Lecture 1 Breast
THE BREAST
ANATOMY and HISTOLOGY

The size and structure of the breast vary with the age, sex, hormonal status and heredity of the individual. The areola is the circular pigmented area that contains sebaceous glands. In its center, the elevated nipple is covered by wrinkled skin lined by stratified squamous epithelium. It contains 15-20 lactiferous ducts (lined by two-layered cuboidal cell mucosa) which branch successively distally, leading eventually into the terminal ducts. Before puberty, this complex system ends blindly but at menarche, it proliferates distally giving rise to 30-epithelium lined ductules or acini. Each terminal duct and its ductules compose the terminal duct lobular unit.
The ductules are covered by cuboidal and myoepithelial lining cells. In addition to ramifying ducts, the female breast consists of connective and adipose tissue, although few alveoli may develop and involute concomitantly with the menstrual cycle. In the male breast, there are only rudimentary ducts surrounded by connective tissue. The female breast is in the unique position of being a gland which is non-functioning except during lactation. However, its extreme sensitivity to hormonal influences disposes it to a number of pathological conditions.
Inflammatory and Related lesions:
Acute Infections (Pyogenic Mastitis and Breast Abscess)
Mastitis, a local or generalized inflammation of the breast, is precipitated by lactation, trauma or infection through the ducts or nipple abrasions. Usually caused by Staph. Aureus which may invade the breast tissue and may progress to the formation of single or multiple abscesses where by the localized collection of pus causes conspicuous tenderness. Less commonly Strept. Pyogenes may cause cellulites. If extensive necrosis occurs the destroyed breast substance will be replaced by fibrous scar which may cause retraction of the overlying skin or nipple, stony hardness and axillary lymphadenopathy; changes mimicking a malignant neoplasm. Chronic inflammation if neglected may lead to fistula formation.
Chronic Infections and Granulomatous Inflammations

Granulomas are caused by different infectious agents:

Tuberculomas: Involving the breast have been described. Although it is relatively rare, but it usually arise from hematogenous, lymphatic or direct spread. It presents as a single caseating lesion which sometimes discharges through the skin.

Sarcoidosis: Reveals similar picture without caseation or acid-fast bacilli.

Fungal infection: actinomycosis are associated with necrotizing granulomas. These are diagnosed by special stains such as PAS or tissue culture.
Idiopathic Granulomatous mastitis (IGM)
This rare condition is seen mainly in young women, usually after pregnancy. Patients present with firm tender mass. It may be complicated by overlying skin ulcerations & multiple draining sinuses.
Non-Inflective Inflammatory Lesions including:

1- Mammary Duct Ectasia:

This disorder tends to affect perimenopausal women usually in the fifth decade of life. Patients are often multiparus and have lactated, but may have had trouble in nursing due to inverted nipples. It begins with dilatation of the terminal collecting ducts beneath the nipple and areola where they become distended with cellular debries and lipid containing material. This may be followed by marked periductal and interstitial chronic granulomatus inflammatory reaction and fibrosis, sometimes associated with a large number of plasma cells (plasma cell mastitis).
Rarely palpable as a “bag of worms”. Fibrosis may cause skin retraction which may be mistaken for carcinoma. Often symptomless but there may be nipple discharge.

Hyper-prolactinemia has been suggested to play a role in its pathogenesis. The pathology described above results in firm mass with adjacent skin dimpling and nipple retraction.
2-Traumatic Fat Necrosis:
It often follows trauma and presents clinically as a firm hard mass (in the fatty tissue of an obese pendulous breast and sometimes associated with skin retraction. It consists of a central focus of liquefactive fat necrosis, surrounded by lipid-layedden macrophages and numerous neutrophilic inflammatory infiltration. This is followed by fibroblastic proliferation, foreign-body giant cell infiltration and ending into scar tissue (which together with the calcification accounts for the hardness of the lump). Extensive fibrous reaction may further cause nipple retraction and fixation thus simulating malignancy.
(Diagram: Traumatic fat necrosis in the breast. Necrotic area is surrounded by lipid filled macrophages and foreign-body giant cells).
Fibrocystic Changes or Cystic Mastopathy

This is a pleomorphic disorder in which variable morphological patterns are encountered in different patients, different areas within the same lesion and even in different microscopical fields within the same slide. It develops in females between puberty and menopause and considered the commonest cause for a lump in the breast. Patients usually presented with ill defined tender thickness of the breast tissue, palpable lumps or physiological nodularity which may vary during the period of the menstrual cycle. It has been postulated that those changes are related to imbalance between estrogens and progestins (with excessive estrogenic stimulation)
In general, it is possible to distinguish 3 dominant patterns of morphological changes:

A-Cystic Formation and Fibrosis (Simple Fibrocytic Changes)
This is the most common type of alteration characterized by an increase in fibrous stroma associated with ductal dilatation and formation of cysts of various sizes, probably due to obstruction. Unopened cysts are brown to blue in colour due to the contained semitranslucent turbid fluid. Sometimes haemorrhage or rupture leads to secondary inflammation. Cysts are lined by columnar, cuboidal or flattened epithelium that may be atrophic in larger ones. The epithelium may consist of large polygonal cells with abundant granular eosinophilic cytoplasm and small hyperchromatic nuclei (apocrine metaplasia), which is virtually always benign. In general, the breast should be palpated again after cystic aspiration and any residual mass should be reaspirated.
Case 62: Fibrocystic disease

cystic dilatation of ducts

interstitial fibrosis
B-Epithelial Hyperplasia (Epitheliosis)

Hyperplasia affecting mammary ducts and ductules is the histological variant that increases the risk of subsequent development of malignancy; especially if it is associated with atypia. May take three main forms: solid, cribriform or papillary. The degree of hyperplasia can be mild, moderate, or severe. In some instances the hyperplastic cells show complex architectural patterns and approaching morphologically those of ductal carcinoma in situ, such hyperplasia is called atypical.
Atypical lobular hyperplasia describes hyperplasias that cytologically resemble lobular carcinoma in situ, but the cells do not fill or distend more than 50% of the acini within a lobule. Atypical lobular hyperplasia is associated with an increased risk of invasive carcinoma. Epithelial hyperplasia per se does not often produce a clinically discrete breast mass. Microscopically, proliferation causes increase in the layers of the ductal epithelium, sometimes encroaching to completely fill the duct lumen obliterating it (solid) or forming fenestrations with gland-like spaces (cribriform). Papillary epithelial projections may grow into the lumen (ductal or florid papillomatosis). The presence of ductal papillomatosis or moderate-severe atypia increase the risk of malignancy. Atypical ductal or lobular hyperplasia may show various degrees of cellular or architectural atypia that should be differentiated from carcinoma in situ.
C-Adenosis and Sclerosing Adenosis

Adenosis: i.e., enlargement of the lobules and/or formation of new lobules, could be a physiological process which occurs during pregnancy and reproductive life; however, it tends to be accentuated in fibrocystic changes.

Sclerosing Adenosis: a significant variant of FCC because its clinical and morphologic features may be deceptively similar to those of carcinoma.
Grossly, the lesion has a hard, rubbery consistency, & thus simulates that of breast cancer. Microscopically, this variant is characterized histologically by intralobular fibrosis and proliferation of small ductules or acini which yield small glandular masses or cellular cords within a fibrous stroma. Well-defined glands may be closely aggregated and backed to each other (adenosis). Stromal overgrowth may distort and compress the glands creating solid cords. Cells from sclerosing adenosis form clusters of up to 30 cells with some nuclear piling and minimal anisonucleosis. Sclerosing adenosis is associated with only a minimally increased risk of progression to carcinoma.
The relationship of the various patterns of fibrocystic Changes to Cancer:

1- Minimal or no increased risk of breast carcinoma: Fibrosis, Cystic changes, Apocrine metaplasia, Mild hyperplasia & Fibroadenomatosis.

2- Slightly increased risk (1.5-2 times): Moderate to florid hyperplasia (without atypia), Ductal papillomatosis & Sclerosing adenosis.

3- Significantly increased risk (5 times): Atypical hyperplasia, ductual or lobular.
Benign Tumours :
Fibroadenoma
This is the most common benign tumor of the female breast. It is a new growth composed of both fibrous and glandular tissue occurring commonly in young women (before the age of 30), and probably caused by hormonal imbalance. Areas resembling fibroadenoma sometimes occur in Fibrocystic Changes (Fibroadenomatosis).
Clinically, palpation reveals a dominant discrete, well-circumscribed elastic round or oval firm mass which resists penetration by the aspiration needle but proves to be mobile when penetrated. Usually small (2-4 cm.) but may reach 7 cm with a uniform tan-white color on cut section. They are usually encapsulated affecting one breast, and rarely multiple in both breasts.
Case 63: Fibroadenoma

- loose connective tissue
- glandular structures

- collagenous fibrous tissue
Phyllodes Tumour (Cystosarcoma Phyllodes)

Infrequently fibroadenoma may grow rapidly often to 10 cm. or more in diameter (Giant Fibroadenoma). Most are benign but few are malignant. On palpation, these are usually large circumscribed, mobile and some may become lobulated and cystic. Grossly they exhibit leaf-like clefts or finger-like projections (phyllodes). They may distort the breast producing pressure necrosis and skin retraction and ulceration. Histologically, these lesions tend to have a more cellular myxoid stroma than do the usual fibroadenoma. Features suggesting its aggressive nature include lack of encapsulation, large dimensions, remarkable nuclear anaplasia, and abnormal mitosis.