Disorders of the Breast

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The initial phase of breast tissue development begins around the fifth to sixth gestational week and continues until around week 20. The breasts develop from two ventral bands of thickened ectoderm, the *mammary ridges*, that extend from the axilla to the inguinal region. By 6 months of gestation, the mammary gland has developed into a tubular structure in a bed of dense fibroconnective tissue stroma. By this time, the breast tissue is evident in both males and females. In a full-term newborn, breast tissue may be palpable persisting for up to 18 months due to the lasting effects of exposure to maternal estrogen. Although this lasting breast enlargement can be a source of concern for parents, it is not pathologic and biopsy or excision should be strictly avoided as this can cause permanent disfigurement. After infancy, the breast tissue involutes and becomes equal between boys and girls until puberty. Secondary breast development in girls begins with thelarche and is driven by the rise of reproductive hormones. The breast continues to develop through the Tanner stages for about 3 years (Table 34.1). Breast asymmetry is quite common during secondary development and the breast bud might be confused with a mass. Again, parents should be reassured that this is normal and no interventions should be performed.

Table 34.1 Tanner stages of breast development

Stage 1	Preadolescence: elevation of the breast papilla only
Stage 2	Elevation of the breast and papilla as a small mound enlargement of the areola diameter
Stage 3	Further enlargement of the breast and areola with no separation of their contours
Stage 4	Further enlargement with projection of the areola and papilla to form a secondary mound above the level of the breast
Stage 5	Mature stage: projection of the papilla only, resulting from recession of the areola to the general contour of the breast

Congenital Anomalies and Disorders of Development

If normal regression of the mammary ridge fails, accessory breasts (polymastia) or supernumerary nipples (polythelia) develop (Fig. 34.1). Because of the location of the mammary ridge, accessory nipples are most commonly found between the normal nipple location and the pubic symphysis in the embryonic milk line. They occur in 1–2% of the population and can be multiple. Because there are reports of an association between accessory nipples and renal disorders, a renal US is indicated in some cases; however, this is not standard practice. Polymastia also occurs most commonly just below the native breast tissue along the milk line, but accessory breast tissue may be located in any location and is often not noted until thelarche or pregnancy. Ectopic breast tissue can also be found in the axilla and patients with this finding can

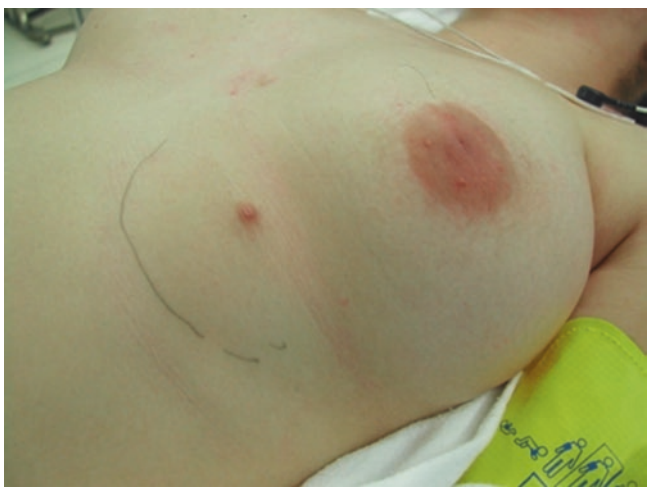

Fig. 34.1 Supernumerary nipple

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present to clinic with an axillary mass. Breast tissue in this location may be confused with a lipoma. It is safe to resect this tissue as it often causes periodic discomfort.

Amastia is the complete absence of the breast tissue and nipple-areola complex, whereas amazia is the absence of breast tissue only. Bilateral amastia is sometimes an isolated occurrence but can be associated with other ectodermal defects (anomalies of the palate and upper extremities) and familial cases have been reported. Unilateral amastia may be due to Poland syndrome. Nipple conditions, including nipple inversion or congenital absence of the nipple (athelia) may be noted at birth. Nipple inversion is normal at birth and is usually bilateral, resolving in the first few weeks of life. If nipple inversion persists, it can cause cosmetic concerns as well as difficulty with breastfeeding. Late-onset nipple inversion can be a sign of an underlying breast lesion. Patients with amastia, amazia, inverted nipples or athelia are most often referred to a plastic surgeon for reconstruction.

Thelarche

The appearance of breast tissue typically occurs between the ages of 8 and 13 years and marks the beginning of puberty. It generally precedes menarche by about 2 years; however, there is significant variation among individuals. Patients with thelarche delayed beyond the age of 13 should be referred for an endocrinology workup to look for evidence of delayed puberty because, though the majority of patients with delayed thelarche will be found to have no underlying endocrinopathy, the causes of delayed puberty can be consequential. These causes include hypogonadotropic hypogonadism, hypopituitarism, constitutional delay, chromosomal abnormalities (Turner syndrome), and hypothalamic dysfunction. Hypothalamic dysfunction may be due to secondary causes, such as hypothyroidism, diabetes, and other chronic illnesses.

Premature thelarche is defined as isolated breast development before 6–8 years of age and is typically isolated. In rare cases, however, it can be an indication of precocious puberty and physical examination should include a thorough search for other signs of early puberty. Hypothyroidism or exposure to exogenous estrogens can be cause premature thelarche. Premature thelarche does not increase the risk of future breast disorders.

Virginal/Juvenile Hypertrophy

Virginal or juvenile breast hypertrophy is a rare disorder of breast development occurring most often during early puberty. It is thought to be the exaggerated response of breast tissue to pubertal hormones. The breast growth is often dramatic and rapid and can be unilateral or bilateral. The management of virginal hypertrophy is focused on making the accurate diagnosis as it can be confused with a giant fibroadenoma or phyllodes tumor, as well identifying the optimal time for intervention. The mainstay of treatment is breast reduction surgery, optimally at the end of puberty. In some cases, the growth is so dramatic that surgery is required prior to the completion of breast development and more than one procedure may be necessary. As the hypertrophy is thought to be due to excessive response to hormones, tamoxifen and other medications have been recommended as adjuvant therapy in certain cases. There is no known association between juvenile hypertrophy and breast cancer.

Trauma

Some developmental disorders are not congenital but traumatic, either iatrogenic or otherwise. Though rare, blunt trauma to the breast can occur due to shoulder restraints in motor vehicle accidents, a direct blow during sports, or due to non-accidental trauma. In some cases, this trauma results in fat necrosis that can present as a painful mass that infrequently necessitates excision. Breast hematomas can be dramatic but rarely require drainage or other intervention.

Iatrogenic injury can occur during procedures in and on the chest, specifically chest tube placement, central line placement, thoracotomy, and thoracoscopy (Fig. 34.2). The areola develops at about 5 months gestation, and the nipple can be nearly invisible in neonates, especially in premature infants. The nipple should be marked before the area is prepped and draped to avoid inadvertent injuries due to an errant incision.

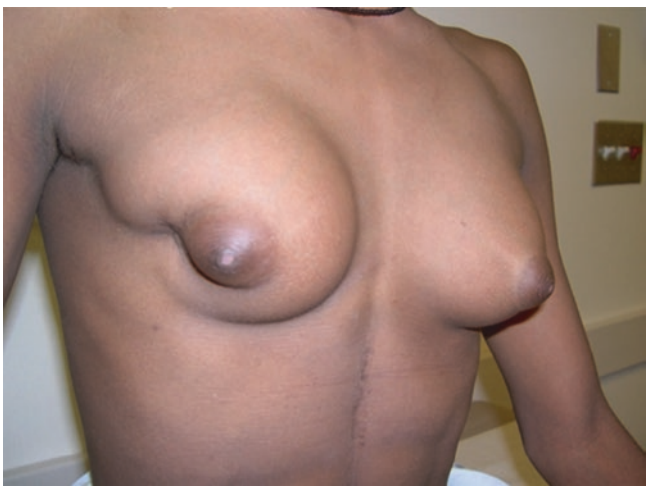

Fig. 34.2 Abnormal breast development in an adolescent due to chest tube placement in infancy

Nipple Discharge

Nipple discharge in nonlactating females can be pathologic but often has a benign or physiologic cause.

Bloody Discharge

While bloody nipple discharge in the adult can be a symptom of an underlying malignancy, in children and adolescents it is almost universally benign and usually self-limited. The most common causes of bloody nipple discharge in the pediatric population are mammary duct ectasia and intraductal papillomas (Fig. 34.3).

Mammary duct ectasia occurs when there is persistent obstruction of the duct with fibrosis, inflammation, and possible bacterial overgrowth. The inflammation can cause bleeding as well as infection. Though the exact etiology of duct ectasia is not known, it is postulated that it may be from an anomaly of duct development. Duct ectasia in children has also been attributed to infection, trauma, or an autoimmune reaction. An US can in some cases help make the diagnosis with findings that include dilated ducts filled with debris or tubular structures and associated cystic lesions. Because of the associated infection, serosanguinous or bloody nipple discharge should be cultured and treated with antibiotics based on culture results. The bleeding from duct ectasia is often self-limited but if persistent may be treated with surgical excision.

Intraductal papillomas are an abnormal proliferation of ductal epithelial cells with epithelium-covered fibrovascular cores. Though most common in women aged 35-55, they can be diagnosed in pediatric patients, albeit rarely. These lesions are often difficult to palpate but cytology of the drainage may demonstrate epithelial cells and aid in the diagnosis. Surgical excision is curative.

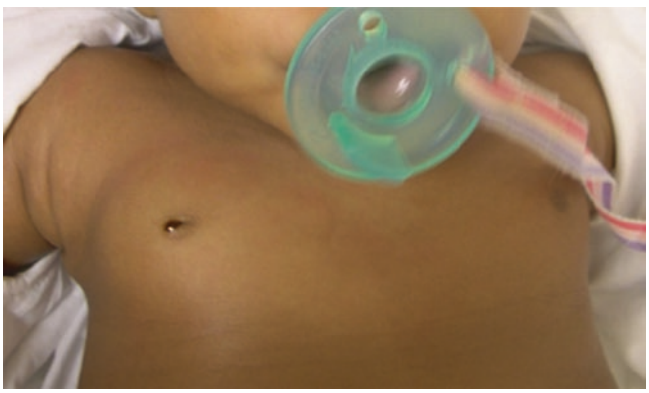

Fig. 34.3 Bloody nipple discharge in an infant

Blood or blood-tinged fluid can also occur from nipple trauma. Local irritation or chafing from prolonged exercise, particularly running or biking, can cause bleeding from the nipple that can be prevented with lubrication or skin coverage with bandages.

Galactorrhea

Galactorrhea in neonates is normal as falling levels of maternal estrogens induce neonatal pituitary gland prolactin production, which precipitates milky discharge from the nipple. This drainage is not pathologic and occurs in up to 7% of term infants. It is sometimes labeled *witches milk* and resolves spontaneously.

In adolescents, galactorrhea is not considered normal and demands a thorough evaluation. Its causes are classified as endocrine (hypothyroidism), neurogenic (trauma or disorders of the chest wall), hypothalamic/pituitary tumors (prolactinomas), drug-induced (psychotropics, oral contraceptives), or idiopathic. In order to establish that the discharge is true galactorrhea, it should be sent for fat staining and, if diagnostic, a workup is warranted.

Infections

Neonatal mastitis occurs most often in term infant girls. The most common organism is *Staph. aureus*, including MRSA and intravenous antibiotics are indicated. Despite adequate treatment, abscesses develop in about half of children with neonatal mastitis.

Mastitis can also occur in adolescent females. Sometimes the induration can be dramatic and cause concern for an underlying mass or an associated abscess. US is helpful in determining if either is present. Mastitis in this age group often responds to oral antibiotics and warm compresses.

If a breast abscess develops, needle aspiration is the preferred means of drainage, with US guidance if necessary. In cases of a large abscess not adequately drained with aspiration, a limited circumareolar incision may be necessary. Aggressive manipulation of the abscess cavity should be avoided.

Fibrocystic Disease

Fibrocystic breast changes are often described as lumpy breasts and can cause discomfort and tenderness, often around the time of menstruation. Adolescent patients with fibrocystic change are frequently referred to pediatric surgeons due to pain or concern for a mass. When no discrete

lesion is identified on physical examination, an US can often be helpful to exclude an underlying small lesion and reassure families. No surgery is indicated and most patients find symptomatic relief with a supportive bra and over-the-counter pain medications. Avoidance of caffeine and chocolate has been advocated, as have vitamin E and evening primrose oil, but these recommendations are primarily based on anecdotal experience.

Masses

Neonatal Lesions

The workup of a breast lesion in infants and babies is different from that of an adolescent patient with a breast mass. The most common lesions seen in the infant, aside from normal breast buds, are vascular and lymphatic malformations. They can involve the chest wall or the breast itself. Just as with lesions diagnosed anywhere in the body, it is important to determine the correct diagnosis, as management differs. Imaging with US, and in select cases MRI, can be helpful to characterize the lesion. Occasionally, FNA helps with diagnosis. Infantile hemangiomas have a typical clinical course of initial growth followed by a slow involution that usually lasts for years. Many patients have lesions elsewhere. Though hemangiomas are benign, if there is rapid growth there may be injury to the immature breast. Other vascular malformations, however, do not regress and require intervention. In cases where surgical resection could be disfiguring the developing breast, other interventions (sclerotherapy) may be considered. Multidisciplinary clinics involving dermatology, radiology, and surgery are available at many institutions and assist in coordinating the nonoperative and operative treatment of these lesions.

Pubertal Masses

Breast masses in children and adolescents are estimated to affect slightly more than 3% of the pediatric population and are commonly managed by pediatric surgeons. The majority of breast lesions are found in females during mid and late adolescence and are almost universally benign. Though the majority of pediatric breast masses are not malignant and some even resolve without intervention, they can often cause symptoms and in many cases, their mere presence can lead to significant anxiety among patients and families. Thus, a thoughtful and focused plan for the workup and treatment is important. A clinical examination with a thorough personal and family medical history is the cornerstone of proper evaluation. Personal history should focus on a history of cancer or chest radiation. Chest radiation therapy for the treatment of other cancers is associated with the development of primary breast carcinoma and metastatic lesions can be found in the breast. Breast masses in patients with these risks should be approached differently. Family history should emphasize the presence of ovarian and breast cancers in family members to assess for a possible undiagnosed BRCA mutation.

Most breast masses are identified by the patient on self-examination and are by definition palpable. US however can be helpful to determine the exact dimensions of lesions, as well as follow size more definitively than with physical examination alone. The Breast Imaging Reporting and Data System (BI-RADS) was developed to risk-stratify lesions on mammogram and US, and it is often incorrectly applied to US obtained in pediatric patients, especially if performed at an adult breast center. Based on the recommendations of the BI-RADS classification, there is sometimes pressure to intervene on a lesion that otherwise does not require it. BI-RADS was developed based on data from adult women and there is no evidence that it is valid in the pediatric population. Educating patients, parents, and referring physicians that BI-RADS does not apply to adolescent breast masses, or having the US repeated by a pediatric radiologist, can obviate the need for unnecessary procedures.

Mammography is not indicated in children or adolescents. Though breast MRI is not routinely used for evaluation of a breast mass in an adolescent patient, it may be used in select patients. In patients who have a known BRCA1 or 2 mutations, a personal history of mantle radiation, or a strong family history of breast cancer, screening breast MRI may be indicated. This screening usually does not begin before age 25 years or less than 8 years after chest radiation therapy. The decision to obtain a screening breast MRI in high-risk populations can be directed in collaboration with an adult breast surgeon or oncologist.

Though the work-up of breast lesions in adults often includes a fine-needle aspiration or core needle biopsy, these procedures have less utility in children. In patients at low risk for malignancy, palpable masses can generally be followed clinically and, when they require intervention, it is usually excision. Needle biopsy is not always diagnostic in differentiating between types of stromal tumors and the indication for intervention is often pain, which is not alleviated with needle-based procedures. In patients with a personal history of cancer or chest radiation, however, a needle biopsy is justified for diagnosis of a malignant lesion. Needle aspiration is also useful for draining cysts.

Most breast masses can be excised using a periareolar incision, with attention to avoiding injuring the nipple complex. There is little morbidity to surgery for adolescent breast masses and, in most cases, even with seemingly large masses, cosmetic results are acceptable after excision. With the generous use of local anesthetic, many patients do not require

narcotics post-operatively. Patients should be counseled to wear a compressive bra after surgery to decrease the risk of a large seroma. The recommendations for immediate follow-up as well as long-term management of breast masses depend on the pathologic diagnosis.

Retro-areolar Cysts (Montgomery Cysts)

The papular tissue in the periareolar regions of the breast are called the glands of Montgomery or Morgagni tubercles. Obstruction of these glands may result in acute inflammation, nipple drainage, or the development of a subareolar mass—a Montgomery cyst. The diagnosis is confirmed with US, which generally shows single or multiple retro-areolar thin-walled unilocular cysts that are smaller than 2 cm and might contain debris. Sometimes the cyst has associated inflammation, pain, and erythema that extends beyond the areola and into the mammary tissue. Symptomatic cysts are managed with NSAIDs, warm compresses, and oral antibiotics as needed. Needle aspiration or incision and drainage is rarely needed and considered only when an abscess forms that does not respond to antibiotics. These cysts usually resolve spontaneously, though this can take up to 2 years.

Fibroadenoma

Fibroadenomas are the most common breast mass of adolescence, accounting for up to 90% of all excised masses. They arise from the overgrowth of the stromal tissue in the breast lobule. The growth of a fibroadenoma is due to an increase in estrogen and therefore most often develops during puberty. They can occur as isolated or multiple lesions and are generally firm and well-defined. On physical examination, they are often described as a mobile rubbery balls. They tend to either grow slowly or not at all and, in adolescents, are almost invariably benign. Some studies have indicated that about 10% of fibroadenomas will regress spontaneously.

Breast masses consistent with a fibroadenoma can be safely followed. The data are mixed about the size of a lesion that demands resection, however, those >3 cm are more often a phyllodes tumor and are therefore generally excised. Furthermore, masses that grow while being followed with physical examination or US also warrant excision. This is due to concern for phyllodes tumor or juvenile fibroadenoma. Many patients also experience pain or extreme anxiety due to a fibroadenoma, both of which can be mitigated with excision.

Juvenile Fibroadenoma

Juvenile (cellular) fibroadenoma is a variant of giant fibroadenoma occurring in young or adolescent females. Giant fibroadenoma is defined as a fibroadenoma >5 cm in diameter or weighing more than 500 g. Pathologically these lesions have increased stromal cellularity. Juvenile fibroadenomas exhibit rapid growth and therefore often have overlying skin changes including ulcerations or distended superficial veins. They cannot be definitively differentiated from a phyllodes tumor by imaging, fine needle aspiration, or core-needle biopsy. Surgery is indicated when there is a concern for a juvenile fibroadenoma for cosmetic reasons as well as to confirm the diagnosis. Preservation of the nipple and normal breast tissue can be challenging, especially in a small breast, and the involvement of an experienced plastic surgeon is often prudent.

Juvenile Papillomatosis

Juvenile papillomatosis, despite its name, differs from intraductal papilloma and does not cause nipple discharge. The mean age of onset is 19 years old and it is caused by hyperplasia of the papillary epithelium of the duct, which creates a mobile mass consisting of multiple cysts. Because of its appearance on pathology and imaging, these lesions have been described as *Swiss-cheese disease*. Juvenile papillomatosis is treated with surgical excision with negative margins. Patients with juvenile papillomatosis often have a strong family history of cancer and, although this lesion is not itself considered premalignant, it can be a marker for increased risk of breast cancer in adulthood. Patients should be counseled accordingly.

Pseudoangiomatous Stromal Hyperplasia (PASH)

PASH is more common in adults but can also rarely occur in children. It is a benign tumor formed from the proliferation of stromal myofibroblasts. PASH can range from a localized incidental finding seen only microscopically to palpable and radiographically visible breast masses. Clinically and sonographically, PASH can mimic fibroadenomas. Generally, PASH is only differentiated from a fibroadenoma on the pathology of an excised lesion and no further intervention is required after excision.

Phyllodes Tumors

Phyllodes tumors are fibroepithelial neoplasms. They are rare in children with a median age of presentation of 45 years. Though they mimic fibroadenomas, phyllodes tumors are often larger or more rapidly growing and physical examination and imaging are unable to conclusively distinguish the two entities. Phyllodes tumors are classified as benign, borderline, or malignant on the basis of histological parameters, but even those with benign histology can recur. The surgical management is wide local excision with clear margins, and, unlike with fibroadenoma, close follow-up with physical examination and US is indicated.

Breast Carcinoma

Primary breast cancer is rare in the pediatric population, accounting for less than 1% of all childhood cancers and less than 0.1% of all breast cancers. There is a >35× increased risk of primary breast cancer in those who have had mantle radiation, particularly at a younger age. The most common primary breast carcinoma in children is secretory carcinoma, which accounts for 80% of all primary breast malignancies in children, making it the most common subtype. It has a favorable prognosis, with a 10-year cause specific survival of over 90%. The management of malignant breast tumors is similar to that used in adult breast cancer. Sarcomas can also develop in breast tissue as can metastatic lesions, typically from lymphoma and rhabdomyosarcoma.

Gynecomastia

Gynecomastia is the benign proliferation of male breast tissue, including glands, stroma, and fat. It is the most common cause of breast enlargement in adolescent boys and occurs to some degree in more than half of pubertal boys. Gynecomastia is most often physiologic and may be due to a local imbalance between estrogen stimulation and the inhibitory action of androgens on breast tissue proliferation. The majority of adolescents with gynecomastia, however, have normal estrogen levels. Secondary causes of gynecomastia are found in <5% of cases but are important to exclude. These secondary causes include estrogen-producing testicular tumors, adrenocortical tumors, gonadotropin-secreting tumors such as hepatoblastoma and fibrolamellar carcinomas, choriocarcinomas, and prolactinomas. Other uncommon causes include liver disease, Klinefelter syndrome, and neurofibromatosis type 1. In addition, the use of drugs such as marijuana, anabolic steroids, corticosteroids, cimetidine, digitalis, and tricyclic antidepressants can cause gynecomastia. A thorough inquiry about medication and drug use is essential in these patients.

In the majority of patients, physiologic gynecomastia is self-limited and resolves over time. Given this natural history, surgical intervention is rarely warranted, despite the often significant psychosocial distress that accompanies the diagnosis. Obesity increases both the prevalence of physiologic gynecomastia and the length of time for it to resolve. Weight loss can be of benefit to some patients with gynecomastia.

Subcutaneous mastectomy might be indicated if there is no regression in size over a year or if there is significant tissue fibrosis. It is also indicated in patients with Klinefelter syndrome due to the risk of malignancy. It is often challenging to get insurance approval for these cases and patients must be prepared that they may have to wait until after they are 18 years old. Subcutaneous mastectomy can be performed with a periareolar or inframmary incision. Liposuction has been used alone or in conjunction with excision in certain cases.

Editor's Comments

Breast masses cause extreme anxiety especially if there is a family history of breast cancer, and it is extremely difficult or impossible to reassure some patients or parents that a lesion is extremely unlikely to be malignant. If it can be performed safely and with a high expectation of a good cosmetic result, biopsy should be considered and is probably appropriate under the circumstances. A breast mass in a toddler on the other hand is almost always a normal breast bud and should never be biopsied, as this will cause partial or complete amazia in adulthood. Reassurance and serial examinations should be the rule, with US performed for enlargement of the mass or extreme parental anxiety.

Most breast masses in teenagers will be fibroadenomas, which can be multiple and bilateral. Unless they are symptomatic, larger than about 4 cm in diameter or growing rapidly, they can safely be observed. As with all potentially worrisome lesions, systematic follow-up is critical. Some resolve spontaneously after a few months or years of observation. Often there is pressure to perform a biopsy because of an US report, usually from an adult radiologist, that states the lesion is suspicious or that biopsy is recommended. Repeat US performed by an experienced pediatric radiologist can sometimes provide the reassurance needed to avoid unnecessary surgery. Unless it is located in the tail of the breast, fibroadenomas are almost always amenable to be removed through a precise periareolar incision, and because they can usually be separated cleanly from the surrounding breast tissue with blunt dissection, the specimen should include little if any normal breast tissue. Furthermore, except in girls with a history of radiation exposure (Hodgkin disease), resection of a breast mass with a margin is rarely necessary.

Fine-needle aspiration can be used to aspirate a cyst but in children is rarely useful for solid masses. Likewise, the needle-localization biopsy is almost never indicated as this is usually performed in women with a nonpalpable lesion detected by screening mammography, which is never indicated in a child. Many adolescents complain of breast pain, for which there is often no effective treatment. When there is pain, many patients think they feel a mass when in fact there is only normal developing breast tissue, which can be very firm and tender to palpation, or fibrocystic change, which is not treated surgically.

Mastitis is treated with antibiotics, while an abscess may need to be aspirated or surgically drained. A judgment needs to be made whether injury to the breast is more likely with incision and drainage or an undrained infection. Needle aspiration or drainage performed carefully through a tiny incision at the areolar border is usually the better choice, especially for an abscess that is symptomatic, tense, or enlarging. Abscess cavities should never be packed with gauze, as this is dated and unnecessarily painful. Ectopic breast tissue most commonly occurs in the axilla and can be cyclically painful. The tissue is usually intimately adherent to the overlying dermis and an acceptable cosmetic result can be difficult to obtain.

Gynecomastia often resolves after puberty. Many surgeons will refuse to operate (and insurance companies will refuse to pay) until the patient has reached 18 years of age and can demonstrate that the breast tissue has failed to begin to diminish in size. Nevertheless, it seems reasonable to consider any significant cosmetic concern that causes severe emotional distress or intense social stigma in a child a reasonable indication for surgical intervention, assuming it can be done safely and successfully. The goal of mastectomy in these cases should be to remove only the breast tissue, although removing a small amount of fat is sometimes necessary, especially in patients who are obese. It is often difficult to know how much tissue should be removed from behind the nipple—removing too much can cause necrosis or nipple inversion, while leaving too much can result in recurrence, especially if the child is still young. It is usually best to leave a small amount and to warn the patient that recurrence is possible but unlikely.

If for some reason an incision needs to be made somewhere other than at the areolar border, traditional teaching suggests that, in order to avoid mutilating or distorting the breast, skin incisions inferior or inferior-medial to the nipple should be oriented radially relative to the areola while those lateral or superior to the nipple should be oriented circumferentially (parallel to the areola). The inframammary incision can be useful and is cosmetically superior to other anterior thoracotomy incisions; however, when the incision is made while the patient is supine and under general anesthesia, it will almost invariably end up being too high (on the breast). If there is any chance that an inframammary incision will need to be made, the site should be marked prior to the operation with the patient in an upright position. There is no reliable way to predict where the inframammary crease will someday be when in a given individual who is Tanner stage 0 with no discernible breast mound. Drains are almost never recommended as a tense seroma can be aspirated painlessly in the office with the needle placed directly through the incision, which is insensate. Although gentle support (a well-fitted sports bra) provides comfort and stability, an old-fashioned pressure dressing or ace-wrap can cause ischemia or pressure injuries and should in most cases be avoided as unnecessary.

Further Reading

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