette Martin
Surgeon-Oncologist

Shailendra Verma
Medical Oncologist

Other contributors:

Kathy White-Williams
Registered Nurse
Nursing Professor
Breast Cancer Survivor

Audrey Friedman
Director, Patient Education Services
Princess Margaret Hospital

Celina Dara
Oncology Pharmacist

Dianne K. Kieren
Professor University of Alberta
Edmonton, Alberta

Ceinwen E. Cumming
Psychologist

Marilyn Hundleby
Psychologist

Linda Harris
Research Assistant

Wendy Schmidt
Editorial Assistant

Colleen Young
Medical Editor (4th Edition)

Amgen Canada would also like to thank the many breast cancer patients who took time to contribute to the development of this booklet.
# Contents

About This Guide ................................................. 1

**The Breast Cancer Team** ........................................ 2
Physicians .................................................. 3
Other Members of the Breast Cancer Team 3

**Understanding Breast Cancer** .................................. 5
How Cancer Develops ........................................ 6
How Breast Cancer Develops ............................. 7
What Causes Breast Cancer? ............................ 8

**Early Detection and Screening for Breast Cancer** .......... 10
Screening Guidelines ..................................... 11
Investigating Breast Lumps ............................ 11

**The Diagnostic Process** ........................................ 12
Diagnosis of Breast Cancer ............................. 14

**Pathology and Staging** .......................................... 16
Staging Breast Cancer .................................... 18
Prognostic Factors ........................................ 21
Predictive Factors ......................................... 23

**Treatment** .......................................................... 24
Treatment Options .......................................... 27
Treatment of Breast Cancer by Stage .............. 45
Clinical Trials ................................................ 59
New Developments in Treatment .................. 62

**Living with Cancer** ............................................... 64
Dealing with Your Emotions ........................... 66
Coping with Age-Related Issues ...................... 66
Coping with Treatment ................................. 67
Coping with Life Changes ............................ 69
Finding Information ................................. 70

**Glossary** ................................................................. 73
Through breast self-examination, physical examination, mammography, ultrasound examination, and sometimes other newer radiological investigations, many women are diagnosed with breast cancer at a very early stage of the disease. In fact, the increased incidence of breast cancer seen in the 1990s is due mostly to an increase in the diagnosis of early breast cancer. The prognosis for these early tumours is very good. Most women with breast cancer survive more than 10 years, making breast cancer one of the most treatable of all cancers. More than 70% of women diagnosed with breast cancer remain cancer-free and never experience a relapse.

Breast cancer patients can look forward to more and more success stories as new investigations and treatments are developed. Your treatment plan will be tailored according to your cancer type and other factors. It is not uncommon for women to receive different types of treatment.

Although the highest risk of relapse is in the first three years after diagnosis, breast cancer can sometimes come back (relapse or recur) many years, even decades, after initial treatment. Rather than referring to “curing” breast cancer, it is more correct to think in terms of “long-term control” or “cancer-free survival.” Late relapses or recurrences are possible; however, new therapies continue to help increasing numbers of women live their lives cancer-free.

This guide was written to help you, a patient diagnosed with breast cancer, find the information and help that you may need. Surveys have found that women diagnosed with breast cancer want several types of information, such as:

- Medical information about the stage of their disease, the likelihood of a cure and their treatment options
- Practical information about procedures and resources
- Information about coping with the emotional effects of cancer on themselves and their families

You can participate in your care and make informed decisions if you understand more about your diagnosis, your treatment options and the results you can expect. You may also be searching for resources, such as books, websites, videos and support groups, to help you cope. This publication has been developed to help meet your information needs.

Definitions of unfamiliar words can be found in the glossary at the back of this guide.
The Breast Cancer Team
The Breast Cancer Team

Your cancer journey will involve a number of healthcare professionals with a variety of specialties. Each diagnosis is unique and your treatment plan will be chosen to suit you. The members of your diagnosis and treatment team may include some of the following healthcare professionals.

**Physicians**

**Primary care physician**
The family doctor, gynecologist or OB/GYN (obstetrician/gynecologist) is often the first physician to be involved in the diagnosis of breast cancer. If, during a routine physical exam, an abnormality is detected in the breast, you may be referred to a breast centre, local radiology centre, local hospital or breast screening facility for further diagnostic investigation.

**Radiologist**
Radiologists are physicians who specialize in the use of radiation and radioactive substances (such as x-rays) to diagnose and treat patients. They interpret the results of diagnostic tests such as mammograms and ultrasounds. Some radiologists also perform image-guided breast biopsies.

**Surgeon**
A surgeon performs breast biopsies, lumpectomies, mastectomies, axillary node dissections or sentinel node biopsies on breast cancer patients. Some breast surgeons work with plastic surgeons who may reconstruct the contour of the breast during the same operation in which the breast is removed.

**Pathologist**
A pathologist specializes in the diagnosis and classification of diseases using laboratory tests. After breast cancer has been detected, the pathologist will study a sample of cancer cells to determine the origin of the disease and whether or not it has invaded nearby tissues. A pathologist will also assign a grade to your breast tumour and identify the type of tumour present, and will help recommend a treatment plan for an optimal outcome.

**Radiation oncologist**
Radiation oncologists specialize in using radiation to treat cancer and work with other cancer specialists to design a customized treatment plan.

**Medical oncologist**
Medical oncologists are trained to use drugs to treat cancer. They may administer chemotherapy, hormonal therapy and/or biological therapy.

**Other Members of the Breast Cancer Team**

Many other health professionals provide very important support in the care of women during their experience with breast cancer.

**Nurse/oncology nurse specialist**
Nurses work in the clinic performing a variety of roles. They may prepare and oversee the administration of treatment, monitor patients and provide supportive care, such as teaching and counselling patients and their families throughout the treatment process. Some are also involved in research.

**Pharmacist**
Pharmacists work in hospitals, cancer centres or retail pharmacies. They prepare chemotherapy drugs and...
can provide information about chemotherapy regimens and advice on drug interactions.

**Physiotherapist**

Physiotherapists help women deal with arm mobility problems as well as arm pain and swelling (lymphedema) that may occur.

**Dietician**

Dieticians offer information and advice on nutrition.

**Oncology social worker**

Oncology social workers can help patients deal with the non-medical crises that can result from cancer. Mental health professionals, psychologists, psychiatrists and spiritual advisers offer support and counselling. These and often other people, including family and friends, are available and ready to assist you in any way you need to be supported throughout your breast cancer journey.
Understanding Breast Cancer
Understanding Breast Cancer

Breast cancer starts in the cells of the breast. Learning about how breast cancer develops and about its causes and risk factors can help you better understand your disease and its treatment.

How Cancer Develops

Even after you stop growing, many cells in your body continue to divide and multiply. They multiply to replace cells damaged by injury or disease and those that have died. Normal cells are programmed to die in response to internal signals (programmed cell death, or apoptosis). Genes direct and coordinate the activities of all the cells in the body. Signals to multiply and instructions to die are controlled by specific genes. As cells divide and multiply, mistakes, known as mutations, can occur.

Mutations can be caused by certain infections, by exposure to chemicals or radiation, or spontaneously and randomly. If there are enough mutations in the genes controlling either growth or programmed cell death, a cell may begin to multiply for no reason or it may ignore instructions to die. When this happens, the cell becomes cancerous, or malignant. It may continue multiplying until it forms a tumour. Cells may break away from the tumour and travel to other parts of the body, where they continue multiplying to form a secondary tumour, or metastasis.

Figure 1: Normal breast
How Breast Cancer Develops

Covering an area larger than just the breast itself, breast tissue extends up to the collarbone and from the armpit to the breastbone. Behind the breast tissue are the muscles of the chest and upper arm.

The breast is made up of milk glands, milk ducts and fatty tissue. The milk glands, which produce milk, are grouped into lobules. The ducts carry the milk to the nipple. The circle of darker skin around the nipple is called the areola. Within the breast, the glands and ducts are surrounded and protected by fatty tissue. Breast tissue changes with age: during adolescence, it consists mostly of milk ducts; in older women it consists mostly of fatty tissue.

Most breast cancers (85%) begin in milk ducts. Most of the remaining breast cancers start in lobules. Other, rarer types of breast cancer include inflammatory breast cancer and Paget’s disease.

Non-invasive (in situ) breast carcinomas are tumours that have remained within the milk ducts or lobules of the breast. They have not spread to the surrounding tissues, lymph nodes or other organs. When the cancer is in milk ducts of the breast, it is called intraductal carcinoma or ductal carcinoma in situ (DCIS). When cancer is in the lobules of the breast, it is called lobular carcinoma in situ (LCIS).

DCIS and LCIS are pre-invasive cancers. They almost never spread outside the breast themselves, but they are associated with a slightly higher risk of developing invasive cancers in the future. If diagnosed early, however, there is no risk of them spreading after they have been removed.

When cancer in a milk duct escapes beyond the duct walls, it is known as invasive ductal cancer. Likewise, invasive lobular cancer is cancer in which the tumour cells have spread beyond the lobules to invade surrounding tissues. If diagnosed early, invasive cancers can be treated effectively. Cancer cells can spread beyond the surrounding tissues by travelling through lymph channels and blood vessels to other parts of the body. Breast cancer that has spread and established a new tumour elsewhere is called metastatic breast cancer.
Although there is no single cause of breast cancer, some factors appear to increase the risk of developing it.

- Age (breast cancer risk increases with age)
- Family history of breast cancer
- Family history of uterine, colorectal or ovarian cancer
- Previous breast disorders with biopsies showing abnormal cells
- No pregnancies or having a first pregnancy after age 30
- Beginning to menstruate at an early age (before age 12) and/or reaching menopause later than average (after age 55)
- Having dense breast tissue
- Taking hormone replacement therapy (estrogen plus progestin) for more than five years
- Increased alcohol consumption may increase breast cancer risk
- Smoking, diet, physical activity level and obesity may affect risk; this is under study

Most women with breast cancer do not have a family history of the disease nor do they have any of the other identified risks.

**Family history and genetics**

Most inherited cases of breast cancer are associated with two specific genes: BRearCancer 1 (BRCA1) and BRearCancer 2 (BRCA2). When they function properly, the BRCA1 and BRCA2 genes keep breast cells growing normally and prevent cancer cell growth, but when either of these genes contains abnormalities or mutations they are associated with a higher risk of developing breast cancer.

Inherited abnormal BRCA1 and BRCA2 genes are responsible for only about 5–10% of all cases of breast cancer. These genes, when abnormal, are also associated with other cancers, including ovarian cancer. In families with the inherited mutation, breast and ovarian cancers often appear in people who are younger than might otherwise be expected. BRCA1 and BRCA2 genetic mutations may also increase the risk of breast cancer developing in men.

There is still a lot more to learn about these genes. All cancer cells contain genetic changes or abnormalities that led to the growth of the tumour. Many of these genetic changes have not yet been identified, but several abnormalities have been found in breast cancer. Abnormalities in the genes that cause cancer cell growth may be relevant to breast cancer treatment decisions for women with and without a family history of the disease.

**Genetic counselling**

If you have a family history of breast or ovarian cancer (or both), you may wish to seek genetic counselling. Because a genetic mutation can be inherited from either the maternal or paternal side of the family, genetic counsellors examine the complete family history, or pedigree, usually going
back three generations. They will assess whether genetic testing may be helpful on a case-by-case basis. Genetic testing will likely be recommended if your family pedigree strongly suggests that an inherited form of the disease is present.

Specialized screening, follow-up and treatments may be considered for women who carry the BRCA 1 or BRCA 2 genes, as well as for their family members. Occasionally, this may include mastectomy before a definite cancer is found in the breast (prophylactic mastectomy) to reduce the likelihood of breast cancer developing, as well as removal of the ovaries to decrease the chance of ovarian cancer. These choices are difficult to make and should be discussed with your doctor, surgeon and family.

**Prevention of breast cancer**

Various clinical trials have shown that tamoxifen, a hormonal therapy (see Hormonal therapy, page 31), can be effective at preventing breast cancer in women who are at a high risk of developing it. Some of the risk factors in the women who were in these studies include:

- Age — risk increases as you get older
- Having relatives diagnosed with breast cancer
- Previous breast biopsy showing abnormal cells

Tamoxifen is the only medication currently considered for the prevention of breast cancer. If you are at high risk for developing this disease, you should discuss the pros and cons of tamoxifen treatment with a qualified healthcare professional, such as an oncologist. In new ongoing studies, researchers are evaluating the effectiveness of raloxifene (Evista®), a drug related to tamoxifen, and another class of drugs called aromatase inhibitors, including anastrozole (Arimidex®), lertozole (Femara®) and exemestane (Aromasin®).
Early Detection and Screening for Breast Cancer
Early Detection and Screening for Breast Cancer

Many breast cancer survivors lead long healthy lives because their breast cancer was detected and treated early. Screening tests, such as an annual clinical breast examination and/or mammography, are the most reliable methods of finding breast cancer. These tests look for signs of disease in women without symptoms.

Screening Guidelines

The Canadian Cancer Society* provides the following screening guidelines:

- If you are 70 or older, talk to your doctor about a screening program suitable for you.
- If you are between 50 and 69, have a mammogram every two years.
- If you are between 40 and 49, discuss with your doctor your risk of breast cancer, along with the benefits and risks of mammography.
- If you are over the age of 40, have a clinical breast examination by a trained health professional at least every two years.

For women in their 20s and 30s, it is recommended that clinical breast examination be part of a periodic health examination, preferably at least every three years.

You may also wish to do regular breast self-examination and report any changes you find to your doctor.

Investigating Breast Lumps

The breast is made up of glands that produce milk, ducts that carry milk to the nipple and fatty tissue. Breast tissue grows and changes in response to alterations in hormone production during puberty and menopause. Women often develop breast lumps, which are usually not cancerous, during these stages in life. Hormone production may also cause changes to the breast or cause lumps to form during a woman’s menstrual cycles, pregnancy or breast feeding (lactation).

For example, women still having their monthly cycles (Pre-menopausal women) often notice such changes or the development of lumps before their periods. These often reappear and disappear with every cycle. Any lump that does not completely disappear after your period should be investigated. If you have stopped having your monthly cycles (are post-menopausal), a new lump or changes in an existing lump should be investigated by your doctor.

Breast lumps may be found by a physician during a physical examination, by you during self-examination or by a screening mammogram. Any new or non-healing skin rash on the breast, lumps or swellings in the armpit or suspicious abnormalities found on a mammogram require further tests and follow-up.

The Diagnostic Process

Diagnosis is the process of identifying a disease from its signs and symptoms. The diagnostic process usually begins with a visit to your family doctor with a specific complaint or symptom, or perhaps because your doctor discovers an abnormality during a routine check-up. Your doctor will take a medical history and perform a physical examination to come up with the initial diagnosis.

The next step is to perform further testing (e.g., mammography, laboratory tests, x-rays) to determine the exact diagnosis. The diagnosis of breast cancer often requires the examination of a tissue sample (biopsy) from the breast.

The diagnostic process involves tests to:

- Confirm the presence of cancer
- Identify the type of cancer
- Locate where the cancer started (primary tumour)
- Help determine the extent or spread of the cancer (stage)
- Aid in treatment decision-making
- Help determine if cancer has returned (recurrence)

“I know when I was first diagnosed — I mean, that fear is raw fear. And that was until the breasts came off. Once the breast came off it was like, that’s it. I’m free, because I’m here, I’m alive and my chances are gonna be good. Once it was gone it was total relief. I was so thankful that it was finally gone.”

~ Breast cancer survivor
Diagnosis of Breast Cancer

Either you or your physician may first discover a lump in your breast. If your doctor suspects cancer, he or she will first perform a physical examination. The examination will involve searching for enlarged lymph glands (nodes) under the arm (axilla) and at the base of the neck.

**Diagnostic tests**

The diagnosis of breast cancer involves more than a physical examination. Most lumps are not cancerous and your doctor will arrange special tests to confirm the diagnosis. Because the results from any one procedure may be uncertain or inconclusive, a combination of tests may be performed, such as:

- Mammography
- Ultrasound examination
- MRI (magnetic resonance imaging)
- Biopsy

**Mammography**

Mammography uses low-dose x-rays to find tumours or other problems in the breast. However, mammograms can miss up to 10% of cancers. Mammograms are less effective in women under 40 because their breast tissue is denser than that of older women. Dense breast tissue can make it difficult to read the mammogram and may hide an underlying cancer. For young women with high breast density, other tests may be recommended in addition to a mammogram.

**Ultrasound**

Examination of the breast using ultrasonography, or ultrasound, can distinguish between a solid lump and a fluid-filled cyst, but may not always distinguish between benign and cancerous tumours.

**MRI**

Magnetic resonance imaging may sometimes be used in identifying a suspicious area for possible biopsy when neither mammogram nor ultrasound results are clear.

**Biopsy**

The appearance of cancer cells and the pattern in which they are growing are important to diagnosing breast cancer correctly. To do this, a small sample of the tumour will be removed and examined under a microscope. Examining this tissue can confirm whether or not cancer is present and if it is present, what type of cancer it is. The procedure used to remove the tumour sample is called a biopsy. A biopsy is usually necessary to make a definite diagnosis of cancer. There are different types of biopsies.

A needle, or core, biopsy, or an open surgical biopsy of the lump may be performed to take a sample of tissue from the suspicious area for microscopic analysis. Your surgeon will try to use the least invasive procedure possible.

During a needle or core biopsy, a needle is inserted into the suspicious area and a small tissue sample is removed. This procedure can be performed under local anesthetic and is often done with the guidance of ultrasound or CT (computed tomography) by a radiologist.

An open, or incisional, biopsy involves removing a piece of the involved tissue through a small cut. An incisional biopsy usually requires only a local anesthetic.

An excisional biopsy is the most involved kind of biopsy. It attempts to remove the entire suspicious lump of tissue from the breast. You may have an
excisional biopsy as an outpatient, usually with only a local anesthetic.

**Other tests**

Once a diagnosis has been made, other tests may be done before or after surgery to see if the cancer has spread outside your breast. These tests may include:

- Axillary or “sentinel” lymph node dissection
- Blood test
- Chest X-ray
- Bone scan

**Axillary lymph node dissection:** Surgical removal of the lymph nodes in the armpit (axilla) is usually done in patients with invasive breast cancer. The lymph nodes are removed and examined under a microscope to find out if they contain cancer or not, thus helping to determine the extent or stage of the breast cancer.

**Sentinel lymph node dissection:** Sentinel lymph node dissection is a new and more selective way of removing and evaluating lymph nodes that is appropriate for women with early-stage, invasive breast cancer who have a low – to – moderate risk of lymph node involvement. It may also be called sentinel lymph node biopsy or lymphatic mapping. By injecting a radioactive and/or blue dye, the surgeon can identify the lymph nodes into which the tumour first drains. These nodes, known as the sentinel nodes, are removed, and if they contain no cancer cells, additional surgery on the lymph nodes in the armpit may not be necessary. This procedure can spare many women extensive surgery in the armpit to remove lymph nodes and can reduce the possibility of subsequent post-operative pain, reduced mobility and swelling in the arm (lymphedema).

Although sentinel node biopsy is used routinely by some surgeons, this procedure is still being studied in several clinical trials to determine when best to use it and for which patients it is most useful.

**Blood tests:** Occasionally, doctors order additional blood tests called tumour marker tests to detect possible cancer activity in the body. These markers may be used as an early indicator of disease progression or recurrence. If you have an elevated marker before treatment, your doctor may check that marker periodically to assess response to chemotherapy.

**Chest X-ray:** A chest x-ray may be done to find out if cancer has spread to the lungs. This test may also assess your heart and lungs before you receive general anesthesia or chemotherapy.

**Bone scan:** A bone scan (also called bone scintigraphy) may be used to determine whether cancer has spread to the bones. You will receive an injection of radioactive material that is taken up by the body’s bone-making cells. These bone-making cells are found mostly in areas damaged by disease, where they are trying to make new bone to repair the damage. Using a special camera, doctors are able to see these areas of extra bone activity by detecting the gamma rays emitted by the injected material.
Pathology and Staging
Pathology and Staging

A pathologist (a physician who diagnoses disease by examining tissue) examines the biopsy tissue of the tumour under a microscope using special stains. The tumour characteristics are evaluated to provide a detailed diagnosis — the pathologic diagnosis.

The pathologic diagnosis includes:

- Whether the cells are cancerous or not
- Tumour stage (tumour size and extent of spread)
- Tumour grade (how closely the cells resemble normal cells and how aggressively they are reproducing and/or spreading)
- Prognostic factors (special cell characteristics or other conditions that might influence how the disease may progress)
- Predictive factors (characteristics that predict the tumour’s response to treatment)

Using the information gathered from the pathologic examination and the results of your physical examination and diagnostic tests, your treatment team will stage the cancer. They will also evaluate the prognostic and predictive factors to make a statement about the likely outcome of the disease and how it may respond to treatment. With this information, you and your treatment team can choose the best treatment options for you.

When discussing your treatment options with you, your doctor may choose to use online assessment tools to illustrate how your cancer may be treated according to the specifics of your case. Adjuvant! Online is one such web-based tool that helps health professionals and patients with early breast cancer discuss the risks and benefits of getting additional therapy after surgery. Because of the complexity of interpreting some of the information required, the information should be entered into Adjuvant! Online by a health professional with experience in cancer medicine.
Staging Breast Cancer

Once the diagnosis of breast cancer has been confirmed, it is important to know what stage your cancer is. Staging describes or classifies cancer according to the extent of cancer involvement within the body.

Stage is determined by:

• The size of the tumour mass
• How much the tumour has spread to nearby tissues
• Whether or not the cancer has spread to the lymph nodes under the arm (axilla)
• Whether or not the cancer has spread to more distant areas of the body (e.g., liver, brain, bones or lungs)

Tumour stage is an important predictor both of how the cancer will behave in the future and of the risk of recurrence. The results of the pathologic diagnosis, physical examination and diagnostic testing are used to determine the stage of your cancer. Your treatment team gathers all this information to predict how your disease may respond to treatment and to determine which treatment options are best for you. Even if cure is not possible, staging assists in determining the treatment that has the best chance of limiting the effects of cancer on your life.

Staging systems

Two staging systems are commonly used to classify breast cancer: the Stage 0 to IV (0 to 4) system and the Tumour Node Metastasis (TNM) system.

The Stage 0 to IV system is the one used in the actual care of patients (clinical practice). Very simply, the lower the stage, the greater the chance of a cure; the higher the stage, the greater the risk of the cancer coming back. This system divides breast cancer into the following, very broad groups:

• Stage 0: non-invasive cancer (in situ)
• Stage I: tumour is less than 2 cm across and has not spread to the axillary lymph nodes under the arm
• Stage II: tumour is between 2 and 5 cm across or has spread to the axillary lymph nodes, or both
• Stage III: tumour is larger than 5 cm across or is a more advanced tumour that involves overlying skin and has spread to the lymph nodes
• Stage IV: a tumour of any size that has spread to sites distant from the primary tumour (metastatic cancer)

The TNM classification is most often used for research and analysis of cancer statistics. This system classifies tumours by tumour size (T), by lymph node involvement (N) and by the presence of metastases (M). See Table 1 for the TNM classification descriptions. Table 2 offers a summary combining the two staging systems.
### Table 1: TNM breast cancer staging

<table>
<thead>
<tr>
<th>Tumour (T) classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis</td>
<td>Localized non-invasive tumour (DCIS, LCIS, Paget’s disease)</td>
</tr>
<tr>
<td>T1</td>
<td>Invasive tumour, 2 cm or less across</td>
</tr>
<tr>
<td>T2</td>
<td>Invasive tumour, more than 2 cm but less than 5 cm across</td>
</tr>
<tr>
<td>T3</td>
<td>Invasive tumour, larger than 5 cm across</td>
</tr>
<tr>
<td>T4</td>
<td>Invasive tumour of any size attached to, or invading, surrounding tissues; includes inflammatory carcinoma</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lymph node (N) classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>Cancer has not spread to lymph nodes (node-negative)</td>
</tr>
<tr>
<td>N1</td>
<td>Cancer has spread to 1 to 3 axillary lymph node(s) on the same side as the breast cancer and/or to internal mammary nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Cancer has spread to 4 to 9 lymph nodes on the same side as the breast cancer or to internal mammary nodes</td>
</tr>
<tr>
<td>N3</td>
<td>This group includes 4 sub-groups:</td>
</tr>
<tr>
<td></td>
<td>• 10 or more positive nodes in the armpit (axilla), OR</td>
</tr>
<tr>
<td></td>
<td>• nodes under the collarbone (infraclavicular), OR</td>
</tr>
<tr>
<td></td>
<td>• nodes in the armpit WITH internal mammary nodes, OR</td>
</tr>
<tr>
<td></td>
<td>• only nodes above the collarbone on the same side as the breast cancer</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastasis (M) classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant spread</td>
</tr>
<tr>
<td>M1</td>
<td>Distant spread (e.g., lung, liver or bones)</td>
</tr>
</tbody>
</table>

### Table 2: Breast cancer staging summary

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumour (T)</th>
<th>Node (N)</th>
<th>Metastasis (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T0</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>No</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T0</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1, N2</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T4</td>
<td>any N</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>any T</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>any T</td>
<td>N3</td>
<td>M1</td>
</tr>
<tr>
<td>Stage IV</td>
<td>any T</td>
<td>any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

Prognostic Factors

Characteristics that affect the risk of your cancer spreading or recurring are known as prognostic factors.

Prognostic factors for breast cancer may include:
- Tumour size
- Spread to lymph nodes
- Microscopic vascular (blood vessel) invasion
- Tumour grade
- Your age
- Hormone receptor status
- Increased HER-2 gene levels

After the physicians in your team assess these factors, your tumour can be given a risk status, or prognosis. Risk status — the chance of the tumour coming back — further contributes to determining the best treatment choices for you.

**Tumour size**

The size of the primary tumour in the breast affects the risk of the disease coming back in the future (relapse). For example, tumours larger than 2 cm have a risk of relapse of 20–30% even if no lymph nodes are affected. Because larger tumours have a greater chance of relapse, most patients with these tumours receive either chemotherapy, hormonal therapy or both after surgery to decrease that risk.

**Figure 2:** Lymph nodes groups near the breast
Spread to lymph nodes
If your tumour has spread to the lymph nodes, the tumour is called node-positive; if it has not spread to lymph nodes, the tumour is node-negative. Lymph nodes that contain cancer cells indicate that the tumour has already spread outside the breast. Detecting breast cancer before it has spread to parts of the body beyond the lymph nodes increases the chance of cure.

Tumours that have spread to the lymph nodes (node-positive) have a higher risk of relapse than node-negative breast cancer does. If you have node-positive cancer, you may receive chemotherapy, hormonal therapy or biological therapy after surgery to reduce your risk of relapse.

Microscopic vascular invasion
The presence of cancer cells in either lymph channels (the lymphatic system) or blood vessels found in the tissue removed with the primary tumour indicates a more aggressive tumour that is more likely to spread or recur in the same region.

Tumour grade
Grading classifies cancer cells based on their appearance and behaviour when viewed under a microscope. Tumour grade is usually determined by the pathologist’s analysis of three features:
- How frequently the cancer cells are dividing (mitotic activity)
- Their tendency to spread to other locations
- How different they look from normal cells

Differentiation is the difference in appearance and function between cancer cells and normal cells. The tumour is graded according to the degree of differentiation and the cell growth rate.

Low-grade
Low-grade tumours most resemble normal breast tissue. The cancer cells are usually well-differentiated and the tumours are slower growing and have a lower risk of spreading.

High-grade
High-grade tumours do not resemble normal breast tissue. The cancer cells are usually poorly differentiated or undifferentiated, the tumours grow quickly and have a greater risk of spreading.

Age
Women who are diagnosed with breast cancer at a younger age, especially those diagnosed before the age of 35, usually have a greater risk of relapse. It is not certain, though, whether this is simply because they have more years ahead of them and therefore more time for cancer to redevelop, or whether the cancer cells themselves are somehow different.
Predictive Factors

Predictive factors are tumour characteristics that suggest whether or not a tumour will respond well to a specific treatment.

Some well-known predictive factors include:

- Increased HER-2 gene levels
- Hormone receptor status

Hormone receptor status and HER-2 gene levels may also be considered prognostic factors.

**Hormone receptor status**

Normal breast cells contain receptors for estrogen (ER) and progesterone (PR). Estrogen and progesterone are the hormones responsible for directing breast development and function. At the time of biopsy, tumour cells are tested to see whether they have estrogen receptors (ERs) or progesterone receptors (PRs).

Tumours that contain receptors for one or both of these hormones are considered receptor-positive. Such tumours tend to be more similar to normal breast tissue than tumours that do not contain these receptors. Hormone receptor-positive tumours are often less aggressive and are less likely to spread than tumours that do not contain estrogen or progesterone receptors (receptor-negative).

Hormone receptor-positive tumours are also more likely to respond to hormonal therapies, such as tamoxifen or the aromatase inhibitors (see Hormonal therapy, page 31.) This is especially true if the tumour is positive for both estrogen and progesterone receptors.

Post-menopausal women usually have receptor-positive tumours and pre-menopausal women are more likely to have receptor-negative tumours.

**HER-2 and the epidermal growth factor receptor family**

Four growth factor receptors form the epidermal growth factor receptor (EGFR) family. Growth factors circulate in the blood and bind or attach to growth factor receptors that sit on the surface of cancer cells. When these growth factors bind to the receptors, they can affect the inside of the cell and promote cell growth. Laboratory analysis of growth factors on breast cancer cells can help predict how that cancer may behave in the future.

Human epidermal growth factor receptor number 2 is called HER-2. It may also be referred to as the c-ErbB-2 or “neu” gene. HER-2 is a gene inside the cell that controls production of the cell’s corresponding growth factor receptor, or protein, on the surface of the cell. In approximately 25–30% of breast cancers, large quantities of this receptor protein are produced because of the increase in the level of the gene HER-2. This is called over-expression.

Normal growth factors in the blood bind to HER-2 and send a signal to the inside of the cell and can stimulate the cancer cells to divide. High levels of HER-2 on breast cancer cells may suggest that the tumour is more likely to recur or spread, and that it may not respond as well to some hormonal therapies or some chemotherapy drug regimens.

Today, there is a biological drug treatment called trastuzumab (Herceptin®) that can specifically help women with breast cancer and abnormally high amounts of the HER-2 receptor (protein) on the cancer cells. Trastuzumab is also called a targeted therapy because it targets breast cancers that make too much of (over-express) the HER-2 gene or protein (See Biological therapy, page 43).
Treatment

Although every woman with breast cancer will respond differently to treatment, the principles on which treatment is based and the terminology used to describe its outcome are the same. The following is a description of some of the terms you may encounter while receiving treatment.

**Primary therapy**
The first or initial therapy given after diagnosis is known as primary therapy.

**Adjuvant and neo-adjuvant therapy**
Adjuvant therapy refers to additional treatment, usually given after surgery during which all detectable disease has been removed, but when there is a chance that microscopic traces remain.

Neo-adjuvant therapy refers to treatment given specifically to help make the next treatment step go more smoothly. For example, in breast cancer chemotherapy, radiation or hormones may be given before surgery to help shrink the tumour.

**Standard therapy**
Standard therapies are treatments that have been used for years and have been tested thoroughly. Standard therapies are considered the most proven and effective therapies. There may be more than one standard therapy for a particular disease. If standard therapy is unlikely to produce a good response, however, you may be offered an investigational, or experimental, treatment as primary therapy.

**Local treatment**
Local treatment refers to any treatment targeted to a specific area of the body (e.g., the breast, the lymph nodes, the lungs) as opposed to the whole body. Treatment of the lymph nodes near the breast may also be referred to as regional treatment, because the lymph nodes lie in the region surrounding the breast. Local treatments for breast cancer include surgery and radiation.

**Systemic treatment**
Systemic treatment is therapy that affects the whole body. The goal of systemic treatments is to get rid of any cancer cells that may have spread to other parts of the body. Systemic treatments for breast cancer include chemotherapy, hormonal therapy and biological therapies.

**Response assessment**
After completing treatment, your physician will repeat some of the tests done during diagnosis to assess the response of your cancer to treatment.

Primary therapy can have four outcomes:

- **Complete remission** or **complete response**: all evidence of disease has been eradicated.
- **Partial remission** or **partial response**: the tumour has shrunk by at least 50%.
- **Stable response**: the disease remains unchanged.
- **Disease progression**: the disease has worsened or the tumour has grown during therapy; this may also be referred to as primary treatment failure.

Your doctors will discuss your treatment response assessment with you and help you understand the prognosis, probable disease outcome and goals of follow-up.
Follow-up after primary therapy

All patients who have been treated for breast cancer are scheduled for routine check-ups or follow-up appointments. Even many years after your initial treatment is over, you should be checked regularly so your doctor can monitor your health and make sure you continue to do well. As well as looking for early signs of relapse, your doctor will monitor you for possible development of long-term consequences of the disease or its treatment.

Some imaging studies may be performed only if relapse is suspected or if imaging is a requirement of a clinical trial (see Clinical Trials, page 58).

Remission and cure

A remission means you show no signs of disease. A long-lasting remission is known as a durable remission. If you experience a complete remission, your doctor will discuss with you the probability of cure, the probability of recurrence and the follow-up monitoring required. Cure means that all evidence of disease has been eradicated and there is very little possibility that the disease will recur. Because the chances of cure vary with the type of disease and the treatment, physicians are reluctant to promise cure unless several years have passed with no recurrence and the probability of recurrence is extremely low.

Relapse and salvage therapy

If the disease returns after a complete remission, it is termed a relapse or recurrence. If you have relapsed, have achieved partial remission or have experienced disease progression, you will be offered second-line, or salvage, therapy. Salvage therapy involves further treatments that may cure the disease or may result in a prolonged remission. Standard salvage therapies used after relapse are often successful in bringing about a second remission.

Risk of relapse

Although breast cancer can seem to be just a lump in the breast (localized disease), the chance, or risk, of it developing into a disease affecting other parts of the body (systemic disease) is important when deciding on a treatment plan.

Breast cancer spreads in two ways:

- As a direct extension from the primary tumour into the local area of the breast, chest wall or lymph nodes
- By travelling through lymphatic channels or blood vessels to create new growths far from the original tumour (metastases)

The risk of a tumour spreading is assessed again after surgery. Your treatment team will determine whether additional treatment is advisable and will help you choose the best treatment plan. They will consider the prognostic and predictive factors to determine how likely it is that the cancer will come back in the breast, chest wall or elsewhere in the body. In other words, they measure the risk assessment.

Palliative therapy

If the disease is not curable with standard therapy and the patient has experienced multiple relapses, the effectiveness of further therapy is expected to be limited. Treatment is given to relieve symptoms and provide comfort. This type of therapy is termed palliative, and may include chemotherapy and radiation therapy.
Treatment Options

Breast cancer treatment today focuses on tailoring an individual treatment plan for each patient. Your plan will be based on the stage of your disease, prognostic and predictive factors as outlined above, and your personal choices. Factors such as other illnesses past and present, age, and whether you are pre- or post-menopausal are also considered.

The various types of treatment used in the management of breast cancer can be divided into two categories: local therapies, which treat the area of the tumour, and systemic therapies, which treat the entire body.

Local treatments include:
- Surgery to remove the tumour
- Radiation to destroy any cancer cells remaining at the site of the tumour

Surgical removal is often used first unless the tumour is considered large or it is felt to be inoperable. Using systemic treatment (either chemotherapy or hormonal therapy) before surgery is common for some groups of women in many hospitals and continues to be studied in clinical trials for a variety of reasons. For most patients, surgery is followed by radiation to the breast (or chest wall after a mastectomy) and often to the lymph nodes.

Systemic therapies are used to attack tumour cell growth, and include:
- Chemotherapy, which kills tumour cells as they grow
- Hormonal therapy, which keeps hormones from sending growth signals to tumour cells
- Biological therapy, which stops growth signals from stimulating the tumour cells

After initial surgery, you will probably receive radiation and chemotherapy, hormonal therapy and/or biological therapy, unless you are at a very low risk of the cancer relapsing or spreading. If you have chemotherapy, radiation is usually administered once the chemotherapy treatments are finished.

Much has been learned over the past 30 years from numerous clinical trials that have looked at the timing and choice of treatment. Combining the results of many trials that together involved many thousands of women (called a meta-analysis of trials) has led to the conclusion that the use of adjuvant systemic therapy either before or, more commonly, after surgery improves cancer-free and overall survival rates in patients with breast cancer.

Prior to starting treatment, your physicians will discuss different treatment options with you. So that you can participate in making important treatment decisions, you may find it useful to understand the types of treatment suggested, their possible results and potential side effects. You may also wish to read the section Treatment of Breast Cancer by Stage (page 45) first and then read about the treatment options being considered for you.

Surgery

Although breast cancer can and does spread outside the breast, local therapy using surgery remains an important part of treatment for several reasons. For some patients, surgery may be all the treatment team
feels is necessary. For other patients, surgery will be part of a larger treatment plan. In addition, surgery provides an opportunity to look at the tumour in the breast (the primary tumour) and glands in the armpit (axillary lymph nodes); this provides valuable information about the cancer itself and about the stage of the tumour. This knowledge will help you and your doctors make a fully informed decision about the treatment options most likely to be beneficial.

With surgical treatment of breast cancer, it is now often possible to remove less of the breast than was usually removed years ago. Even mastectomy (breast removal) is a more refined, less drastic option than it was a generation ago. As well, in many cases, fewer lymph nodes are removed.

Breast cancer surgery can be divided into two main types: mastectomy and breast-conserving surgery.

**Mastectomy**
The original surgery for breast cancer, developed approximately 100 years ago, was called a radical mastectomy. It removed the entire breast, skin, muscles in the chest wall and lymph nodes in the armpit. This drastic and deforming surgery is no longer performed. It has been replaced by the modified radical mastectomy.

A modified radical mastectomy removes the entire breast and some of the axillary lymph nodes but leaves the chest wall muscle, thus greatly reducing the risk of post-surgical pain, loss of mobility and lymphedema (swelling). Modified radical mastectomy usually involves one or two incisions over the chest wall and in the armpit.

A simple mastectomy removes only the breast without removing the lymph nodes.

A mastectomy usually means a short hospital stay and the temporary use of tubes to drain fluid from your armpit. Generally, pain after the operation can be easily managed using painkillers.

**Breast-conserving surgery**
Between the 1970s and 1990s, doctors gradually achieved a better understanding of the behaviour of breast cancer. Surgeons began to test the idea of removing less of the breast tissue along with the cancer in operations much smaller than a mastectomy. This approach, based on the idea that it is unnecessary to remove too much healthy breast tissue as long as the tumour is completely removed, is known as breast-conserving surgery.

Breast-conserving operations remove the tumour along with a margin of healthy tissue surrounding the tumour. Breast-conserving surgery makes it possible to remove the tumour completely while allowing a woman to keep her breast.

Types of breast-conserving surgery include:
- **Lumpectomy**: removal of the lump and a small amount of surrounding normal tissue (surgical margin)
- **Quadrantectomy**: removing about one quadrant, or quarter, of the breast
- **Segmental or partial mastectomy**: removal of a piece, or segment, of the breast

Breast-conserving surgery is often coupled with the surgical removal of some lymph nodes under the arm (axillary dissection).

**Axillary dissection**
Axillary lymph node dissection is the surgical removal of the lymph nodes in the armpit (axilla) and is often used in patients with invasive breast cancer. This surgery can be done using a general anesthetic (you will be unconscious) but without an overnight stay at the hospital (outpatient procedure). Most patients experience little pain except for a stiff or sore arm. Mild pain tablets are usually taken.

At some hospitals, a sentinel lymph node dissection may first be performed to confirm whether the cancer has spread to the lymph nodes. If the sentinel nodes are not cancerous, surgery to the armpit itself may be unnecessary. If the sentinel nodes are positive for cancer, then the surgeon will do the axillary node dissection.
Sentinel lymph node dissection is still being studied in several clinical trials and may not be available at your treatment centre.

“I think you need to have time to think about the changes to one’s body (lumpectomy and mastectomy), to grow into it, to absorb and become accustomed to it, whatever it is, because right away there’s often a feeling of ‘I didn’t want to look’.” ~ Breast cancer survivor

Choosing between mastectomy and breast-conserving surgery

Most women are able to have breast-conserving surgery. Clinical trials have proven that breast-conserving surgery plus radiation provides the same benefit as a modified radical mastectomy in terms of cancer-free, or overall survival rates. The choice, however, is yours.

Factors to consider when choosing between the two surgical options include:

- **Size of the tumour**: small tumours can be removed with breast-conserving surgery without noticeably changing the shape of the breast; larger tumours may require a mastectomy.
- **Size of the breast**: removing a large tumour from a small breast without changing the shape of the breast is difficult. In these cases, a mastectomy may be preferable.
- **Location of the tumour**: if the nipple or areola is involved, a mastectomy may be necessary.
- **Extent of the tumour**: if the tumour has spread throughout the milk duct system in the breast (extensive intraductal disease) a mastectomy may be recommended to remove as much of the disease as possible. If there are several tumours in one breast, or during an earlier surgery it was not possible to obtain tumour-free margins, a mastectomy may be the preferred option.
- **Where you live**: radiation therapy following breast-conserving surgery is usually given daily, Monday through Friday, for three to five weeks. This schedule may lead some women to choose mastectomy instead.

- **Your general health or personal situation**: for some women a mastectomy may be the better option because radiation therapy after breast-conserving surgery is inadvisable. For example, if you are pregnant, have other medical problems, have poor general health or have had previous radiation to the breast, you may be advised to choose a mastectomy.

- **Personal preference**: some women simply do not wish to have radiation therapy, and therefore choose a mastectomy. For some women it is important to keep their breast; for others, removing the entire breast allows them peace of mind.

If the breast cancer comes back in the breast itself (local relapse or recurrence), mastectomy is usually recommended because radiation to the breast usually cannot be repeated.

Some women prefer to have a mastectomy. They feel more comfortable having the whole breast removed because they feel they will not need to worry about the cancer coming back in the breast afterwards. If a mastectomy is done, radiation may still be given to the chest wall and lymph glands. Later, you can consider a breast replacement (called a prosthesis) or breast reconstruction surgery. Breast reconstruction can decrease the personal distress of losing a breast. It usually requires at least one and sometimes several operations.

Although it is possible to have a mastectomy and breast reconstruction done at the same time at some hospitals, this is usually not suitable for women who will need radiation after surgery. Many of the reconstruction techniques, such as abdominal tram flap surgery, involve moving tissue from other areas of the body to the breast, and this new tissue may not look acceptable if the area is treated with radiation afterwards.
Radiation

To kill tumour cells, radiation therapy, also called radiotherapy, uses a special type of radiation called ionizing radiation. Ionizing radiation affects the molecules of a cell and damages any cells in the radiation beam’s path. The doses of radiation are called “fractions.” Fractions are usually given once daily, Monday through Friday.

The goal of radiation therapy is to deliver high enough doses of ionizing radiation to kill or sterilize the cancer cells while causing minimal damage to healthy tissue. Because cancer cells divide rapidly they are more likely to be affected by repeated daily doses. Over the course of the radiation treatment, the number of tumour cells steadily declines until, hopefully, all the cancer cells are killed. Normal cells can recover after each radiation dose, or fraction, in about three to six hours. After several weeks of treatment even normal cells will be damaged, but they will recover as time passes.

After radiation to a breast, it will not usually be radiated again even if cancer recurs in the same breast. Radiation therapy may be used in other areas of the body, however.

How radiation therapy is administered

When breast cancer is treated with radiation after surgery, the treatment is usually given for a few minutes daily, five days a week, for three to five weeks. Radiation can be given at the same time as hormonal therapy and some mild forms of chemotherapy. Certain chemotherapy drugs, however, should not be combined with radiation. In those cases the chemotherapy is given before radiation because the sooner chemotherapy is started after surgery the more likely it will be successful in stopping the cancer from coming back.

Radiation in the primary management of breast cancer

Radiation is used in several different ways for women with breast cancer. When radiation is given to the breast, the main goal is to kill the microscopic tumour cells that may be there. In early-stage breast cancer, radiation may be as important as the surgery itself. For patients with very small carcinoma in situ (DCIS or LCIS), radiation might not be used after breast-conserving surgery.

Radiation after breast-conserving surgery

Receiving radiation after surgery helps destroy microscopic tumour cells that might be present. The chance of local relapse or recurrence is 5–10%. If you don’t have radiation after breast-conserving surgery, the chance of local recurrence is about 35%, or one in every three patients.

Radiation is administered to the whole breast and an extra dose, called a boost of radiation, may be given to the site of the original tumour because it is the most likely site of recurrence. To avoid radiating more normal tissues than absolutely necessary, the radiation is directed across the chest from one side of the breast to the other.

Radiation after mastectomy

Radiation may be applied to your chest wall after mastectomy if your tumour has a high risk of relapse or recurrence. The decision to give radiation after a mastectomy is based on the pathology information gathered at diagnosis.

If the whole tumour could not be removed during surgery, radiation is given to the chest wall to reduce the risk of local recurrence. Without radiation, there is a very high chance of the cancer starting to grow again at the sites where cancer cells are known to be (called residual disease). To avoid radiating more normal tissue than necessary, the radiation beam is directed across the chest wall from one side of the breast to the other.

Radiation in node-positive patients

If cancer was found in your lymph nodes (node-positive cancer), your doctors may recommend
that after mastectomy, you have radiation to your chest wall and lymph glands, especially if four or more nodes were involved.

In women with node-positive cancer who have had breast-conserving surgery, radiation is usually given to treat the remaining breast tissue and the lymph node areas in the armpit. If the lymph nodes in the armpit are given radiation, often the lymph nodes above the collarbone, called the supraclavicular lymph nodes, are also treated.

**Radiation side effects**

You may notice changes to the healthy part of the remaining breast in the years after you undergo radiation treatment. It may not be as soft and may develop small blood vessels on the skin surface.

During local radiation treatment of the breast, the amount of normal tissue treated and the radiation dose are kept as small as possible to avoid radiating the heart or more of the lung than is absolutely necessary. You may experience slight to moderate reddening of the skin, much like sunburn, which is often uncomfortable. If the sunburn effect is more severe, then itching and flaking may occur. Moist areas in the skin crease under the breast are more sensitive to radiation and may be more affected. These skin changes usually disappear over a few weeks. Radiation may also cause some breast swelling and tenderness, which may last for several months.

Radiation treatment makes some patients feel very tired. Nausea caused by radiation treatment for breast cancer is uncommon. It is most likely to occur in heavy-set women with large breasts and when the lymph node areas are treated as well as the breast, because of the large amount of tissue receiving radiation.

Some medical conditions may be made worse by radiation. If you have severe heart or lung diseases such as chronic bronchitis or emphysema, you may not be offered radiation therapy. Women with connective tissue diseases like systemic lupus or scleroderma may develop severe reactions and scarring, so if you have this type of condition, avoid radiation if at all possible.

**Hormonal therapy**

Hormonal drug therapy is a systemic therapy that slows the growth and spread of cancer cells by changing hormone levels in your body.

Hormones are chemical substances produced by glands in the body. Estrogen and progesterone are hormones produced by the ovaries, other tissues such as fat cells and the adrenal glands. Estrogen and progesterone control changes during puberty, menstruation, pregnancy and menopause, travel across the cell membrane and attach themselves to receptors within the cell’s nucleus in breast tissue, areas around the vagina, and the uterus, or womb, and change the activity of these cells.

Hormonal therapy for breast cancer is designed to reduce the amount of estrogen produced in your body or to block the action of estrogen on the hormone receptors (ER and/or PR). This action prevents the hormones from stimulating tumour growth and helps to cause tumour cell death. A receptor-positive tumour exposed to hormonal therapy will shrink both because cancer cells are not dividing and multiplying and because some cancer cells are dying. Women with visible or measurable breast tumours that are both ER- and PR-positive have a 50–60% chance of having their tumours shrink in response to hormonal therapy. If your cancer is positive for only one type of receptor you may have a lower chance of responding to hormonal therapy.

**Hormonal therapy and the management of breast cancer**

At diagnosis, about two-thirds of all breast cancers in women under age 50 and three-quarters of those in women over 50 have protein receptors
for estrogen, progesterone or both. These tumours are referred to as hormone receptor-positive. The growth of hormone receptor-positive tumours is promoted in part by the body’s regular estrogen and progesterone production.

Because of good results achieved with hormonal therapy given after surgery to patients with hormone receptor-positive tumours, you may choose to have hormonal therapy instead of chemotherapy, or to have it following completion of chemotherapy. Hormonal therapy is often used alone in women over age 65 with node-positive, hormone receptor-positive breast cancer, and in women of any age with node-negative, receptor-positive cancer when there is a low risk of the disease coming back in the future.

If you were taking hormone replacement therapy (HRT) before you were diagnosed with breast cancer, you should stop taking your HRT prescription. The safety of resuming this therapy after a diagnosis of breast cancer is not known, although two studies done in Sweden were stopped early because use of HRT was associated with an increase in breast cancer recurrence.

Types of hormonal therapy

**Luteinizing hormone-releasing hormone agonists**

The time of life between puberty and menopause is called the Pre-menopausal stage. During this time, a woman menstruates, or has her period. Estrogen in Pre-menopausal women is produced primarily in the ovaries. Therefore, for Pre-menopausal women with hormone receptor-positive cancer, the goal of hormonal treatment is to stop the natural production of hormones by the ovaries. In the past, surgery to remove the ovaries (oophorectomy) to stop estrogen production, or radiation to impair the production of estrogen, were commonly used. Using surgery or radiation to stop or impair the action of the ovaries is called ovarian ablation.

Now drugs such as goserelin (Zoladex®), leuprolide (Lupron Depot®) or buserelin (Suprefact®) are used to reduce the production of estrogen by inhibiting (slowing down) the pituitary gland’s signal to the ovaries to make estrogen. These drugs are called luteinizing hormone-releasing hormone (LH-RH) agonists. They cause you to go into menopause for up to three years. These drugs can be given only by injection once a month or once every three months. Possible long-term side effects of these drugs are the same long-term risks associated with menopause, such as possible increased risk of heart disease and osteoporosis (brittle bones). Some of the clinical trials that used these LH-RH agonists also used tamoxifen (Table 3).

**Anti-estrogen agents (selective estrogen receptor modulators)**

Estrogen-positive tumours need estrogen to survive. Anti-estrogen drugs block estrogen from binding to the breast cancer cells, thereby either “starving” them to death or hindering their growth.

Selective estrogen receptor modulators (SERMs) are a new class of anti-estrogen drug. As the name implies, they are selective and have the ability to block the estrogen receptors in some tissues, such as breast cells, and stimulate estrogen receptors in other tissues (bone and liver).

Tamoxifen is the most widely used SERM in Canada. Other SERMs being tested for use in breast cancer include raloxifene (Evista®) and toremifene (Fareston®).

**Tamoxifen:** Tamoxifen is the oldest and best-known hormonal therapy for receptor-positive premenopausal and post-menopausal women with breast cancer. It causes multiple hormonal actions, including blocking the effects of estrogen on the tumour but stimulating an estrogen-like effect on the lining of the uterus (the endometrium), the cardiovascular system and the bones.
Table 3: Commonly prescribed hormonal therapies

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Effect</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ovarian ablation</strong></td>
<td>Reduce ovarian hormone levels</td>
<td>Premenopausal women</td>
</tr>
<tr>
<td>(i.e., stop ovary action)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiation</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LH-RH agonists</strong></td>
<td>Suppress ovarian hormone production (injections once per month or once every 3 months)</td>
<td>Premenopausal women</td>
</tr>
<tr>
<td>Goserelin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buserelin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leuprolide</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Anti-estrogen agents</strong></td>
<td>Block estrogen effects on tumour</td>
<td>Premenopausal and post-menopausal women</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Aromatase inhibitors</strong></td>
<td>Prevent adrenal and other tissues from producing estrogen</td>
<td>Post-menopausal women only</td>
</tr>
<tr>
<td>Letrozole</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anastrozole</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exemestane</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Tamoxifen is taken as a tablet, usually once a day. Currently, tamoxifen is recommended as an adjuvant therapy to be taken for five years. Clinical trials suggest that tamoxifen treatment for five years is better than for two years, but that 10 years may not be better than five, and could be worse. Tamoxifen’s side effects are usually mild and may include hot flashes and vaginal problems like discharge and itching. Hot flashes usually improve with time, but if they are severe, several medications are available to help make this side effect more tolerable.

Tamoxifen is linked to a slightly increased risk of developing uterine cancer — about one in every 1,000 women treated. If you take tamoxifen, you should report any unexplained vaginal bleeding to your physician and ask for a referral to a gynecologist. Tamoxifen has also been associated with an increased risk of developing blood clots in veins or, very rarely, in arteries. Deeper blood clots in the leg (called deep vein thrombosis) are reported in about two to five of every 100 women treated, which is similar to the risk of this side effect associated with birth control pills. Sometimes, deep vein clots may break off and travel to the lungs, causing a pulmonary embolism, which is a potentially life-threatening situation. The risk of blood clots is generally higher if you are over age 65, overweight, have a history of smoking, don’t
exercise, have recently had surgery or have a previous history of blood clots. If you develop painful swelling in one or both legs, see your doctor immediately. There is also a very low risk of stroke associated with taking tamoxifen.

Keep in mind that when it is used appropriately, the benefits of tamoxifen in preventing the recurrence of breast cancer outweigh these risks substantially.

**Aromatase inhibitors:** Aromatase inhibitors are used for the adjuvant treatment of hormone receptor-positive breast cancer in post-menopausal women only. Before menopause, most of a woman’s estrogen is produced in the ovaries. But in post-menopausal women, most estrogen is made from another hormone, androgen. Aromatase inhibitors stop, or inhibit, an enzyme called aromatase from turning androgen into estrogen. This lowers the amount of estrogen produced outside of the ovaries, which means less estrogen reaches the estrogen receptors and there is less cancer-cell growth.

Aromatase inhibitor medications include anastrozole (Arimidex®), exemestane (Aromasin®) and letrozole (Femara®). Each is taken by pill once a day, usually for up to five years. But for women with advanced (metastatic) disease, the medicine is continued as long as it is working well. All three aromatase inhibitors work in similar ways. Your doctor will help you decide which of the three medicines is best for you based on the results of thorough testing.

Clinical trials involving thousands of women have tested these medicines in different ways:

- Adjuvant use of an aromatase inhibitor (anastrozole or letrozole) instead of tamoxifen
- Use of an aromatase inhibitor (letrozole) after five years of tamoxifen
- Switching from tamoxifen to one of two aromatase inhibitors (exemestane or anastrozole) after two to three years of tamoxifen for a total treatment of five years

Studies show that using an aromatase inhibitor for 5 years of treatment up front or as extended treatment for 5 years after tamoxifen will prolong the time that women live without their breast cancer coming back (recurrence) compared to just using tamoxifen. However, individual studies have yet to definitively show an improvement in the overall length of life (overall survival). It is possible this may change with longer follow-up. For patients who are treated for 2-3 years with tamoxifen, then switched to an aromatase inhibitor for the balance of 5 years, there appears to be a small overall survival benefit in addition to prolonging the time that women live without a recurrence.

The main side effect of therapy with an aromatase inhibitor is osteoporosis caused by a lack of estrogen supply to the bones. The risk of developing osteoporosis from these drugs is often estimated at one in 100 (1%). If you are on one of these drugs for adjuvant treatment of breast cancer, you should take 1500 mg of calcium and 400 to 800 IU of vitamin D per day and have a bone density test (called DEXA) done every two years, or more often if required. Aromatase inhibitors cause fewer blood clots and hot flashes than tamoxifen does and they are not associated with cancer of the endometrium (uterine lining). They do, however, cause muscle aches and pains, which are severe enough in 5% of women to cause them to stop treatment. Aromatase inhibitors may also elevate cholesterol levels, whereas tamoxifen can lower cholesterol levels.

**Chemotherapy**

Chemotherapy is the treatment of cancer with drugs. Although each chemotherapy drug works differently, they all kill cancer cells or prevent their growth. Chemotherapy for breast cancer can consist of one drug or a combination of drugs. Generally, chemotherapy is given in multiple cycles. When several
cycles of treatment are prescribed, this is termed a course of therapy. You will usually receive chemotherapy treatment as an outpatient.

**How chemotherapy works**

Tumour cells divide and multiply, causing the tumour to get bigger. Chemotherapy kills tumour cells by interfering with one or more of the steps involved in cell division and multiplication. Unfortunately, chemotherapy does not target cancer cells specifically. It can also damage normal cells, especially those that divide rapidly or frequently. This damage, referred to as toxicity, is responsible for the common side effects of chemotherapy. Medications to reduce or prevent many chemotherapy side effects are available.

Fortunately, normal tissues are able to recover after chemotherapy and damage is usually short-lived.

Chemotherapy can also damage the tissues in the ovaries; early menopause (called premature menopause) can occur as a result. If the breast cancer is hormone-positive, this chemotherapy side effect can be beneficial because the effect on your hormones also helps fight the cancer cells.

**Chemotherapy and the management of breast cancer**

Chemotherapy is most often used alone or just before hormonal therapy in premenopausal women and post-menopausal women with node-positive breast cancer. In some ER/PR positive, node-negative patients, both types of treatment are often used. Chemotherapy has been shown to reduce rates of relapse and improve survival, especially for women under 50.

Chemotherapy for early-stage (stages I and II) breast cancer is usually started a few weeks after surgery. In general, chemotherapy is not given at the same time as radiation. Usually radiation is administered once chemotherapy is finished.

Chemotherapy given before surgery (called pre-operative or neo-adjuvant therapy) is used to shrink larger tumours or those that cannot be treated easily by surgery at the time they are found. If the tumour shrinks well, then these cancers are often removed by surgery after the chemotherapy. Chemotherapy should be considered as a first treatment for what is called locally advanced breast cancer (see Treatment choices for larger cancers in the breast or in lymph nodes found before surgery [Stage III], page 48). When the cancer has to be treated for the second time (either because of a relapse in the breast area or because it has metastasized), chemotherapy is used to stop or slow the spread of the disease.

**Chemotherapy regimens**

Chemotherapy is usually administered as a combination of drugs, called a regimen. The development of chemotherapy regimens has been based on the belief that the most effective way to kill cancer cells is to attack many different cell-growing mechanisms all at the same time. Because different chemotherapy drugs damage cancer cells in different ways, a combination of drugs theoretically kills more tumour cells than a single drug and leads to a higher chance of cure. In addition, using several drugs with slightly different side effects allows sometimes two, three or even more drugs to be used together in one regimen. Chemotherapy combinations are often used as standard treatment for many types of cancer.

Many chemotherapy combinations originally found effective in treating later stages of breast cancer are now used to improve cure rates or survival for patients in early stages of breast cancer. When these combinations are given after initial surgery, the treatment is called adjuvant systemic therapy. Several proven chemotherapy regimens are currently considered standard treatments for breast cancer (Table 4). As clinical information
<table>
<thead>
<tr>
<th>Regimen</th>
<th>Agents</th>
<th>Number of cycles</th>
<th>Cycle length (days)</th>
<th>Treatment duration (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEF</td>
<td>Cyclophosphamide (by tablet) Epirubicin</td>
<td>6</td>
<td>28</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Fluorouracil</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMF</td>
<td>Cyclophosphamide (by tablet) Methotrexate</td>
<td>6</td>
<td>28</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Fluorouracil</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AC</td>
<td>Doxorubicin Cyclophosphamide (into a vein)</td>
<td>4</td>
<td>21</td>
<td>3</td>
</tr>
<tr>
<td>FAC</td>
<td>Fluorouracil Doxorubicin Cyclophosphamide</td>
<td>6</td>
<td>21</td>
<td>4–6 (pace of treatment administration depends on ability to tolerate side effects)</td>
</tr>
<tr>
<td></td>
<td>(into a vein)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEC</td>
<td>Fluorouracil Epirubicin Cyclophosphamide</td>
<td>6</td>
<td>21</td>
<td>4–6 (pace of treatment administration depends on ability to tolerate side effects)</td>
</tr>
<tr>
<td></td>
<td>(into a vein)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEC followed by docetaxel</td>
<td>Fluorouracil Epirubicin Cyclophosphamide (into a vein) x 4 then docetaxel x 4</td>
<td>6–8</td>
<td>21</td>
<td>4–6</td>
</tr>
<tr>
<td>AC+T</td>
<td>Doxorubicin x 4 Cyclophosphamide (into a vein) x 4 then paclitaxel alone x 4</td>
<td>8</td>
<td>14 (high-dose)</td>
<td>4</td>
</tr>
<tr>
<td>AC+T* + filgrastim support</td>
<td>Doxorubicin x 4 Cyclophosphamide (into a vein) x 4 then paclitaxel alone x 4</td>
<td>8</td>
<td>14 (high-dose)</td>
<td>4</td>
</tr>
<tr>
<td>TAC</td>
<td>Docetaxel Adriamycin Cyclophosphamide (into a vein)</td>
<td>6</td>
<td>21</td>
<td>4–6 (pace of treatment administration depends on ability to tolerate side effects)</td>
</tr>
</tbody>
</table>

*See the section on Neutropenia on Page 41 for an explanation of filgrastim support.
increases, however, standard therapies may change. It is important that you discuss any questions you have about chemotherapy with your physician and the team looking after you.

Clinical trials involving many thousands of women have taught us a lot about the different effects of each chemotherapy regimen. Here are some of the more important conclusions:

- Six cycles of CMF and four cycles of AC have the same benefit in terms of improving cure rates. CMF, however, takes longer to give and has a higher rate of nausea because cyclophosphamide is given by tablet. Although AC chemotherapy always causes hair loss, CMF does not always cause complete hair loss and does not have the small associated risk of damage to the heart that AC has.
- Six cycles of CEF or FEC or a similar type of chemotherapy is better than CMF-like chemotherapy. Six cycles of CEF or FEC has been the best option for many node-positive women younger or older than 50. However, CEF, FEC and similar treatments are regimens that may not be tolerated by all patients. They have a higher chance of causing a low white blood cell count with fever (called febrile neutropenia) than CMF does (see Chemotherapy side effects, page 39).
- AC is given for a shorter time; thus, only four doses of cyclophosphamide are given rather than the six doses included in the CMF, CEF and FEC regimens. AC is also slightly better at preserving fertility than the six-cycle treatments.

Information coming from clinical trials suggests that a new class of drugs called taxanes, such as paclitaxel (Taxol®) and docetaxel (Taxotere®), can also improve your chances of surviving early-stage breast cancer. The AC regimen for four cycles followed by paclitaxel for four cycles, or the three-drug combination of docetaxel with AC (called TAC) for six cycles, may result in slightly better outcomes than AC alone for four cycles or CMF, FAC and others for six cycles. Growth factor support with filgrastim has been shown to help patients better tolerate high-dose AC regimens. Many of these treatments have not been directly compared with one another in clinical studies, however.

Your choice of treatment will be made after discussion with your cancer specialist (usually a medical oncologist) and may depend in part on provincial or territorial guidelines that direct treatment choices. In addition, there are often various ongoing studies (clinical trials) taking place at a cancer centre that may offer other options.

Variations of the commonly used regimens (CEF, FEC, AC then paclitaxel, or TAC), other combinations and newer agents are frequently used for patients with larger breast tumours or when the cancer is considered inoperable. In cases where the tumour is large at the beginning of treatment, chemotherapy may be used to shrink the tumour enough to make surgery possible. The best treatment for these locally advanced breast cancers has not been precisely defined and if you are in this situation you may wish to consider entering a clinical trial if one is available.

For recurrent metastatic breast cancer, there are many different chemotherapy regimens or single drugs that can be used. Some are quite similar to the regimens used in early-stage disease. The choices for a particular woman may vary depending on the previous treatment of the original early-stage cancer, what drugs or drug regimens were used and the total number of drug doses given. Some of the possible choices are outlined in Table 5.

**Importance of dose and schedule**

Clinical trials have defined standard chemotherapy regimens that specify the drugs, dosages and scheduling (timing) of their administration to produce the best outcomes. Clinical trials have also shown, however, that to achieve these outcomes, the full
**Table 5:** Standard chemotherapy regimens and agents for relapsed cancer

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Number of cycles</th>
<th>Cycle length (days)</th>
<th>Treatment duration (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single agents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Docetaxel</td>
<td>6–8</td>
<td>21</td>
<td>4–6</td>
</tr>
<tr>
<td></td>
<td>12–20</td>
<td>7</td>
<td>4–6</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>6–8</td>
<td>21</td>
<td>4–6</td>
</tr>
<tr>
<td></td>
<td>12–20</td>
<td>7</td>
<td>4–6</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>10–20</td>
<td>7</td>
<td>4–6</td>
</tr>
<tr>
<td>Capecitabine (by tablet)</td>
<td>6–15</td>
<td>21</td>
<td>6–8</td>
</tr>
<tr>
<td>Liposomal doxorubicin</td>
<td>6–8</td>
<td>28</td>
<td>6–8</td>
</tr>
<tr>
<td><strong>Combinations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adriamycin + docetaxel (AT)</td>
<td>6–8</td>
<td>21</td>
<td>4–6</td>
</tr>
<tr>
<td>AC x 4 then paclitaxel</td>
<td>4</td>
<td>21</td>
<td>6</td>
</tr>
<tr>
<td>Docetaxel Capecitabine</td>
<td>6–8</td>
<td>21</td>
<td>4–6</td>
</tr>
<tr>
<td>5-Fluorouracil (5-FU) Adriamycin Cyclophosphamide (by injection)</td>
<td>6–8</td>
<td>21</td>
<td>4–6</td>
</tr>
<tr>
<td>Gemcitabine Paclitaxel</td>
<td>6–8</td>
<td>21</td>
<td>4–6</td>
</tr>
<tr>
<td><strong>Biological agents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trastuzumab alone</td>
<td>Until relapse</td>
<td>21 or 7</td>
<td>Until relapse</td>
</tr>
<tr>
<td>Trastuzumab with chemotherapy* then trastuzumab alone</td>
<td>Until relapse</td>
<td>21 or 7 (usually while on chemotherapy) 21 (once chemotherapy finishes)</td>
<td>Until relapse</td>
</tr>
</tbody>
</table>

*Drugs include docetaxel, paclitaxel, vinorelbine, cisplatin, carboplatin or capecitabine as single agents or in combinations: docetaxel + cisplatin; docetaxel + carboplatin; paclitaxel + cisplatin; paclitaxel + carboplatin*
chemotherapy dose must be given without deviating from the schedule.

For most patients, standard doses of chemotherapy kill the maximum number of tumour cells possible, producing some side effects that can be well managed. The development of drug resistance may be responsible for the lower cure rates seen when lower chemotherapy doses are used. Since a single dose of chemotherapy kills only a certain number of cancer cells, multiple doses, or cycles, are necessary to destroy all cancer cells. Chemotherapy is scheduled as frequently as possible to:

- Minimize tumour growth between cycles
- Prevent the development of resistance
- Achieve the best outcome

Clinical trials have determined which combinations of drugs given according to what schedules kill the most tumour cells while keeping side effects to a minimum. Nevertheless, every patient's body is different, and sometimes chemotherapy is delayed or the dose is lowered to allow patients to recover from side effects. Reducing chemotherapy doses, postponing treatment or giving cycles of chemotherapy less frequently may reduce cure and survival rates.

Because chemotherapy damages rapidly dividing cells, including white blood cells, your white blood cell count may drop dramatically during chemotherapy treatment. In this situation, your immune system may not be able to fight infection very well, making you vulnerable to serious or even life-threatening infections. In some cases it may be necessary to delay chemotherapy treatment until the white blood cell count recovers. Patients may also experience other side effects such as severe fatigue or nausea. In many cases, however, these side effects can be managed successfully with medication so that the chemotherapy schedule can be maintained.

**Chemotherapy side effects**

*Introduction*

In addition to killing cancer cells, all chemotherapy regimens damage normal cells — in particular, rapidly dividing cells — and commonly produce side effects. However, the popular perception that chemotherapy causes intolerable side effects is incorrect. This misconception causes people to fear chemotherapy unnecessarily. You may experience only some of the side effects. In most cases, effective medications eliminate many side effects or at least reduce them significantly. Techniques to reduce anxiety, such as meditation or relaxation, may help you cope with concerns about side effects. Side effects resolve when therapy is completed.

Acute (sudden, severe) chemotherapy side effects generally happen during the first few cycles of treatment and get better after therapy is finished. Side effects such as mouth sores and hair loss are common and you will usually be able to manage them at home with advice from, and treatments suggested by, your cancer-care team. Side effects that may require more serious medical attention include:

- Low white blood cell count (neutropenia), especially if you also have a fever (febrile neutropenia)
- Severe vomiting or diarrhea resulting in dehydration
- Unexplained bleeding
- Low red blood cell count (anemia) and the fatigue it causes

It is important that you know how to contact your family physician, have the correct phone numbers for the cancer centre and know when to go to the emergency ward if any of these potentially serious side effects occur. Some of the most effective chemotherapy regimens, which may use high doses of chemotherapy drugs, may cause the most side effects.
There are also some rare long-term side-effect risks associated with chemotherapy, including heart disease and leukemia.

**Hair loss**

Damage to fast-growing cells in hair follicles can cause hair loss (alopecia). Many patients experience temporary hair loss, although hair loss depends on the drugs used. With the taxane class of drugs (paclitaxel and docetaxel), in about one in 100 patients, hair might not grow back with its original thickness after treatment. Even though lost hair always grows back, the psychological impact of losing your hair can be immense. Hair loss is the chemotherapy side effect some patients fear the most.

You may want to consider purchasing a wig, scarves or hats before chemotherapy begins. You may also choose to cut your hair very short or even shave your head if you start to lose your hair. By taking these steps, you can maintain control of your appearance. This may help you feel more in control of the disease and its treatment.

**Fatigue**

Fatigue is a very common side effect of chemotherapy. Several factors contribute to fatigue, including:

- The stress of adjusting to being diagnosed with cancer
- Recent surgery and anesthesia
- Reduced red blood cell counts
- The effects of the chemotherapy drugs themselves

Getting enough sleep, eating well and minimizing stress at home and on the job are all important to managing fatigue. Relaxation therapies can be very useful. Fatigue due to a low red blood cell count is called anemia; anemia resulting from chemotherapy can be treated. See Anemia on page 42 for details on managing this condition.

**Mucositis (mouth sores)**

Damage to fast-growing cells lining the mouth may cause mouth sores (mucositis). Mucositis is common and may occur several days after chemotherapy starts. Mouth sores and tenderness often appear when your white blood cell count is low.

Before beginning chemotherapy, a dental check-up and cleaning are advisable. When chemotherapy begins, rinsing with a mild mouthwash that contains no alcohol is helpful. Mouthwashes may contain some pain relievers (anesthetics) as well as an antifungal agent that will help control infections such as candidiasis, or thrush. It is recommended that you keep your mouth clean using a soft toothbrush and avoid foods that may irritate the inside of the mouth or throat.

Further research is ongoing to clarify the possible role of the new agent palifermin (Kepivance™), a specifically designed keratinocyte growth factor (KGF)-like agent that may reduce the incidence and duration of severe oral mucositis in solid tumours (for example, lung or breast cancer) setting. Currently, Kepivance™ is used only in patients with hematological malignancies (cancers that affect blood, bone marrow or lymph nodes) with a very high risk of mucositis because of the use of specific treatments, such as bone marrow transplantation.

**Nausea and vomiting**

If you experience nausea or vomiting at all, they will occur on the day of, and possibly for a few days after, chemotherapy. Fortunately, very effective anti-nausea medications, such as ondansetron (Zofran®), granisetron (Kytril®), dolasetron mesylate (Anzemet®) and dexamethasone (Decadron®) can completely prevent or significantly reduce these symptoms when given before and up to 48 hours after chemotherapy. For delayed nausea — occurring more than 48 hours after treatment — your doctor may suggest taking prochlorperazine (Stemetil®), domperidone (Motilium®), dimenhydrinate (Gravol®) or metoclopramide (Maxeran® or Reglan®).

If you experience vomiting, be sure to drink plenty of fluids to avoid dehydration.
**Diarrhea**

Damage to cells lining the gastrointestinal tract may cause diarrhea. Although diarrhea is common with certain chemotherapy drugs, it is generally not severe or long lasting. It can usually be managed with non-prescription anti-diarrheal agents.

If you experience diarrhea you should be sure to drink plenty of fluids to avoid dehydration. If diarrhea is severe, your physician must be notified, because medically serious loss of body fluid (dehydration) can occur and admission to hospital might be needed.

**Cystitis**

Chemotherapy may cause cystitis, or inflammation of the bladder. Cystitis is seen more often with high doses of intravenous cyclophosphamide than with oral cyclophosphamide. Cyclophosphamide by-products excreted in the urine can damage the lining of the bladder causing blood to appear in the urine. Blood in the urine should not be confused with red urine, which is produced by some drugs (such as doxorubicin).

To prevent severe cystitis, lots of fluids need to be taken (at least eight glasses per day) to ensure that the bladder gets emptied frequently during the first 24 hours after a cyclophosphamide dose. If you receive chemotherapy late in the day, it is helpful to make sure you get up and empty your bladder during the night and to take in more fluids.

When very high doses of cyclophosphamide or a related drug, ifosfamide (Mitoxana®), are used, a protective medication, mesna, is given to counteract the effects of these drugs’ by-products on the lining of the bladder.

**Neutropenia**

Neutrophils are special white blood cells that play a very important role in fighting infections. A low neutrophil count is called neutropenia. A low neutrophil count resulting from cancer chemotherapy may predispose you to developing serious or even life-threatening infections. Prolonged neutropenia may also mean that your next chemotherapy dose needs to be reduced or delayed.

Virtually all patients receiving chemotherapy develop neutropenia, but the degree of neutropenia that a particular patient experiences is variable and cannot be predicted. Patients who experience slight neutropenia, with the white blood cell count rapidly returning to normal, do not require any specific treatment. If, however, you experience a fever higher than 38°C or other symptoms of infection when you have neutropenia, you should contact your physician immediately. In this situation, you would usually be admitted to hospital and treated with intravenous antibiotics. The likelihood of patients experiencing severe neutropenia that would result in infections requiring intravenous antibiotics and hospitalization depends in part on the chemotherapy regimen being used. It can be as low as one in 100 women treated or as high as almost 20 in 100.

It is very important that you know who to contact — and when — if you have these symptoms. You must not wait to contact your doctor or cancer centre if your fever is higher than 38°C or if you have other signs of infection. An infection left untreated while you have a low white blood cell count can be life-threatening.

Because neutropenia is a potentially serious complication of chemotherapy, white blood cell counts are closely monitored during chemotherapy. On the day you are scheduled to receive your next cycle of chemotherapy, your white blood cell count will be measured to ensure that you are able to receive the next dose. If the white blood cell count has not recovered to a level that allows chemotherapy to be given safely, the next cycle of chemotherapy could be delayed until the level has recovered. If you have had severe or long-lasting neutropenia, it may be necessary to use reduced doses during future cycles of chemotherapy.
Neutropenia can be treated, however, and the incidence of it reduced often by administering medication (growth factors) that stimulates the development of white blood cells. Filgrastim (Neupogen®) and pegfilgrastim (Neulasta®), also known as granulocyte colony-stimulating factors (G-CSF), are two growth factors used to decrease the incidence of neutropenia. If you have already experienced severe neutropenia, or are given a chemotherapy regimen that is known to cause severe neutropenia, your doctor might suggest that you take filgrastim or pegfilgrastim before receiving chemotherapy. The use of G-CSFs may prevent risk of fever associated with neutropenia (febrile neutropenia) during cycles of chemotherapy, thus avoiding dose reductions and/or delays.

Pegfilgrastim is like filgrastim, but it lasts much longer. Thus the advantage of pegfilgrastim is that you require only one injection after each chemotherapy cycle instead of five to 10 days of daily injections with filgrastim.

Severe neutropenia requiring treatment is more common with intensified chemotherapy regimens and in older patients. You may have medical conditions in addition to cancer (called co-morbid conditions) that may affect your ability to receive a full chemotherapy dose. You may wish to discuss with your physician ways of ensuring that you are able to receive a full and effective dose of chemotherapy.

**Anemia**

Feeling unusually tired may be a result of anemia, a common side effect of many chemotherapy regimens. Anemia occurs when there is a significant decrease in your red blood cell level. Because it is the hemoglobin in your red blood cells that carries oxygen throughout your body, a decrease in the number of these oxygen-rich cells can cause your energy level to drop. Although it is not life-threatening, many patients report that the fatigue resulting from anemia has a negative impact on their day-to-day activities.

Your doctor will check your blood count often during treatment. Mild or moderate anemia is common with some chemotherapies and treatment is usually unnecessary. The severity of anemia may increase with certain types of chemotherapy regimens; it can also get worse when chemotherapy continues for several months. If you experience severe anemia, a blood transfusion or medication (growth factors) that stimulate the development of red blood cells may be considered.

Red blood cell growth factors are called erythropoietic-stimulating agents. In Canada, there are two erythropoietic-stimulating agents available: darbepoetin alfa (Aranesp®) and epoetin alfa (Eprex®). These medications are given as an injection under the skin. Treatment is usually given for up to nine weeks before it is certain that the hemoglobin level (or red blood cell count) is increasing. The treatment is then continued until chemotherapy is complete and for a few weeks afterwards until red blood cell production returns to normal.

Darbepoetin alfa is similar to epoetin alfa, but it lasts much longer. This means that fewer injections of darbepoetin alfa than of epoetin alfa are required for the treatment of anemia. Most provinces and territories have treatment guidelines for the use of erythropoietic-stimulating agents for patients receiving chemotherapy.

**Thrombocytopenia**

Thrombocytopenia is when the number of blood platelets drops below normal. Although chemotherapy can cause thrombocytopenia, severe thrombocytopenia is very unusual. Thrombocytopenia can have serious consequences because blood platelets help prevent bleeding. A severe drop in your platelet count can cause bleeding and bruising in the skin. Rarely, thrombocytopenia can also cause bleeding from the gums, in the urinary tract (hematuria) or in the stomach or lower bowel. If there is bleeding...
in the bowel, the blood always passes through quickly as it irritates the lining of the bowel wall. This means the blood may be passed upwards and is vomited (the vomit is black or looks like coffee grounds) or it may be passed downwards into the stool, which becomes very dark or black and may even show fresh blood with diarrhea.

Platelet transfusions may be given if bleeding occurs or if your platelet count drops to severely low levels. Experimental platelet growth factors that stimulate platelet counts are being investigated in clinical trials.

**Potential long-term side effects**

**Premature menopause:** One long-term result of chemotherapy is that a woman’s periods may stop and may not return (called early or premature menopause). This is more common in women who start chemotherapy when they are more than 40 years of age. This side effect may be considered a good thing if you have hormone-positive (ER- or PR-positive) breast cancer, since the hormone changes that occur with menopause may also improve your chances of beating breast cancer as well, though this has not been definitively proven.

**Leukemia:** Leukemia is a very rare long-term toxicity that can occur months or years after chemotherapy has been finished. Leukemia is cancer of the white cells in the blood and in the bone marrow, where blood cells are made. It is believed that the risk is greater with the most intensive chemotherapy regimens. This is understandably a greatly feared side effect. It must be remembered that it is unlikely to happen, and has been reported in very few women for every thousand treated. Unfortunately, the risk cannot be predicted with certainty for any individual woman needing chemotherapy to treat her breast cancer.

**Heart problems:** Heart failure is another possible chemotherapy side effect. The drugs known to cause this rare side effect are doxorubicin and epirubicin. However, the safe doses of these medications are well known and breast cancer regimens are designed to be within the safe dose range.

With new drugs like the taxanes (especially paclitaxel) and new biological treatments like trastuzumab, there are some interactions with the drugs known to potentially affect the heart (doxorubicin and epirubicin). If there are concerns about heart problems because of previous or ongoing treatments, then special tests may be done, such as a scan called a MUGA (multiple gated acquisition) to check the heart muscle or an ultrasound test called an echocardiogram. If specific heart treatment is needed, it might also be necessary to stop cancer treatment for a while, or possibly switch to a different chemotherapy regimen.

**Biological therapy**

A major drawback of both chemotherapy and radiation is the inevitable damage that these treatments cause to normal cells. The need to limit this damage restricts the chemotherapy and radiation doses that can be used. The concept of delivering treatment to kill only cancer cells has led to the development of biological therapy, also known as immunotherapy.

Biological therapy uses the immune system to fight cancer. Substances made by the body or made in a laboratory are used to boost, direct or restore the body's natural defences against cancer. Biological therapy may be used alone or in combination with chemotherapy.

**Trastuzumab**

The most common biological therapy drug used to treat breast cancer is trastuzumab (Herceptin®). Trastuzumab is a monoclonal antibody therapy. Monoclonal antibody therapy uses antibodies made in the laboratory. These antibodies can target cancer cells by identifying substances (protein
receptors) on the surface of the cancer cells that signal growth. Trastuzumab is designed to block HER-2 protein receptors.

HER-2 protein receptors, when activated, send growth signals to the cell. In certain breast cancers, HER-2 protein receptors are produced in excessive amounts (over-expressed). Breast tumours that over-express HER-2 tend to grow faster, are hormone receptor-negative and are more likely to recur after initial treatment, usually in areas distant from the primary tumour (metastases) (see HER-2 and the epidermal growth factor receptor family, page 23).

There have been a number of clinical trials evaluating how best to use trastuzumab. In Stage IV disease (metastatic breast cancer), this biological agent can be given alone, although clinical trial results suggest that it is best to give it with certain chemotherapy drugs. Trastuzumab may also be used in women newly diagnosed with early-stage invasive and locally advanced breast cancer who have a high risk of cancer recurring.

Only women who have tested positive for HER-2 are likely to benefit from trastuzumab. Approximately 25–30% of women with breast cancer test HER-2-positive.

Trastuzumab is given as an injection into the vein (intravenously). Dosing and scheduling vary from patient to patient.

Side effects are generally mild and can include fever, chills, muscle aches and nausea. These side effects usually become less severe after the first treatment. Before starting trastuzumab therapy, you should have your heart tested (with an echocardiogram or a MUGA scan) to check how well it is functioning because trastuzumab can cause heart problems.
Treatment of Breast Cancer by Stage

**Treatment choices for pre-invasive breast cancer (DCIS or LCIS, Stage 0)**

**Description**
Ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) are pre-invasive cancers and are classified as Stage 0. These tumours rarely spread outside the breast themselves, but are associated with a slightly higher risk of developing more dangerous, invasive cancers in the future.

**Initial treatment options**
Lymph node removal: Lymph node removal is unnecessary if you have DCIS or LCIS but lymph nodes are removed when invasive cancer is suspected. The role of sentinel lymph node biopsy in women with only pre-invasive (in situ) cancer is still being investigated, although some surgeons already use it.

*Ductal carcinoma in situ*
DCIS is treated with surgery that removes part of the breast (lumpectomy) plus radiation, or removal of the whole breast without radiation. Your cancer-care team may suggest that you take tamoxifen to decrease the chance of DCIS coming back in either breast and also to decrease the chance of invasive cancer in the future.

*Lobular carcinoma in situ*
A diagnosis of LCIS is followed up using physical examination and either mammography alone or in combination with ultrasound examinations. Because LCIS is considered a pre-cancerous condition, surgery is usually not used to remove it. Although LCIS is a risk factor for developing invasive breast cancer in the future, only about 25% of women with LCIS will go on to develop invasive cancer, even if both breasts have LCIS. Sometimes it is difficult to follow LCIS because mammograms and ultrasound may not find the area of abnormality. In some cases, tamoxifen may be given to prevent the development of invasive cancer.

**Chance of cancer-free survival**
Your chances of surviving cancer-free if you are diagnosed with pre-invasive breast cancer are usually excellent. Nevertheless, some women can develop DCIS again, or may develop invasive breast cancer in the same, or opposite, breast. The risk depends on the size of the initial DCIS, the type of DCIS (as reported by what it looks like under the microscope) and whether tamoxifen was prescribed and taken.
**Flowchart 1:** Initial management of Stage 0 breast cancer

![Flowchart](image-url)

**Treatment choices for early invasive breast cancer (node-negative, Stage I)**

**Description**
Stage I tumours are smaller than 2 cm and do not involve lymph nodes (that is, they are node-negative).

**Treatment options**

**Local treatment:** Local treatment involves breast-conserving surgery (lumpectomy or partial mastectomy) and radiation, or mastectomy with no radiation.

**Hormonal therapy:** Hormonal therapy alone may be recommended if the tumour is hormone receptor-positive and has a generally good prognosis. As well, hormonal therapy alone may be recommended for older post-menopausal women because it is more effective than chemotherapy for this group of women and has fewer side effects.

Hormone receptor-positive tumours that are approximately 1 cm in size may be treated with hormonal therapy alone or with surgery followed by hormonal therapy.

**Aggressive Stage I tumours:** Patients with more aggressive tumours are usually offered chemotherapy. Following chemotherapy, you may be given hormonal therapy if your cancer is ER- or PR-positive (see Predictive Factors, page 23). Aggressive tumours may be high grade and/or cancer cells may be present in the nearby blood or lymph vessels (vascular invasion). If an aggressive tumour is ER- and
PR-negative, treatment with chemotherapy alone may be recommended. (Hormonal treatments are effective only for ER- and PR-positive tumours.) If your HER-2 test results are positive, your team may recommend biological therapy, such as the antibody trastuzumab (Herceptin®), to further decrease your risk of cancer recurrence. Trastuzumab may be given either along with or after chemotherapy treatment. Trastuzumab can be administered simultaneously with hormonal therapy.

If you have a tumour larger than 1 cm and test positive for the HER-2 gene, you may be offered therapy for one year with trastuzumab, given either with or after chemotherapy. This targeted treatment is suitable for high-risk node-negative breast tumours.

If your risk is average or moderate, you may decide to accept chemotherapy and/or hormonal therapy, depending on your individual situation and risk factors.

For tumours less than 1 cm across, ER- or PR-positive and of low grade, usually only surgery (and radiation if breast-conserving surgery is performed) is needed. Your cancer-care team may also suggest hormonal therapy.

**Chance of cancer-free survival**

If you have early-stage invasive breast cancer, your chances of surviving cancer-free are often excellent, but this will vary depending on your particular risk factors. The spectrum of risk for node-negative patients is very large. Some women with tumours of less than 1 cm in size and no other aggressive features may have only a 5–10% chance of recurrence. Others who have more aggressive tumours may have up to a 40–50% chance of disease recurrence. In all cases, treatment plans are individualized based on the particular risk that each woman faces from her breast cancer, taking into consideration her preferences and overall health. This is why treatment plans can vary so widely among patients.

**Figure 3:** Stage I breast cancer

![Stage I breast cancer](image)
Flowchart 2: Node-negative treatment options (Stage I)

Stage I

- Breast-conserving surgery
- Mastectomy

Assess risk of relapse

- Low risk
  - Radiation only
- Moderate risk
  - Hormonal therapy (if hormone-positive)
  - Radiation
  - Follow-up
- High risk
  - Systemic therapy
    - Chemotherapy
    - +/- Hormonal therapy (if hormone positive)
    - +/- Biological therapy (if HER-2 positive)
  - Radiation
**Treatment choices for invasive breast cancer (lymph node-positive at surgery, Stage II)**

**Description**
Tumours classified as Stage II can be described as:
- Smaller than 2 cm with positive lymph nodes
- Between 2 and 5 cm with either negative or positive lymph nodes
- Larger than 5 cm with negative lymph nodes

**Treatment options**

**Local treatment:** This involves breast-conserving surgery (either lumpectomy or partial mastectomy) and radiation, or mastectomy (sometimes with radiation afterwards). Whichever surgery you have, you should expect to receive adjuvant chemotherapy, hormonal therapy and/or biological therapy as well. Some oncologists are exploring the benefits of neo-adjuvant chemotherapy (chemotherapy before surgery) for this type of breast cancer.

**Systemic adjuvant therapy:** Depending on individual risk factors, almost 50%, or perhaps more, of women with Stage II cancer probably have microscopic metastatic disease (that is, disease somewhere else in the body but too small to be detected with x-rays or other tests).

Chemotherapy and hormonal therapy each decrease the risk of developing metastatic disease by 5–10%. When both treatments are given, the decrease is therefore 10–20%. Using the biological therapy trastuzumab after chemotherapy in women whose tumours have high HER-2 levels further decreases the risk of recurrence by about 15%.

Radiation after mastectomy in certain situations can also decrease risk of later metastatic disease by about 5–10%. Radiation after mastectomy is currently given primarily to women in whom four or more nodes are found to contain breast cancer cells or when the tumour is larger than 4–5 cm.

**Chance of cancer-free survival**
Because patients with Stage II invasive breast cancer can include women with 2 cm tumours and only one small metastasis in a lymph node (node-positive) as well as women with larger tumours up to 5 cm with many positive nodes, the risk of the disease returning varies from about 40 – 75% if a woman remains untreated.

**Figure 4:** Stage II breast cancer showing positive nodes (not all Stage II tumours have positive nodes)
**Flowchart 3:** Treatment options for node-positive breast cancer (Stage II)

**Stage II**

- Breast-conserving surgery
- Mastectomy

**Systemic therapy**
- Chemotherapy
- +/- Hormonal therapy (if hormone positive)
- +/- Biological therapy (if HER-2 positive)

- Radiation
- Follow-up

**Radiation**
(offered in some cases where many nodes in armpit are positive and/or very large cancer in breast)

**Treatment choices for larger cancers in the breast or in lymph nodes found before surgery (Stage III)**

**Description**
Stage III breast cancer patients include women:

- With any large tumour (over 5 cm)
- With between four and nine cancerous nodes in the armpit at surgery
- Whose only cancerous lymph nodes are very obvious ones under the ribs near the breastbone (that is, internal mammary tumours seen on some kind of radiology exam or seen or felt by the physician)
- With a breast tumour with lymph nodes involved above the collarbone on the same side (called supraclavicular)

**Treatment options**

**Neo-adjuvant therapy:** Treatment often starts with neo-adjuvant systemic chemotherapy, which means receiving chemotherapy before surgery as the first treatment. There are studies that have also looked at using high-dose, or dose-dense, treatments for neo-adjuvant therapy. Most good-quality studies suggest that the treatment should include a doxorubicin- or epirubicin-based chemotherapy (FAC, FEC or CEF).

In addition, the taxanes have been included in several clinical trials and are often used in routine management of Stage III breast cancer. If the drug docetaxel (Taxotere®) is used for neo-adjuvant therapy, it seems that fewer cancer cells are left at the time of surgery than if no taxane had been used. Hormonal therapy is also added, usually after
surgery, for all hormone-positive (ER- or PR-positive) tumours. Trastuzumab may also be administered after surgery if the tumour over-expresses HER-2. Your cancer-care team will most likely recommend post-surgery radiation.

**Radiation for Stage III:** If you undergo chemotherapy first, your cancer-care team will probably suggest that you have radiation afterwards. This is because in many women with Stage III breast cancer, cancerous lymph nodes are found before chemotherapy is started. Since radiation is offered to most women who have positive nodes found at surgery, it is advisable to offer women at Stage III radiation even when the nodes seem to have disappeared after the chemotherapy.

**Radiation in inoperable tumours:** For the initial treatment of inoperable breast cancer, radiation can be the primary therapy to control local problems. Radiation is usually combined with chemotherapy, hormonal therapy or both. The chemotherapy is often tried before radiation but you could choose to try hormonal treatment after initial radiation. This approach may also be tried if aggressive chemotherapy options are felt to be unsuitable.

**Surgery:** Depending on which subgroup of Stage III cancer you have at the time of diagnosis, surgery may be done after the chemotherapy and before radiation. Occasionally, surgery will have been done first, before other treatment is suggested.

**Mastectomy:** Is the most common surgery suggested even if cancer in the breast shrinks dramatically with chemotherapy or hormonal therapy. If only a part of the breast is removed, cancer cells that could grow back may be left in the remaining breast tissue. It is usually considered safer to remove the whole breast and have the tissue examined under a microscope.

**Chance of cancer-free survival**

Long-term control of Stage III breast cancer is often possible if you have good tumour shrinkage while on chemotherapy and few cancer cells are found at surgery, assuming surgery is possible after chemotherapy has finished. However, because these tumours are often aggressive and can grow quickly, and because they are larger than Stage I or Stage II tumours, patients with Stage III cancer generally do not have quite as good an outlook.

**Figure 5:** Example of Stage III breast cancer
**Flowchart 4:** Common treatment options for more advanced local breast cancer (Early Stage III or Stage IIIA)

- **Large operable tumour**
  - Referral to cancer centre
    - 1. Consideration of clinical trial
    - 2. Consideration of neo-adjuvant treatment for increasing chance of breast-conserving surgery
  - Neo-adjuvant chemotherapy*
    - Reassessment for breast-conserving surgery
      - Segmental resection + radiation therapy
      - Mastectomy + radiation therapy
  - Referral to cancer centre for adjuvant chemotherapy +/- radiation therapy

*Regimens suitable for neo-adjuvant chemotherapy:
- 4 cycles FEC100 (fluorouracil, epirubicin and cyclophosphamide) followed by 4 cycles docetaxel
- 4 cycles AC (adriamycin and cyclophosphamide) followed by 4 cycles docetaxel
- 6 cycles FAC (fluorouracil, adriamycin and cyclophosphamide)
- 6 cycles CMF (oral cyclophosphamide, methotrexate and fluorouracil) if regimens above are not suitable

- Hormonal therapy (if hormone positive)
- Biological therapy for one year (if HER-2 positive)
Flowchart 5: Common treatment of locally advanced breast cancer (Stage IIIB)

Locally advanced breast cancer Stage IIIB

- Neo-adjuvant chemotherapy*

  - Assess response of tumour to chemotherapy**
    - Segmental resection + radiation therapy
    - Mastectomy + radiation therapy
    - Radiation therapy***

  - Hormonal therapy (if hormone positive)
  - Biological therapy for one year (if HER-2 positive)

*Regimens suitable for neo-adjuvant chemotherapy:
- 4 cycles FEC100 (fluorouracil, epirubicin and cyclophosphamide) followed by 4 cycles docetaxel
- 4 cycles AC (adriamycin and cyclophosphamide) followed by 4 cycles docetaxel
- 6 cycles FAC (fluorouracil, adriamycin and cyclophosphamide)
- 6 cycles CMF (oral cyclophosphamide, methotrexate and fluorouracil) if regimens above are not suitable

**Proposal of surgery is based on tumour shrinkage after chemotherapy. Patient's choice is considered, as is whether or not surgery is an option.

***Radiation therapy for local control of tumour if tumour does not shrink after treatment and when surgery is not an option. Medical, radiation and surgical specialists may recommend surgery at some point.
Rare types of breast cancer

Treatment choices for inflammatory breast cancer

Inflammatory breast cancer is rare — only about 5% of breast cancers are classified as inflammatory. The distinguishing feature of inflammatory breast cancer is redness involving part or all of the breast. The red area often feels warm and redness may come and go. The breast is often swollen and tender. Your skin is red and swollen because cancer cells may have blocked the lymph drainage of the skin and of the breast tissue. Your skin may also look dimpled, resembling the peel of an orange.

Taking a mammogram may be very difficult in this situation. Diagnosis of inflammatory breast cancer is usually made based on the results of a biopsy or fine-needle sample of skin tissue (fine-needle aspiration). The cancer cells have usually spread throughout the breast, rather than remaining in a well-defined lump.

If you have this type of Stage IIIB cancer, you will probably be sent to a cancer specialist or cancer centre and will be considered for chemotherapy rather than surgery first. After chemotherapy is completed, use of surgery, radiation treatment or both depends on how well your cancer responds to the chemotherapy (how much it shrinks). In rare

Flowchart 6: Treatment choices for inflammatory breast cancer (Stage IIIB)

*Regimens suitable for neo-adjuvant chemotherapy:
- 4 cycles FEC100 (fluorouracil, epirubicin and cyclophosphamide) followed by 4 cycles docetaxel
- 4 cycles AC (adriamycin and cyclophosphamide) followed by 4 cycles docetaxel
- 6 cycles FAC (fluorouracil, adriamycin and cyclophosphamide)
- 6 cycles CMF (oral cyclophosphamide, methotrexate and fluorouracil) if regimens above are not suitable
cases, if a woman cannot tolerate chemotherapy, hormonal therapy or biological therapy may be used. This is not standard, however. See the treatment chart below for the usual way in which these cancers are treated.

**Treatment choices for Paget’s disease**

Paget’s disease of the breast is a unique condition that affects the nipple area, making it dry, itchy and scaly. Sometimes the condition persists for months or more before being identified because it is thought to be a skin problem. In 50% of cases, when a biopsy is taken of the nipple and the underlying breast, pre-invasive cancer (ductal carcinoma in situ) is diagnoses. The other 50% of patients will have invasive breast cancer somewhere deeper in the breast. Paget’s disease is diagnoses when the pathologist finds special cells in the nipple tissue called Paget’s cells.

If you have problems with the skin on one nipple and it does not get better with skin treatments, you should see a specialist in breast problems (usually a general surgeon). If needed, a biopsy can be done to check for Paget’s disease.

Paget’s disease is treated by removing the nipple area and the pre-cancer (DCIS) or invasive cancer in the breast tissue underneath the nipple. Removing the nipple area usually leaves a poor cosmetic result, so it is quite common for women with Paget’s disease to have a mastectomy.

Treatment after surgery depends on the type and extent of DCIS or on the stage of the invasive cancer found in the breast (see sections on treatments for stage 0, I or II, as appropriate).

**Patient follow-up after treatment for stages 0 to III**

Most patients with early-stage breast cancer who receive treatment will never have a relapse or recurrence. If you have a small cancer (less than 1 cm) with no other negative factors associated with it (as discussed in the Pathology and Risk of relapse sections), you have a better than 90% chance of being alive five and even 10 years after diagnosis. For larger breast cancers, and depending on all the other factors relevant at the time of diagnosis, there are some groups of women that have a 50–80% chance of the disease coming back elsewhere in the body.

If you have been diagnosed with breast cancer, you should receive follow-up care according to either cancer-centre or provincial or territorial guidelines. The highest chance of relapse is in the first three years after initial diagnosis and treatment, but relapse is possible even seven or 10 years after initial treatment has been finished. It’s possible to see problems 15 to 25 years later, although this is less likely.

Follow-up for Stage I and Stage II breast cancer consists of periodic examinations (every three to six months) by a physician for five years, after which an examination once a year is sufficient. A routine follow-up examination should include a physical examination of both breasts (or the chest wall if you have had a mastectomy), examination of the lymph nodes in the area and a mammogram once a year.

If you have had Stage III cancer you will be followed more closely. If the disease is metastatic (Stage IV), you will see your doctor at more frequent intervals, depending on the particular problems you have and type of treatment you are receiving. Specific tests to look at the internal organs or bones are usually arranged only when symptoms occur that suggest that the cancer has come back.

**Treatment for local recurrence**

If the initial treatment did not eliminate all the cancer cells, the cancer may recur. Breast cancer recurring at the site of the primary tumour either in the breast (if breast-conserving surgery was done) or at the mastectomy site is known as local recurrence and can potentially be cured with further treatment. Disease that recurs in the nearby lymph
nodes under the arm (axilla), near the breastbone (internal mammary nodes) or around the collarbone (supraclavicular if above the collarbone, infraclavicular if below it) is called a local-regional recurrence. This area can also include the skin of the chest wall after a mastectomy. This type of recurrence may or may not be completely cured, even with aggressive treatment. The result of treatment in the local-regional area often depends on a variety of factors.

The diagnosis and approach for a local recurrence is often very similar to that for the initial disease. Taking a biopsy of a lump can confirm recurrence and complete removal, or excision, of a smaller lump can sometimes provide both diagnosis and treatment.

You and your cancer-care team will choose treatments based on:

• The area involved
• The type of cancer cells present (especially whether they are hormone-positive or not)
• Previous treatments
• Time from original treatment to recurrence

For example, if you experience a local recurrence after breast-conserving surgery and radiation treatments, it may be treated by a second breast-conserving operation or by a mastectomy. Chemotherapy, hormonal therapy or both, can follow the operation. Surgery and systemic therapy might be used to treat a local recurrence on the chest wall after mastectomy. Radiation is usually not an option if you have had previous radiation at the same site.

Development of a second breast tumour, either as a new unrelated primary tumour in the same breast or in the opposite breast, is a less common type of recurrence, but it can also be curable, especially if diagnosed early.

You may choose chemotherapy, hormonal therapy or both, depending on your particular situation. Previous chemotherapy may or may not have an effect on your ability to tolerate more chemotherapy. This is especially true if the same or a similar type of chemotherapy is an option. Patient choice and quality-of-life issues play a large role in decisions about treatment of local recurrences, especially those involving repeat surgery and chemotherapy. Because the types of local and local-regional recurrences are so varied, clinical studies are difficult to perform, and so there is a lack of good study information to help provide definitive answers.

**Treatment for metastatic breast cancer (Stage IV)**

**Description**

Stage IV breast cancer is diagnosed when distant metastases are found.

**Investigations**

Once breast cancer has been classified as Stage IV, it is likely that tests will be done to determine the extent of the disease because this will affect treatment. A chest x-ray, ultrasound exam of the abdomen and a bone scan are usually the first, and perhaps only, tests required. Frequently, a CT (computed tomography) scan of the chest or abdomen is done. For other diseases (e.g., in the spine) sometimes a CT or MRI (magnetic resonance imaging) scan will be done. Occasionally, and where facilities exist, a PET (positron emission tomography) scan will be done to distinguish the difference between cancer recurrence and other lumps, especially where biopsy may be difficult to perform. Once all the sites of the disease have been identified, these areas will be followed when treatment begins.

**Treatment options**

**Hormonal therapy:** If you originally had hormone-positive disease, then use of hormonal therapy is probably a good option. Your choice of hormonal therapy or chemotherapy may be influenced by the extent of cancer spread, the particular organs affected, symptoms caused by the disease spread and personal preference.
**Biological therapy**: Biological therapy may be used if the breast cancer tumour over-expresses HER-2.

**Chemotherapy**: If all the hormonal therapies have been used, or if the disease is progressing rapidly, women with hormone-positive tumours may need chemotherapy. If your original tumour was hormone-negative, then chemotherapy is the best choice if you need systemic treatment.

**Radiation**: Treatment of painful cancers, such as tumours in bones, is usually best done with radiation. However, radiation can be applied to certain areas (especially of the spine, spinal cord or brain) only a limited number of times because of potential damage to normal tissues. Radiation doses and the size of the areas treated vary depending on previous treatments with radiation and the need for chemotherapy or hormonal therapy for particular sites of disease at any one time.

There are types of radiation that are not administered from outside the body but instead are given by a special radioactive injection, as is done with bone-seeking radiation (called isotopes) like strontium. This kind of radiation therapy treats all bones that may be involved and is usually used for women who have many painful bone cancer sites. Specialists called nuclear medicine physicians usually give the injections. The availability of this treatment varies around the country. After a strontium injection, your blood cell counts can go quite low for several weeks and follow-up blood tests are needed. The use of strontium causing low blood counts means that chemotherapy cannot be given at the same time as strontium. Radiation is usually also given after surgery for bone problems resulting from breast cancer (such as operations to prevent bones from breaking or when a bone is very weak).

**Supportive treatments for bone disease**: Bone disease can be found in up to 70% of women with Stage IV breast cancer. You may experience bone pain, bone fracture, weakening of the bone or spinal cord compression. In addition to anti-cancer treatment, drugs called bisphosphonates are used to try to strengthen bone. The three most common bisphosphonates are clodronate (Bonefos®, Ostac®) given orally; pamidronate (Aredia®) infused into a vein (intravenously) for two hours once every four weeks; and zoledronate (Zometa®) given intravenously for 15 minutes every four weeks.

**Figure 6**: Stage IV breast cancer (number and location of metastasis may vary)
Management of accompanying problems in metastatic breast cancer: Pain — and the fear of experiencing severe pain — are major concerns for many women with metastatic disease. Cancer pain can generally be effectively controlled.

Pain is usually managed in what is described as a stepwise approach. The first drug used is often acetaminophen or similar drugs such as ibuprofen or acetylsalicylic acid (ASA). If these are not strong enough, combinations with drugs like codeine may be tried.

Stronger painkillers, called narcotics, are available to control more severe pain. These very effective painkillers can be given by tablet or injection, as suppositories (medications that are inserted into the rectum and are absorbed directly into the bloodstream through the tissue of the colon) and sometimes using a skin patch that can stay on for a few days. Narcotic injections can sometimes be given using a pump that you control yourself — the pain reliever goes into your skin and from there into your bloodstream. The dose can be preset, with an extra or boost dose (which you can choose when to give yourself) determined by the level of pain. Unfortunately, many patients resist taking narcotics because they are afraid of becoming addicted. This fear is unfounded, however: the vast majority of patients taking narcotics to manage pain do not become addicted to them.

Clinical trials have shown that in patients with cancer that has spread to their bones, early use of bisphosphonates may reduce the number of metastases to bone, the number of bone problems (including fractures) and the need for radiation therapy. Bisphosphonates currently available include clodronate, an oral or injectable medication, and pamidronate and zoledronate, which are both given only by injection. Other experimental therapies to treat bone metastases are being investigated in clinical trials.

Other problems you may experience if you have metastatic disease, such as heartburn or nausea, can usually be controlled by using acid-suppressing or anti-nausea drugs.

Not surprisingly, many women with metastatic breast cancer experience depression, anxiety and difficulty sleeping as they attempt to cope with their disease. If you experience any of these problems, it is important to discuss them with your physician, clinic nurse or another member of the care team. Numerous effective antidepressants and anti-anxiety agents are available to help you. As well, all women in this situation need ongoing support and encouragement that can be obtained from a variety of sources linked to the cancer centre and in your community. Ask your oncologist and oncology nurse about them.
Clinical Trials

Until the time comes when breast cancer can be cured or permanently controlled in the majority of women, research into all aspects of this disease will continue. There continues to be a need for women who have had, or currently have, breast cancer to participate in research studies. Over the past few decades these volunteers have helped researchers learn so much, meaning that women with breast cancer today receive better treatment than ever before. But a lot of work remains to be done.

Participating in a clinical trial gives you the opportunity to test newer and potentially more effective treatments. Understanding what clinical trials are, why they are conducted and the risks and benefits of participating in one can help you decide whether clinical trial participation is right for you.

A clinical trial is a way in which new ideas and treatments can be tested. Studies are needed to prove the importance of treatments for specific groups of patients. Clinical trials often compare two or more treatments in well-defined patient groups. These trials usually follow up patients for several years to determine which treatment most improves cancer-free survival. Some patients participating in clinical trials have now been followed for 20 years. Trials also measure short- and long-term side effects in more detail than is done for patients not participating in trials.

An important feature of some clinical trials is that during treatment, neither patients nor physicians and other researchers are aware of which treatment is given to each individual patient. This is called a double-blind study. An additional feature of some trials is that neither researchers nor participants can choose which treatment a specific individual will receive. This is called randomization.

Randomization ensures that results in each group being compared will come from differences between the drug treatments or treatment approaches being compared and not from differences in the kinds of patients chosen for each treatment group through conscious or unconscious choices (called biases).

By removing biases, double-blind, randomized trials eliminate an important source of mistakes or errors, particularly when subjective factors such as pain relief or treatment side effects are being studied. Clinical trials need not always be blinded and randomized, however, especially if they are done during the early stages of testing a new treatment. When the effect of a particular treatment on the natural course of an illness is unclear, a placebo-controlled trial may be done. In this type of study, some patients will be given a treatment with no therapeutic or medicinal value (called a placebo), while others will receive the drug being tested.

Clinical trial results help physicians gain a better idea of what approaches might help certain groups of women the most and therefore help them suggest the most appropriate treatment. For example, if two treatment possibilities give equally good results, but one has far fewer side effects, the treatment that causes fewer problems will likely be favoured.
For instance, early breast cancer clinical trial results showed that radical mastectomy did not improve survival in breast cancer. As a result, breast-conserving surgery has become an important standard treatment choice.

Most often, clinical trials provide information about the best treatment for groups of patients, not necessarily about the best treatment for an individual. Results from a clinical trial in which all patients had certain tumour factors might not apply to patients with slightly different tumour characteristics. Therefore, in spite of the large amount of information already gathered from clinical trials, factors such as a physician's clinical judgment and each patient's age, general health and personal preferences are always considered when planning treatment for breast cancer.

Standard therapies are those that have been well studied in one or two large clinical trials, or in several smaller ones, and in specific patient populations. The treatments that become standard are the ones that have been shown to give the best results for the most patients. Several clinical trials and many years of follow-up are usually necessary before a treatment can be considered a standard therapy.

**Clinical trial participation**

Theoretically, any cancer patient can participate in a clinical trial. Your opportunity to do so depends on whether a suitable trial is being conducted at a treatment centre you can reach. Sometimes the trial might be looking at new ways of giving drugs that are known to be useful in some groups of women with breast cancer. Sometimes the trial will be for a new or investigational treatment. There are some studies that ask survey-type questions; take blood, urine or tumour tissue samples; measure weight and fitness; or involve diet, but do not involve drug treatments at all.

Research is also finding the best length of time over which specific treatments should be given, establishing the smallest or largest doses that work and investigating the problems of side effects. No one cure exists for all patients with breast cancer. Many promising therapies must be studied to allow a few to become standard treatments in the future.

The search for treatments to improve survival in metastatic disease is intense, and many clinical trials continue to study treatments that are thought to have potential.

Many cancer centres commonly offer women with all stages of breast cancer the opportunity to participate in clinical trials. By participating in a trial, you are not only helping increase our understanding of breast cancer treatments, but you may also discover how an investigational approach might benefit your own illness. Individual trials vary from centre to centre because many new treatments are being tested across the country at the same time. You can inquire as to whether or not any clinical trials are open for your participation at any time during your evaluation and treatment for breast cancer; you will always be free to choose whether or not to participate, and you will be free to withdraw from a trial at any time.

Whether you participate in a clinical trial or not, you are assured of receiving the best possible treatment. It is important that you take all the time you need to make this very important decision, read the written explanation of the trial and, if you decide to participate, sign a consent form.

Clinical trials must be approved by Health Canada and the research ethics board of the institution, hospital or university conducting them to be allowed to enrol patients. This process ensures that trials are designed and conducted fairly, honestly, safely and with high ethical standards. For more information about participating in clinical trials and about which trials are currently being conducted in Canada, call the Canadian Cancer Society’s Cancer Information Service (CIS) at 1-888-939-3333.
**Weighing the risks and benefits of clinical trial participation**

Every treatment, whether it is standard or investigational, is associated with both risks and benefits. The major risk associated with investigational treatments is that little information is available about rare toxicities and about the effectiveness of the new treatment in different types of patients. The major benefit is that the new therapy might be the best one for you. Clinical trial participants are monitored closely and are often required to make more frequent visits to the clinic than are patients not participating in a trial. For some, this offers comfort; for others, the time commitment is too disruptive.

You should weigh these factors carefully before deciding to participate in a clinical trial.
Currently, several different approaches to improving cure rates and survival rates are being investigated. These include new drugs and combinations, hormonal and biological therapies and new radiation therapies.

New chemotherapy agents and combinations

Researchers are still evaluating the specific situations and patient groups in which some of the newer drugs and drug combinations (regimens, schedules or protocols) are the most effective, and how chemotherapy should be combined with other biological treatments. Combination therapies including two or more chemotherapy drugs have been shown to improve cure rates in some groups of women with breast cancer.

Although the use of tamoxifen is already standard therapy, results from some important international trials looking at the benefit of using tamoxifen after chemotherapy in Pre-menopausal women will be available in the future. Information from clinical trials seems to confirm the idea that when post-menopausal women use tamoxifen, it should be started at the end of chemotherapy. These trials are also helping to clarify the role of new drugs called aromatase inhibitors. Data on whether radiation and tamoxifen should be given together, versus delaying the tamoxifen until after radiation is finished, have not been conclusive.

New biological agents

Researchers are investigating the development of biological therapies in addition to trastuzumab (Herceptin®). Herceptin® blocks the abnormal function of a gene that is prevalent in breast tumours, called erbB2. Researchers are identifying and testing other potential drugs that may block this gene as well as other members of the erbB family of genes, such as the epidermal growth factor receptor.

Other biological and gene therapies are being developed, but they are far from being in routine clinical use. Gene therapy can use a genetically altered virus to replace an abnormal gene with a normally functioning gene, and thereby affect cancer cell growth. These are very promising treatments for the future.

One avenue that has already produced important results in clinical trials is the study of anti-angiogenesis drugs, which stop the formation of new blood vessels required for a tumour to grow (blood vessels in tumours are abnormal). The drug bevacizumab (Avastin®) has been used with paclitaxel (Taxol®) in Stage IV (metastatic) breast cancer and has been found to provide an improvement in cancer progression survival of several months. More studies with bevacizumab are being undertaken but as yet the treatment is not available in North America for the treatment of breast cancer except in clinical trials.
Immune therapy (also called immunotherapy) refers to a group of treatments, including tumour vaccines, intended to stimulate the body’s immune system to fight the tumour more effectively. The best outcomes from all this promising research would be to improve results from treatments we already have, develop more biological treatments (like trastuzumab) and to reduce side effects of treatments. Some new studies will be done using samples (biopsies) of cancerous breast tissue taken before and again after therapy. This will allow important biological tests to be done on the tumour tissue. Breast-conserving surgery or mastectomy will be arranged after the new treatment has been given and its effects on the tumour can then be studied directly.

**Radiation therapy standards**

Research involving radiation therapy has been directed at finding the lowest dose and the shortest time over which to administer radiation while maintaining its effectiveness. Although most cancer centres give between three and five weeks of radiation as adjuvant treatment, there is no standard treatment schedule used by all centres across the country.
Living with Cancer
In addition to the medical aspects of cancer, you will have to cope with many different emotional, psychological and practical issues. You will need to make decisions about priorities that you would not otherwise have had to make. Remember that you are an individual and your situation is unique. Only you can decide how you can best cope with your cancer and its treatments and how to manage your daily life.

However, many concerns are common to most people with cancer. Some of the issues you will face are described in this section, as are coping techniques that many patients have found useful. This section also lists resources that you can use to find the help and information you need.
Dealing with Your Emotions

Receiving a diagnosis of cancer is always shocking and overwhelming. You may alternate between feeling numb and feeling intense emotions such as panic, outrage, anger, guilt and despair. It is important to acknowledge, experience and talk about how you feel. You may prefer to talk to family, friends, a member of your healthcare team or other patients in a support group. A support group can be a good place to talk with people who have dealt with similar problems, to learn how they coped and to share your feelings and experiences. You may also wish to talk with a professional counsellor, such as a psychologist, to help you deal with your emotions. Whatever you decide, make sure you get the help you need.

Fear may make you want to start treatment immediately. In many cases, this is unnecessary. It is important to take the time to calm down, learn about your options, think things over and gain some perspective before deciding on a course of treatment. Try to manage your fear by getting accurate information, learning about useful resources and getting support.

Dealing with relationships

Cancer changes not only your life, but also the lives of those around you. Sharing your cancer experience with others is important, but while many relationships will grow stronger, others may become strained or even dissolve. Most people are supportive and caring when they learn that someone close to them has cancer. Some may have difficulty dealing with their own emotions about your diagnosis. They may respond by withdrawing, by blaming you for having cancer, by making insensitive remarks such as “be grateful it can be treated” or by giving you unwanted advice. Their reactions may hurt you or leave you angry at a time when you really need support.

People who respond this way do so because of their own fears, not because they don’t care. Having someone else you can talk to can be very helpful in this situation. In addition, you must decide whom you will tell about your diagnosis and what you will say.

Coping with Age-Related Issues

Cancer can affect people at any stage in their lives. Each stage has its special concerns, and you might find it useful to talk to people your own age. Young people are often concerned about the effect of cancer on completing their education, establishing a career, dating, social relationships and starting a family. Middle-aged individuals often find that cancer interrupts their careers and makes it more difficult to look after others who depend on them, such as children and aging parents. Older patients may worry about the effect of cancer on other health problems, about not having enough support or about losing the opportunity to enjoy their retirement. It is important to deal with your concerns and to come to terms with them. You may be able to find a support group specifically for cancer patients your age who have similar experiences and concerns.
Coping with Treatment

Participating in your treatment
All cancer patients face treatment decision-making challenges during their cancer journey. Your need for information and the degree to which you may wish to participate in or control decisions about your treatment are entirely up to you. Remember, though, that you are a partner in your treatment, and you will feel better if you participate actively in managing your disease.

Attitude is also very important. Patients who believe they will defeat cancer will do better than those who believe they will not. The first step in participating in your treatment is to believe it will be successful. To participate fully in managing your disease, ask questions, determine your options and work closely with your physician to make choices.

You will need to understand some aspects of the following:
- The disease and how it is likely to behave in your individual situation at diagnosis
- Your own risk of recurrence
- The treatment choices available to you at diagnosis
- The effect treatment choices may have on your future health

Treatment decisions should be made once you understand as best you can what your options are and the likely results of each choice.

Breast cancer usually grows more slowly than you might imagine. By the time a breast lump is large enough to be seen on a mammogram or felt during an examination, it may have been growing for many years. When a woman first hears the diagnosis of breast cancer, the natural reaction is to want immediate treatment. However, it is very important to take some time to understand the disease, its risks and your options. Many people find it helpful to write questions down or to bring one or more family members to the consultation during which your physician will discuss treatment choices and your prognosis with you.

You must be comfortable with your physician and the approach he or she takes to treatment. If you are not comfortable, discuss your concerns. If it becomes apparent that you and your doctor are not a good match, ask for a referral to another.

Managing side effects
The side effects of cancer treatment can usually be managed effectively with medications. The emotional and psychological impact of side effects is more difficult to deal with.

Feeling unattractive
Hair loss and other changes in appearance caused by treatment make many people feel unattractive. These feelings are best addressed by learning how to improve your appearance: how to hide hair loss and manage temporary changes such as dry skin, brittle nails and a blotchy complexion. The “Look Good...Feel Better” program teaches women with cancer how to use makeup and skin care techniques effectively and how to choose a wig or hat. Information for men is also available. To inquire about the services and materials offered by “Look Good...Feel Better,” call 1-800-914-5665 or visit http://www.lookgoodfeelbetter.ca/.

Feeling tired
Fatigue is a common side effect that may limit what you can accomplish on any given day. You will need to decide whether you can continue working or going to school full-time. You will need to set priorities. Pace yourself and listen to your body. Stop your activities and rest when you are tired. See Fatigue in the Chemotherapy side effects section on page 40 for more information.
“The sudden reminder that life is finite can promote an evaluation of one’s life. This can reveal a sometimes pressing need to make the best of one’s life. Making changes can be a much more difficult process than merely acknowledging the need to do something differently. An important learning opportunity has been to put one’s troubles into perspective and to relax more. This comes, however, with the realization that this is an ongoing and challenging learning process.”
~ Breast cancer survivor

Using complementary or alternative therapies
Many women are interested in investigating various alternative or complementary therapies. Many non-drug therapies, such as meditation, relaxation and visualization, are frequently used to help cancer patients reduce stress and anxiety levels and maintain a positive attitude. There are many different types of therapy that promote relaxation. Your healthcare team or support group can help you find workshops that teach these techniques. Exercise is also important in reducing stress and frustration. Experiment with different techniques or activities to find those that are best for you and that help improve your feelings of well-being. At this time in your life, you come first.

You may also be interested in experimenting with “natural” medicines, vitamins, herbal remedies or other unproven therapies advertised as cures for cancer. Using them may make your cancer therapy work less effectively — unproven treatments have not been scientifically tested and can contain unknown products or additives that may conflict with treatment prescribed by your treatment team. To ensure the most effective treatment for yourself, discuss your interest in alternative therapies with the members of your care team.
Coping with Life Changes

Living in remission

Living in remission can be a source of both relief and anxiety: relief that the tumour is gone and anxiety that it may recur. You may feel that successful treatment has given you another chance at life. It is not uncommon for cancer to change people’s priorities or career directions. It is important for you to deal with changes in your attitude to your life, your relationships and yourself. It is also important, while hoping that the disease stays in remission, to remember that it can recur. Therefore, take the appropriate steps to maintain your health and follow your physician’s recommendations for follow-up visits.

Dealing with relapse

If you experience a relapse, you may feel even worse than when you were first diagnosed, because you had hoped and believed that the cancer was cured. But it may actually be easier for you to cope the second time around; you already know what to expect, how to find support and how to manage your disease. Remember, if your cancer was successfully treated once, it may be successfully treated again. Use whatever support you need to get through a relapse.

Facing sterility

If you want to have children and you are not able to as a result of your cancer treatment, you will face several practical and emotional issues. You may be able to deal with your disappointment on your own, or you may need help. Your partner, friends, family or support groups can help.

“Of course breast cancer affected who I am as a woman. I am a different person, a person in progress, learning about each new piece of me — who I am, what I am thinking, how my body works and what I look like. I am in the process of becoming the new me — piece by piece. I am not there yet, but I know there is no timeline in this journey.” ~ Breast cancer survivor
Finding Information

When you are diagnosed with breast cancer, you may seek information to help with making decisions. If you cannot remember much of what your doctor said when you were given your diagnosis, you may want to make another appointment with your physician to learn more about your disease and to discuss treatment options. Writing out your questions before the appointment, taking a family member with you and making notes can help you get the information you need.

Numerous other sources of information are also available, including other patients, books, Internet websites and newsgroups, and other members of your healthcare team. Patients who have more information generally do better because they feel more in control and are more able to participate in their treatment.

Putting statistics in perspective
Statistics indicate only how groups of patients respond to a particular disease or treatment; they cannot predict an individual's response. In addition, because they are based on older treatments, many published statistics are outdated. Treatment and cure rates have changed significantly. Like all cancer patients, you want to know what your chances are, but do not allow a positive attitude to be negatively affected by statistics. To cope effectively with cancer, you need all your mental and emotional resources.

Finding a support group
If you are interested in talking to, and learning from, people who have had similar experiences, ask your oncologist, your cancer nurse or the oncology social worker if they know of any groups in your area. You can also find a support group by calling the Canadian Cancer Society's Cancer Information Service (CIS) at 1-888-939-3333. CIS maintains a national database of support groups listed by postal code, but does not rate them. You will have to use your own judgment to find a group that appeals to you. CIS may also refer you to your provincial Canadian Cancer Society office for additional information on local groups. Call CIS between 9 AM and 6 PM from anywhere in Canada.

Finding resources
Some important things to remember when you are reading about your disease or about coping with cancer:

- Make sure the treatment information you are reading is current. Much of what is published may already be outdated because cure rates, survival statistics and treatments are constantly changing.
- Find an author whose writing makes sense to you. All authors try to write clearly, but writing styles, terminology and approaches to discussing cancer vary from author to author.
• You do not need to spend money buying books unless you want to. You can borrow books from a support group or your local library.
• Evaluate the credibility of any publication you find. Books may be inaccurate. Although authors try to give you accurate information, some may be biased or misinformed.

**Useful books**

Only you can determine what books are useful to you, but the following is a list of books that many patients have found helpful. The Cancer Information Service of the Canadian Cancer Society also has lists of useful books.

**General cancer books**

*Anatomy of an illness as perceived by the patient: Reflections on healing and regeneration*, by Norman Cousins.

*Cancer. Your guide through the first few months*, by Wendy S. Harpham.

*Cancer as a turning point: A handbook for people with cancer, their families, and health professionals*, by Lawrence LeShan.

*Cancer is a word, not a sentence: A step-by-step practical guide to cancer and cancer treatment*, by Robert Buckman.

*Everyone’s guide to cancer therapy: How cancer is diagnosed, treated and managed today*, by Malin Dollinger, Ernest H. Rosenbaum and Greg Cable.


*Oh my God, I thought you’d died*, by Claude Dosdel and Joanne Broatch.

*Peace, love and healing*, by Bernie S. Siegel.

*Reflections: Illness and healing; the art of Robert Pope*, by Jock T. Murray.


*What you really need to know about cancer: A comprehensive guide for patients and their families*, by Robert Buckman.

**Breast cancer books and CDs**


*Intelligent patient guide. Breast cancer: All you need to know to take an active part in your treatment, 2nd edition*, by Ivo Olivotto, Karen Gelman and Urve Kuusk.

*Survivors’ guide to breast cancer: A couple’s story of faith, hope and love*, by Robert C. Fore and Rorie E. Fore.

*That other place: A personal account of breast cancer*, by Penelope M. Williams.

*The breast book: The essential guide to breast care and breast health for women of all ages*, by Miriam Stoppard and Rachael Simmons.

*The complete breast book*, by June Engel.


*What you need to know about breast cancer. Diagnosis, treatment and beyond*, by Pat Kelly with Mark Levine.
Using the Internet

The World Wide Web has thousands of websites devoted to cancer. Websites can provide huge amounts of information about treatment, alternative medicine, personal experiences, specific types of cancer and general cancer issues. Many sites link to related sites; therefore, if you access the websites listed below, you will be able to link to many others. It is important to note, however, that information on the Internet is not screened for accuracy, so be sure to assess the credibility of information you find there.

General cancer resources
Chemotherapy Side Effects:
www.chemotherapysideeffects.ca

Canadian Association of Provincial Cancer Agencies:
http://www.capca.ca

Canadian Cancer Society:
http://www.cancer.ca

CancerGuide: Steve Dunn’s Cancer Information Page:
http://cancerguide.org

CancerNet (National Cancer Institute, Department of Health and Human Services, United States Government):
http://wwwncic.cancer.gov

OncoLink (University of Pennsylvania Cancer Centre):
http://www.oncolink.upenn.edu

Wellspring (cancer support group):
http://www.wellspring.ca

People Living with Cancer (American Society of Clinical Oncology):
http://www.plwc.org

Breast cancer resources

Alberta Breast Cancer Program:
http://www.albertabreast.com

Breastcancer.org:
http://www.breastcancer.org

Canadian Breast Cancer Network:
http://www.cbcc.ca

Gilda’s Club Greater Toronto:
http://www.gildasclubtoronto.org

Ontario Breast Cancer Information Exchange Partnership:
http://www.obciep.on.ca

Willow’s Breast Cancer Support & Resource Services:
http://www.willow.org

Imaginis, the Breast Cancer Resource:
http://www.imaginis.com

Canadian Cancer Society’s Cancer Information Service

The Canadian Cancer Society’s Cancer Information Service (CIS) is a clearing house for information about cancer. Call CIS at 1-888-939-3333 for information about the following topics:

• All types of cancer
• Prevention and early detection
• Cancer treatment and side effects
• Drugs and clinical trials
• Unconventional therapies
• Emotional and financial issues
• Cancer statistics
• Resources available in your community
**adjuvant therapy:** treatment (called systemic) with chemotherapy and/or hormonal therapy given after surgery to improve cure rates

**alopecia:** the absence of hair from areas of the body where it usually grows; hair loss

**anastrozole:** an aromatase inhibitor drug that prevents the adrenal glands and other tissues from producing estrogen; used to treat hormone receptor-positive breast cancer in post-menopausal women; brand name, Arimidex®

**anemia:** a reduction in hemoglobin, which is a measure of the red blood cell count, to below normal levels; chemotherapy may cause anemia

**antibody:** a substance used in treatments directed against an antigen (see below). Examples are trastuzumab (Herceptin®) and bevacizumab (Avastin®). The antibody is made to fit into the antigen like a key into a lock, with exact precision. Many of these treatments have fewer side effects than traditional chemotherapy owing to they are specific to the targeted antigen

**antigen:** a unique identifying structure found on the surface of all cells and organisms that allows the immune system to determine whether the cell is foreign to the body

**Anzemet®:** see dolasetron mesylate

**apoptosis:** programmed cell death, or built-in instructions for cells to die after a specific lifespan; tumours may grow because cancer cells have evaded this mechanism

**Aranesp®:** see darbepoetin alfa

**Aredia®:** see bisphosphonates

**Arimidex®:** see anastrozole

**Aromasin®:** see exemestane

**aromatase inhibitors:** hormonal therapies. In post-menopausal women, the ovaries do not produce estrogen; rather, it is produced by conversion of pre-estrogen to estrogen in fat and muscle cells. The pre-estrogen can be converted to estrogen only by a reaction involving an enzyme called aromatase. The drugs anastrozole, letrozole and exemestane block aromatase and decrease circulating estrogen to almost zero, thus starving the cancer cells of estrogen, which is required for growth.

**Avastin®:** see bevacizumab

**axillary lymph nodes:** glands in the armpit that are part of the body’s defence against infection

**benign growth:** a non-cancerous lump or growth
**bevacizumab**: a drug that fights cancer by stopping the growth of blood vessels in tumours; brand name, Avastin® (approved in North America for the treatment of colorectal cancer)

**biopsy**: removal of tissue sample for examination. Biopsies are sometimes done with a fine needle and local anesthetic, or they can be taken during surgery

**bisphosphonates**: bone-strengthening drugs used in the treatment of metastatic cancer in bones; it can also reduce the number of metastatic tumours in bones; drugs include clodronate (Bonefos®, Ostac®), pamidronate (Aredia®) and zoledronate (Zometa®)

**Bonefos®**: see bisphosphonates

**breast-conserving surgery**: breast cancer surgery that removes the tumour without removing the breast

**buserelin**: a luteinizing hormone-releasing hormone agonist drug used to reduce the production of estrogen by reducing the pituitary gland’s signal to the ovaries to make estrogen; brand name, Suprefact®

**carcinoma in situ**: ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) are both non-invasive, or non-spreading, tumours. They are sometimes referred to as pre-cancer

**chemotherapy**: systemic drugs usually given by intravenous injection that are used to kill cancer cells

**climacteric**: see menopause

**clinical trial**: a study comparing the benefits and safety of different treatments in specific groups of patients

**clodronate**: see bisphosphonates

**computed tomography (CT or CAT) scan**: an imaging study that produces a three-dimensional X-ray

**core biopsy**: a needle biopsy using a large hollow needle to remove a core of tissue from a tumour

**CT scan**: see computed tomography

**cycle**: one course of a fixed dose of a chemotherapy drug or combination of drugs, usually with a defined schedule over a predetermined period of time, such as three or four weeks

**cyst**: a fluid-filled sac, usually benign

**cystitis**: inflammation of the bladder

**darbepoetin alfa**: a manufactured biological response modifier similar to erythropoietin, a natural hematopoietic growth factor in your body that stimulates the production of red blood cells; used to treat anemia (low red blood cell count) after chemotherapy; a modified version of recombinant human erythropoietin that stays in the body longer and can therefore be administered less frequently; brand name, Aranesp®
Decadron®: see dexamethasone

dexamethasone: an anti-nausea medication; brand name, Decadron®

dimenhydrinate: an anti-nausea medication used for nausea occurring more than 48 hours after chemotherapy; brand name, Gravol®

docetaxel: a synthetic derivative of the naturally occurring compound paclitaxel

dolasetron mesylate: an anti-nausea medication; brand name, Anzemet®

domperidone: an anti-nausea medication used for nausea occurring more than 48 hours after chemotherapy; brand name, Motilium®

dose escalation: increasing the dose of a drug to intensify the therapeutic effect

drug resistance: the ability of some tumors to develop immunity to one or more chemotherapy drugs

ductal carcinoma in situ (DCIS): see intraductal carcinoma

epoetin alfa: a manufactured biological response modifier that mimics erythropoietin, a natural hematopoietic growth factor in your body which stimulates the production of red blood cells; used to treat anemia (low red blood cell count) after chemotherapy; brand name, Eprex®

Eprex®: see epoetin alfa

ER-positive: see hormone receptors

erthropoietin: the body “manufactures” its own blood, and erythropoietin is involved in this process as a hematopoietic growth factor, in that it is involved in the production of blood. Specifically, erythropoietin stimulates the development of red blood cells from immature cells. Recombinant human erythropoietin (epoetin alfa) has been manufactured under the brand name Eprex®.

Evista®: see raloxifene

exemestane: an aromatase inhibitor drug that prevents the adrenal glands and other tissues from producing estrogen; used to treat hormone receptor-positive breast cancer in post-menopausal women; brand name, Aromasin®

Fareston®: see toremifene

Femara®: see letrozole

filgrastim: a manufactured hematopoietic growth factor that stimulates the development and differen-
fraction: a dose of radiation used in radiation therapy

G-CSF: see granulocyte-colony stimulating factor

gene: a segment of material inherited from your parents — a section of DNA — that specifies the manufacture of a particular product, often a protein

goserelin: a luteinizing hormone-releasing hormone agonist drug used to reduce the production of estrogen by reducing the pituitary gland’s signal to the ovaries to make estrogen; brand name, Zoladex®

granisetron: an anti-nausea medication; brand name, Kytril®

granulocyte colony-stimulating factor: a hematopoietic growth factor made in the body that stimulates the development of neutrophils from stem cells, and which has also been manufactured for therapeutic use

Gravol®: see dimenhydrinate

growth factor support: giving manufactured hematopoietic growth factors filgrastim or pegfilgrastim after chemotherapy to help the neutrophil count recover more rapidly; brand names, Neupogen® and Neulasta®

hemoglobin: the oxygen-carrying protein in red blood cells; hemoglobin levels are measured to determine the presence of anemia

HER-2: human epidermal growth factor receptor number 2 — part of the epidermal growth factor (EGFR) family. A gene inside the cell that controls production of the cell’s growth factor receptor; high levels of HER-2 on breast cancer cells may suggest that the tumour is more likely to recur or spread

Herceptin®: see trastuzumab

high-dose chemotherapy: an investigational technique using very high doses of chemotherapy after bone marrow or stem cells from the patient have first been saved (so that the patient does not lose the ability to manufacture his or her own blood)

histopathological diagnosis: a diagnosis reached by microscopic examination of tissue samples

hormone receptors: cell structures to which hormones attach themselves, and so affect the behaviour of that cell. Some types of cancer cells have receptors for the hormones estrogen (ER-positive) or progesterone (PR-positive), and will often respond to hormonal therapy
**hormonal therapy**: cancer therapy that prevents natural hormones from causing the growth of tumour cells

**immune response**: the normal response of the immune system to protect the body from foreign substances

**immune system**: the body system responsible for maintaining health by removing abnormal cells and fighting infection

**immunologic treatment**: a group of investigational treatments attempting to stimulate the body’s defence (i.e., immune) system to attack cancer cells more effectively; also called immunotherapy

**in situ**: Latin for “in its original position”; cancer that has not spread beyond where it began; non-invasive

**inflammatory carcinoma**: an uncommon, rapidly growing type of breast cancer that is characterized by redness and swelling in the breast resembling an infection

**intraductal carcinoma**: breast cancer that began in the milk ducts and has not spread beyond the ducts; also called ductal carcinoma in situ

**investigational treatments**: treatments that are still being studied to determine their most appropriate use in particular types of patients

**Kepivance™**: see palifermin

**Kytril®**: see granisetron

**letrozole**: an aromatase inhibitor drug that prevents the adrenal glands and other tissues from producing estrogen; used to treat hormone receptor-positive breast cancer in post-menopausal women; brand name, Femara®

**leuprolide**: a luteinizing hormone-releasing hormone agonist drug used to reduce the production of estrogen by reducing the pituitary gland’s signal to the ovaries to make estrogen; brand name, Lupron Depot®

**lobular carcinoma in situ (LCIS)**: cancer that began in the lobules of the breast and has not spread beyond the lobules

**lobule**: a grouping of milk glands in the breast, leading to milk ducts

**Lupron Depot®**: see leuprolide

**lymph channel**: a network of vessels connecting lymph nodes

**lymph glands**: see lymph nodes

**lymph nodes**: glands that are part of the body’s system of defence against infection
**magnetic resonance imaging (MRI):** a type of imaging study that uses radiofrequency waves to produce a three-dimensional image

**malignant growth:** a tumour that can spread somewhere else in the body; cancer

**mammogram:** see mammography

**mammography:** an imaging technique using low-dose X-rays to get a better look at changes found in the breast during physical examination, or to check the breast even when no obvious changes have been discovered; the resulting image is called a mammogram

**mastectomy:** removal of the whole breast

**Maxeran®:** see metoclopramide

**medical oncologist:** a cancer physician specializing in the use of drugs (chemotherapy or hormones) to treat cancer

**menopause:** the natural process that comes with age and marks the end of a woman’s child-bearing years, when a woman’s ovaries stop functioning and her menstrual periods stop. Women are Pre-menopausal if they have regular periods and post-menopausal after their periods have stopped. The peri-menopause is the few years before, during and after menopause. The point when a woman’s periods actually stop is called the climacteric. If a woman has had a hysterectomy and has no menopausal symptoms (like hot flashes), blood tests can be done to see if she is pre- or post-menopausal.

**metastatic:** cancer that has spread through the blood vessels or lymph channels to sites in the body distant from its origin

**metoclopramide:** an anti-nausea medication used for nausea occurring more than 48 hours after chemotherapy; brand names, Maxeran® and Reglan®

**Motilium®:** see domperidone

**mutation:** a genetic change in a cell; it can be spontaneous or induced by exposure to toxins, carcinogens or radiation

**neo-adjuvant therapy:** systemic therapy (a treatment that goes into the blood by injection or tablet) administered before surgery rather than after it

**Neulasta®:** see pegfilgrastim

**NEUPOGEN®:** see filgrastim
neutropenia: a reduction in the neutrophil count to below normal levels, which can be caused by chemotherapy; neutropenia places patients at risk of serious infection and chemotherapy dose reductions and delays

dnode-negative, node-positive: breast cancer is classified as node-negative if it has not spread to the lymph nodes, and node-positive if it has

Nolvadex®: see tamoxifen

nuclear grade: see tumour grade

ondansetron: an anti-nausea medication; brand name, Zofran®

Ostac®: see bisphosphonates

ovarian ablation: using surgery or radiation to stop or impair the production of estrogen by the ovaries; formerly used to treat hormone receptor-positive cancer in Pre-menopausal women

paclitaxel: a drug developed from the toxin of specific types of Yew trees and bushes and used to kill dividing cells, especially tumour cells

Paget’s disease: a rare form of breast cancer that involves the nipple and areola, causing itchy, scaly skin; diagnosed by the presence of Paget’s cells

palifermin: a growth factor protein used to increase the number of keratinocytes (the major cell type of the outermost layer of the skin) to help speed up the growth of cells in the lining of the mouth to replace those damaged by chemotherapy or after bone marrow transplant; brand name Kepivance™

palliative therapy: treatment given to relieve symptoms and provide comfort when a cure is not likely

pamidronate: see bisphosphonates

pathologist: a physician who diagnoses disease by studying tissues removed by biopsy or surgery

pegfilgrastim: a manufactured hematopoietic growth factor that stimulates the development and differentiation of neutrophils from stem cells; also known as granulocyte colony-stimulating factor (G-CSF); a modified version of filgrastim that stays in the body longer; brand name Neulasta®

peri-menopause: see menopause

platelets: blood cells responsible for preventing bleeding and for stopping bleeding after any injury

positron emission tomography (PET): an imaging technique in which short-lived radioactive tracers are injected to produce images of the body’s biological functions
post-menopausal: see menopause

predictive factors: the special factors found in a tumour that suggest how it might react to specific types of anti-cancer treatments

Pre-menopausal: see menopause

prochlorperazine: an anti-nausea medication used for nausea occurring more than 48 hours after chemotherapy; brand name, Stemetil®

prognosis: a forecast or prediction of the likely course of a disease or outcome of treatment, based on specific aspects of the disease seen in an individual. Often expressed as the risk of relapse

prognostic factors: patient or tumour characteristics that affect the risk of spread or recurrence of the tumour

prophylactic mastectomy: removal of a breast with no known cancer in it; considered for women who are at a high risk of developing cancer

prosthesis: an artificial breast replacement

PR-positive: see hormone receptors

radiation oncologist: a cancer physician specializing in the use of radiation to treat cancer

radiation: ionizing radiation used to kill tumour cells

raloxifene: a selective estrogen receptor modulator; brand name, Evista®

recurrence: the return (relapse) of detectable cancer after initial treatment had produced no detectable signs of cancer (remission)

red blood cells: blood cells responsible for carrying oxygen to the tissues

regimen: a medication recipe that specifies the drugs, doses, timing, frequency and total amounts

Reglan®: see metoclopramide

relapse: see recurrence

remission: the absence of any detectable signs of a tumour after treatment has been completed

salvage therapy: second-line therapy used after relapse, partial remission or disease progression
sentinel node biopsy: surgery in which the lymph nodes into which a tumour drains are removed and examined for cancer

staging: a system for looking at a tumour to determine its extent, risk of spread or recurrence and appropriate treatment choices

standard therapy: any therapy that is well accepted and often used by healthcare professionals in a specific medical condition, against which new therapies are often compared based on the standard therapy’s record of effectiveness and safety

stem cells: immature cells, found in bone marrow and blood, that eventually produce red blood cells, white blood cells and platelets

Stemetil®: see prochlorperazine

Suprefact®: see buserelin

surgical oncologist: physician specializing in the use of surgery to treat cancer

systemic disease: a disease affecting the whole body

systemic treatment: any treatment that goes into the bloodstream because it is given by injection or tablet

tamoxifen: a hormonal therapy (a selective estrogen receptor modulator) that has been effective in preventing breast cancer in women at high risk; brand name, Nolvadex®

Taxol®: A trademark used for the drug paclitaxel, a drug developed from the toxin of specific types of Yew trees and bushes and used to kill dividing cells, especially tumour cells

Taxotere®: A trademark used for the drug docetaxel, a synthetic derivative of the naturally occurring compound paclitaxel, which is used to treat breast cancer and non–small-cell lung carcinoma

thrombocytopenia: a below-normal number of platelets in the blood; platelets help prevent bleeding

toremifene: a selective estrogen receptor modulator; brand name, Fareston®

toxicity: unwanted damage to normal cells caused by chemotherapy, radiation hormonal therapy or other treatment

trastuzumab: a biological drug used in treating women with breast cancer who have high levels of HER-2; brand name, Herceptin®

tumour grade: a score, assigned to a tumour by a pathologist, representing how aggressive a tumour is in
terms of risk to a patient. Nuclear grade is a contributing factor to the tumour grade, specifically measuring a tumour’s degree of abnormality and how quickly it is growing

**tumour node metastasis (TNM) system**: a cancer staging system used mostly for research and statistical purposes; it considers tumour size (T), lymph node involvement (N) and metastases (M)

**ultrasonography**: a diagnostic technique using sound waves to view different parts of the body, especially internal organs

**ultrasound**: see ultrasonography

**vascular invasion**: cancer that has spread to lymph or blood vessels near the original site of the disease

**Zofran®**: see ondansetron

**Zoladex®**: see goserelin

**zoledronate**: see bisphosphonates

**Zometa®**: see bisphosphonates