

# Effusion Cytology

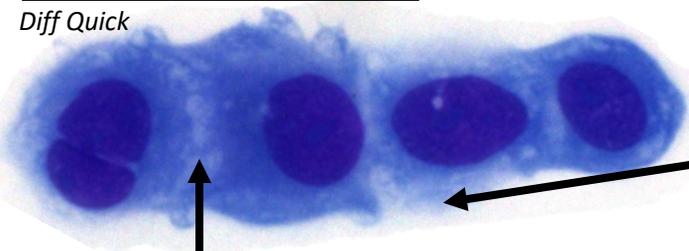
## Normal Components

Fluid sources: Peritoneum, Pleura, and Pericardium  
(Mesothelium-lined cavities)

### Mesothelial Cells

“Mesos”

Diff Quick

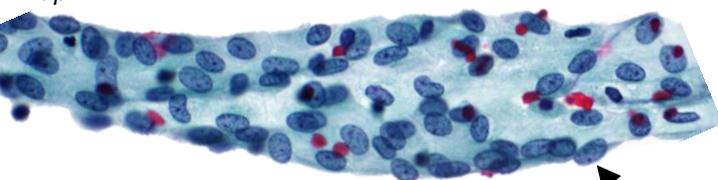


**Round, central nucleus** with coarse chromatin.  
Abundant dense cytoplasm.

“**Lacy skirt**” (where the cytoplasm is denser closer to the nucleus) due to surface microvilli (visible on EM) → causes characteristic “**windows**” between mesothelial

Pap

Window



Can be multinucleated.  
Variably prominent nucleoli.

#### In effusions:

Cells often present as dispersed single cells.  
Mesos often adhere to each other in pairs

Cell block: H&E



#### In washes:

(take during surgery → larger tissue fragments)  
Mesos often present in large monolayer sheets  
Well-organized, honey-comb appearance  
Little nuclear overlap

Mesothelial cells can take on phagocytic roles and essentially exist on a morphologic spectrum with histiocytes, making them sometimes impossible to tell apart morphologically.

In response to inflammation/trauma, mesothelial cells can become “**Activated**” and look very scary!

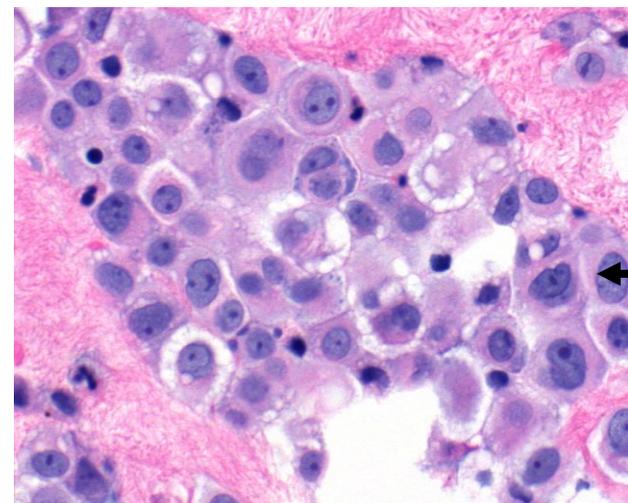
#### Activated findings include:

- Prominent nucleoli
- Larger cell size and Multinucleation
- Denser, two-toned cytoplasm
- Mitotic figures
- Vacuolization (mimicking signet ring cells)
- Cytoplasmic blebs
- Hugging (engulfing/canibalization) other mesos

BUT, they should still have smooth nuclear contours

**Positive stains:** Calretinin, D2-40, CK AE1/AE3, CK7, CK5/6, WT-1, Mesothelin,

**Pericardial** mesos are famous for being **SUPER “activated”** (think of all the trauma of continuous beating!). Be very cautious diagnosing metastatic carcinoma there and do stains!



# Histiocytes

**Peripherally located grooved/folded/indented/curved nuclei**

(smaller than mesothelial cell nucleus)

**Abundant foamy cytoplasm**, often containing debris

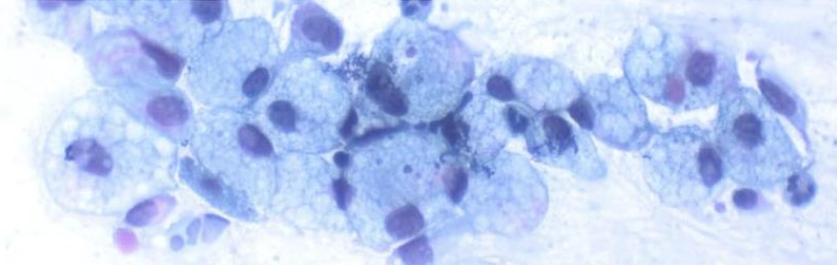
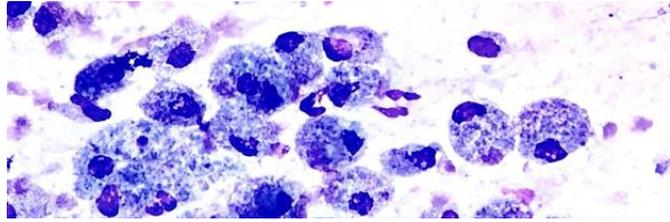
(more cytoplasm than lymphocyte)

Sometimes can also see monocytes (which become macrophages after activation), derived from marrow.

Smaller, rounder cells with oval, indented nuclei.

“Raked” chromatin

**Positive stains:** CD68, CD163



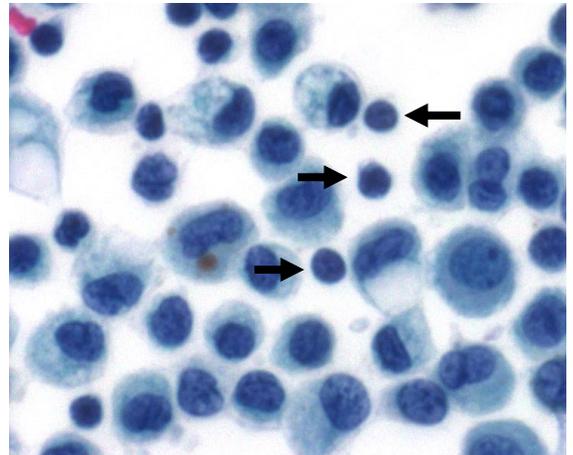
# Lymphocytes

Small cells with a single round nucleus.

Thin rim of cytoplasm.

A few is normal, especially in chronic effusions, but if there are A LOT of lymphs think about:

- Lymphoma (Consider flow, or stain a cell block)
- Tuberculous effusion
- Chylous effusion
- Metastases

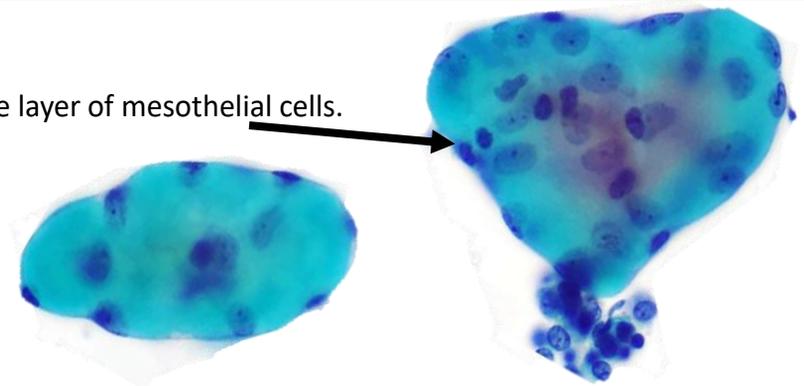


# Collagen Balls

Sphere of collagen surrounded by a single layer of mesothelial cells.

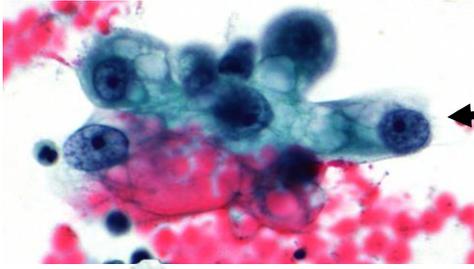
See in pelvic washes, likely from ovary.

Benign, incidental finding.



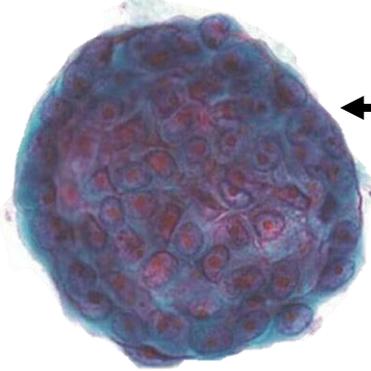
# Malignant Effusions

## Metastatic Adenocarcinoma



Second population of “**Foreign**” epithelioid cells (in addition to mesos)

Cytologic **atypia** (although sometimes bland)  
**Mucin** production/intracytoplasmic lumina  
 Often larger than Medium-sized mesos  
 Well-defined cell borders (no lacy skirts)  
 Delicate cytoplasm (with mucin vacuoles)



**Large cell groups** (Often balls, papillae, or caterpillars)  
 “**Cannon balls**” → specifically suggests breast origin  
 Classically with “**smooth community borders**”  
 (Knobby borders favor mesos)  
 On cell block, often a “**halo**” around tumor cluster  
 (other cell/material retracted away)

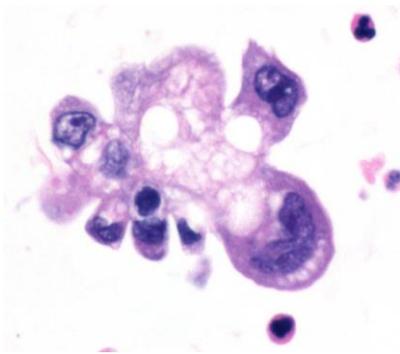
Beware, some adenocarcinomas (notably lobular breast and gastric signet-ring carcinoma) shed as single-cells, making them hard to spot on H&E

Often best to have a low threshold for IHC.

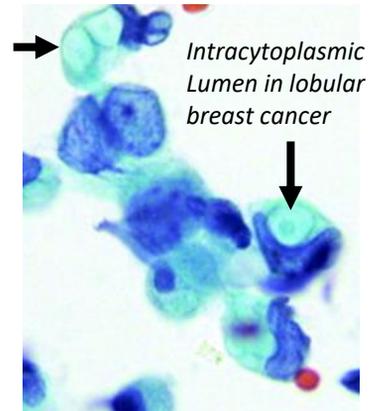
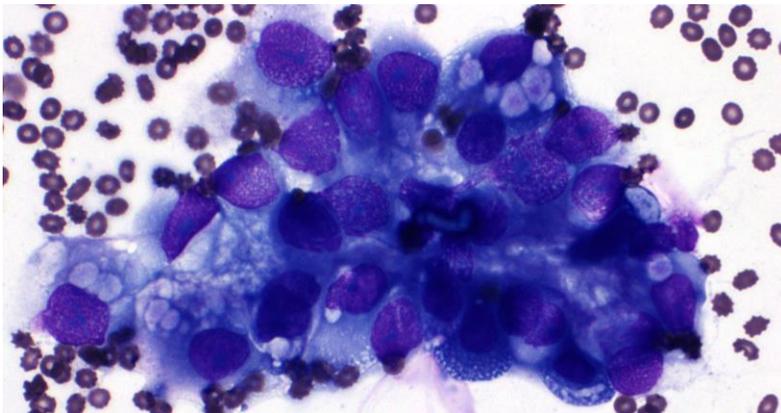
### IHC Panel to differentiate from mesos (*Generally*):

Metastatic Adenocarcinoma	Mesothelial cells
BerEP4	Calretinin
MOC31	D2-40
B72.3	WT-1
Claudin-4	CK5/6

Adeno stains that can also get mesos: PAX8, CK7, AE1/AE3  
 Meso stains that can also get carcinomas: WT-1, CK5/6



Look at how **BIG** these cells are (note RBC for comparison)!



Intracytoplasmic Lumen in lobular breast cancer

## Lymphoma

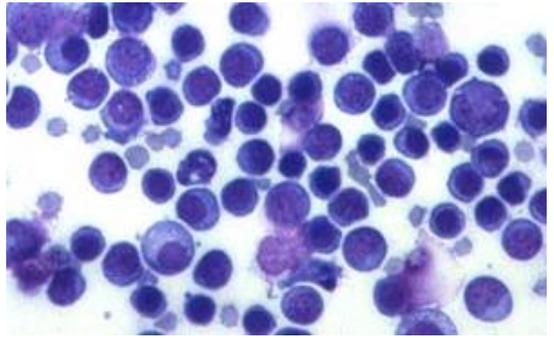
Often occur late (with an established Dx)  
Cause chylous effusions often (milky white)  
Dominated by lymphocytes

**Single disclosive cells** (of varying size depending on type)  
If high-grade: Lots of big cells, mits, and karyorrhexis  
Consider sending flow or staining cell block.

### Primary Effusion Lymphoma:

Occurs in immunocompromised patients (often AIDs). Aggressive. Involves pleura, peritoneal fluid, or pericardium without solid component. Big, ugly cells (high-grade). Positive: HHV8, EBV, CD30. MYC overexpressed.

Interestingly, there is a form of this lymphoma that occurs in the setting of breast implants. However, this seems to be rare and indolent in comparison.



## Malignant Mesothelioma

Most commonly older men in pleural cavity due to asbestos exposure.  
Poor prognosis. Classically forms rind-like encasement of lung.  
Histologically, can be epithelioid, sarcomatoid, or both (biphasic)

First specimen often pleural fluid, but classically very hard to dx.

All mesothelial cells (no "foreign" second population)

Often maintain similar cytologic features (lacy skirts, etc...)

Can be cytologically malignant or relatively bland

**"More and bigger cells, in more and bigger clusters."**

Large clusters with knobby, flower-like contours

The diagnosis of mesothelioma has medical and legal implications, so the diagnosis often requires special studies or a tissue biopsy for definitive diagnosis. Otherwise, often signed out as *"Atypical mesothelial proliferation."*



**Special Studies that support the diagnosis of mesothelioma with good specificity (not fantastic sensitivity though):**

**IHC:** BAP1 or MTAP loss

**FISH:** CDKN2A (p16) deletion

Multigene expression profiling panels

### **Mesothelioma on Tissue biopsy:**

- Stromal invasion usually apparent
- Dense cellularity
- Complex papillae, tubules, and cellular stratification
- Cells surrounded by stroma
- Expansile nodules with disorganized growth
- Minimal inflammation

**Useful Article:** Husain AN et al. Guidelines for Pathologic Diagnosis of Malignant Mesothelioma 2017 Update of the Consensus Statement From the International Mesothelioma Interest Group. Arch Pathol Lab Med. 2018 Jan;142(1):89-108.

# Benign Effusions

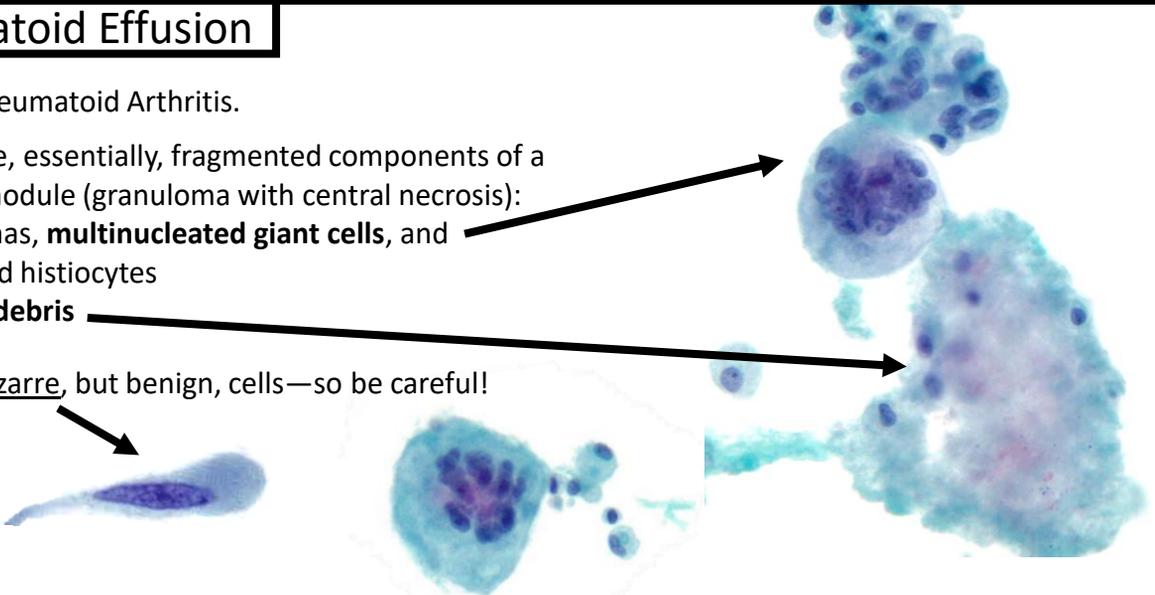
## Rheumatoid Effusion

Seen with Rheumatoid Arthritis.

Classically see, essentially, fragmented components of a rheumatoid nodule (granuloma with central necrosis):

1. Granulomas, **multinucleated giant cells**, and epithelioid histiocytes
2. **Necrotic debris**

Often very Bizarre, but benign, cells—so be careful!

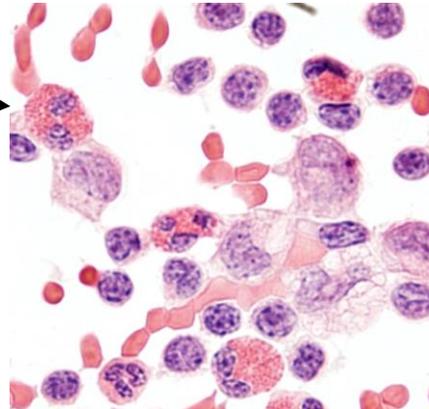


## Eosinophilic Effusion

Abundant eosinophils.  
Rarely malignant.

Often idiopathic, but also associated with:

- Pneumothorax,
- Prior procedure,
- hypersensitivity reaction,
- infection,



## Lupus Effusion

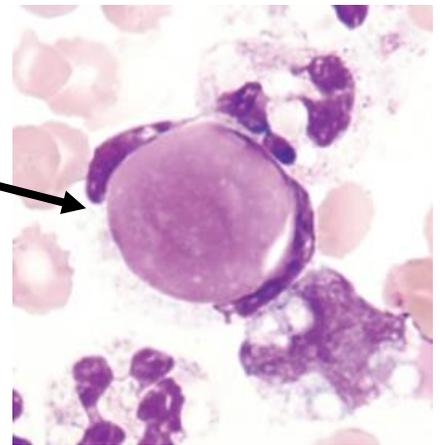
Seen in systemic lupus erythematosus (LE) due to pleuritis.

Classically see "**LE**" cells, which are neutrophils with a phagocytosed nucleus.

Auto-antibodies (e.g., Anti-DNA) attack a cell → the cell dies and the nucleus is shed creating a LE body → this is phagocytosed by a neutrophil.

This finding is not too sensitive or specific, but it is classic and can prompt further testing.

"Tart cells" (phagocytosed nucleus in a macrophage) are more common and even *less* specific.

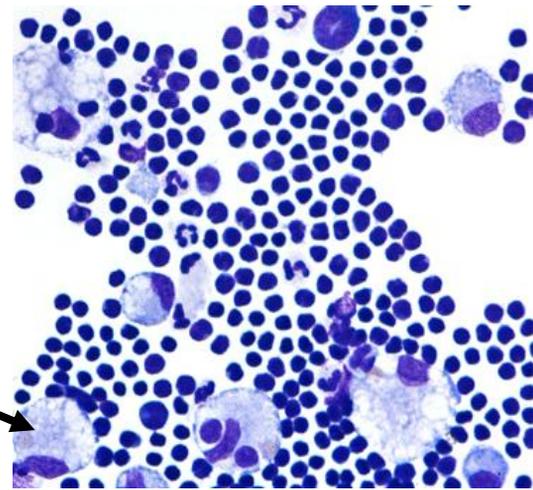


## Chylous Effusion

Caused by leakage of thoracic duct → leaks fatty lymphatic fluid.  
Often caused by lymphoma.

Rich in triglycerides → milky white.

Mostly lymphocytes with some lipophages and mesos.



## Tuberculous effusion

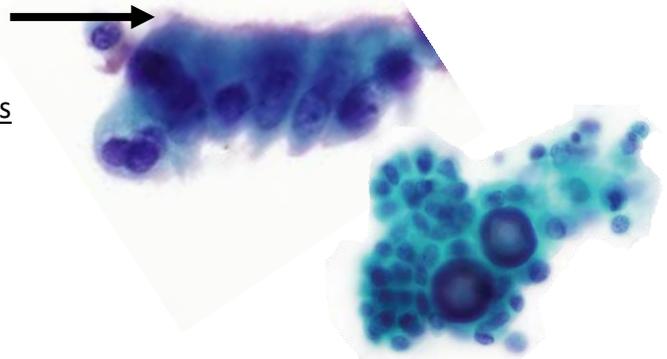
Abundant lymphocytes (T-cells) with sparse mesos.

Histiocytes are present, but giant cells are rare.

## Endosalpingiosis

Fallopian tube-type epithelium present elsewhere.  
Columnar to cuboidal cells with bland nuclear features  
Cilia are unique finding that can be very helpful.  
Can have psammoma bodies

PAX8 positive (like many GYN tumors), so be careful!



## Endometriosis

Can be hard to diagnose without history, but always something to keep in the back of your mind.

Triad:

1. Hemosiderin-laden macrophages
2. Endometrial glands (small columnar cells, similar to mesos)
3. Endometrial stroma (like histiocytes or lymphs)

Cell block can be very helpful!

