BREAST HEALTH

I. BREAST HEALTH

A. Embyrology, Development, and Anatomy: The mammary glands begin to develop in the 6 week embryo, when an ectodermal ridge (the milk line) begins as a bilateral thickening extending from the axilla to the groin. This ridge eventually atrophies, with the exception of bilateral small portions in the pectoral regions that become the breasts. During the fifth embryonic month, each breast develops 15 to 20 solid cords (primary milk ducts) which branch. The ends of the primary milk ducts dilate. The ducts become hollow during the seventh and eighth month. At the same time, a small depression develops in the skin that corresponds to the nipple.

Nearing the onset of puberty, the first change in the breast is the formation of the breast bud. The areola subsequently enlarges, and then the nipple begins to grow outwards. A few years later there is progressive subareolar growth, so that the areola is raised above the breast outline, producing the appearance of a secondary mound. In the adult breast, the level of the areola has recessed to the level of the surrounding breast tissue so that only the nipple protrudes. It appears that estrogen is responsible for the initial stages of breast development, but that further development of the lobules requires adult levels of progesterone. Other hormones that play a role in the breast development are prolactin, insulin, growth hormone, and corticosteroids.

The breast is at the level of the second to sixth ribs, its medial boundary being the sternum and its lateral border the midaxillary line. The upper and medial two-thirds of the breast lie on the fascia above the pectoralis major muscle, and the lower outer one-third of the breast rests on the serratus anterior muscle. The upper, lattermost portion of the breast, the tail of Spence, extends into the axilla and the passes through an opening in the axillary fascia (the foramen of Langer). A disproportionately large percentage of the breast tissue is the upper outer quadrant; therefore, a large proportion of both benign and malignant lesions arise in that area.

The nipple, which contains smooth muscle, is raised approximately 5 to 10 mm above the areolar skin; the areola, which is darkly pigmented ring of epithelium surrounding the nipple, contains many small openings of Montgomery's glands (sebaceous glands).

The breast is comprised of approximately 12 to 20 lobes, which are arranged like spokes of a wheel. Lobes contain their own excretory duct, which has its own opening into the nipple surface. Collectin ducts extend from the surface of the nipple to the lactiferous sinus, a dilated sinus that contains secretions from the segmental duct, which in turn has received secretions from the subsegmental duct. Each lobe of the breast is

comprised of many lobules, each containing 10 to 100 acini. The acini are arranged around an intralobular ductule that ultimately drains into the subsegmental duct. The lobule contains the epithelial units that are ultimately responsible for milk production.

Ten to 15 percent of breast tissue is epithelium, the rest being stroma. Cooper's ligaments are the supporting framework of the breast lobes.

Two major arteries provide most of the blood supply for the breast. More than 50 percent of the vascular supply is from the anterior perforating branches of the internal mammary artery. The other major component of blood supply to the breast is from the axillary artery via the lateral thoracic and thoracoacromial arteries. Most of the superficial veins of the breast drain into the internal mammary vein. The deep venous drainage corresponds roughly to the arterial supply.

The lymphatics of the breast have great clinical significance, because breast cancer can spread via the lymphatics. Most of the lymphatic drainage is to the ipsilateral axillary nodes. Some of the medial breast has drainage through the intercostal spaces and into the internal mammary nodes inside the thorax. Lesser areas of drainage include supraclavicular and anterior cervical lymphatics.

B. **Physiology:** During pregnancy, aveolar growth and early colostrum production are stimulated by steroids produced by the placenta and ovary, human placenta lactogen (HPL), growth hormone, insulin, and cortisol. Although prolactin is elevated, the high concentrations of circulating estrogen and progesterone exert and inhibitory effect during pregnancy. Within the first few days postpartum, this inhibition is no longer present, circulating estrogen and progesterone levels fall, the role of prolactin predominates, and milk is produced. Suckling of the infant elevates prolactin levels. If a woman does not breast-feed, her prolactin level decreases to normal at approximately one week postpartum. In the woman who is breast-feeding, by 6 to 12 weeks postpartum, prolactin levels fall to prepregnancy values. High prolactin seems to be a requirement for the initiation of lactation, but subsequent lactation can proceed without these high levels.

C. **Benign Breast Lesions:** Although the clinician, when performing a breast examination, places the greatest emphasis on the early detection of malignancy or on the identification of pre-malignant lesions, it is more likely that benign pathology will be identified. Therefore, the clinician must be familiar with the spectrum of benign entities that may be encountered.

The Cancer Committee of the College of American Pathologists arrived at a consensus statement on the relative risk for invasive breast cancer based on pathologic examination of benign breast tissue. The Committee agreed that the

following histologic reports are not associated with any increased risk of malignancy.

1. Adenosis (sclerosing of florid)
2. Apocrine metaplasia
3. Cysts (macro and/or micro)
4. Duct ectasia
5. Fibroadenoma
6. Fibrosis
7. Mild hyperplasia (more than two but not more than four epithelial cells in depth)
8. Mastitis
9. Periductal mastitis
10. Squamous metaplasia

D. **Fibrocystic Changes:** Probably the most common benign problem that the physician sees relates to patients with fibrocystic changes, those who complain of painful and/or "lumpy" breasts. The incidence of fibrocystic changes is uncommon before the age of 21, occurs in greater numbers of women in the reproductive years coming for routine health care, and has an incidence that continues to increase during the late pre-menopausal years, being most common in the fifth decade of life.

Patients with fibrocystic changes most commonly complain of bilateral breast tenderness, often beginning 7 to 14 days prior to the onset of menses, and this problem may be even more common in anovulatory women.

It is essential when the diagnosis of fibrocystic changes is made that the presence of malignancy be considered and that every effort be made to rule it out. Fibrocystic changes are usually bilateral and diffuse. If a dominant lesion is present, a diagnosis must be made. Mammography and/or ultrasound can be utilized to make certain that the lesion is cyctic and that there are no radiographic findings suggestive of malignancy. Ultrasound may be useful in demonstrating the presence of cystic lesions, whereas mammography, where indicated, is more sensitive in identifying early, non-palpable malignancies. If a lesion is clearly cyctic, and there is no suggestion of malignancy, aspiration of the fluid should be performed. If the fluid is not bloody, and if the cyst completely collapses and does not recur, the patient can be carefully followed.

In a patient with a questionable physical exam, it is helpful to re-examine the breasts one week after the onset of her next period to make certain that these changes regress. Obviously patients who have bilateral fibrocystic changes may also be harboring a sub-clinical malignancy, so even when the clinical diagnosis of fibrocystic changes seems clear, it is important that standard protocols to rule out malignancy are not inadvertently omitted. In some circumstances, a biopsy will be needed if there is any remaining question of malignancy.

Treatment of symptomatic fibrocystic changes are, to avoid caffeine and other methylaxanthines (which are present in coffee, tea, chocolate, and many soft drinks), because fibrocystic changes may be correlated with caffeine consumption and the amount of caffeine consumed. Wearing a tight fitting brassiere my also be helpful. The use of oral contraceptive may alleviate symptoms, but the risks and benefits must be considered for the individual patient. Provera from days 15 to 25 of the cycle has been shown to relieve symptoms. Danazol may reduce the discomfort of fibrocystic changes. Tamoxifen has also been suggested for this problem.

E. **Fibroadenoma:** Another common benign breast problem is the fibroadenoma that is most often found in patients between the late teenage years and age 40. It is rare in postmenopausal women. These are usually mobile, rubbery, well-delineated lesions.

Despite being benign, fibroadenomas almost always undergo core biopsy or are removed. This is done for several reasons, to make certain that the diagnosis is correct. Occasionally, the fibroadenoma can become large and distort the breast. If the patient becomes pregnant, fibroadenomas can grow rapidly, and even infarct. Patients usually want to have the lesion removed.

F. **Intraductal Papilloma:** Intraductal papilloma is a benign papillary lesion that is not very common. It is usually solitary, but in about 10 percent of cases it is multiple. It often causes a serous or bloody discharge. Approximately 50 percent of patients have a palpable subareolar mass. The mean age of patients with this lesion is 48, although there is great variability.

G. **Mammary Duct Ectasia:** Mammary duct ectasia is an uncommon benign inflammatory problem in which subareolar ducts are dilated and there is periductal mastitis. It may present with nipple discharge, which may range from grumous to serous to bloody. Ductal fibrosis may result in nipple flattening or inversion, and it is important to distinguish this from breast cancer.

H. **Mastitis:** Is a relatively uncommon postpartum complication. Approximately 11 percent of patients with postpartum mastitis subsequently develop a breast abscess, most commonly due to Staphylococcus aureus. It may be difficult to distinguish between inflammatory breast cancer and postpartum mastitis, which can lead to a delay in the diagnosis of malignancy.

I. **Fat Necrosis:** The usual etiology of this rare condition is trauma, although the patient may not remember or be unaware of the causative injury. The patient presents with a breast mass that may be tender. The condition must be differentiated from carcinoma, and it may be confusing. This is the only benign lesion that can cause skin dimpling. Furthermore, on mammography, it appears as a spiculated area.

J. **Oversized, Underdeveloped, and Asymmetrical Breasts:** Many women consult their physicians because they consider their breasts to be overly large, or unduly small, or asymmetrical, and these problems are often of considerable concern to many women. The only treatment available for excessively large or small breasts, or markedly asymmetrical breasts, is corrective plastic surgery. The only exception is underdeveloped breasts due to primary ovarian failure (such as that related to gonadal dysgensis or Turner's syndrome, or secondary to pituitary failure); in such cases, estrogen therapy is highly successful and achieves full breast development.

K. **Accessory Nipples:** Sometimes associated with accessory breasts, can occur anywhere along the milk line from the neck to the groin. They may be single or multiple. They require no therapy except for explanation, many women thinking that they are moles or skin growths.

L. **Nipple Discharge**: Approximately 5 percent of women who seek medical care for breast complaints will have nipple discharge. It is a more common complaint among patients with benign tumors than in women with malignancies. The physician should make certain when a woman presents with a complaint that no malignant or pre-malignant pathology exits.

The first step in the evaluation is a careful history. Include the color of the discharge, if it is from a single duct, or bilateral, frequency and duration, and whether it is intermittent. One of the most important facts about nipple discharge is whether it is spontaneous. Most pre-menopausal women, and some postmenopausal women taking hormone replacement therapy, can produce a small amount of discharge when squeezing the nipple or the breast just behind it.

The physician should attempt to determine and record the duct or ducts that are involved, what the color and character of the discharge are, and whether the patient has any abnormalities on physical exam, particularly a mass in the subareolar region.

If the patient has not had a recent mammogram, such testing is appropriate, unless she is a patient under age 30 with no history or physical findings that are at all suspicious. (For instance, it would not be appropriate to obtain a mammogram for a 25-year-old with bilateral milky discharge.)

Galactorrhea can be distinguished clinically from other types of discharge, and must be, because the evaluation is different. Galactorrhea is usually from multiple ducts, bilateral, milky, and non-spontaneous. This is not uncommon in parous women, and also may be found in patients using phenothiazines, drugs that deplete dopamine, and hormones. It may be secondary to mechanical stimulation.

It is important to distinguish a nipple lesion that is eczematous and bloody from a bloodtinged nipple discharge, because the former may be Paget's disease of the nipple.

If the patient has a breast mass and a nipple discharge, both must be fully evaluated.

Nipple discharge may be grumous, purulent, milky, watery, serous, serosanguinous, or grossly bloody. Grumous discharge is usually associated with duct ectasia. Watery or serous discharge is most commonly associated with cancer or papillomas. Bloody or blood-tinged discharge may be related to malignancy, but it is more commonly related to benign lesions. Other than for patients with Galactorrhea, the diagnosis and treatment of nipple discharge usually involves surgery.

M. Epidemiology of Breast Cancer: Breast cancer is the most common malignancy diagnosed in women in the United States, with an estimated 175,000 new cases of invasive cancer diagnosed in 1999. Breast cancer is the second most common cause of cancer death in U.S. women, surpassed only by lung cancer.

One in eight women born in the United States today will develop breast cancer. The incidence of breast cancer shows international variation, with the United States, Canada, and Northern Europe having the highest rates in the world.

Approximately 10 percent of breast cancers are attributable to specific, inherited, single-gene mutations. The BRCA1 gene encodes a tumor-suppressor protein that acts to inhibit tumor. Various alterations within the BRCA1 gene may be responsible for as much as half of all breast cancers resulting from a single-gene mutation.

BRCA2 gene mutation also results in an elevation in breast cancer risk. It also predicts an increased breast cancer risk among men who carry the mutated gene

Another risk factor for breast cancer, is age. The older a woman becomes, the greater her likelihood of developing breast cancer. Breast cancer is not completely unknown in women in their teens and 20s, so any mass in the breast, even in young women, must be evaluated, and malignancy ruled out.

Having had a cancer in the contralateral breast also places a woman at greatly increased risk for a new primary breast cancer.

Menstrual and reproductive history are significant factors. Women who have an early menarche or late menopause are at increased risk. Having a first child before the age of 18 reduces the risk of breast cancer to one-third the risk of a woman who has her first child at age 35 or later. On the other hand, having

multiple pregnancies is not protective. Earlier studies had suggested that breast-feeding might reduce breast cancer risk, but this is debated.

Wynder and many others have presented laboratory data and experimental evidence to support the association of high-fat diets and breast cancer. He demonstrated an almost linear relationship between the daily dietary fat intake in a country and its death rates from breast cancer. However, more recent studies using improved dietary assessment methods have also consistently failed to incriminate dietary fat as an established risk factor. Some investigators have suggested that dietary fat indirectly influences risk by determining obesity, which is a risk factor, particularly among postmenopausal women.

Others have suggested that breast cancer risk can be reduced by increasing the fiber content of the diet, and by increasing consumption of foods rich in vitamins A and C.

Although there has been evidence that caffeine consumption exacerbates fibrocystic changes o f the breast, it doe not appear to increase the likelihood of developing breast cancer.

Other factors that seem to increase breast cancer risk include radiation exposure (e.g., survivors of Hiroshima and Nagasaki atomic bombs, those with multiple chest fluoroscopies for tuberculosis, and those treated with x-rays for acute postpartum mastitis). The strength of the association of radiation and breast cancer risk is related, first and foremost, to young age at radiation exposure, level of radiation exposure, and length of time after exposure. Findings suggest that exposure to radiation at a young age when estrogen stimulation begins (menarche or beyond) may initiate the process that ultimately leads to breast cancer.

Additional factors that appear to increase risk include residence in the north, urban residence, upper socioeconomic status, and other primary cancer in the ovary, endometrium, or colon.

The issue of breast cancer risk and exogenous hormone use has been one of some controversy. There are data that suggest that oral contraceptives do not increase breast cancer risk, and conflicting data that suggest that for certain subsets of women it does increase risk. Further research into this question must continue. In the meantime, women and their physicians must remember that in addition to making an enormous contribution to providing women with the capability to control their reproductive lives, the birth control pill has important side benefits, such as reducing the risk of salpingo-oophoritis and the risk of ovarian and endometrial cancer.

The relationship between hormone replacement therapy and risk of breast cancer may relate to such factors as the duration of use and the dose, or level of hormones during use, as well as the recency of hormone replacement therapy.

However, in assisting patients in making risk-benefit decisions on the use of post-menopausal exogenous estrogens, the positive impact on cardiovascular disease, prevention of osteoporosis, and clinical symptomatology often outweigh the as yet incompletely defined issue of the role of exogenous estrogen in breast cancer risk.

Risk factors for Breast Carcinoma

- Age
- Previous cancer in the contralateral breast
- Residence in North America or Northern Europe
- Family History
- Nulliparity
- First birth age 35 or older
- Previous biopsy with premalignant histology
- Early menarche
- Late menopause
- Obesity
- High-fat, low-fiber diet
- Radiation exposure
- Caucasian
- Upper socioeconomic status
- Residence in cold climate
- Urban residence
- Other primary cancer in ovary, endometrium, or colon

N. **Screening for Breast Cancer:** Women should be involved in a program for the early detection of breast cancer that includes mammography, breast self-examination, and examination by a health care provider.

1. Mammography and Other Breast-Imaging Techniques: At present, mammography is the best technique available for the early detection of breast cancer. It does, however, have a false-negative rate of approximately 10 percent, making breast self-examination and clinical breast examination essential supplemental modalities. If a mass is present in a woman's breast, despite the presence of a normal mammogram, it is essential that the etiology of the mass determined. Mammography is not perfect, but it has made a remarkable contribution to the early diagnosis and ultimate reduced likelihood of mortality for women with breast cancer.

The American Cancer Society now recommends yearly mammography for women in their 40s.

There are two basic indications for mammography: screening and evaluation of a possible problem (diagnostic). Routine screening is performed for an asymptomatic patient. Diagnostic mammography is performed to evaluate a clinical sign or symptom or to evaluate further an imaging finding identified on a screening mammogram.

A screening mammogram consists of two views per breast – usually a craniocaudad view and a mediolateral oblique view.

A diagnostic mammogram is performed for problem solving. The need for a diagnostic mammogram is sometimes generated by a finding identified on screening mammography. It is sometimes generated by the referring primary health care provider who orders a mammogram to help assist in evaluating a clinical problem, such as a palpable mass, focal tenderness, new nipple inversion, nipple discharge, or breast skin changes, such as dimpling or unexplained erythema.

In diagnostic mammography communication between the referring health care provider and the radiologist is essential. The mammographer must be made aware that there is a clinical issue to be evaluated. When ordering a diagnostic mammogram, it is extremely helpful to provide the mammographer with a diagram of the breast indicating the location of the palpable mass or skin change. Another method to describe the location of a lesion is to view the breast as a clock face with the patient facing the observer. For example, an upper outer quadrant mass on the right may be described as being in the 11 o'clock position. A mass should also be described in terms of approximate size and distance from the nipple. Improved accuracy of diagnosis can be achieved if the written prescription for mammography indicates, for example, possible 1-cm mass, left 12 o'clock, 2cm from the nipple.

F. **The Mammography Report**: Should include the patient's name and date of birth. The basic format includes the following;

a. **Clinical Indication:** screening exam or diagnostic problem.

b. **Pertinent History:** include surgical or radiation history, factors increasing the risk for breast cancer, history of hormone replacement therapy.

c. **Comparison:** Documentation that the current study was compared to prior mammograms.

d. **Images:** At least 15 standard mammographic positions are defined by the American College of Radiology. Prior to obtaining an image, the technologist confirms that the patient is not wearing powder, perfume, or deodorant because residue from these products can mimic microcalcifications. The technologist affixes radiopaque markers to the breast to demarcate scars and palpable masses. Prominent lesions on the skin surface are marked so that the mammographer does not misinterpret a shadow created by the skin lesions as being within the breast parenchyma. In some facilities , the nipple is routinely marked.

The two basic positions for routine screening are the craniocaudad (CC) and the mediolateral oblique (MLO) views. To obtain a craniocaudad view, the film cassette is placed under the breast, the breast is compressed between two plastic plates, and the x-ray beam is directed from the top of the breast to the bottom. This view allows evaluation of the breast from medial to lateral. The goal is to image as much posterior breast tissue as possible. Inclusion of the pectoral muscle assures that this goal has been accomplished. In the MLO view, the film cassette is located on the lateral aspect of the breast. The breast is compressed between two plates that are oriented 45 to 60 degrees oblique relative to vertical. This view allows evaluation of the breast from superior to inferior. A properly positioned MLO view images the pectoral muscle to the level of the nipple and the nipple is viewed in profile.

In some women, glandular tissue extends laterally beyond the lateral edge of the CC view. In this case, a third view called the exaggerated craniocaudad view (XCCL) is added; the patient is rotated to include the lateral tissue on the film. A "spot compression" view uses a compression device smaller than the conventional compression plates to cone down to a small area of interest. Spot images are usually more painful to the patient than full paddle images because the forces of compression in one small area.

A mediolateral view (ML) in the 90-degree position (non-angled) is used to triangulate the location of a lesion for preoperative needle localization. Tanagential views (TAN) are performed by positioning the breast so that the area of interest is in tangent to the x-ray beam.

e. **Findings:** The overall density of the breast is described. Any positive findings are reported .

f. **Impression:** A summary and interpretation of the important findings.

g. **Recommendations:** The recommended time interval for the next follow-up, or recommendation for further evaluation, is made.

h. **Assessment:** A number from 0 to 5 is assigned to designate a specific BI-RADS category. According to BI-RADS, the breast composition is described as one of four types:

1. The breast is almost entirely fat.
2. There are scattered fibroglandular densities.
3. The breast tissue is heterogeneously dense. This may lower the sensitivity of mammography.
4. The breast tissue is extremely dense, which could obscure a lesion on mammography.

If a lesion can be seen on one view only, it is called a density. A mass has volume. A lesion can be classified as a mass if it can be imaged in two orthogonal planes, which allows it to be described in three dimensions. According to BI-RADS criteria, masses are described as follows:

1. Shape – round, oval, lobular, irregular
2. Margins – circumscribed (well defined or sharply defined), microlobulated, obscured, indistinct (ill-defined), spiculated (lines radiating from the margins of a mass)
3. Density – describes the opacity of a lesion relative to the adjacent breast parenchyma. Masses denser than the surrounding breast are regarded with a higher degree of suspicion than low-opacity lesions.

The radiologist, at the completion of the report, indicates her or his degree of suspicion for malignancy by assigning one of the following assessment categories:

Category 0 – Need additional Imaging Evaluation
Category 1 – Negative
Category 2 – Benign Finding
Category 3 – Probably Benign Finding – Short Interval Follow-up Suggested.

Category 4 – Suspicious Abnormality – Biopsy Should Be Considered
Category 5 – Highly Suggestive of Malignancy – appropriate Action Should Be Taken: These lesions have a high probability of being cancer.

Findings described to have spiculated margins, irregular shape, linear morphology, and/or segmental or linear distribution are the most suspicious for breast carcinoma and should be assessed as Category 5 lesions.

2. Physical Examination: Although mammography is the most sensitive technique for the early diagnosis of breast cancer, physical examination by the health care provider does play an important complementary role.

If the physician finds an abnormality on physical examination, the physician must not be lulled into a false sense of security by a normal mammogram. Because 8 to 15 percent of women with breast cancer have normal mammograms, the etiology of the abnormal physical findings should be determined, and the physician should avoid placing excessive reliance on a normal mammogram in this situation.

Not only is it important that women have regular breast exams by their health care provider, but it is also important that when an abnormality is identified on physical examination the reason for this finding should be determined, even in the presence of a normal mammogram.

The American Cancer Society guidelines for physical examination for the detection of breast cancer in women with no symptoms are: women 20 years of age and older should perform breast self-exam every month; women ages 20 to 39 should have a physical exam of the breasts by a professional, usually a physician every 3 years; and women 40 and older should have a physical exam of the breasts performed by a trained health care professional every year, and a mammogram every year.

In addition, women who are at higher-than average risk may need to be examined more often than annually. Of course, any woman with a breast complaint should be examined, regardless of when her most recent prior examination took place.

The first step in the breast examination is inspection. This is usually done with the arms raised overhead, then with tension on the pectoralis muscles (which can be accomplished by having the patient place her hands on her hips and press inward), and finally with the patient relaxed and leaning forward. The physician is looking for skin and contour changes such as retraction, edema, or erythematic, and for nipple changes such as retraction, eczema, or erosion. The breasts are then examined with the patient in both the sitting and supine positions. The examination must be systematic, with a thorough evaluation of all breast tissue for masses. This is commonly done in concentric circles, starting with the outermost

breast tissue. The physician should attempt to elicit nipple discharge and should examine the axilla carefully for nodes.

The breast examination should be documented in the medical record.

3. Teaching Breast Self-Examination: Women should be taught how to perform breast self-examination and encouraged to do so. This can be reinforced while the clinical breast examination is being performed.

The patient should be instructed that if she does note any abnormalities, she must report them to her physician so that the doctor can promptly perform an evaluation. Breast cancer may develop in the interval between radiographic examinations, and therefore monthly self-examination may result in earlier diagnosis.

O. **Staging:** Staging refers to the grouping of patients according to the extent of their disease. Staging is either clinical, meaning before surgical treatment, or pathologic, based on findings on the specimen and any testing. Staging is important in determining the kind of pretreatment evaluation; determining the choice of treatment for an individual; assessing the patient's prognosis; and comparing the results of different treatment programs.

Currently, staging of cancer is determined by the American Joint Committee on Cancer (AJCC), which is jointly sponsored by the American Cancer Society, The National Cancer Institute, The College of American Pathologists, and The American Colleges of Physicians, Radiologists, and Surgeons.

Clinical staging is based on all information prior to definitive treatment and includes the findings on physical exam, imaging studies (mammography and ultrasound), operative findings, and findings of biopsy material. Clinical stage is useful in selecting and evaluating therapy.

Stage 0 means that the cancer is in situ only. Stage 1 cancers are less than 2cm with no suspicious lymph nodes and no suspicion of distant metastases.

Stage IIA are patients who have cancers less than 2 cm but who have suspicion of cancer in the axillary lymph nodes, although the lymph nodes are not fixed to each other and are not fixed to any other structures. Also included in Stage IIA are cancers that are more than 2cm but not more than 5cm in greatest dimension but the axillary lymph node exam is negative, in Stage IIB, the cancer is also between 2 and 5 cm, but there can be suspicion of cancer in the lymph nodes, although the lymph nodes are not fixed to each other (matted) nor fixed to any other structures (such as the pectoralis minor muscle). Also included in IIB are cancers greater than 5 cm in greatest dimension, but with the lymph node exam normal.

Stage IIIA, a tumor that has lymph nodes that are matted or fixed to each other is included, regardless of the size of the cancer. Also included in Stage IIIA are cancers that are greater than 5cm with an exam that suggests cancer in the lymph nodes, in which the lymph nodes are not fixed to each other or to any other structures.

Stage IIIB includes any cancer of any size with direct extension to the chest wall or skin. Extension to skin may have the appearance of "peau d'orange," ulceration of the skin or satellite skin nodules, as well as inflammatory breast cancer, as noted clinically. With those special skin changes, the cancer may be of any size, and the lymph node involvement may be none, or of any degree, and it is still Stage IIIB. Also included in Stage IIIB are cancers of any size if there is metastasis found in the internal mammary lymph nodes.

Stage IV only includes patients with distant metastasis. Ipsilateral supraclavicular lymph node metastasis is considered distant metastasis.

Staging is very important for considering what kind of diagnostic tests are obtained before definitive treatment. Because bones are the most common first-diagnosed site of metastatic disease for breast cancer, a bone scan is often performed, especially as a baseline. It is not indicated for Stage 0 breast cancer, and is not usually performed before treatment of Stage I or Stage II breast cancer. The exception may be where the plan is to do a mastectomy for Stage I/II patients. In this case, it becomes more important to rule out any small possibility of metastatic disease before a major operation.

P. SURGICAL PROCEDURES

1. Cyst Aspiration: Cysts in the breast are a common occurrence. The cyst is typically found as a smooth, round, slippery mass, and can be distinguished from solid masses with a similar palpatory sensation by the simple technique of cyst aspiration.

Palpable cysts are drained for four reasons: to establish the diagnosis of a cyst; to provide a quick diagnosis; occasionally to provide relief of pain if the cyst is causing pressure; and to provide for an optimal clinical breast exam free of the interfering mass.

The key issue in the evaluation and management of a cystic breast lesion is to make certain that a malignancy is not present, either in that location or elsewhere in the breasts. If the patient has not had her appropriate mammography screening it is preferable to do this prior to aspirating the cyst so as to avoid distortion of the mammography films. In addition, a sonogram is often done to confirm the fact that the lesion is indeed, cystic.

The advantages of ultrasound are that it uses no ionizing radiation, is usually well tolerated by the patient, and can be rapidly performed. A main goal of sonography is to determine whether a mass is cystic or solid.

To perform cyst aspiration, the cyst is stabilized between two fingers of the non-dominant hand, and a 20-guage needle and syringe are used to aspirate the cyst. Several conditions must be satisfied for a cyst aspiration to be considered adequate treatment. The cyst must fully collapse and there must be no residual mass following aspiration. The cyst fluid must be clear or cloudy. If it is brown or red, this suggestive of previous bleeding into the mass. Finally, the cyst must not repeatedly re-accumulate.

If the cyst does not completely collapse, if it repeatedly re-accumulates, or if the cyst fluid is bloody, a breast biopsy is indicated.

2. Fine-Needle Aspiration Biopsy, Needle Localization, and Stereotaxic Core Biopsy: Fine-needle aspiration (FNA) biopsy can be performed using either sonographic or mammographic guidance, with or without stereotactic technique. It requires minimal equipment, can be done rapidly, and is relatively inexpensive. When compared to gun-fired core biopsy needles, the FNA needle is smaller gauge (21 or 25 G) and is easier to control for sonographically guided procedures. For these reasons, and to avoid the risk of pneumothorax, it is often the chosen percutaneous technique if the breast is very thin or if the target is deep against the chest wall. The lesion is suspected to be a cyst, FNA is the procedure of choice; it allows fluid aspiration with minimal breast intervention.

FNA samples cannot accurately diagnose atypical ductal hyperplasia, carcinoma in situ, or infiltrating carcinoma because the architecture surrounding the abnormal cells is not evaluated.

Needle-wire localization involves use of a compression plate with fenestrations or open alphanumeric grid. The shortest distance to the targeted lesion is calculated with use of two orthogonal views-usually a CC and a 90-degree lateral. The needle length is chosen. The patient's breast is placed in compression with the compression plate open to the side planned for needle entry. A mammographic film is obtained to identify the target. Using sterile technique, the needle is advanced into the breast. The needle has a hollow core through which a wire passes. The position of the needle-wire apparatus is confirmed in orthogonal planes. When it is determined that the needle is adequately located with respect to the lesion, the wire is advanced. The patient is taken to the operating room with the needle and/or wire in situ. After the biopsy is performed, the surgical specimen is usually radiographed to assure that the target tissue has been removed.

Core-needle biopsy is a highly accurate method of biopsy. The procedure is fast and cost-effective when compared to surgery. The goal of core biopsy is to make

a diagnosis percutaneously. If the results are malignant, theoretically the patient will then only need one operation – a lumpectomy or mastectomy, with or without axillary lymph node dissection. In comparison, a surgical biopsy requires an operation to make the diagnosis and a second operation for therapy. If the lesion is very small, it is possible to remove the entire mass with core biopsy. In this case, it is essential to leave a marker to enable localization for excisional biopsy if warranted by pathology results.

In sonographically guided core biopsy, the needle trajectory is planned so that it traverses the breast parallel to the chest wall to avoid misfire into the pleura or pericardium. Using sterile technique, the skin entry site is anesthetized with lidocaine. The mass is continuously observed in real-time. A 14-gauge cutting needle attached to a biopsy gun is advanced into the breast through a small skin nick. The needle is advance or fired with use of the biopsy gun. The area is scanned to assure that the lesion is traversed by the needle and to assure that the needle tip is safely within breast parenchyma.

Stereotactic biopsy uses a computer to calculate the three-dimensional location of a lesion using x, y, and z. coordinates. To perform this calculation, two images of a lesion are obtained mammographically. The x-ray tube is angled 15 degrees relative to the lesion in one direction and 15 degrees relative to the lesion in the other direction. Stereotactic technique can be used for fine-needle, core-needle, or vacuum-assisted core-needle biopsy. The patient can be imaged prone with the use of a special table that has an opening to allow the breast to hang down pendulously. The target is identified and using sterile technique, the skin site is anesthetized and a small skin nick is made. A 14-gauge needle is advanced to the proper depth. A prefire image is obtained. If correct needle placement relative to the lesion is confirmed, the needle is fired. Several passes can be made. The needle must be removed from the breast to retrieve the specimen after each pass.

3. Incisional and Excisional Biopsy: Incisional biopsy may be performed for a patient with a breast malignancy to confirm a diagnosis prior to definitive therapy as well as to obtain tissue for hormone receptor analysis. If the histological analysis shows malignancy, treatment planning can be initiated with the patient. In a patient with a suspicious lesion, if no malignancy is identified utilizing this technique, it is essential to perform an excisional biopsy to confirm that there is no malignancy. If it is possible that the patient will be undergoing further surgery, the incision must be made within the boundaries of the area that would subsequently be removed, with a secondary goal being to achieve an optimal cosmetic result.

4. Surgery for Breast Cancer: In 1992, the American Colleges of Surgeons, Radiology, and pathologists and the Society of Surgical Oncology held a conference on Standards for Breast Conservation Treatment. The result was published in CA: A Cancer Journal for Clinicians.

Given that the goal of lumpectomy, axillary dissection, and radiation is to attain maximum cosmetic results while achieving a high probability of local control and survival rates at least as good as those found with total mastectomy and axillary dissection, the consensus conference made recommendations regarding surgical technique and radiation therapy to assist in achieving these ends.

Some surgical recommendations relate to those factors that would ultimately result in optimal cosmetic effect. They noted that particularly for lesions in the upper quadrants, arcuate incisions with the skin lines with thick flaps centered over the lesion are preferable to radial incisions. Except when tumors are quite superficial, overlying skin does not require excision. Meticulous hemostasis is important, drains are rarely needed, and the surgeon should refrain from suture reapproximation of breast tissue if possible, and leave the "dead space" cavity.

Regarding the amount of tissue to be removed and the margins, approximately 1 cm of normal margin should be removed. The removal of excessive tissue adversely affects the cosmetic result. Conversely, the surgeon should remove the tumor so that the margins are grossly negative (or further resection is indicated) and should attempt to achieve microscopically negative margins. It is important to ink the resection margins and mark the excised tissue to assist the pathologist with proper orientation.

Both for staging and to prevent axillary recurrence, and axillary dissection is important in most women. However, some women may have no suspicious palpable lymph nodes, and thereby may not necessarily require an axillary dissection for local control. Furthermore, elderly women may not require accurate staging, their treatment will be the same regardless of microscopic cancer found in the lymph nodes. These women do not have the same indications as the other patients for axillary dissection.

A great deal of investigation is ongoing with dye and tracer techniques to accurately find the "sentinel" lymph node…the lymph node predictive of the rest of the axillary lymph nodes. If the sentinel lymph node does not contain metastases, the rest of the lymph nodes are also presumed to be normal, and an axillary dissection can be avoided.

The consensus conference also made recommendations regarding radiation therapy. At present, all patients who have lumpectomy and axillary dissection should have radiation following the surgery. Although some patients can be cured with this limited surgery alone, it is not known which, if any, subgroups of patients can be safely treated with limited surgery without radiation.

Patients should routinely receive 4500 to 5000 cGy to the whole breast using megavoltage radiation. Most trials have utilized boost irradiation as well, although the precise indications for this are not fully defined.

Boost irradiation is either by electron beam or, less commonly, by implantation, with doses of 1000 to 1500 cGy.

5. Reconstructive Surgery: The timing of reconstructive surgery is occasionally an issue that evokes some controversy. Often it can be done at the time of mastectomy, especially in earlier stage patients. However, depending on the extent of disease and the therapy to be utilized postoperatively (chemotherapy, chest wall radiation), physicians sometimes prefer to have the reconstructive procedure delayed.

Most plastic surgeons who deal extensively with breast reconstruction like to see the patient as soon as the diagnosis of breast cancer is made. That way, assurances can be offered to allay her anxiety. It also provides the best opportunity to plan for the appropriate type and timing of the reconstruction, and to establish the plan with the oncologic surgeon. Breast reconstruction is not a purely "cosmetic" operation, but rather one that restores to normal tissues altered by disease and surgery.

Q. **Prognostic Factors:** A variety of factors will have an impact on any individual patient's likelihood of cure;

- Lymph node involvement
- Tumor size
- Receptor status
- Distant metastases
- Peritumoral lymphatic and blood vessel invasion
- Histology
- Nuclear grade
- Ploidy
- Protease cathepsin D

One of the most significant factors affecting prognosis and length of survival is the presence of metastatic disease at the time of diagnosis.

R. **Adjuvant Chemotherapy:** During the past 20 years, studies have addressed the question of what is the optimal adjuvant therapy regimen. Studies that compare single agents to combination therapy are under way. A potential problem with combination therapy is that doses of each agent in the combination often must be reduced because of overlapping toxicity. Administration of each of the agents in a combination regimen sequentially, and at optimal dose, instead of in their combination, is currently under investigation. Longer duration versus shorter duration chemotherapy is being investigated, and some issues have been settled. For CMF (Cytoxan, Methotrexate, and 5-Fluorouracil) based regimens, 6 months of treatment is as effective as 1 year.

Perioperative chemotherapy – given at the time of or just after surgery – offers several theoretical advantages in that drugs may kill circulating tumor cells that conceivably were dislodged at the time of surgery. On the other hand, this timing may decrease healing capability.

Currently, patients who require chemotherapy but who are lower risk are usually given a 6 month course of CMF, which is eight cycles. Higher risk patients are usually given an Adriamycin-based regimen, with the "Bonnadonna" regimen (named after the medical oncologist in Milan, Italy where the publications originated) being the most common. It consists of four cycles of Adriamycin followed by the standard course of CMF as in lower-risk cancers. Recently, the trend has been to give Adriamycin and Cytoxan for four cycles followed by Taxol for four cycles to the higher risk patients.

Treatment side effects, long-term toxicity, and a decrease in the quality of life are additional important gauges of adjuvant treatment and need to be further studied. An accurate side effect profile is also important for women to make an informed decision about the adjuvant treatment, especially patients with a low risk of disease recurrence.

Certain "side effects" of Tamoxifen may contribute to its overall net benefit. The estrogen like properties may result in reduced serum cholesterol and a more favorable lipid profile, and may reduce the risk of cardiovascular disease. The estrogen-like properties of Tamoxifen also may stabilize and sometimes increase bone density.

The side effects of Tamoxifen are menopausal symptoms with at least 50 to 60 percent of patients reporting hot flashes. Eye toxicity in the form of retinopathy is rare. Tamoxifen use is clearly related to increased incidence of endometrial cancer, with as much as a 2 percent estimate of developing this disease in a 5 to 10 year course of treatment.

In the past several years, there have been more and more indications for prescribing Tamoxifen. The course of treatment is almost always five years. Among its many uses, Tamoxifen is given to most women after chemotherapy whose cancer had positive hormone receptors. The only exception may be for women who maintain their menstrual cycles after chemotherapy.

Adjuvant Therapy for Women with negative Lymph Nodes

		Menopausal Status	
Tumor Size	**Hormone Receptor Status**	**Premenopausal**	**Postmemopausal**
≤1α	ER+	None	None
	ER-	None	None
>1 cm	ER+	Chemotherapy (e.g., CMF) usually followed by tamoxifen	Either tamoxifen alone or chemotherapy (e.g., CMF)

			followed by tamoxifen
	ER-	Chemotherapy (e.g., CMF)	Chemotherapy (e.g., CMF)
In general, for all cancers <1 cm with negative lymph nodes, the long-term risk of distant metastases without chemotherapy is less than 9%. It is usually the case that the side effects of tamoxifen or any chemotherapy are not worth the benefit. The recommended course of tamoxifen currently is 5 years for adjuvant treatment. Five percent or less of ER- cancers are thought to respond to tamoxifen. Depending on age and comorbid status, older women may not have enough estimated benefit from chemotherapy to justify the more serious side effects in the elderly.			

Adjuvant Therapy for Women with Positive Lymph Nodes

		Menopausal Status	
Tumor Size	**Hormone Receptor Status**	**Premenopausal**	**Postmenopausal**
Any tumor size	ER+	Chemotherapy (e.g., a doxorubicin-based program) usually followed by tamoxifn	Chemotherapy (e.g., a doxorubicin-based-program or CMF) followed by tamoxifen
	ER-	Chemotherapy (e.g., a doxorubicin-based program)	Chemotherapy (e.g., a doxorubicin-based program or CMF)
If the lymph nodes have cancer, tumor size is of no prognostic value. Rather, the increasing number of positive lymph nodes is directly proportional to the worse prognosis.			

S. Carcinoma In Situ: There are two types of carcinoma in situ of the breast, ductal carcinoma in situ (DCIS) and lobular (LCIS).

Historically, patients with ductal carcinoma in situ were treated by mastectomy. This was particularly appropriate then, because patients presented with large palpable tumors. Currently, the majority of intraductal carcinomas are small and mammographically detected. Because breast conservation has been proven to be effective for invasive cancer, preserving the breast, with or without radiotherapy, has been explored for successful treatment of pre-invasive cancers.

There is some suggestion that if the breast is conserved, postoperative radiation will reduce or delay the risk of recurrence.

In any event, patients must be followed very carefully if they elect to have breast-conserving treatment, because there is a significant subsequent risk for either in situ or invasive disease, with at least 1 percent per year developing recurrence in the breast.

Mammography assists greatly in identifying lesions that prove to be ductal carcinoma in situ, but it is not as helpful in identifying lobular carcinoma in situ, mainly because LCIS does not contain calcifications. One-quarter to one third of patients with lobular carcinoma in situ will develop invasive cancer in the next 20 years, which may be in either breast. Some of the invasive cancers will be

lobular, but most will be ductal. When LCIS is found on biopsy, as opposed to DCIS, it is not useful to re-operate for "clean" margins.

Recommendations for treatment of LCIS have ranged from careful follow-up to bilateral total mastectomy with reconstructive surgery. Recent trends are clearly toward a more conservative approach, and tamoxifen chemoprevention should be considered.

T. Treatment of Advanced and Recurrent Breast Cancer: Stage III breast cancer is considered locally advanced disease. Patients are usually treated with a multimodality approach. One approach is to begin with chemotherapy, followed by mastectomy, followed once again by chemotherapy to complete the program, and then chest wall radiation. If the patient's primary tumor disappears after the initial chemotherapy, the patient's chances of survival are much greater. The amount of residual disease in the mastectomy specimen is also of prognostic significance, as is the number of positive nodes following initial chemotherapy.

Inflammatory breast cancer also is treated with multimodality therapy beginning with systemic treatment. The prognosis is very poor, but fortunately only 1 to2 percent of breast cancers are inflammatory tumors.

The issue of breast recurrence following breast-conserving primary therapy is becoming increasingly important. Kurtz studied 1593 women with stage I and II breast cancer who had been treated initially by macroscopic complete tumor excision and radiotherapy. He reported an actuarial freedom from mammary recurrence of 93 percent at 5 years, 86 percent at 10 years, 82 percent at 15 years, and 80 percent at 20 years. Although 79 percent of recurrences were in the vicinity of the tumor bed, as the time from treatment lengthened, an increasing percentage of the tumors were located elsewhere in the breast and may have been new tumors. Only 10 of 181 women with recurrence had distant metastases either concurrently or previously.

Local recurrence after breast-conserving surgery and radiation has a better prognosis than does chest wall recurrence following primary treatment by mastectomy. The five prognostic factors that influenced survival were length of disease-free interval, axillary node status, primary T stage, and number and size of recurrences. If a woman had three or more of these five favorable prognostic factors, her 5-year survival was 75 percent.

Despite improvements in primary and adjuvant therapy, a percentage of women initially diagnosed with early stage disease will experience systemic recurrence in the next 20 to 25 years. The site of recurrence or metastatic disease is important in determining prognosis. The development of visceral metastases is usually associated with a shorter disease-free interval after treatment for the metastases and a subsequent decreased survival. Brain metastases have a particularly poor prognosis; these patients have a median survival as short as three to six months.

On the other hand, women with metastatic disease confined to the bone frequently have indolent disease and survive, on average, for 4 to 5 year with treatment.

Response to therapy will also depend upon tumor burden and disease-free interval.

Therapy for recurrent disease almost always includes chemotherapy and/or hormonal therapy. Surgery or radiation may be utilized in addition to systemic therapy under certain circumstances. Emergency radiotherapy may be lifesaving in cases of superior vena caval syndrome (respiratory distress, venous distension of the chest wall and neck, puffiness of the face and neck, and central nervous system effects such as visual and mental disturbances and headaches), spinal cord compression, or bronchial obstruction.

Fifty to 70 percent of patients with estrogen-receptor-positive tumors will respond to endocrine therapy, but only 10 percent of those who are receptor-negative will. Women with recurrent breast cancer that is not life-threatening, who have estrogen-receptor-positive tumors may be treated initially with hormonal therapy. This would usually be tamoxifen for postmenopausal women and usually for premenopausal women as well, although sometimes oophorectomy is recommended. High-dose medroxyprogesterone acetate may produce responses in some patients. Patients who have previously responded to tamoxifen but then suffer a relapse may respond to other hormonal agents. In some circumstances, chemohormonal therapy may be useful either as primary or secondary therapy for recurrent disease.

Women with metastatic breast cancer may live comfortably for several years, and it is important that their routine health needs receive regular attention. In addition, women with breast cancer are at high risk to develop primary endometrial, ovarian, and colon cancers, and they should be appropriately screened for these diseases.