

Breast cytology

EOE FRCPATH cytology course

Dr Preethi Gopinath

MBBS, MRCS, PGDipMedEd, FRCPATH

Consultant Histopathologist

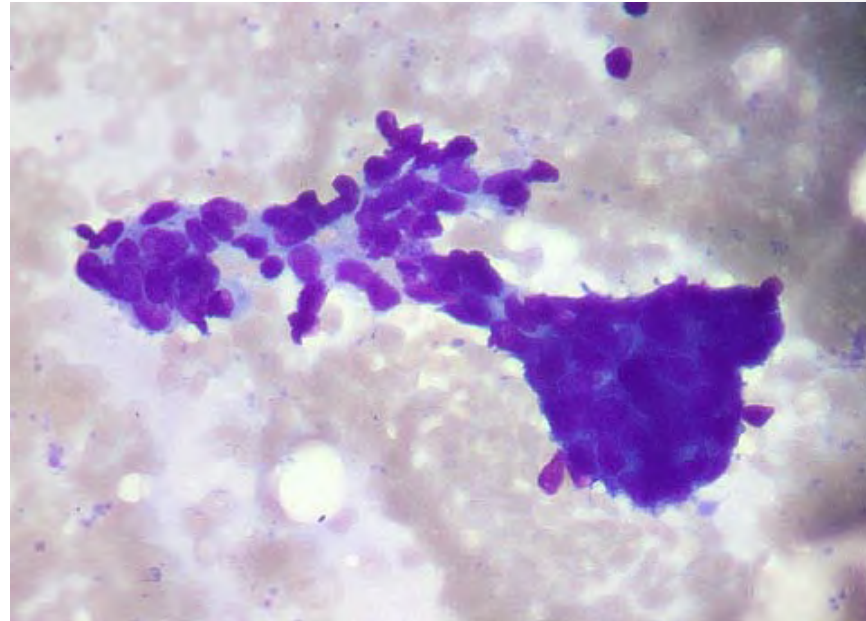
Princess Alexandra Hospital NHS Trust

Honorary Senior Clinical Lecturer

Queen Mary University of London and Anglia Ruskin University

Introduction

- FNA technique (21-25 gauge needle, since 1930's)
- Advantages – minimal discomfort, rapid results
- Accuracy – operator dependent, 82-98% sensitivity for malignancy, 77-100% specificity
- False negative results related to sampling and interpretation
- Indications – All palpable lesions, radiologically detected cystic lesions
- Low incidence of complications, occasional bleeding, infection and infarction



Techniques

- Usually performed under US or mammogram guidance
- 2-4 passes through the lesion for adequacy
- Direct smear – MGG and Pap stain are optimal
- Adequacy – no specific requirements for a minimum number of ductal cells, only adequate when represents lesion sampled

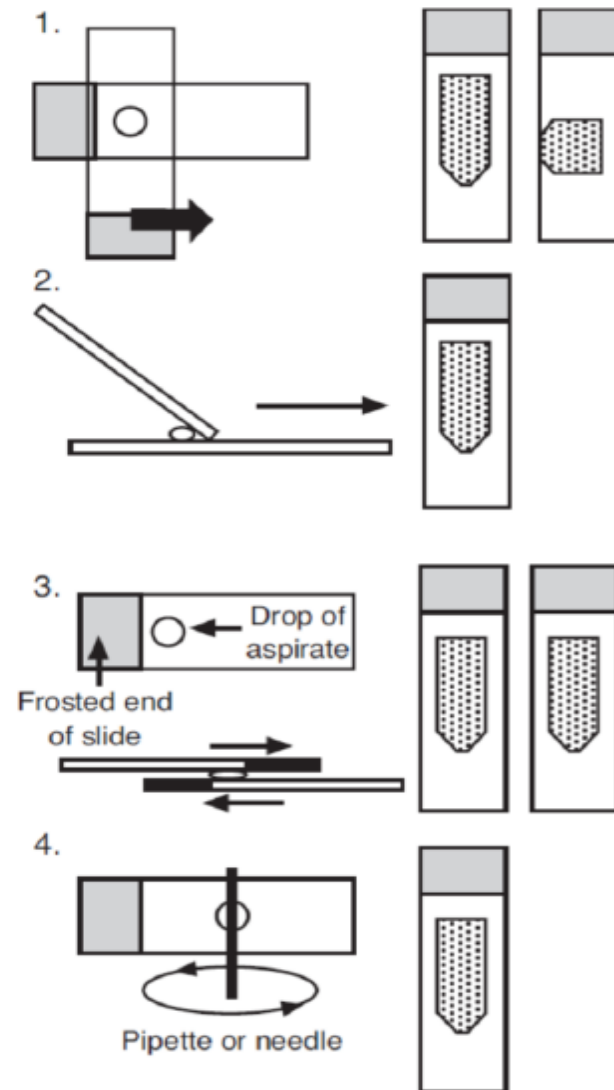
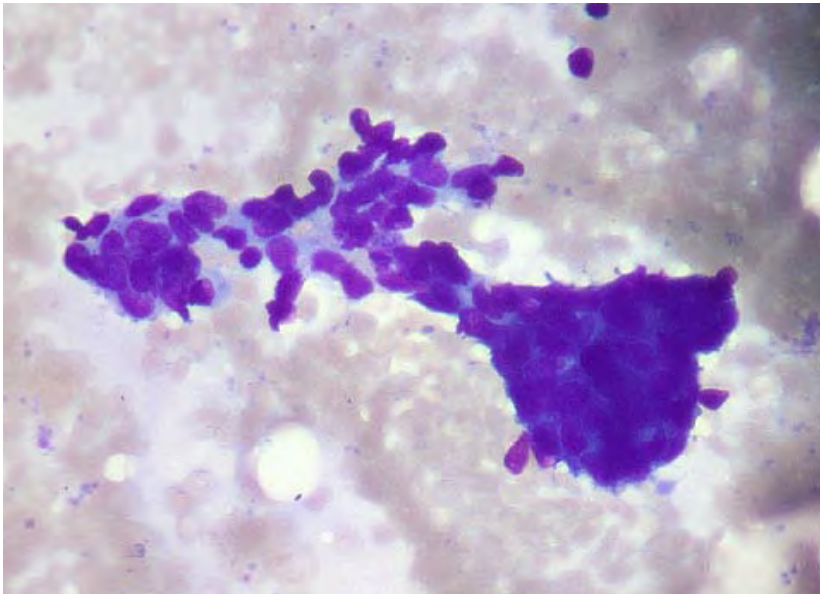
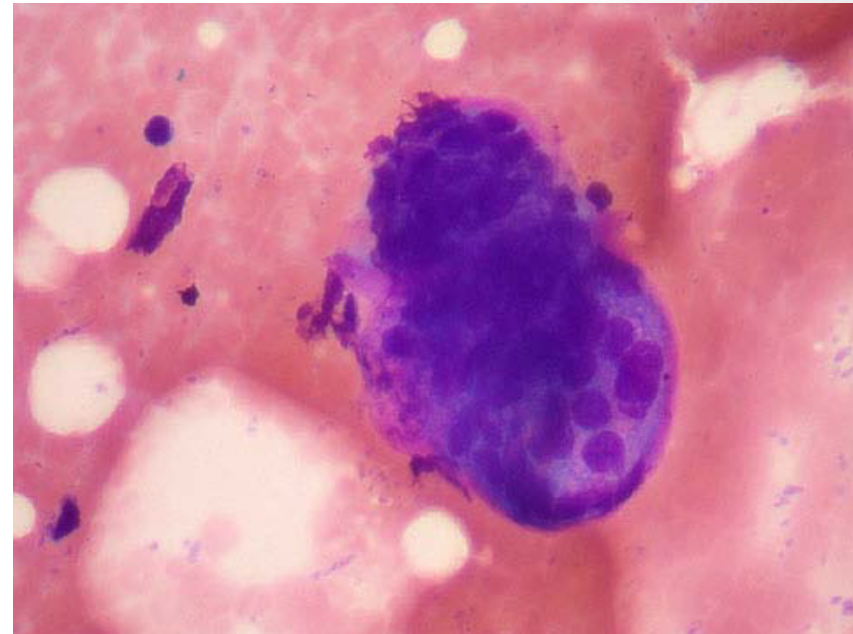


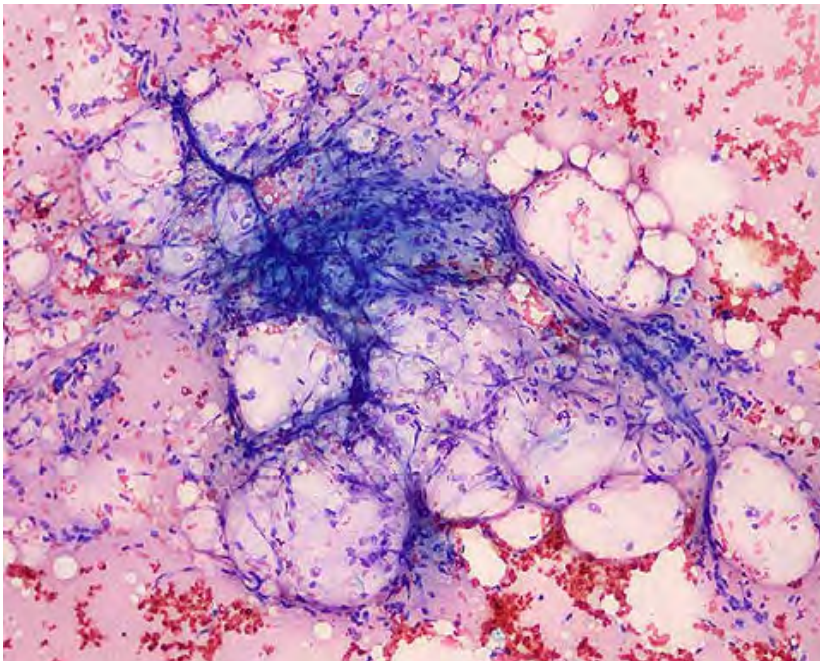
Figure 1: Spreading with a slide. Three basic methods (1, 2 or 3) can be used, all producing similar effects. Alternatively, the slide may be spread using a pipette or a needle (4).



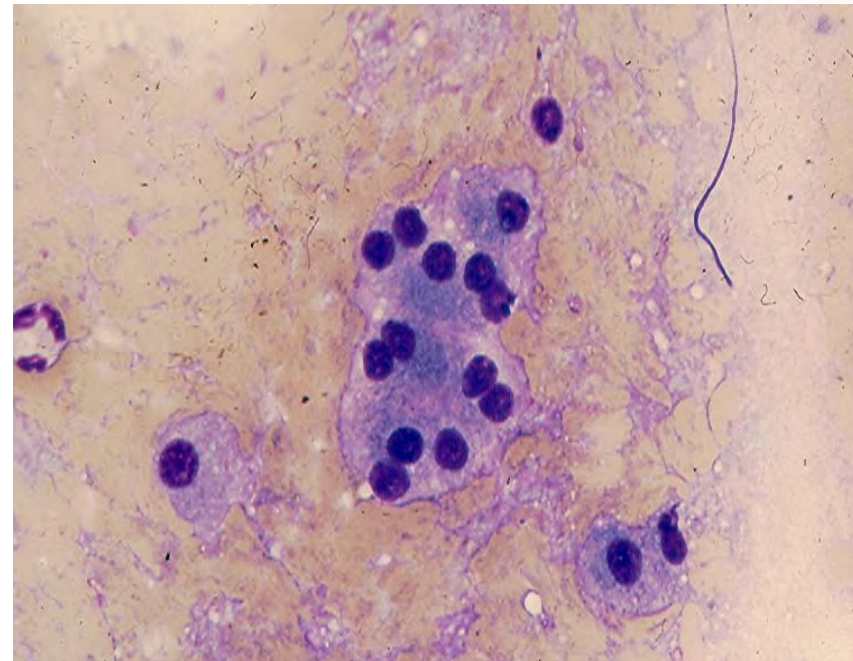
Ductal epithelial cells & myoepithelial cells



Lobular unit

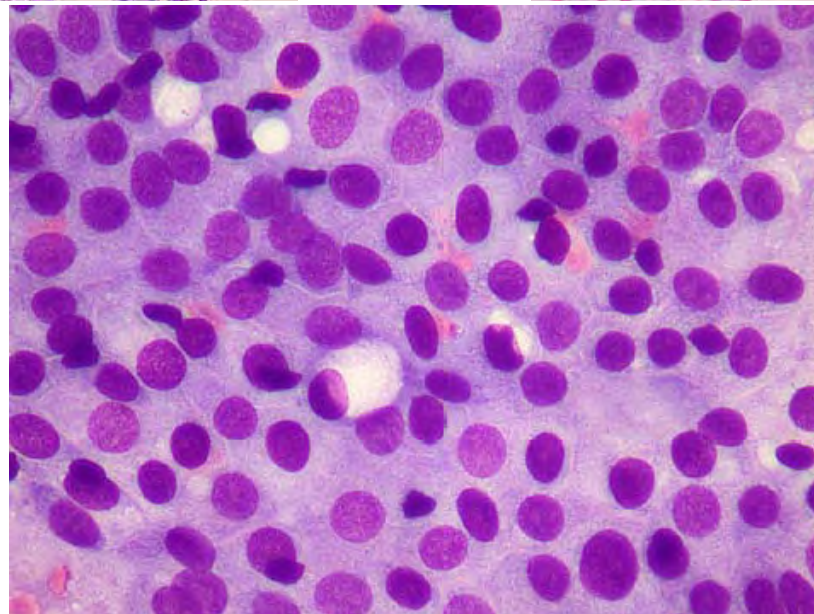
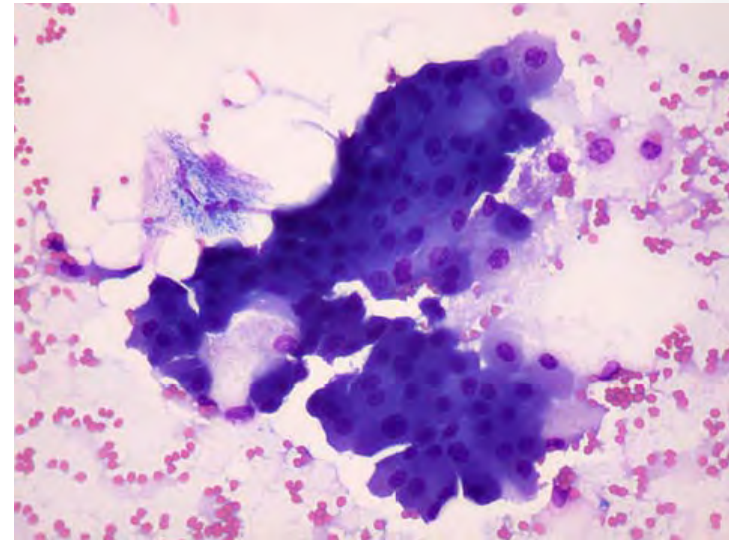
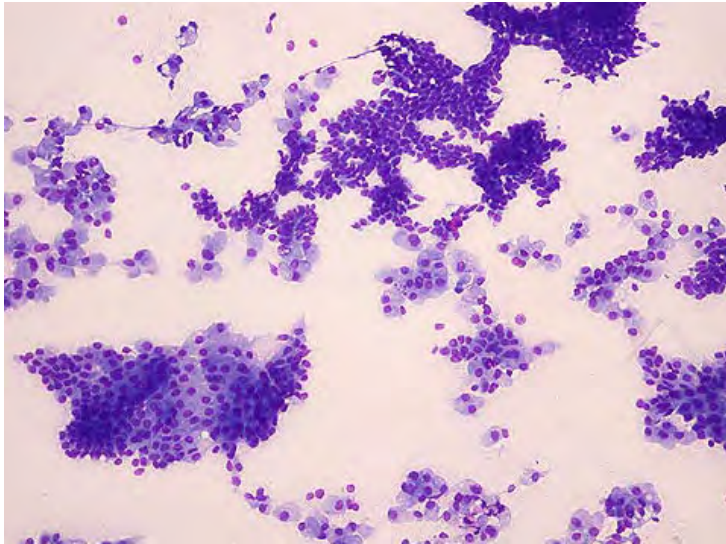


Stroma with capillaries

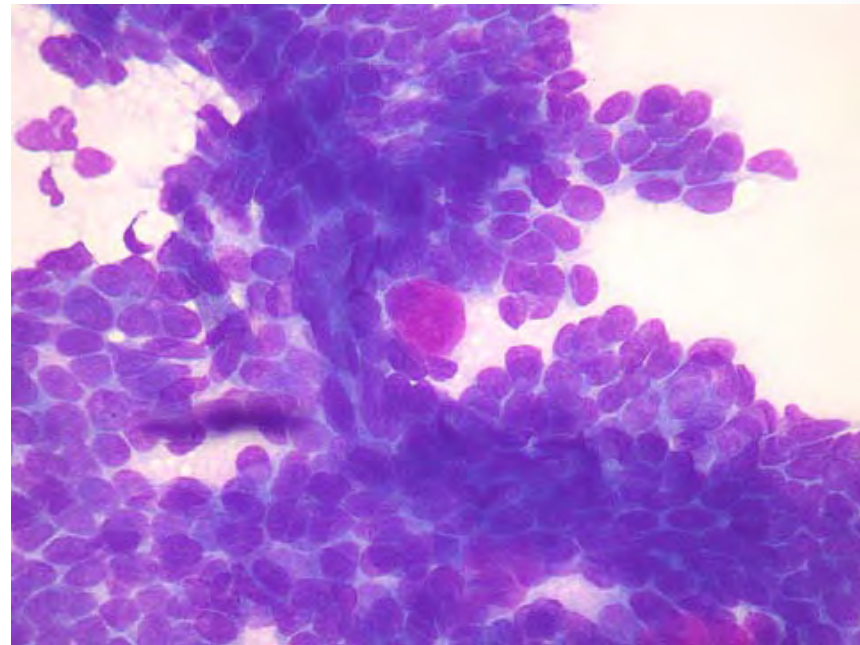
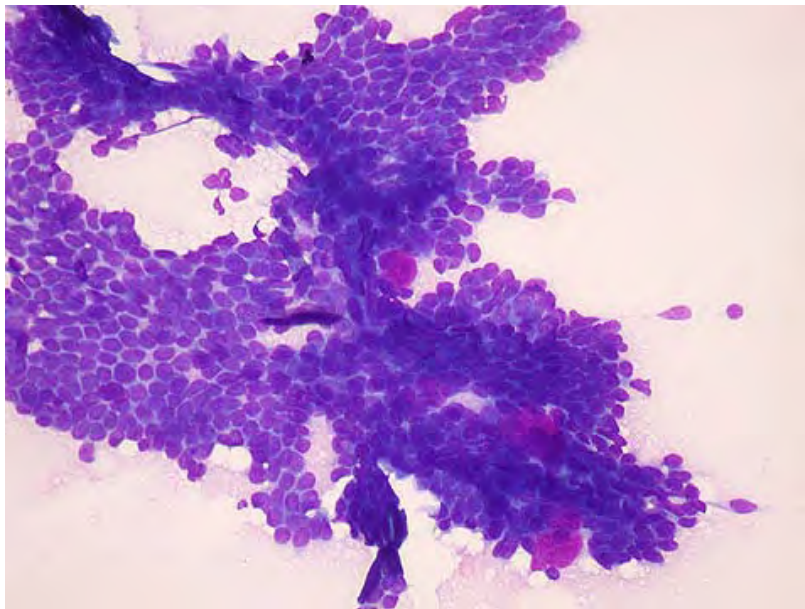


Lobular (acinar) cells

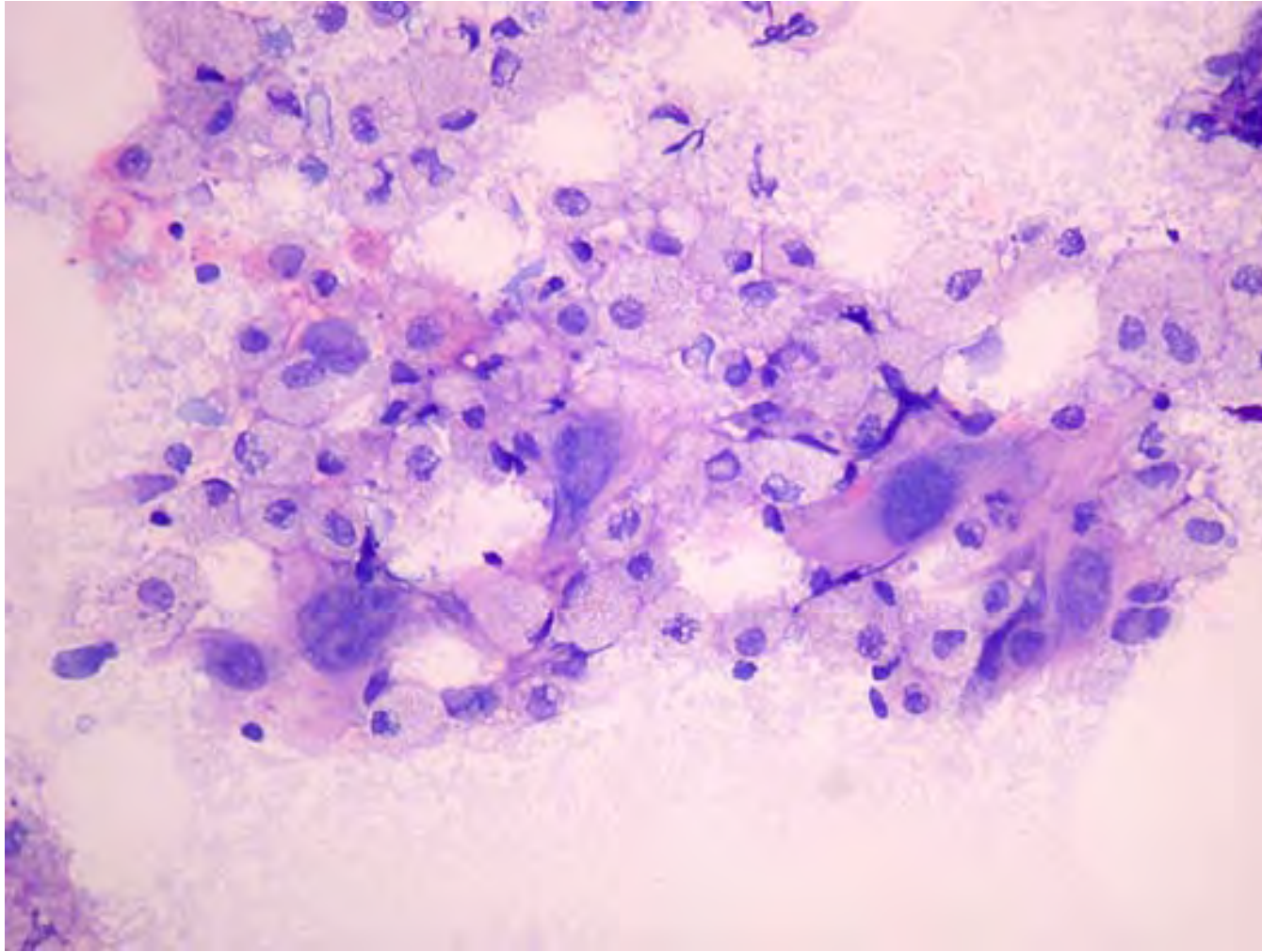
Fibrocystic change



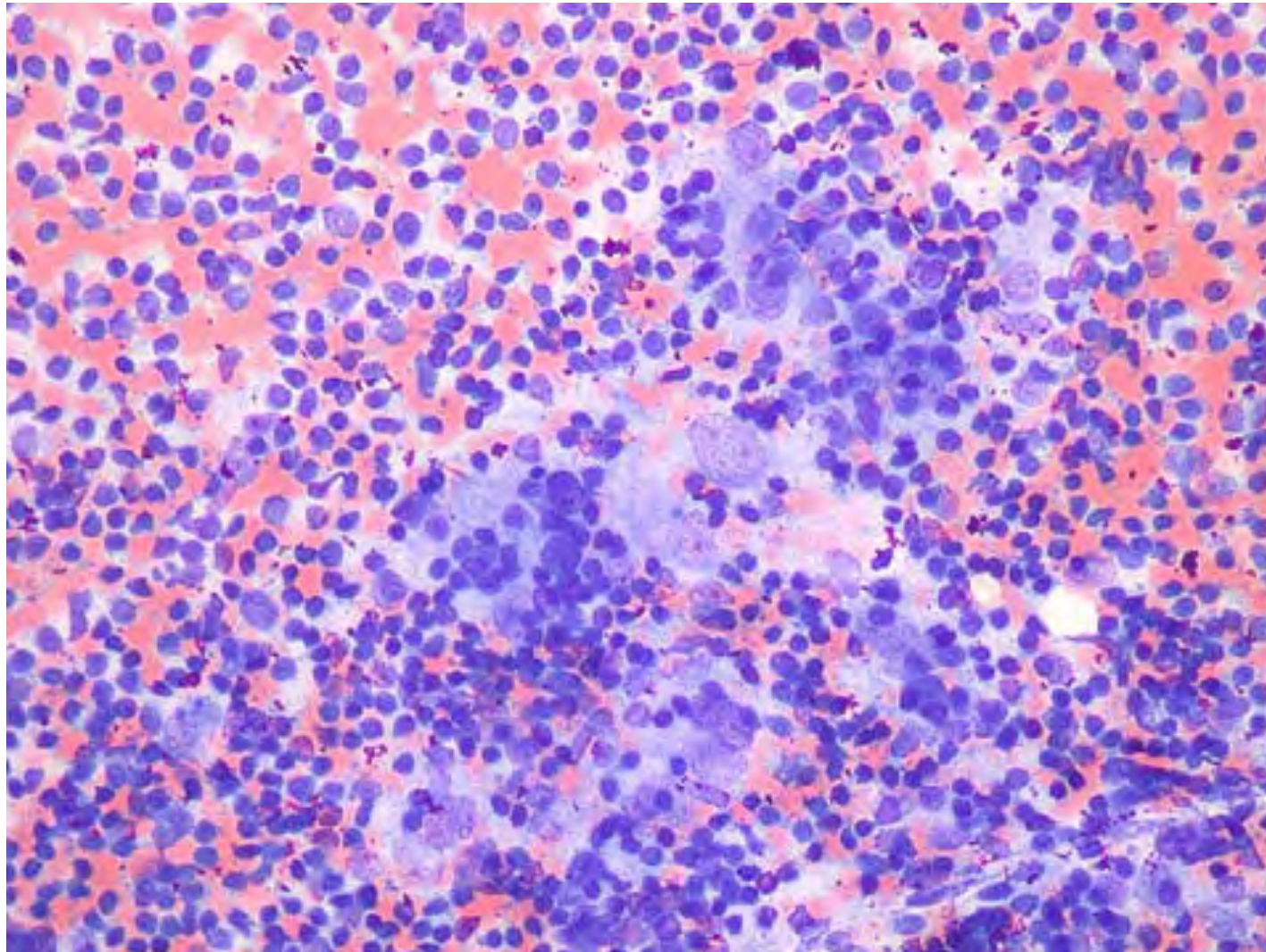
Collagenous spherulosis



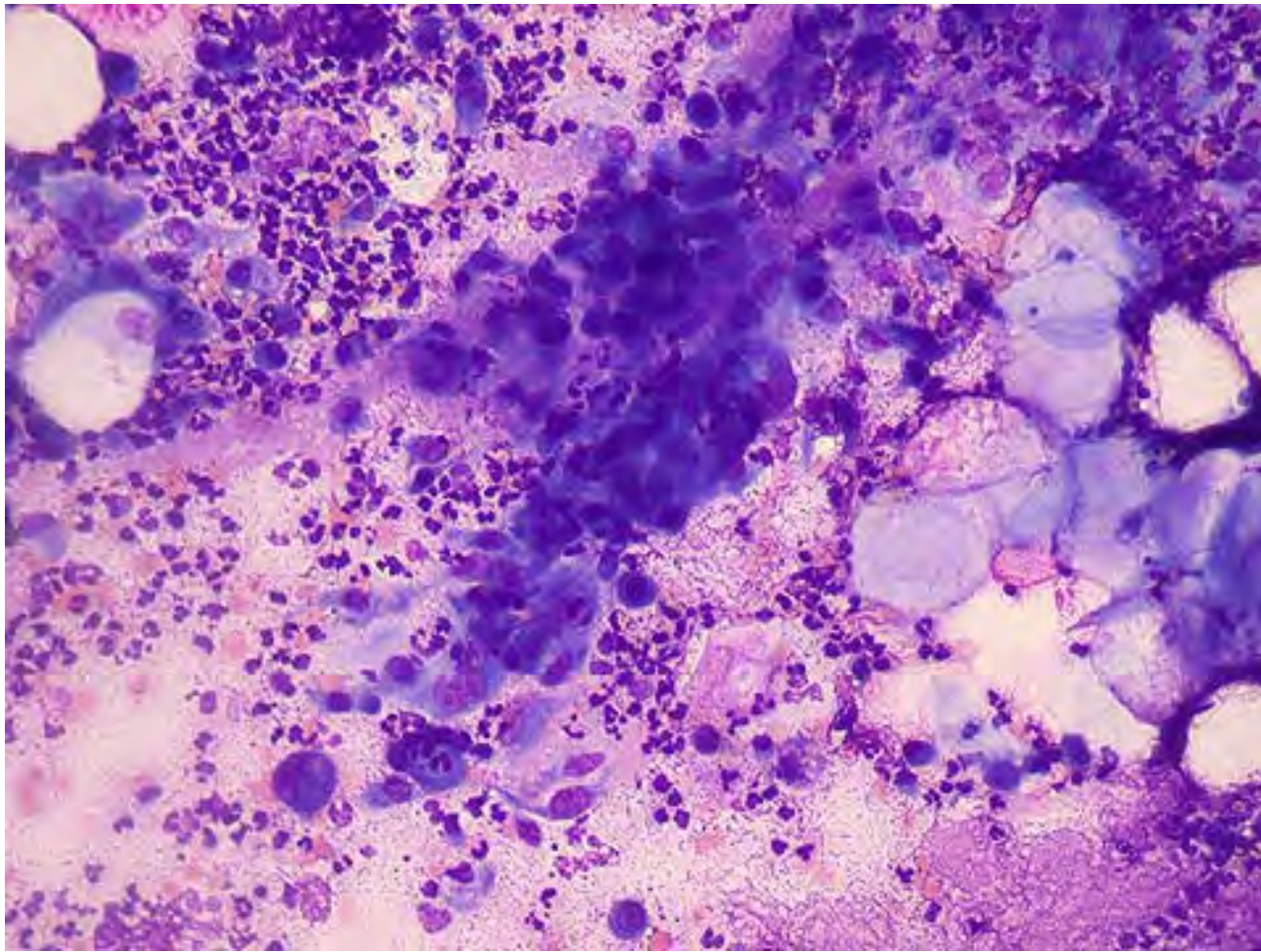
Atypia in inflamed cysts



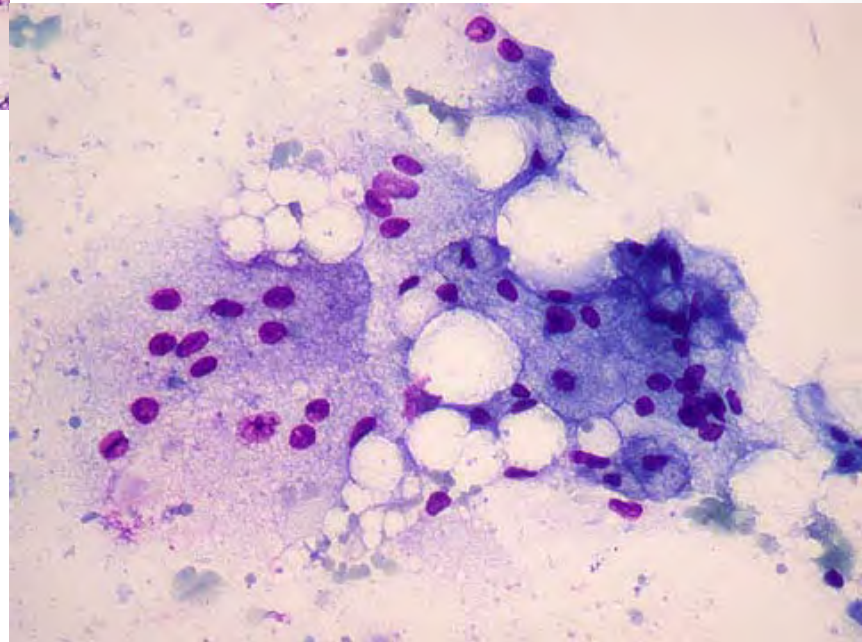
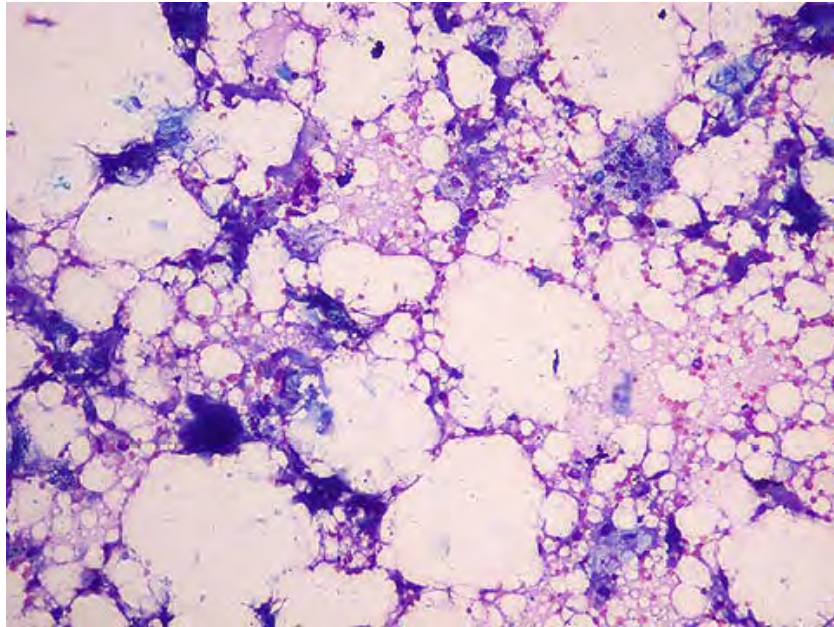
Breast abscess



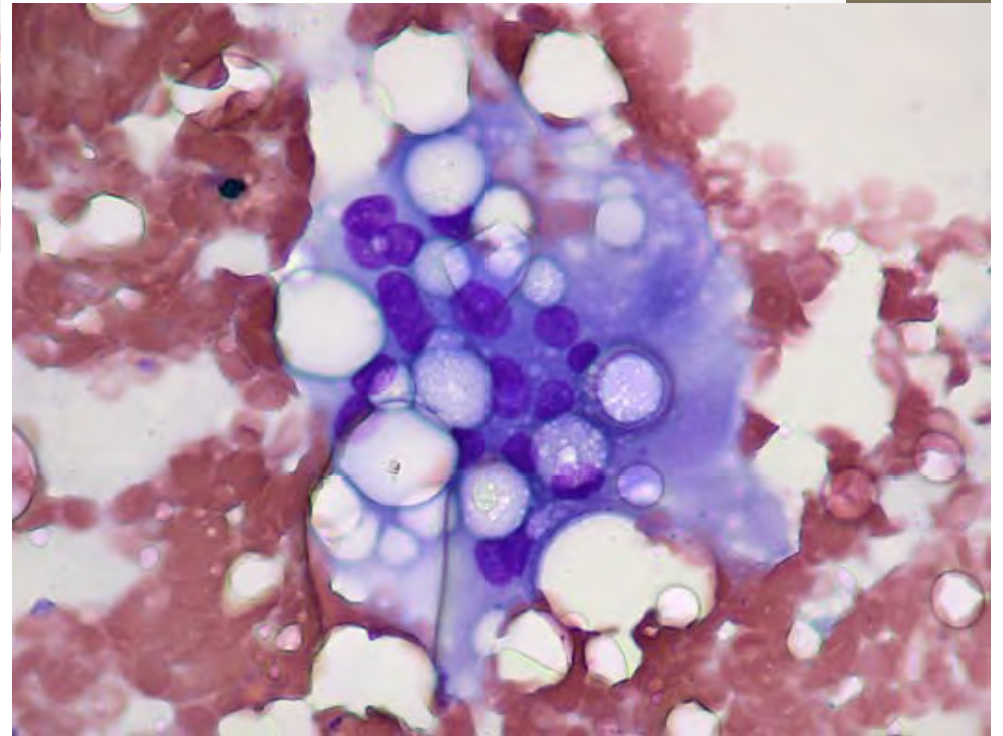
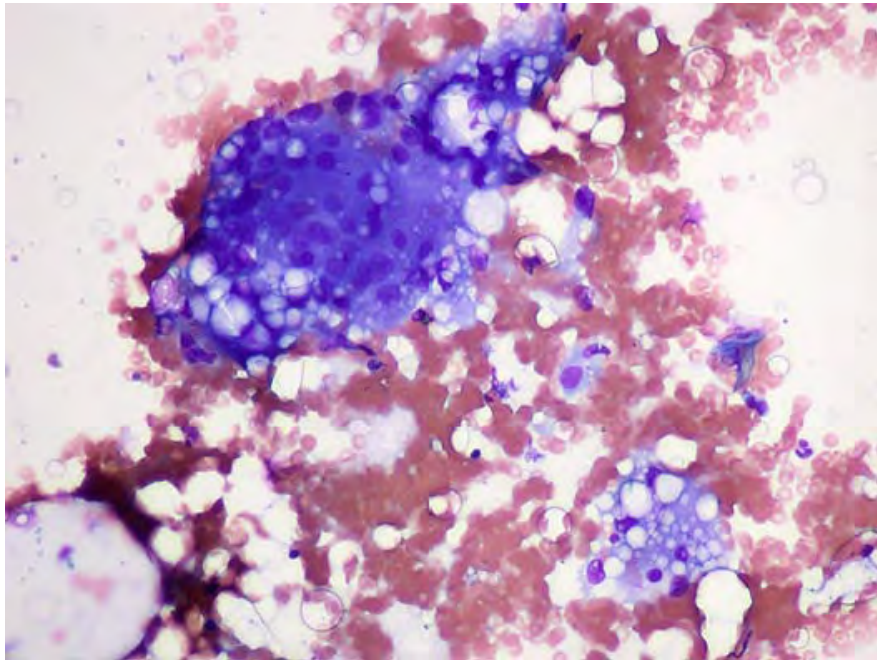
Peri-areolar abscess



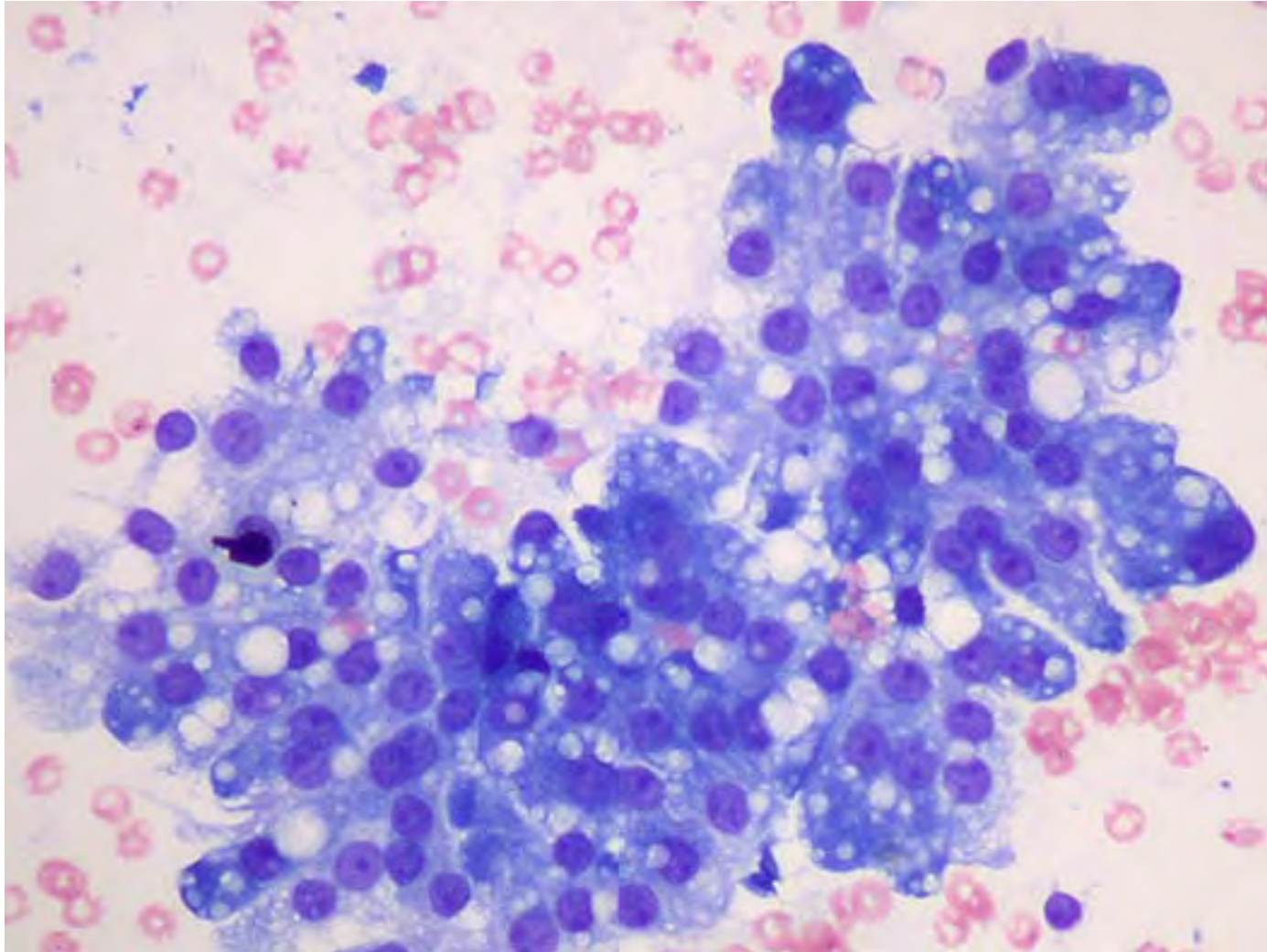
Fat necrosis



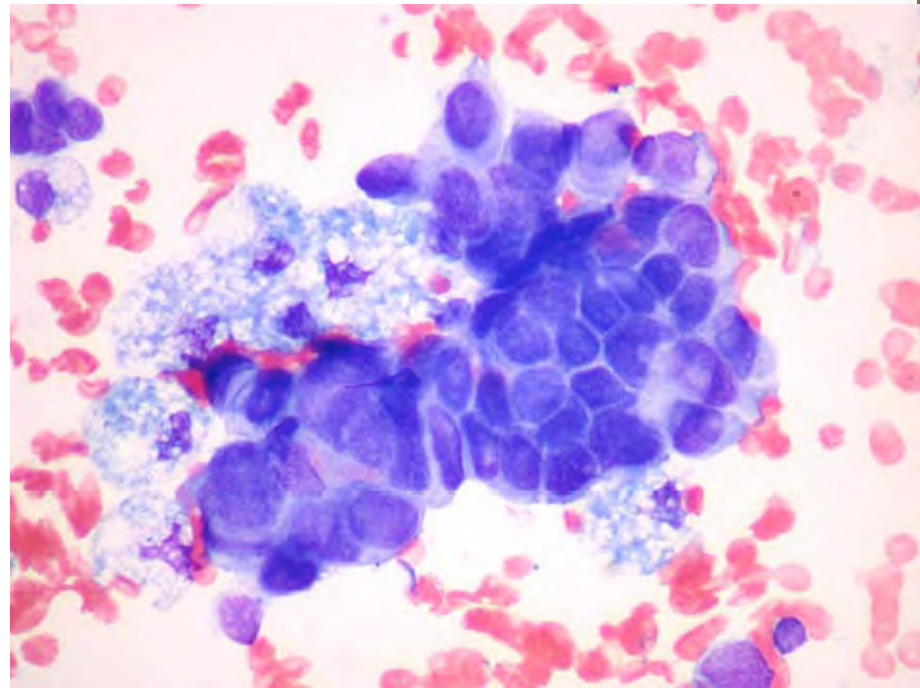
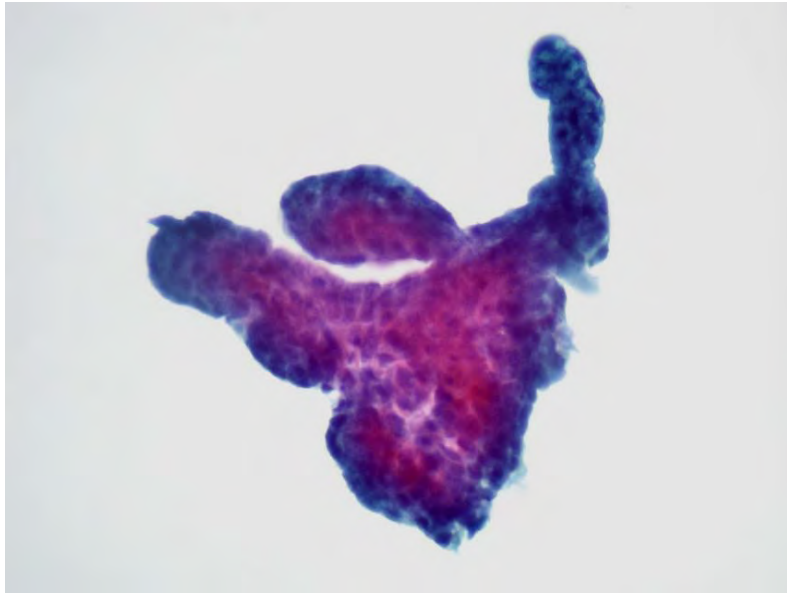
Silicone



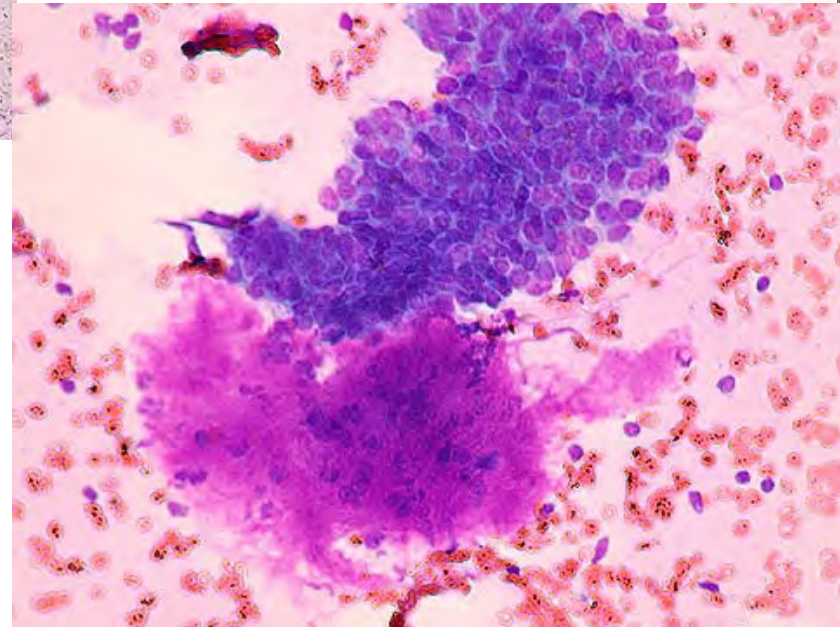
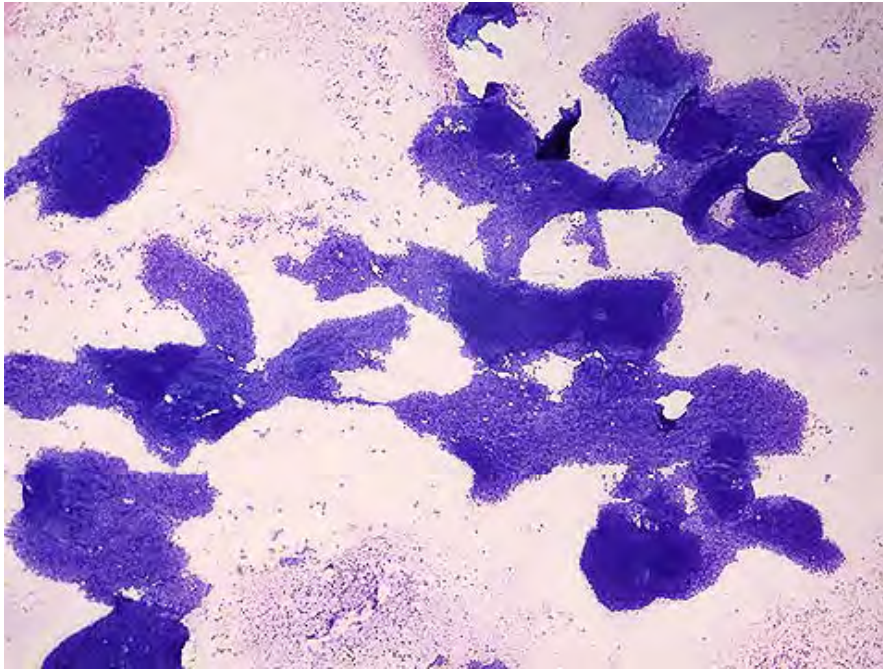
Lactational/secretory change



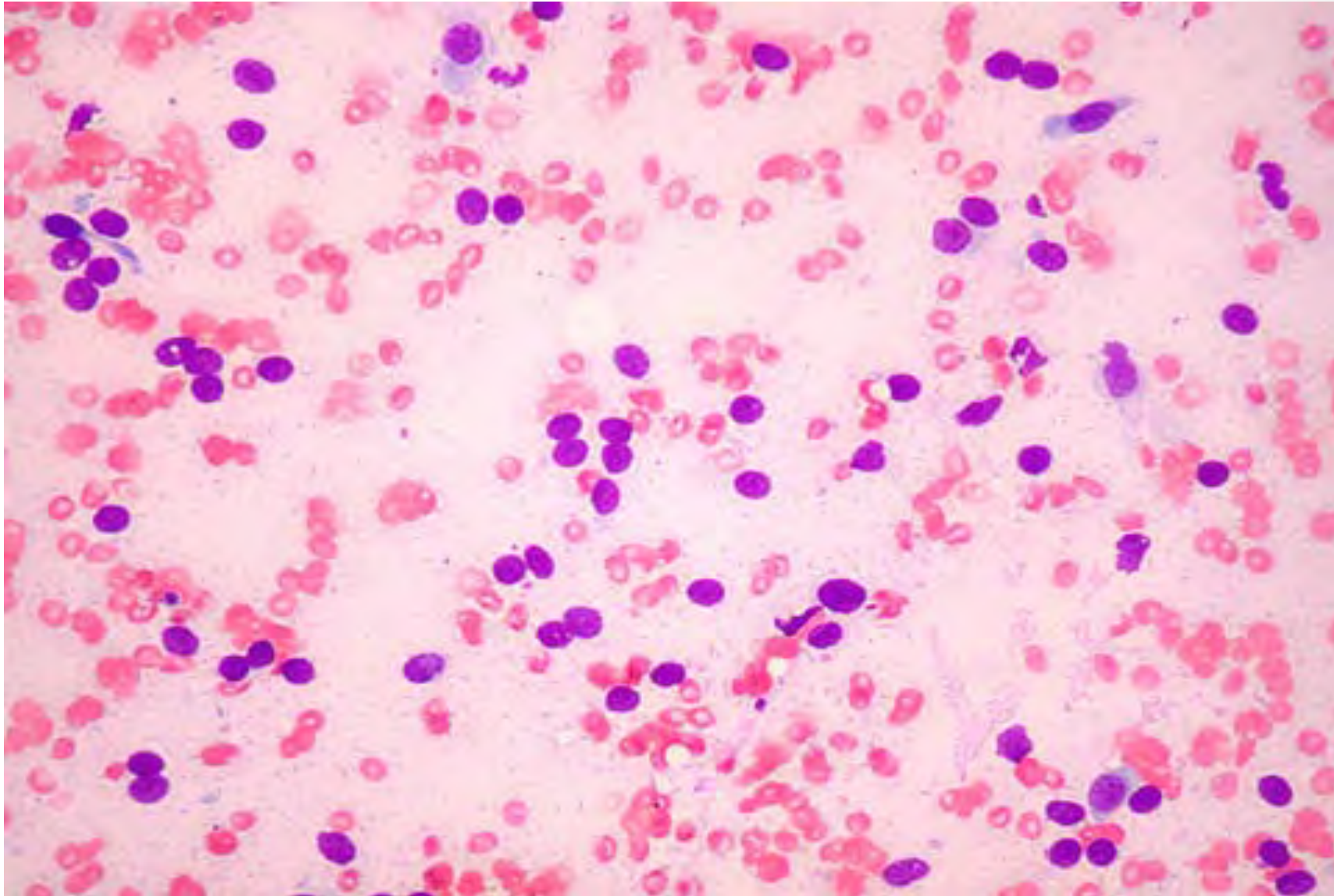
Papillary lesions



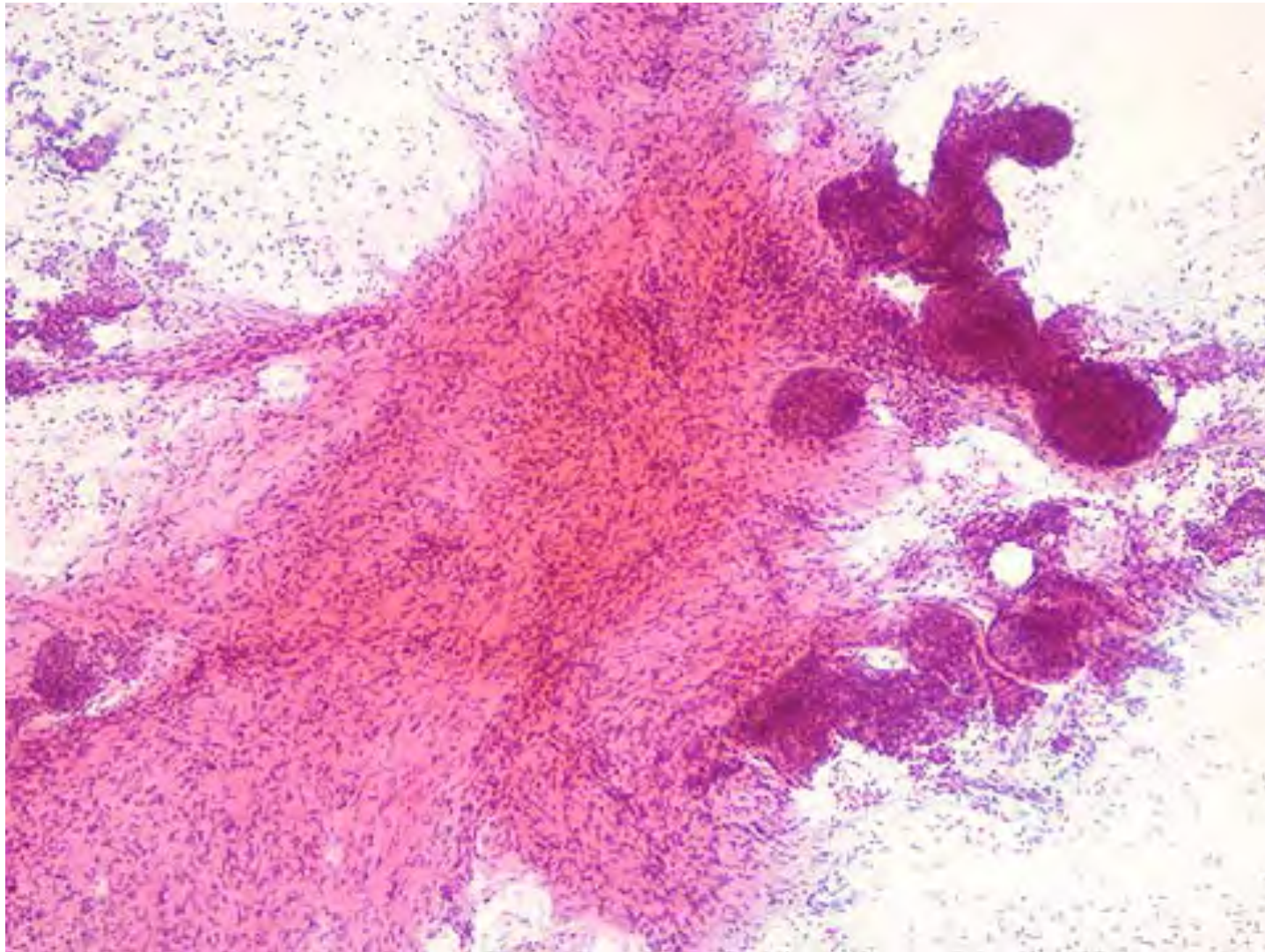
Fibroadenoma



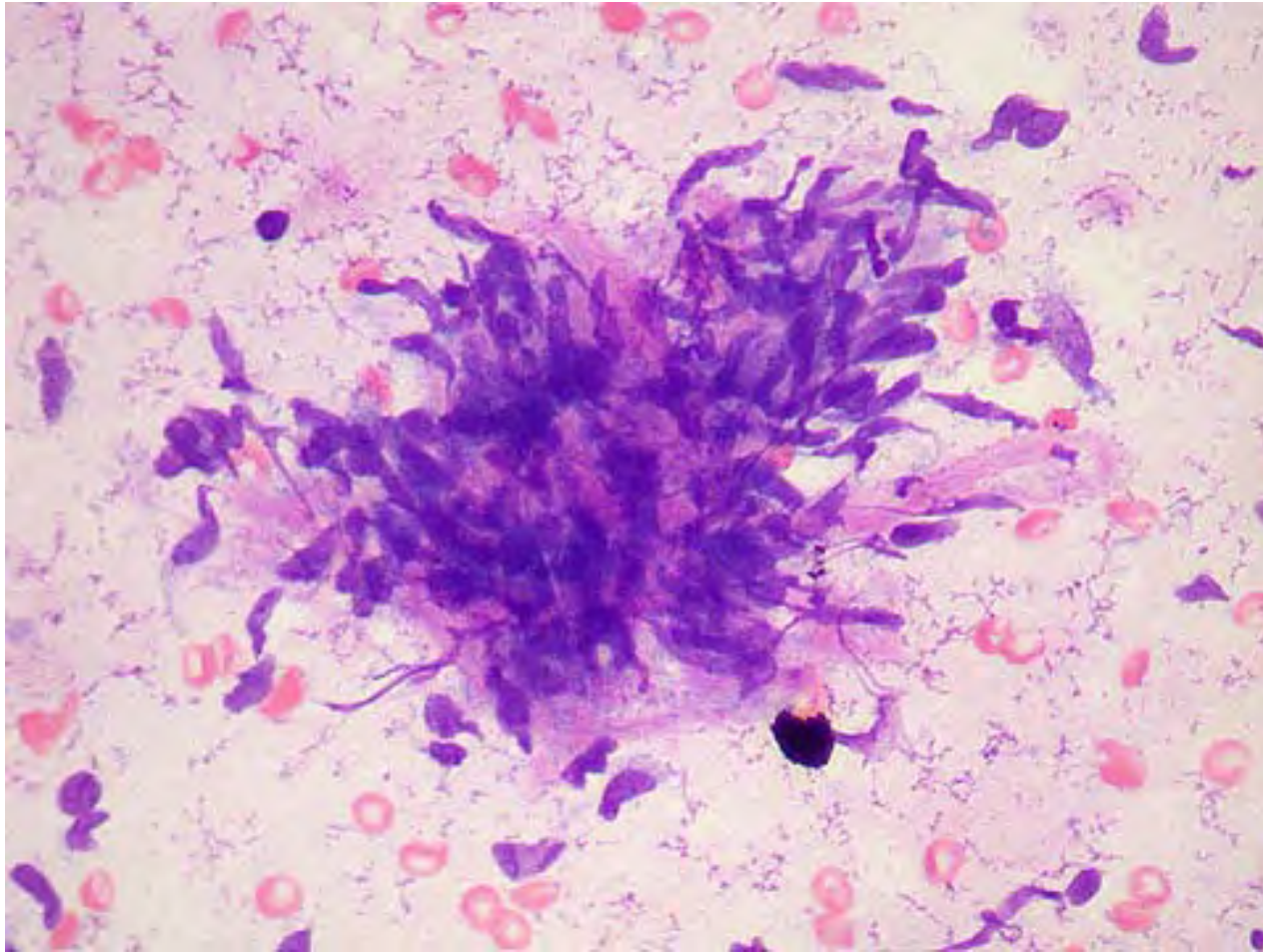
Bare bipolar nuclei



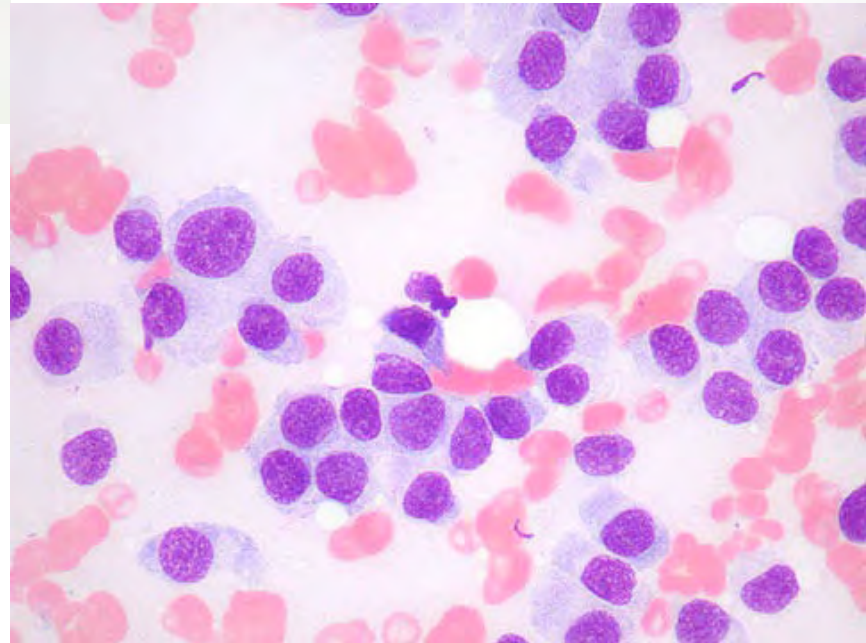
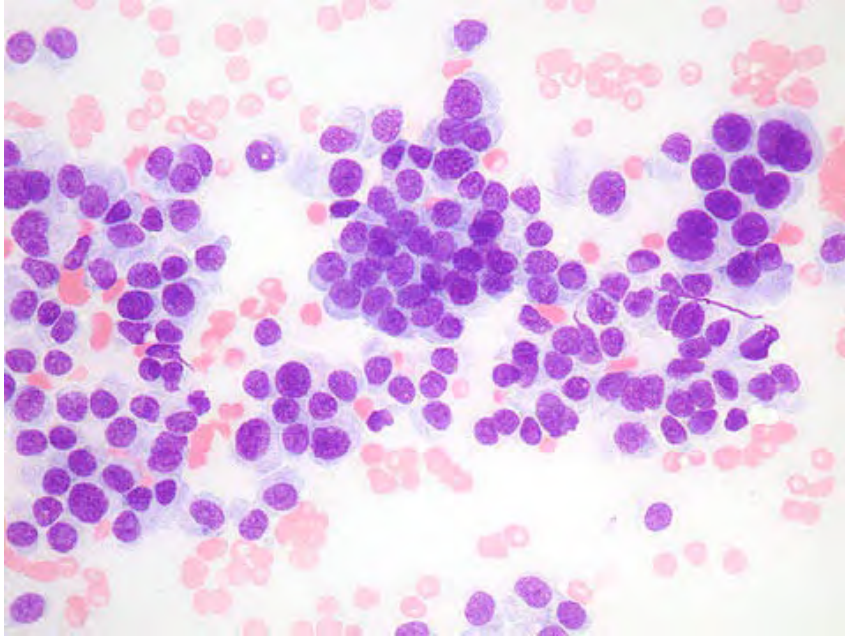
Juvenile fibroadenoma



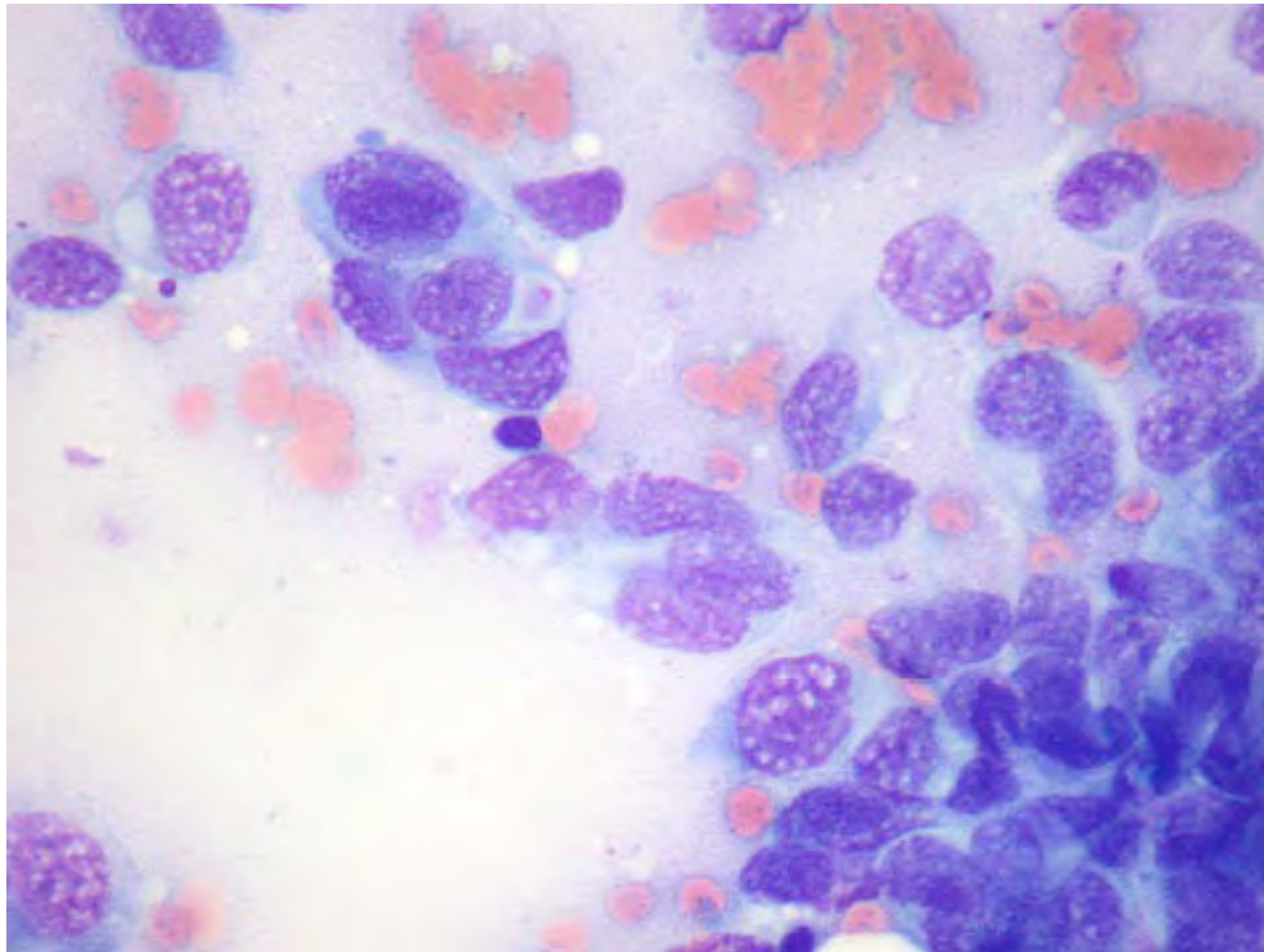
Phyllodes



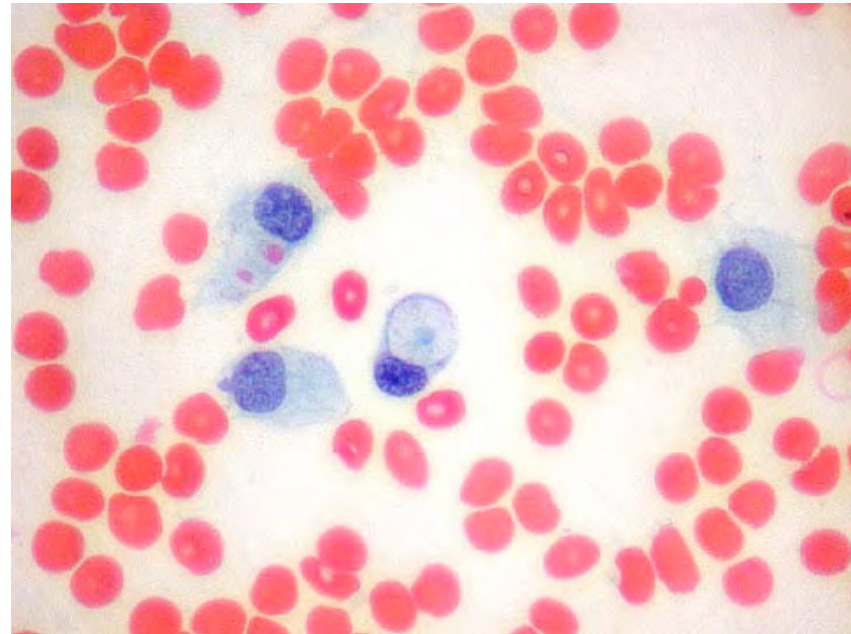
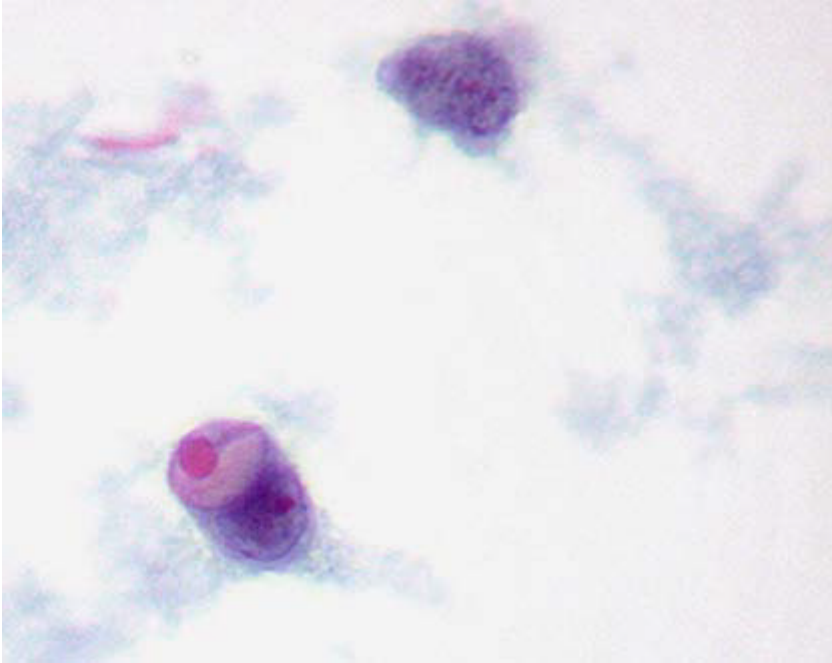
Low grade IDC



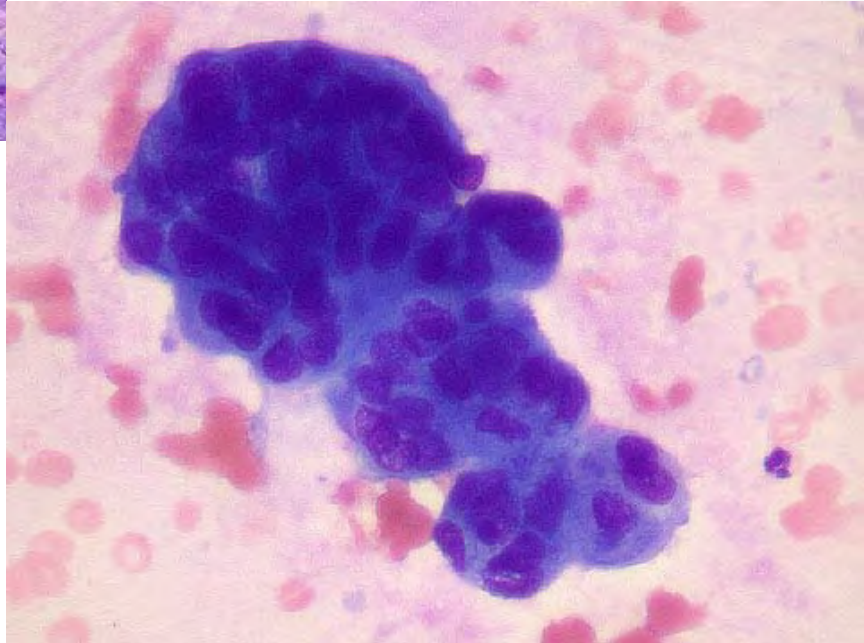
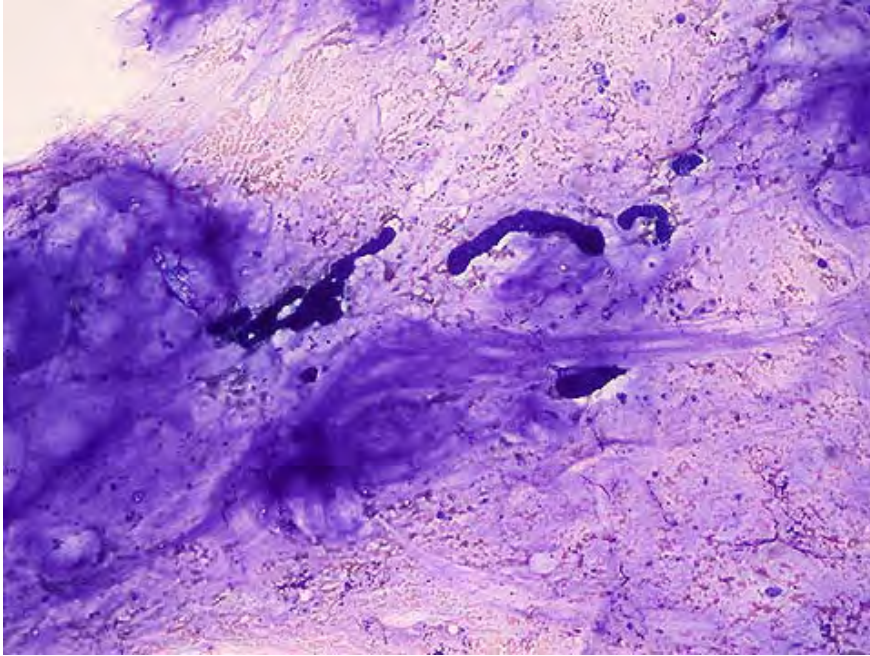
High grade IDC



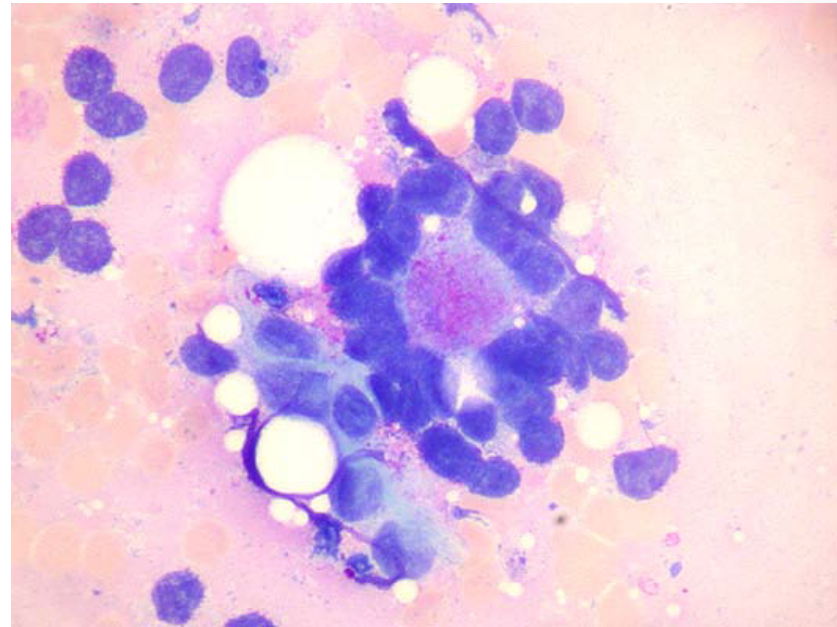
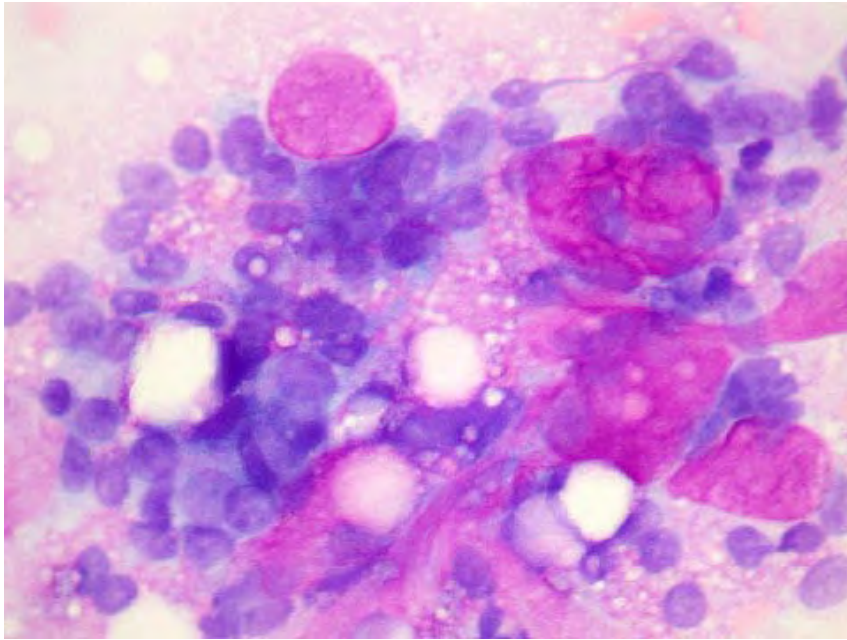
Lobular carcinoma



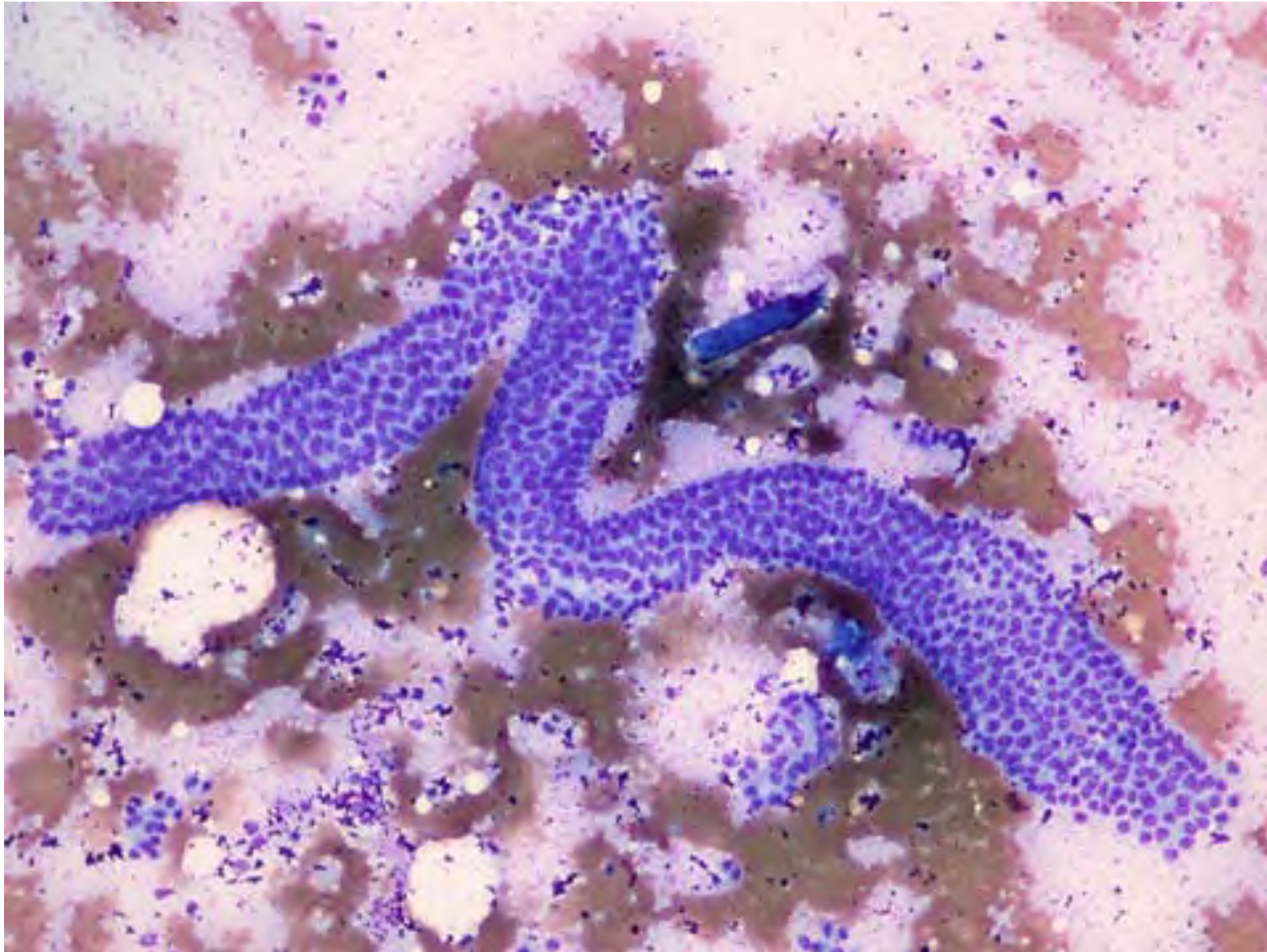
Mucinous carcinoma



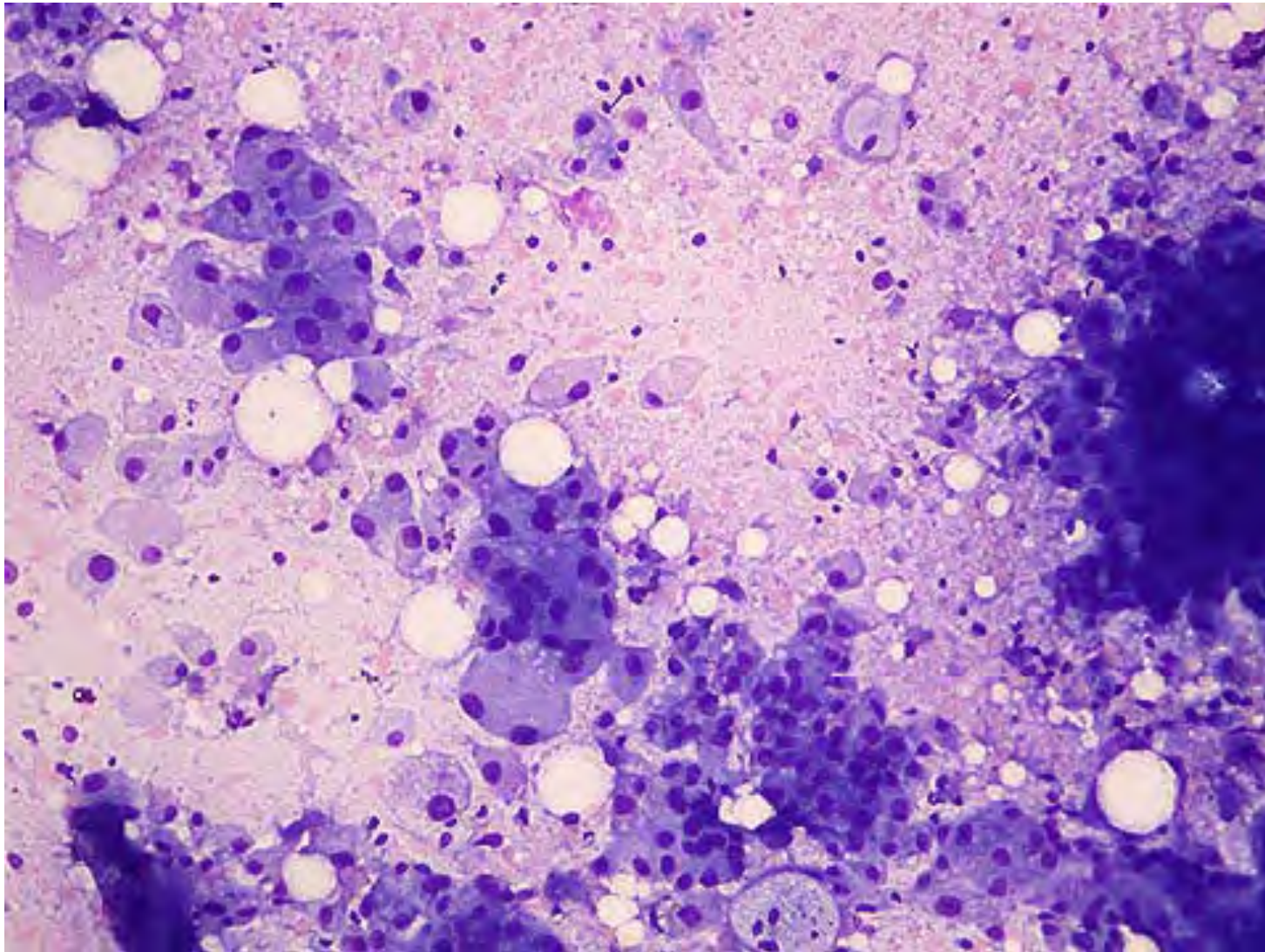
Adenoid cystic carcinoma



Tubular carcinoma



Apocrine carcinoma



What breast cytology cannot do

- Assess architecture
- Cannot be used alone to investigate screen detected lesions and should not be performed for calcification
- Cannot distinguish invasive vs in situ, UTH vs ADH, LVI
- Follicular vs diffuse lymphoma
- ALH vs LCIS vs ILC

Nipple discharge cytology

- Non-invasive, minimal discomfort
- Unilateral discharge
- Not helpful as a screening test, only cells from intraductal processes.
- Sensitivity for malignancy – 41-60%
- No requirements for adequacy, based on judgement –
acellular specimen in nipple discharge can be reported as C2
as no epithelial cells in sample is a benign feature
- A single group with atypical/papillaroid features can warrant a
C3 diagnosis if there is a suspicion of papilloma radiologically

RCPATH 2016 guidance

Table 1: General diagnostic criteria for the recognition of benign and malignant conditions

Criterion	Benign	Malignant
Cellularity	Usually poor or moderate	Usually high
Cell-to-cell cohesion	Good with large defined clusters of cells	Poor with cell separation resulting in dissociated cells with cytoplasm or small groups of intact cells
Cell arrangement	Even, usually in flat sheets (monolayers)	Irregular with overlapping and three-dimensional arrangement
Cell types	Mixtures of epithelial, myoepithelial and other cells with fragments of stroma	Usually uniform cell population
Bipolar (elliptical) bare nuclei	Present, often in high numbers	Not conspicuous
Background	Generally clean except in inflammatory conditions	Occasionally with necrotic debris and sometimes inflammatory cells including macrophages
Nuclear characteristics		
Size (in relation to RBC diameter)	Small	Variable, often large, depending on tumour type
Pleomorphism	Rare	Common
Nuclear membranes (PAP stain)	Smooth	Irregular with indentations
Nucleoli (PAP stain)	Indistinct or small and single	Variable but may be prominent, large and multiple
Chromatin (PAP stain)	Smooth or fine	Clumped and may be irregular
Additional features	Apocrine metaplasia, foamy macrophages	Mucin, intracytoplasmic lumina

Reporting categories - breast

Reporting C codes	Definition	Other comments
C1	Inadequate (subjective) Does not include cysts, abscess, IM lymph node, fat necrosis	Hypocellular, error in spreading/staining, excessive blood, crush
C2	Benign (includes FA, fat necrosis, granulomatous mastitis, abscess, lymph node)	Regular ductal epithelium, cyst, fibrofatty fragments
C3	Atypia probably benign (inc papillary lesions and suspected phyllodes)	Pleomorphism, loss of cohesion, increased cellularity (no definitive surgery)
C4	Suspicious of malignancy	Scant/poor preservation but some features of malignancy/occasional malignant cells (no definitive surgery)
C5	Malignant	Overt malignant features, not based on a single criterion

Pitfalls

- ADH vs DCIS vs IDC low grade
- Columnar cell change (mimic ILC)
- Lactational change (dissociation)
- Radiotherapy changes (dissociation and pleomorphism)
- Intramammary lymph nodes
- Degenerate cells in cyst fluid
- Granulomatous mastitis (MNGC, inflammation)
- Granular cell tumour – eosinophilic granular cytoplasm on Pap
- Adenomyoepithelial lesions – presence of bare nuclei
- Collagenous spherulosis – granular purple globules – AdCC

- Tubular carcinoma – more regular and monotonous
- Lobular carcinoma – low cellularity, sparse cells
- Apocrine carcinoma – cellular smears, resemblance to benign, uniform cells with nuclear atypia, necrosis
- DCIS – Cannot be distinguished from invasive on cytology alone
- Carcinoma with fibro-elastosis – sparse cellularity
- Phyllodes – intact stromal cells, may see mitoses, crossover with fibroadenoma
- Metastatic tumour – Melanoma, small cell carcinoma, RCC, SCC
- Lymphoma
- Malignant stromal tumours – dissociated malignant spindle cells – spindle cell carcinoma (metaplastic) versus sarcoma

Axillary lymph node FNA

- 21 gauge needle, more common than biopsy
- Biopsy appropriate for C1-3 from suspicious node/node >20mm
- Longitudinal to transverse axis ratio less than 2
- Concentric/eccentric thickening of cortex >2-2.5mm
- Loss of fatty hilum
- US plus FNA/CNB will detect metastases in 45-50% of cases
- All patients with primary breast cancer and negative FNA/Core are candidates for SLNB/other axillary procedure

Reporting categories – lymph node

Reporting C codes	Definition	Other comments
LC1	Inadequate	No lymphoid cells/ technically inadequate
LC2	Benign	Benign lymphoid cells regardless of whether reactive features seen
LC3	Atypia	Atypical cells present (lymphoid/other) can be used for LG lymphoma
LC4	Suspicious of malignancy	Lymphoma/metastasis – single/small groups only
LC5	Malignant	Metastatic carcinoma or other malignancy

Pitfalls

- Benign lymph node inclusions – melanocyte rests, epithelial inclusions
- Macrophages – mimic carcinoma cells, granulomatous lymphadenitis, dermatopathic lymphadenitis
- Lymphocytes from inflammatory skin disorder

Exam tips

- Fewer centres performing breast cytology routinely so more challenging to gain experience
- Expect a C2 or a C5 case, C3 cases are unlikely due to inter-observer variation and issues regarding appeals
- Fibroadenoma, fibrocystic change, fat necrosis are common C2
- Reactive axillary lymph node aspirate LC2
- Metastatic carcinoma in axillary lymph node
- Malignant breast cytology (unusual to have these cases as M5 U5 lesions are not usually FNA'd), more likely to be as a metastatic lymph node aspirate
- Don't panic, stick to low power first and make your mind up then only go higher to check for bare nuclei
- Include C and LC codes in diagnosis as per RCPATH dataset

References

- Westenend PJ, Sever AR, Beekman-De Volder HJ, et al. A comparison of aspiration cytology and core needle biopsy in the evaluation of breast lesions. Cancer 2001;93:146-150.
- RCPATH -Guidelines for non-operative diagnostic procedures and reporting in breast cancer screening June 2016
- Rosen PP. Rosen's Breast Pathology, 3rd Edition, 2009; Walter Kluwer/Lippincott Williams & Wilkins, Philadelphia.
- Differential Diagnosis in Cytopathology Book 2nd Edition
- [Paolo Gattuso](#), [Vijaya B. Reddy](#), [Shahla Masood](#)

Any Questions?
Thanks for listening