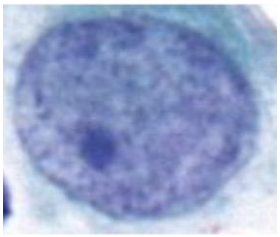
Prepared by Kurt Schaberg

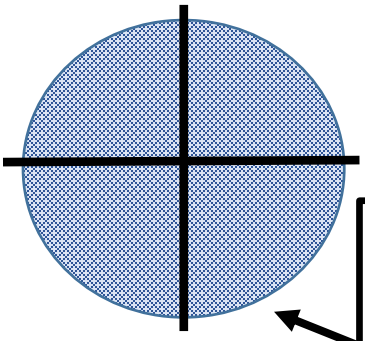
Cytology Basics

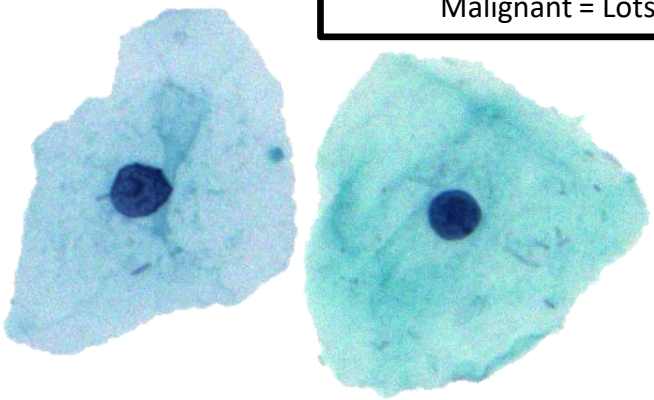
Benign



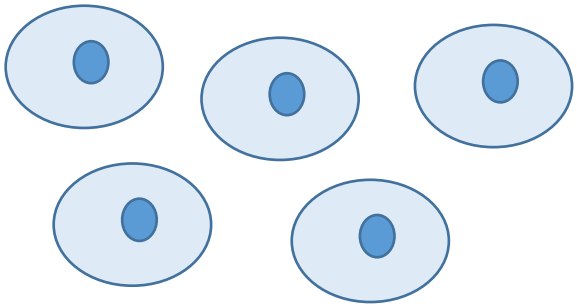
Round nuclei
"Smooth" evenly distributed chromatin

Think: Like a robin's egg

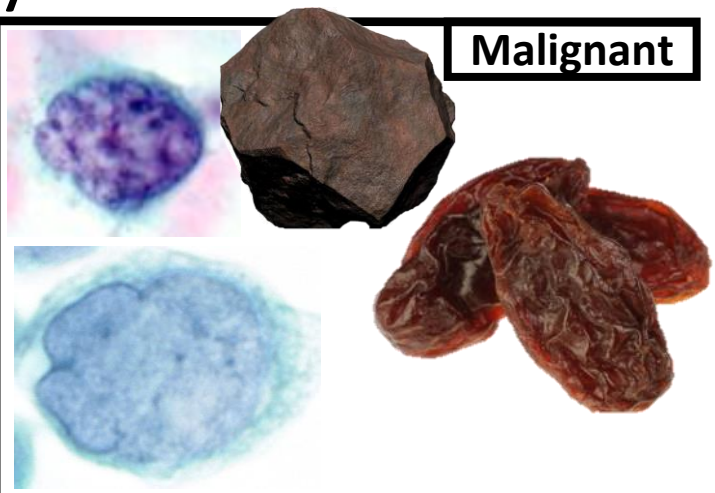




Cells/nuclei look similar to neighbors

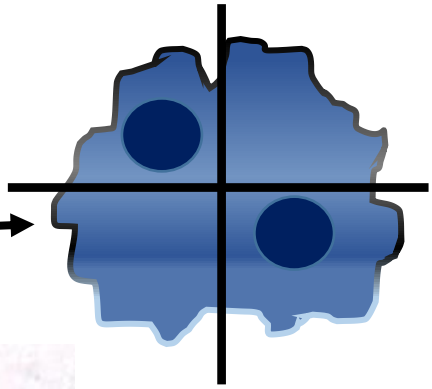


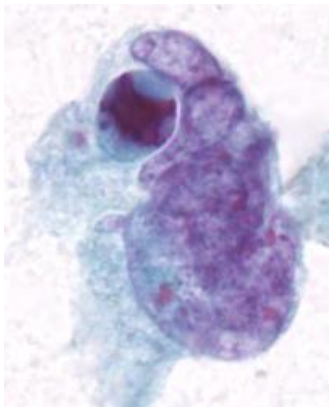
Malignant

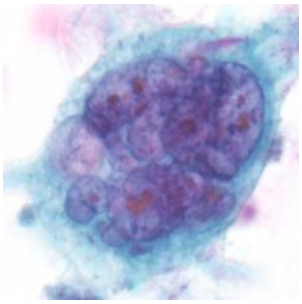


Irregular nuclear contours
Clumped, uneven, vesicular or hyperchromatic chromatin

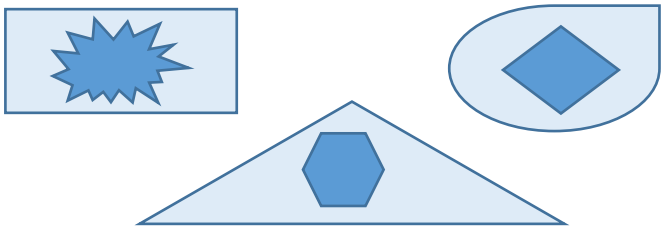
Think: Like a boulder or raisin







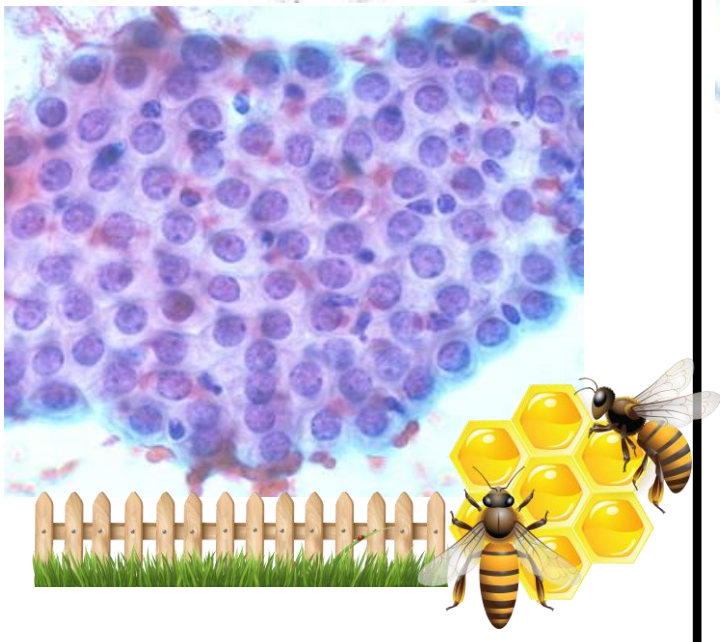
Lots of variation in size/shape of neighboring cells (Pleomorphism)



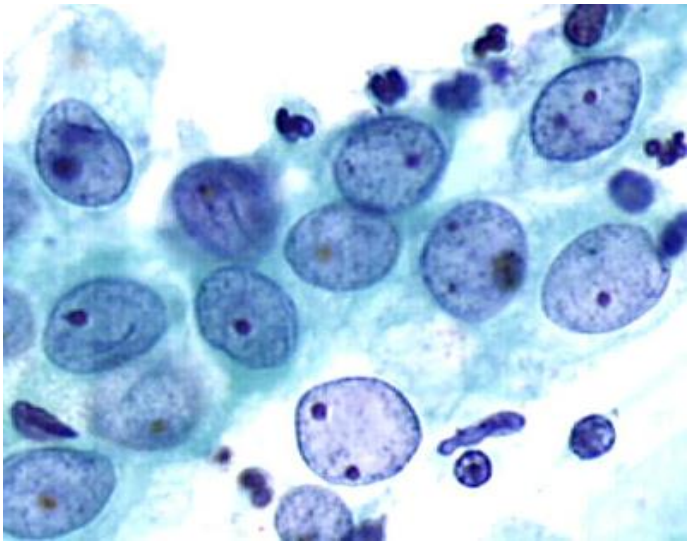
One approach: Mentally divide a nucleus into quarters and compare the chromatin and nuclear contours of each quarter.
Benign = Mostly the same
Malignant = Lots of variability

Benign

Organized cell clusters
Polarized cells (that know which way is up)
"Honeycomb" or "Picket-fence" glandular architecture

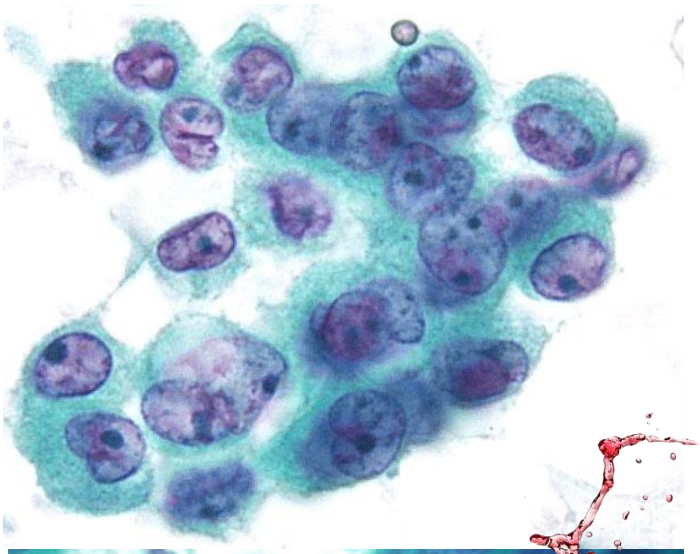


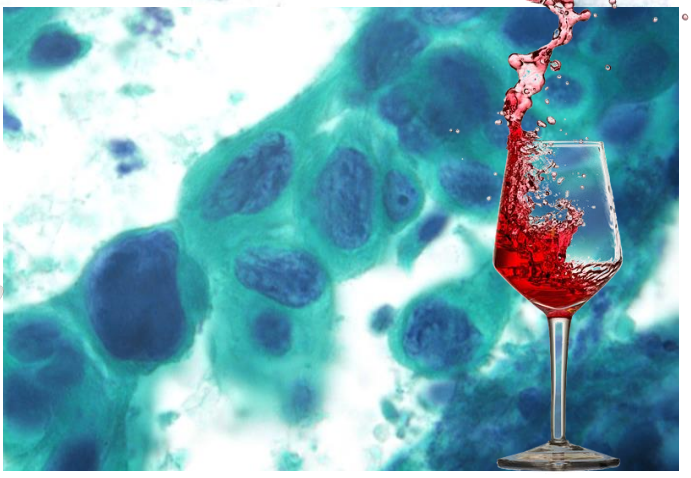
Small, usually inconspicuous nucleoli
Rare mitoses



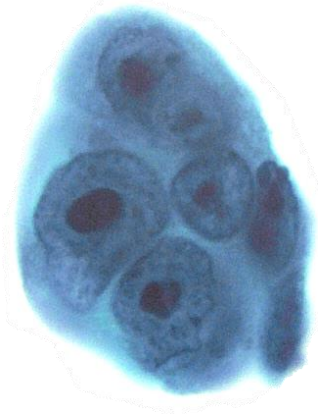
Malignant

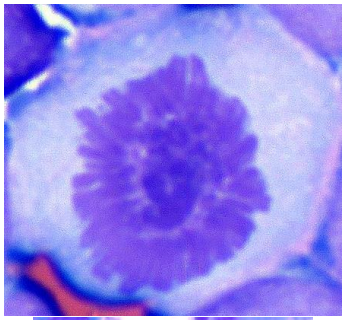
Irregular "Drunken" architecture
Tightly packed together

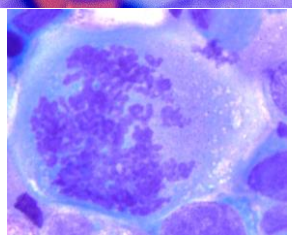




Large, prominent nucleoli (sometimes)
Frequent mitoses, especially atypical

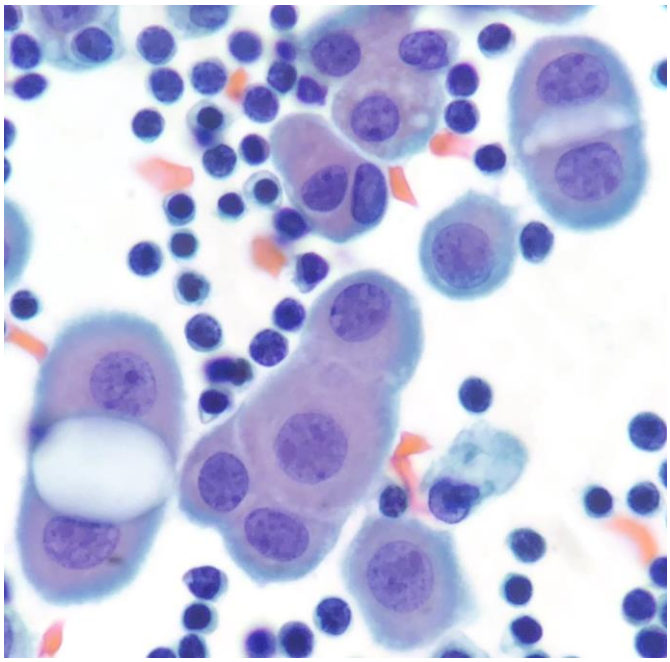




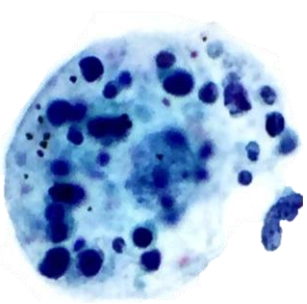


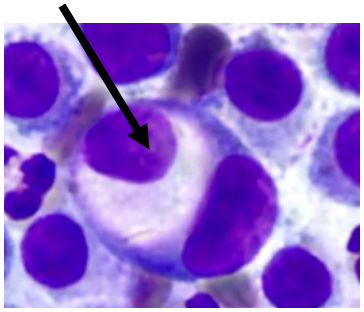
Benign

No nuclear molding



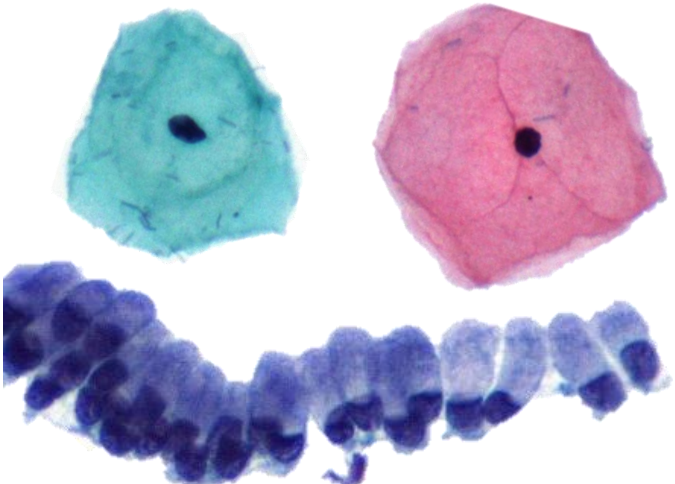
The main phagocytosis of cells in benign processes is by macrophages





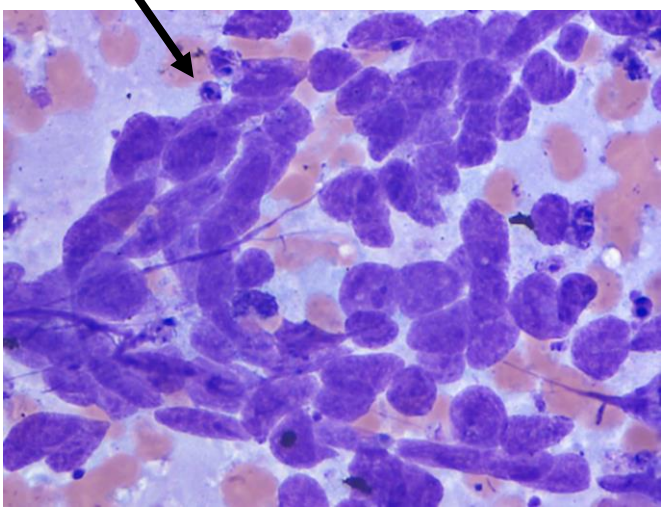
Often Low N:C Ratios

(However, there are obvious exceptions to this, like benign lymphocytes or reserve cells having scant cytoplasm)



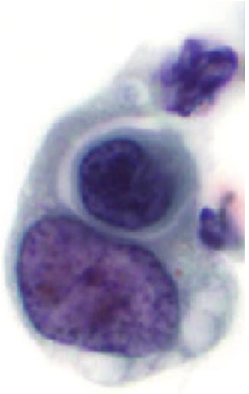
Malignant

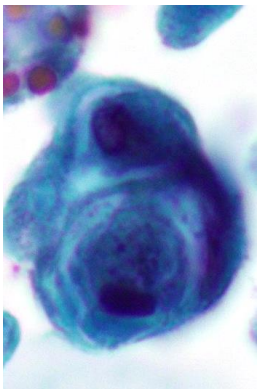
Nuclear molding



"Cannibalism"

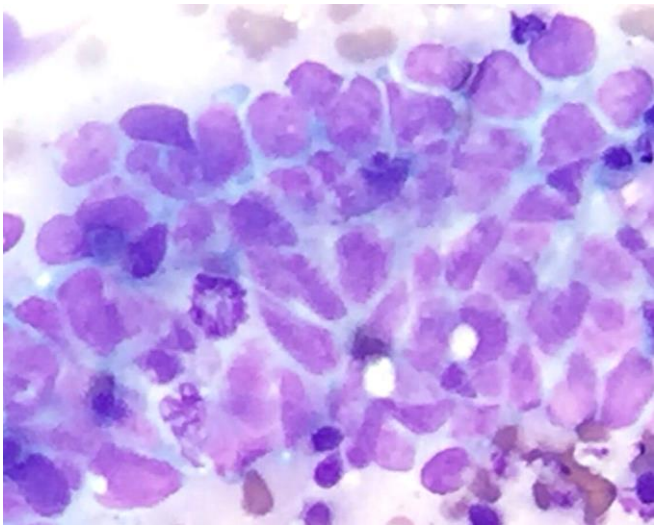
(tumor cells eating other tumor cells)





Often High N:C ratios

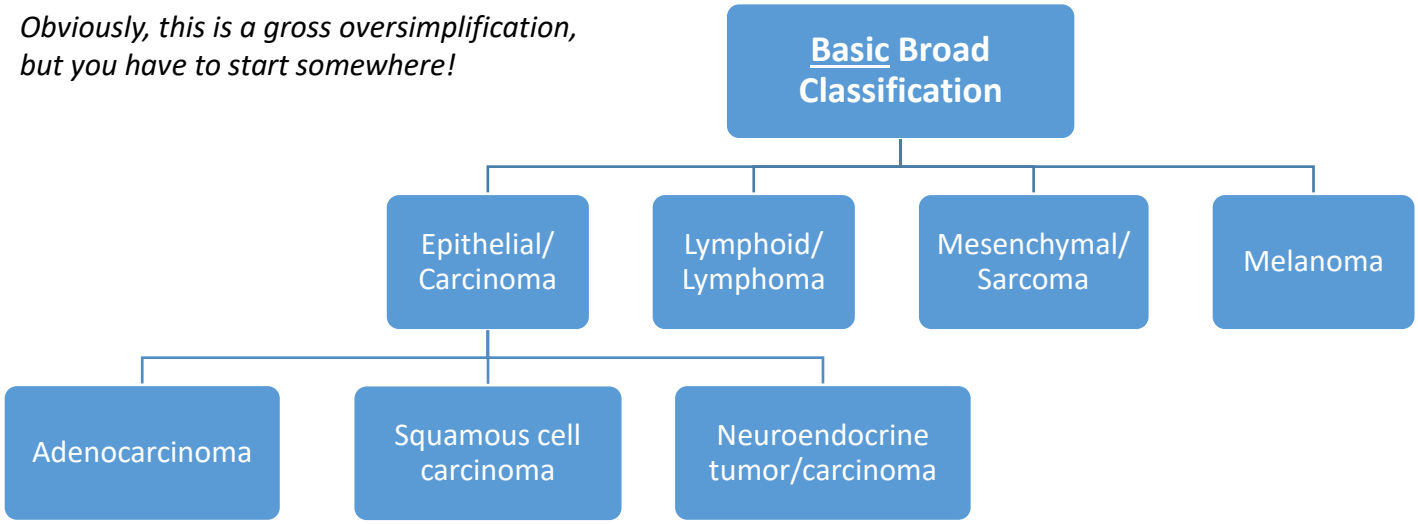
(There are plenty of exceptions to this, for example mucinous carcinomas)



Basic Lines of Differentiation

Always think broadly and first try to put things into a "bucket," then you can get more specific after.

Obviously, this is a gross oversimplification, but you have to start somewhere!

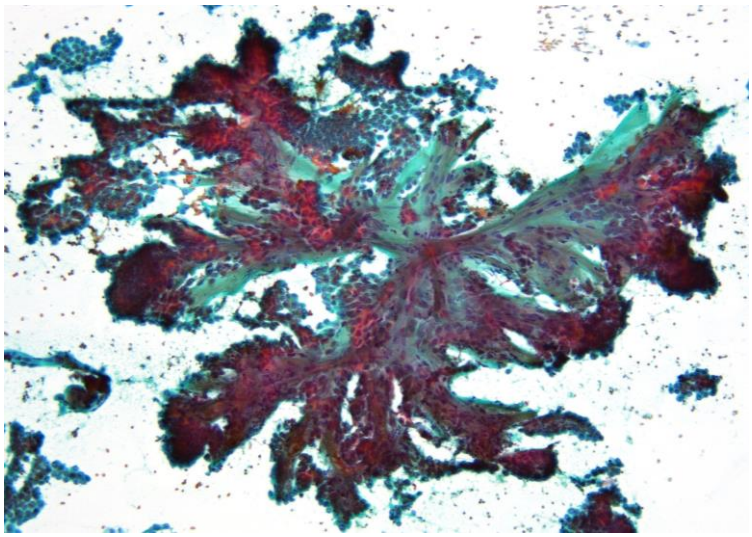


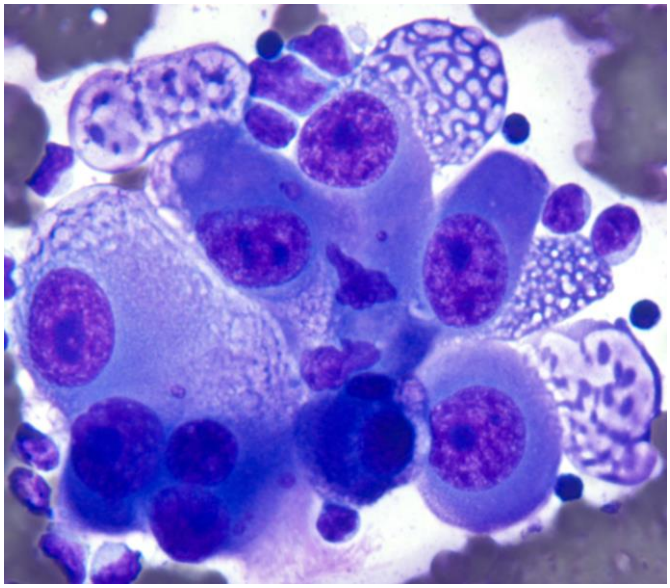
Epithelial cells/Carcinoma

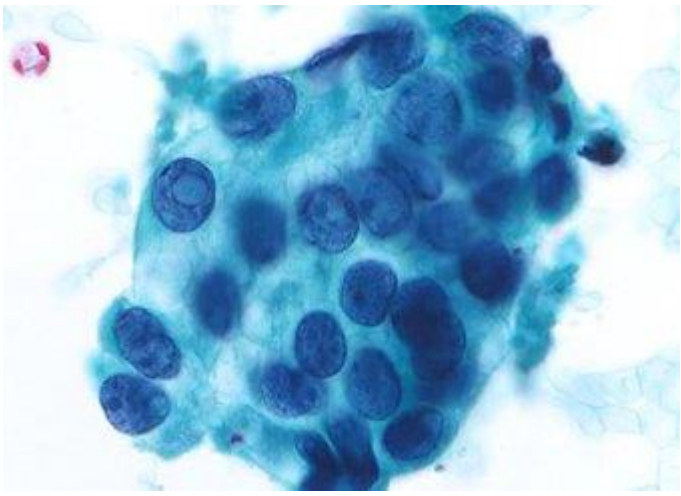
Epithelial cells form structures, so even when smeared, they remain in **cohesive clusters**

Compared to blood cells, they are also **relatively large in size**

They often have moderate to **abundant cytoplasm** (obviously not true of all carcinomas though… I'm looking at you small cell carcinoma!) and therefore appear "*epithelioid.*"







Glandular Cells/ Adenocarcinoma

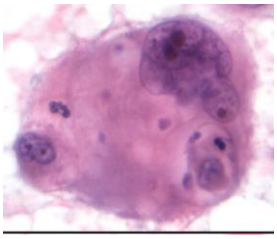
May **form glands** or papillae

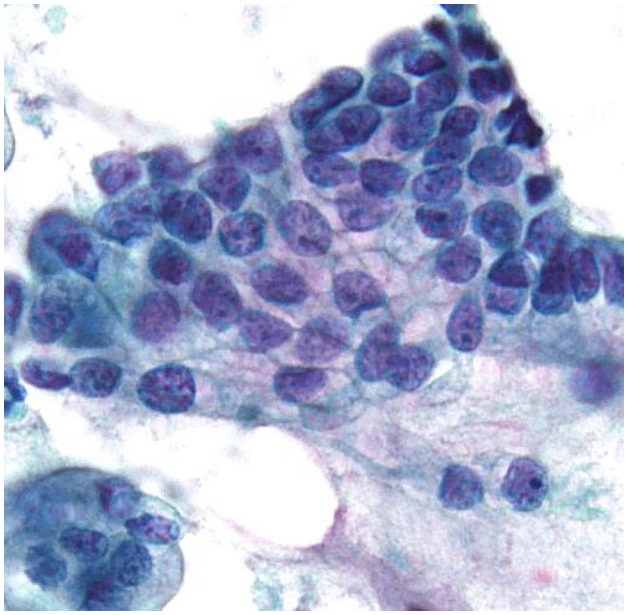
Characteristically **produce mucin**, which may be visible in cytoplasm.

Cytoplasm often appears "**delicate**" (fluffy to granular) with **less distinct cell borders**. Blueish cytoplasm on Pap usually.

Often columnar with nucleus **polarized** at one end.
Can see **Signet ring cells**.

Intracytoplasmic lumina

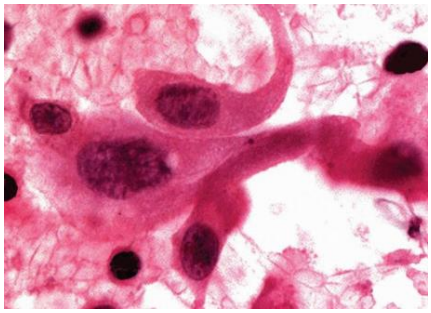




Squamous cell cells/carcinoma

Produce keratin → **Bright orangish on Pap stains**. Can see keratin pearls

Cytoplasm appears "**dense**" with **distinct cell borders**

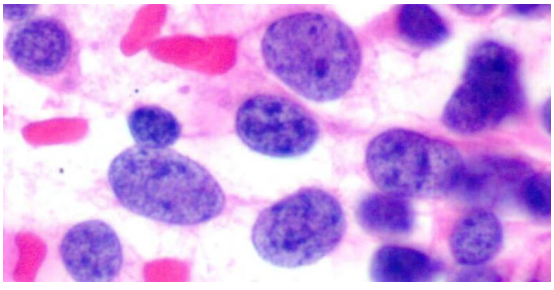


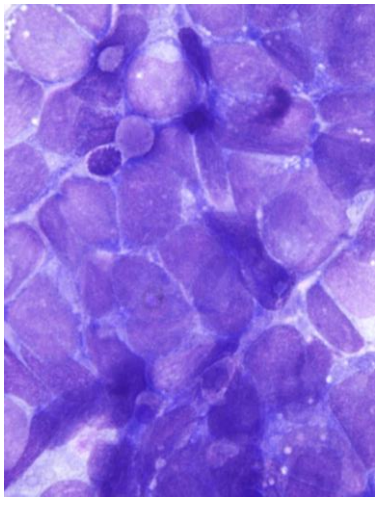
Neuroendocrine Cells/ Tumors

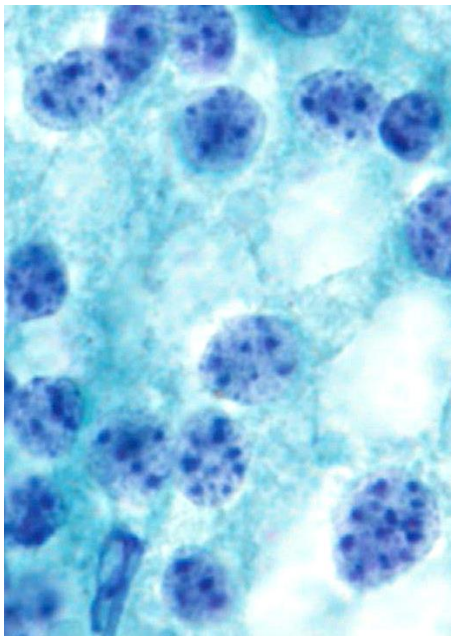
Nuclear **chromatin appears stippled** like "**Salt and Pepper**"

Cells are often **discohesive**

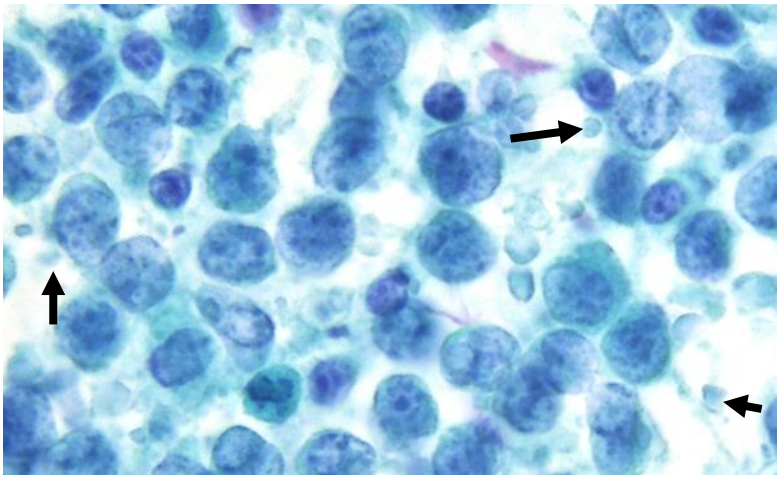
May have granular cytoplasm with secretory granules.







Lymphocytes/Lymphoma



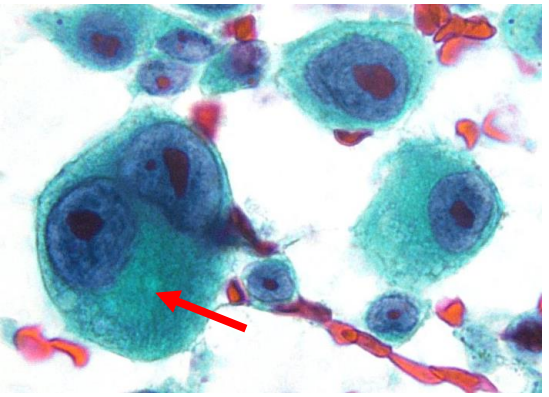
Discohesive small cells (remember, they must circulate through vessels, so they have to be small and loose)

Scant cytoplasm

Lymphoglandular bodies (pieces of lymphocyte cytoplasm that peel off during smearing →)

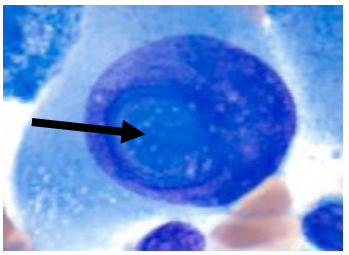
Consider **sending for flow cytometry** at time of adequacy to evaluate for lymphoma

Melanocytes/Melanoma



Large, discohesive cells. Often **very cellular** aspirates.

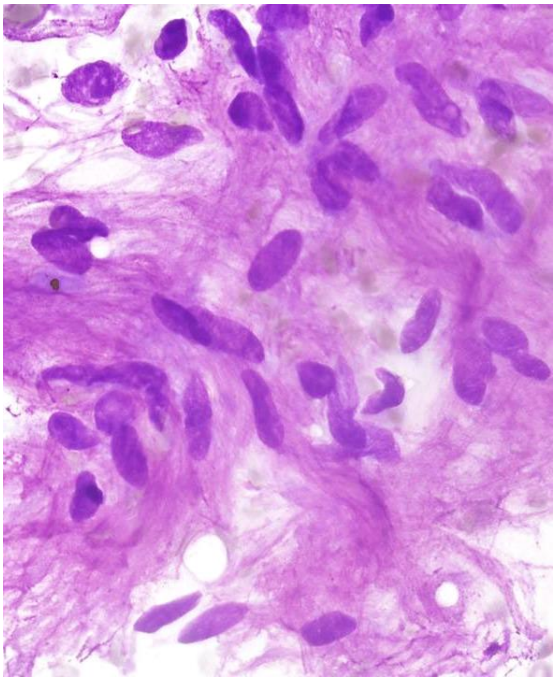
Frequently prominent nucleoli
Double mirror image nuclei (DMIN)
("bug-eyed demons")



Cytoplasmic melanin pigment (→)

Intranuclear pseudoinclusions (→)

Mesenchymal/Sarcoma



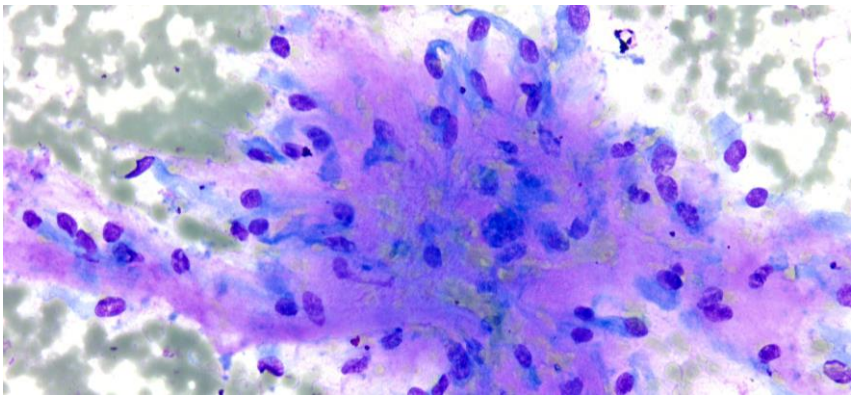
Spindled cells = long, narrow cells with relatively scant cytoplasm and cigar-like nuclei.

Frequent **extracellular matrix**

Neural tumors often have "buckled" or "fishhook" nuclei.

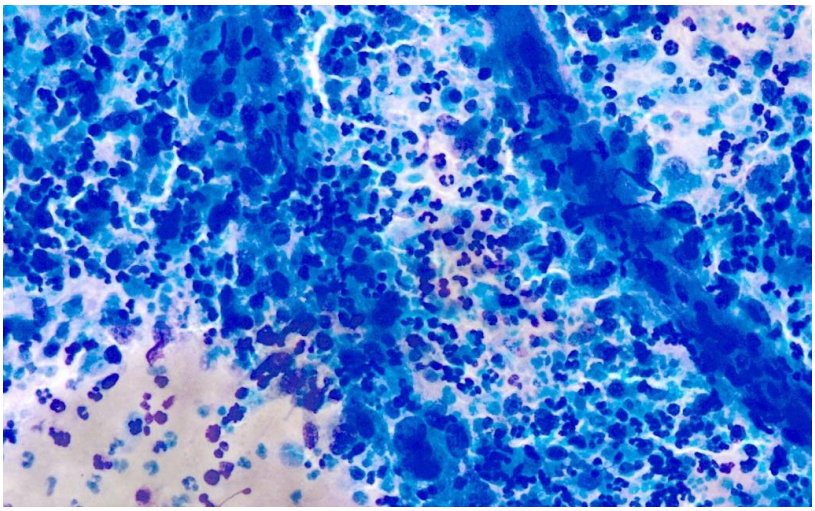
Very variable pleomorphism

Often paucicellular aspirates due to dense extracellular fibrous stroma



Common Non-Neoplastic Findings

Abscess



Abundant Neutrophils (some of which may be degenerating)

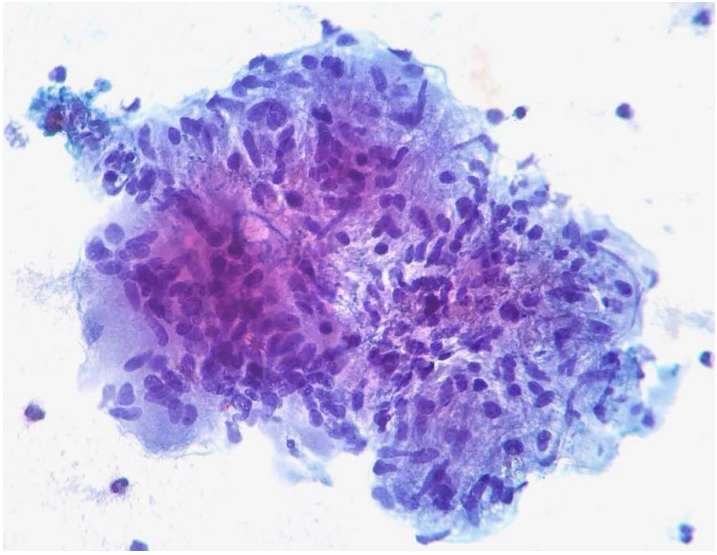
Necrosis and fibrin

Macrophages, bacteria, foreign material

At time of adequacy assessment one will see frank pus. If this happens, remember to **culture it!**

Clinically: Warm, Red, Tender

Granulomas



Nodular collections of **epithelioid histiocytes**
Often in loose **syncytial aggregates**
Can resemble a swirling school of fish

Histiocytes may be spindled or epithelioid with elongated nuclei resembling bananas or boomerangs
Can see **Multinucleated Giant Cells**

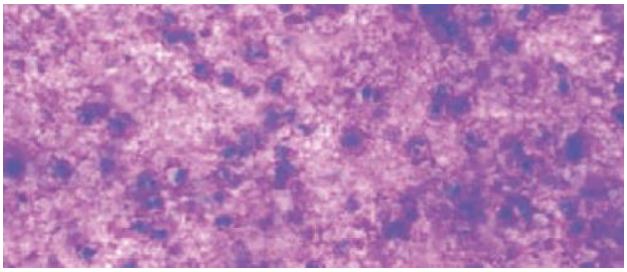
DDX: Infection (esp. TB & Fungi), Sarcoidosis, foreign material→ so try to do **cultures** or at least **bug stains**!

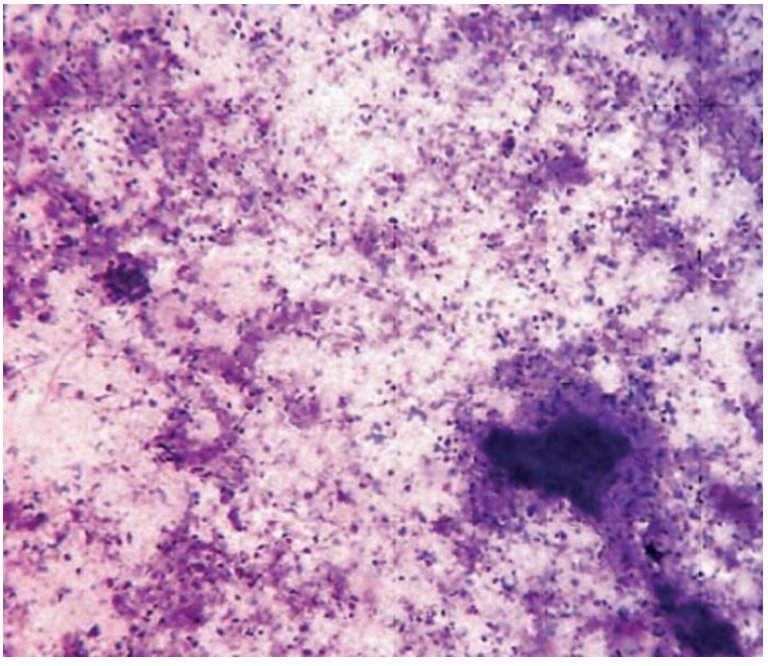
Necrosis

Lots of "**grungy" particle fragments and fibrin** without any nucleated cells.

Can be seen in non-neoplastic processes and neoplastic processes (so look around for viable cells to suggest what might have caused it).

May see **macrophages** trying to clean up.



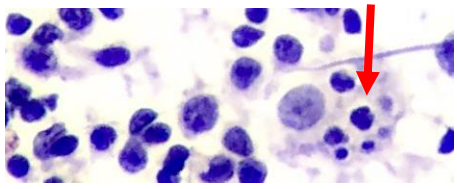


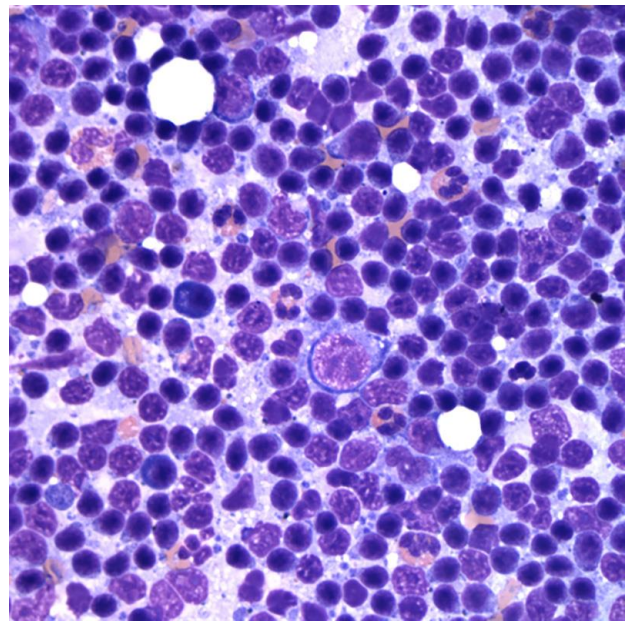
Reactive Lymphoid Hyperplasia

Often very cellular aspirate.
Mixture of small and large lymphocytes (range of maturation) with a **predominance of small lymphocytes**.
Frequently plasma cells and **tingible macrophages** (↓)

May see mitoses

Consider sending for **flow cytometry** at time of adequacy to evaluate for lymphoma





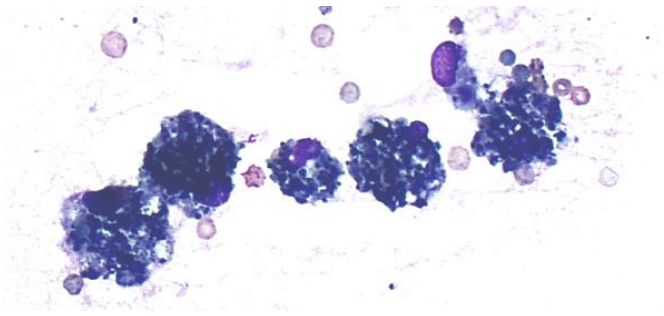
Cyst Fluid

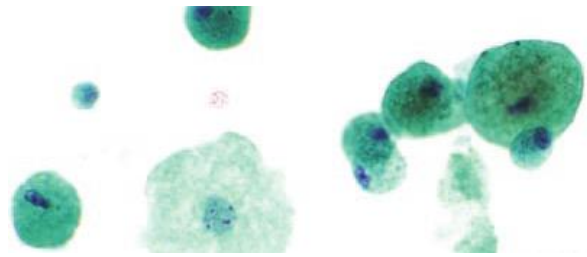
Paucicellular with **scattered macrophages**, which may contain **hemosiderin pigment**

May see scattered debris.

These elements are often non-specific and don't indicate the composition of the cyst lining/wall, so may be "unsatisfactory" for diagnosis.

If possible, drain the cyst and then reaspirate the area in attempt to sample the cyst wall.

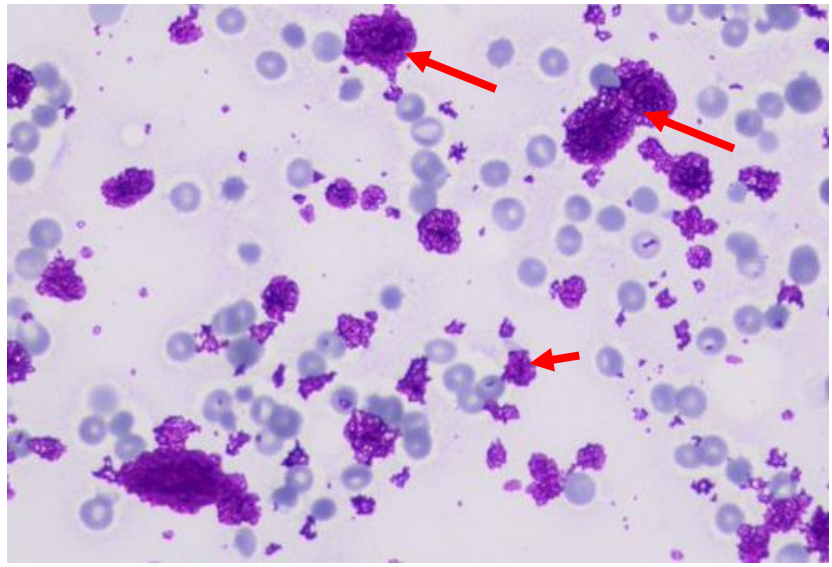




Ultrasound Gel

Coarsely granular metachromatic material on Romanowsky stains.

Can obscure diagnostic material.



(some) Differential Diagnoses

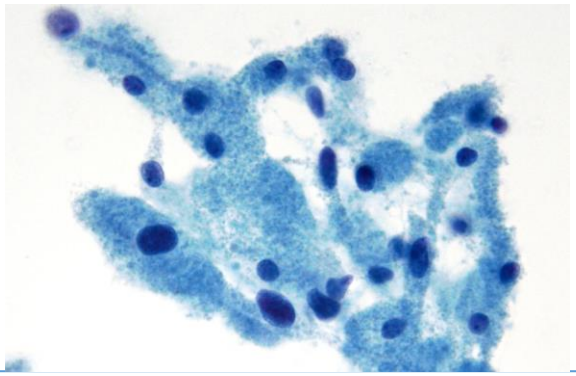
Intranuclear Pseudoinclusions

Develop when the cytoplasm pushes into the nucleus (think: a balloon within a balloon)

- Papillary thyroid carcinoma
- Medullary thyroid carcinoma
- Melanoma
- Liver (benign *and* malignant hepatocytes)
- Meningioma
- Lung adenocarcinoma

Very Granular Cytoplasm

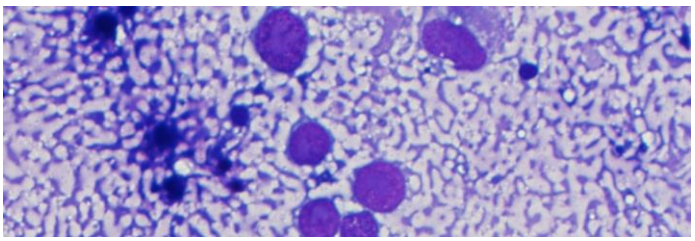
- Granular cell tumor (lysosomes)
- Acinar cell carcinoma (zymogens)
- Oncocytic/Hürthle cell neoplasms (mitochondria)
- Neuroendocrine tumors (neurosecretory granules)
- Hepatocytes/tumors
- Melanoma (melanosomes)
- Adrenal cortical/tumors
- Leydig cells/tumors



Tigroid Background

Seen with glycogen-rich lesions

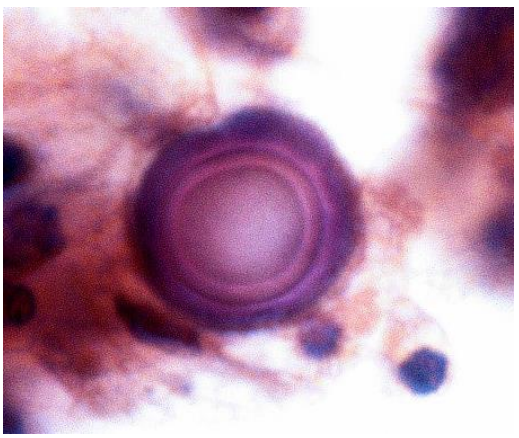
- Seminoma/Dysgerminoma (most classic!)
- Clear cell renal cell carcinoma
- Ewing sarcoma/PNET
- Other glycogen-rich tumors



Psammoma Bodies

Frequently seen in papillary tumors

- Papillary thyroid carcinoma
- Serous ovarian tumors
- Mesothelioma
- Papillary renal cell carcinoma
- Meningioma
- Somatostatinoma (duodenum)
- Prolactinoma (pituitary)
- Lung micropapillary adenocarcinoma



Based on: The Book of Cells: A Breviary of Cytopathology, by Dr. Richard Mac DeMay