

Cytopathology Of Effusions – Clues and Caveats

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Serous Effusion Cytopathology

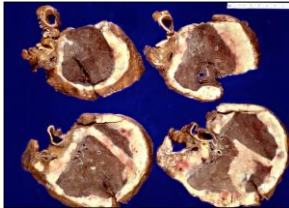
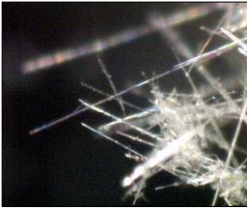
“Diagnostic Issues”

- **Reactive Mesothelial Hyperplasia Vs. Malignant Mesothelioma**
- Malignant Mesothelioma Vs. Metastatic Adenocarcinoma
- Unusual Phenotypes of Metastatic Carcinoma
- Non-epithelial, Non-mesothelial Malignancies Mimicking Adenocarcinoma
- Sarcomatous Effusions
- Effusions In Children
- Lymphocytic Effusions

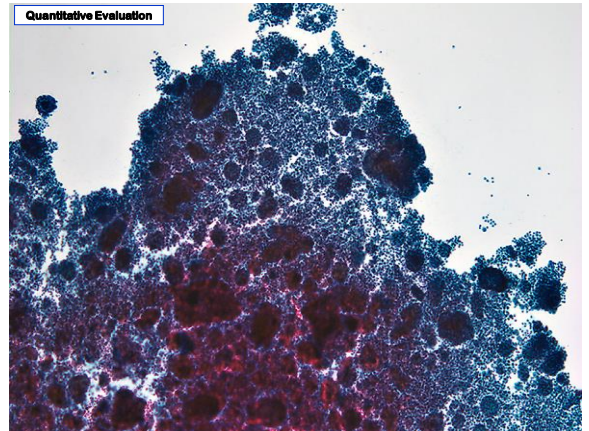
Malignant Mesothelioma

“A Potential Litigation Diagnosis”

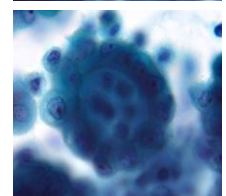
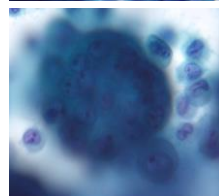
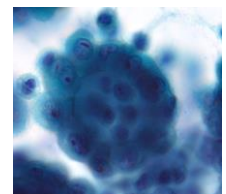
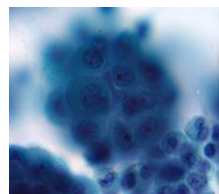
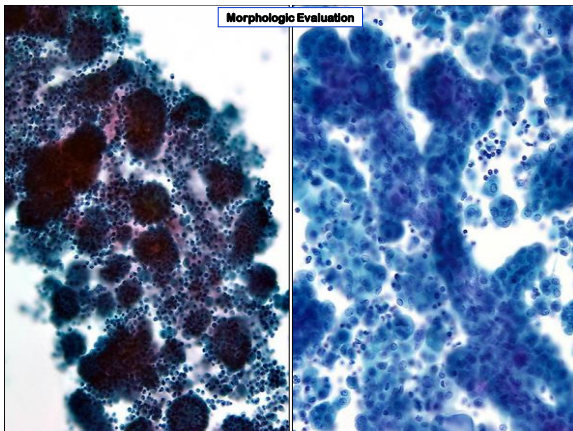
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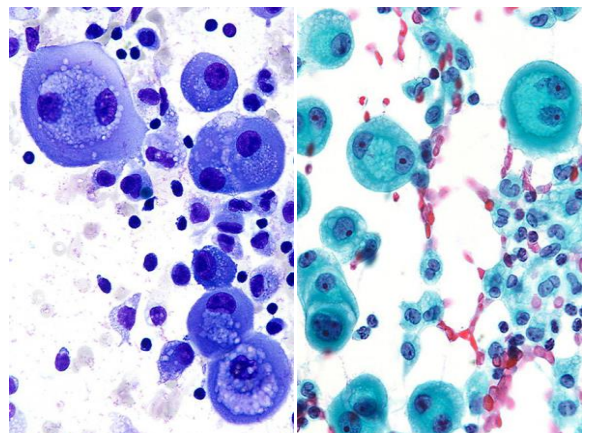
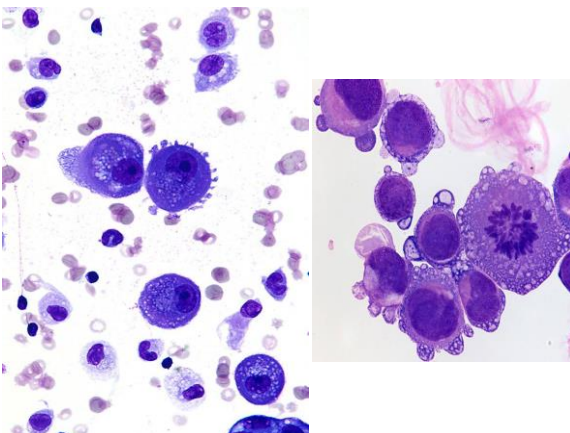
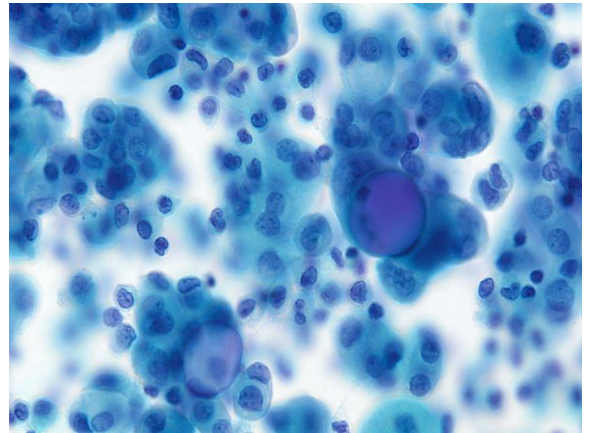
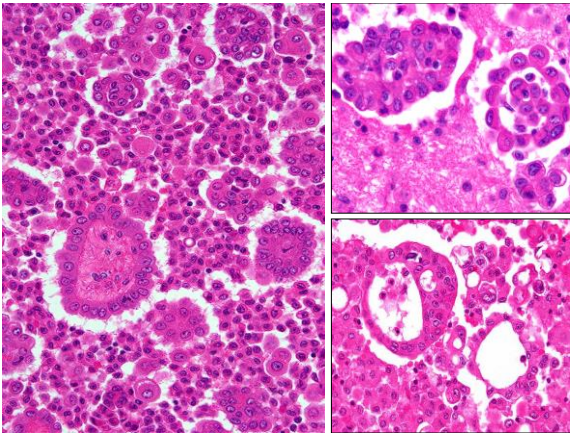
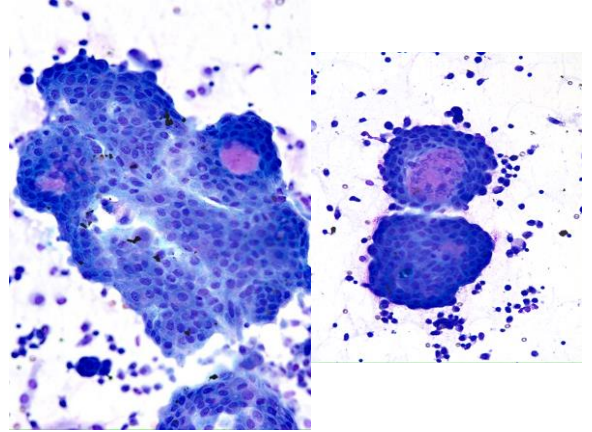
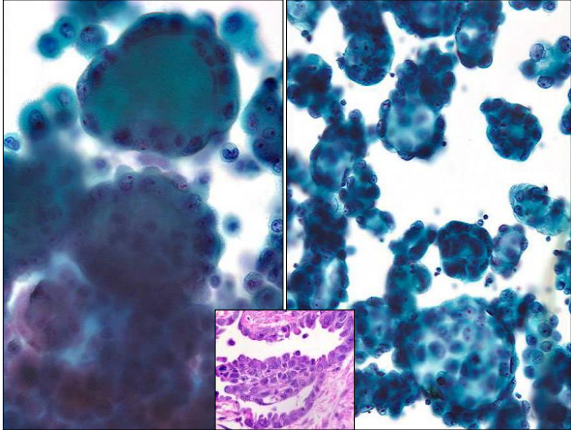


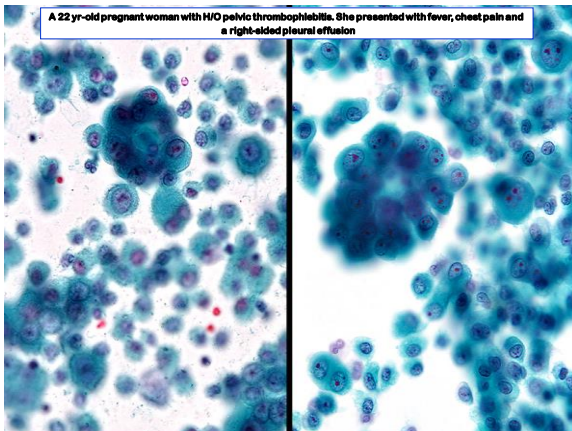
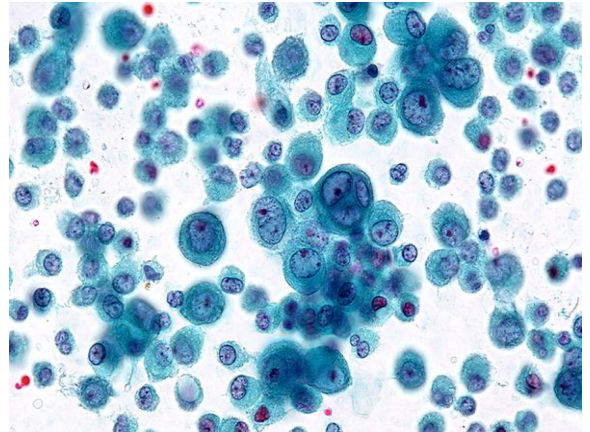
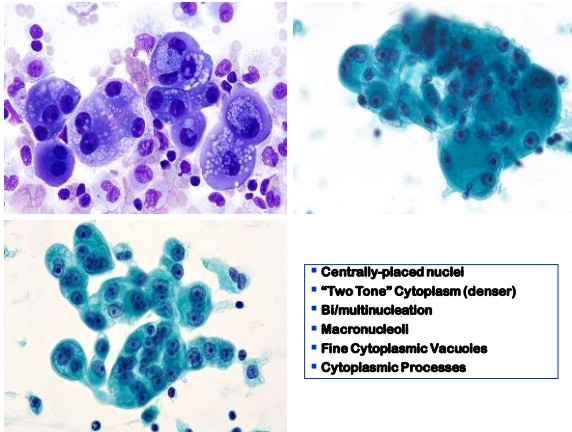
Quantitative Evaluation



Morphologic Evaluation

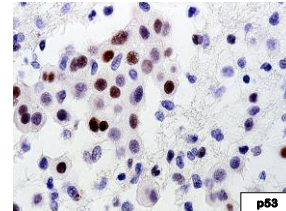






p53 Immunostaining In Mesothelial Hyperplasia Vs. Malignancy

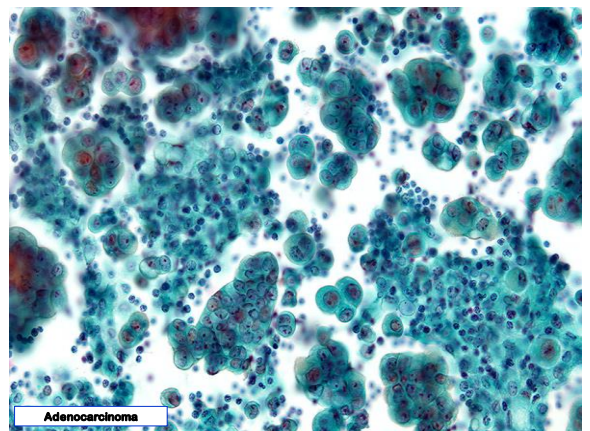
- mo AB Do -7
- Positivity In Malignancy - 32% To 55%
- None Of The Benign Effusions Stained
- Highly Specific (100%)
- Moderately Sensitive

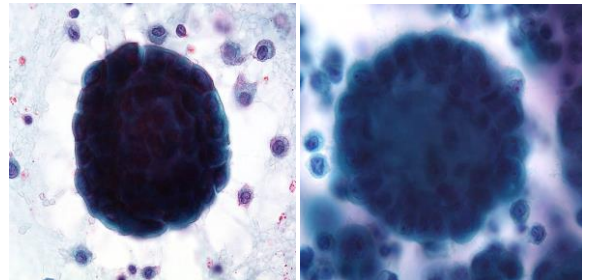
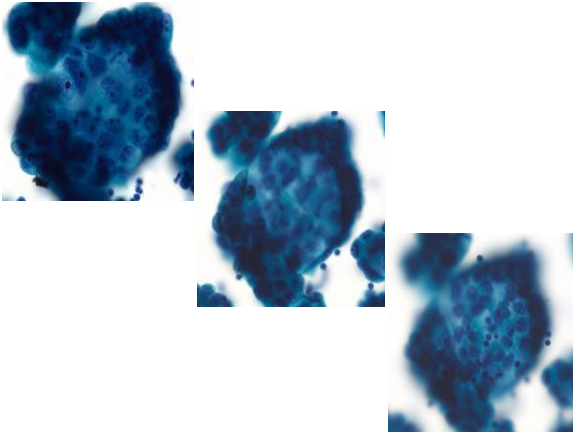


Serous Effusion Cytopathology

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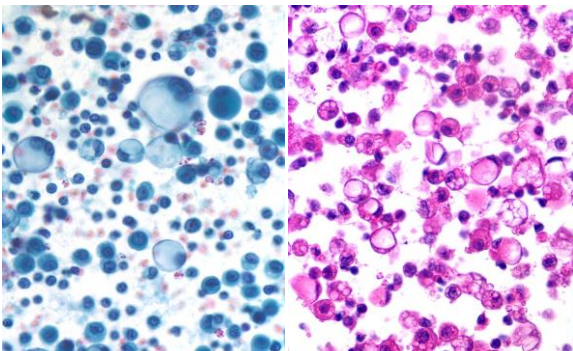
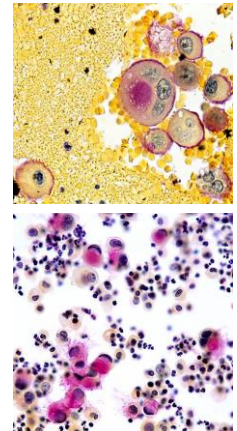
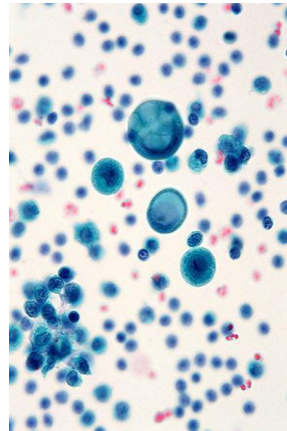


■ Cytochemical Staining

■ IPOX Studies

- Mucicarmine
- PAS, D-PAS
- Alcian Blue, Alcian Blue With Hyaluronidase, (Colloidal Iron)
- Oil Red O

- Mesothelioma – Acidic (mesenchymal) mucin, hyaluronic acid
- Adenocarcinoma – Neutral (epithelial) mucin



Mesothelioma Vs. Adenocarcinoma

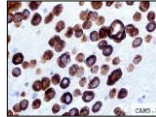
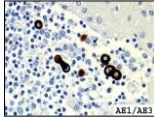
IPOX Markers

- Cytoskeletal Proteins
- Cell Surface Glycoproteins
- Oncoplacental Antigens
- Myelomonocytic Antigens
- Intracellular Calcium-binding Proteins
- Cadherins
- Other Antigens

Cytoskeletal Proteins (Intermediate Filaments)

- Cytokeratins
- Vimentin

- CK (AE1/AE3, CAM 5.2)
 - Almost All Mesotheliomas And Adenocarcinomas Are Positive
- Vimentin
 - Mesothelioma (Epithelial) - Scant Or Undetectable Reaction,
 - Adenocarcinoma - Seldom (Lung) To 50% Positivity
- Very Confusing Profile - Limited Value

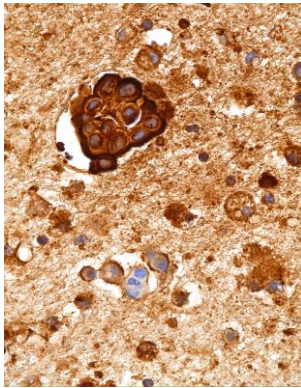
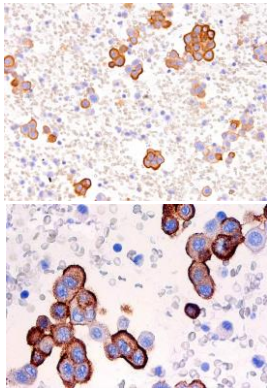


Cell Surface Glycoproteins

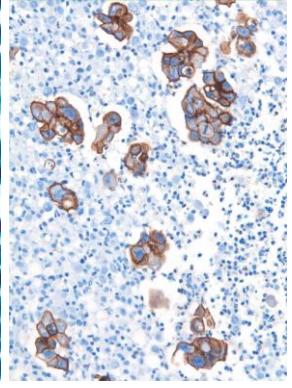
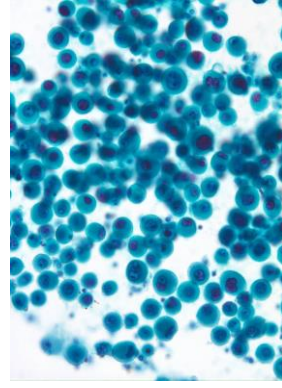
- Epithelial Membrane Antigen (EMA)
- B72.3
- Ber-EP4
- Others (HEA-125, MOC-31, 44-3A6, And BG Antigens)

EMA

- Polymorphic Epithelial Mucin
- Mesothelioma - 5% To 42%
- Adenocarcinoma - 50% To 100%
- Membranous/ Spiky Staining Pattern In Mesothelioma, Focal Staining In Benign Mesothelium
- Limited Practical Value



ACA



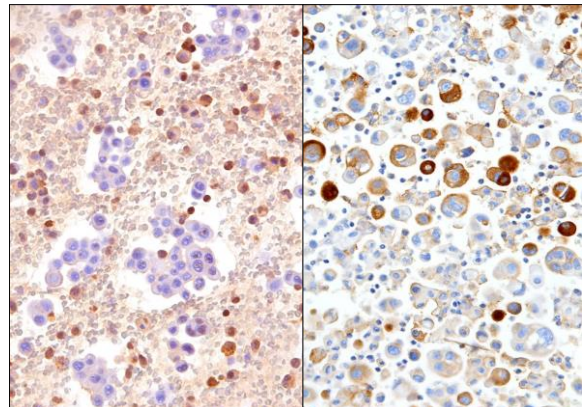
Ber-EP4

Oncoplacental Antigens

- Carcinoembryonic Antigen (CEA)
- Placental Antigens (PLAP)

CEA

- Oldest, And Most Widely Used Antibody
- Mesothelioma - 15% TO 45% - pCEA, ~3% -mCEA
- Adenocarcinoma - 85% To 95% (Lung)
- Papillary Serous Carcinoma - 16%

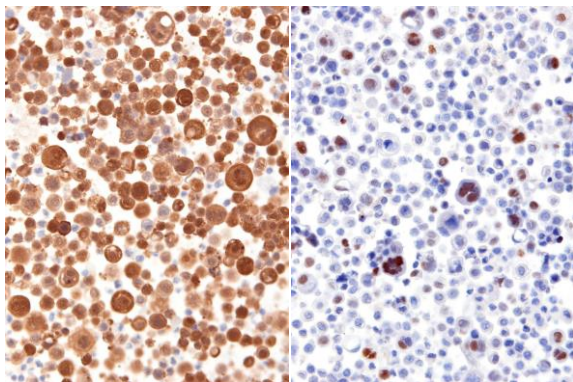


Myelomonocytic Antigens

- Leu-M1 (CD15)
- LN2 (CD74)

LEU-M1 (CD 15)

- Monoclonal AB, Recognizes Glycolipid Sugar Sequence
- Hodgkin Lymphoma Marker
- Mesothelioma - 0% To 32%
- Adenocarcinoma - 42% To 94%
- Highly Useful And Specific Marker (Although Less Sensitive)



p53

IC Ca++ Binding Proteins

- S-100 Protein
- Calretinin

Calretinin

- 29 Kda Ca++ Binding Protein
- Expressed By Neurons, Gonads, Adipose Tissue, Kidney, Sweat Glands, Thymus And Mesothelium
- Mesothelioma – 42% To 100% (~80%)
- Adenocarcinoma – 6% To 30% (Focal)
- Most Useful Positive Marker For Mesothelioma

Other Antibodies For Mesothelioma

- | | |
|------------------------------------|-----------------------------|
| ▪ CK7 +, CK 20 - | (Breast, Lung, Ovary, Panc) |
| ▪ CK 5/6 (Epithelial Mesothelioma) | [83 to 91% Vs ~ 25-35%] |
| ▪ WT-1 | [76-100% Vs 100% Ov Serous] |
| ▪ Thrombomodulin | [77% Vs 14%] |
| ▪ Mesothelin | [100% Vs 39-91%] |
| ▪ AMAD-2 | [100% Vs 7%] |
| ▪ D2-40 | [90% Vs 36% weak] |

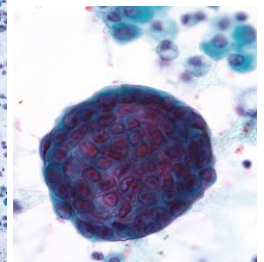
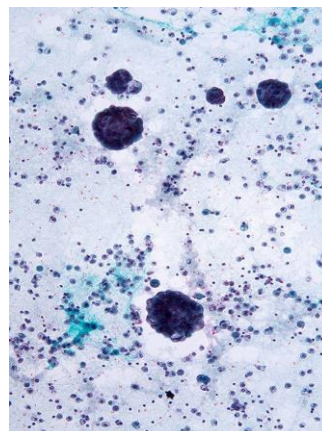
JHH Panel

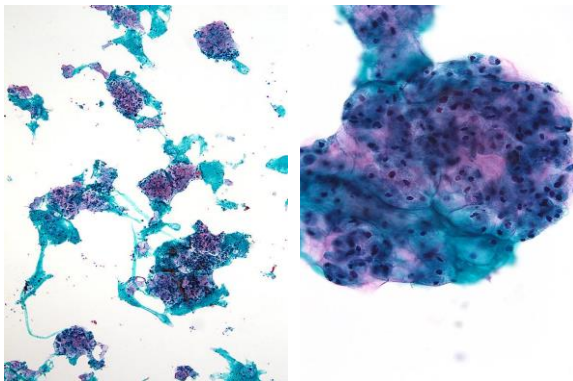
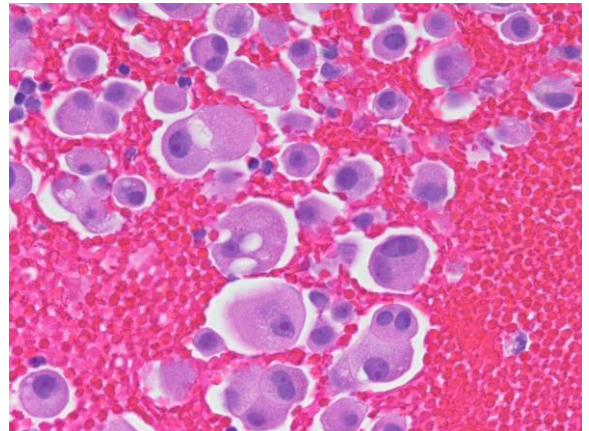
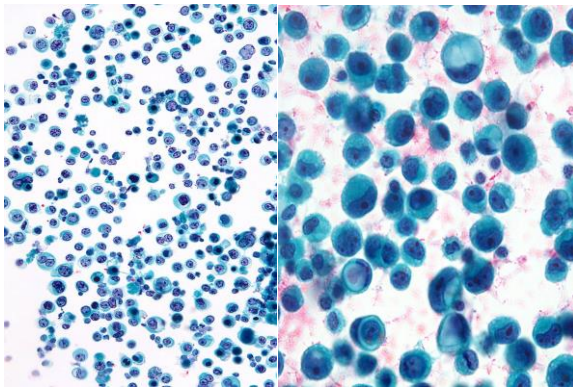
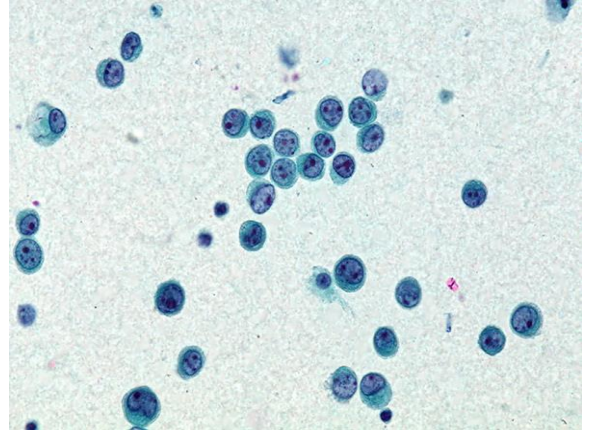
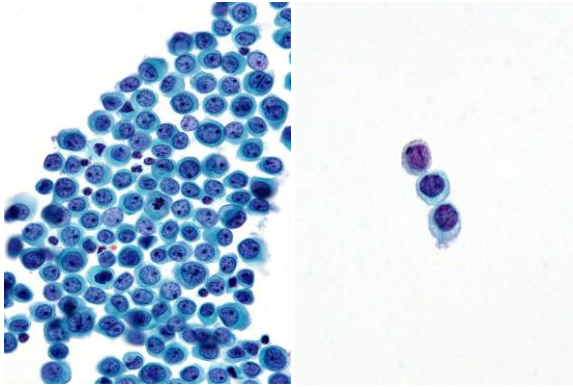
- Calretinin, WT-1, CK 5/6 (D2-40, p53)
- Ber EP4, mCEA (Napsin-A, TTF-1, PAX-8, Other specific markers)

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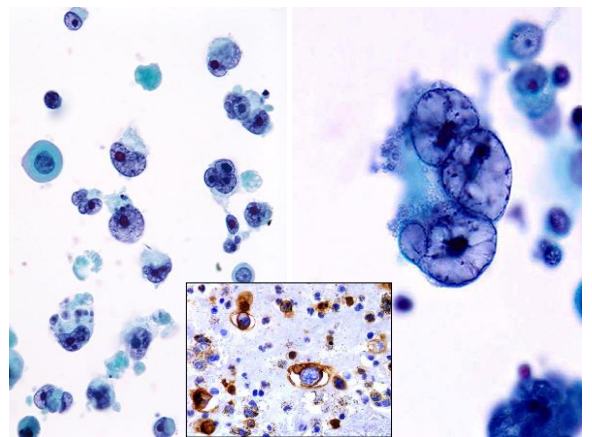
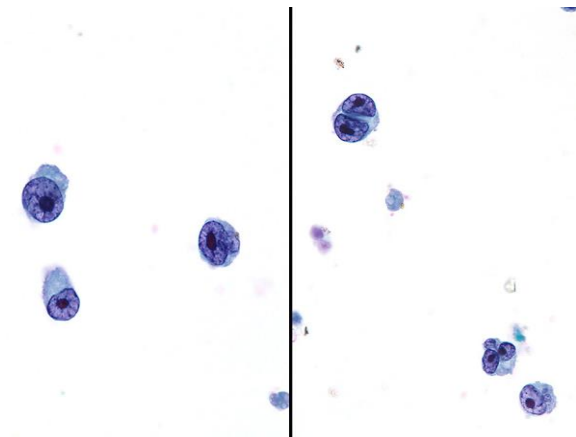
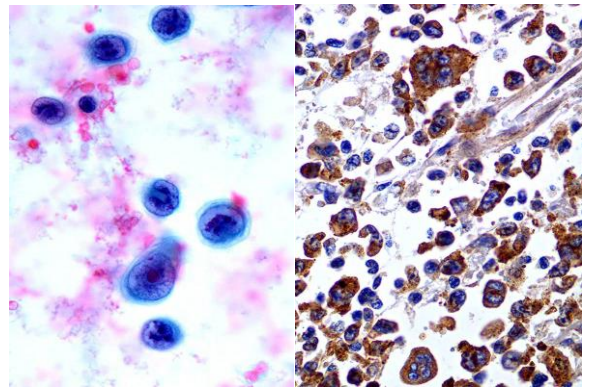
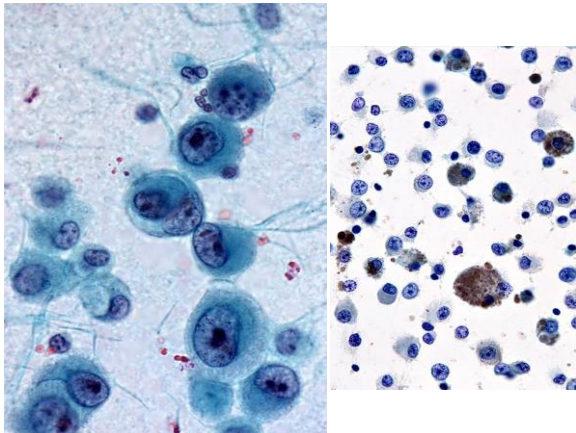
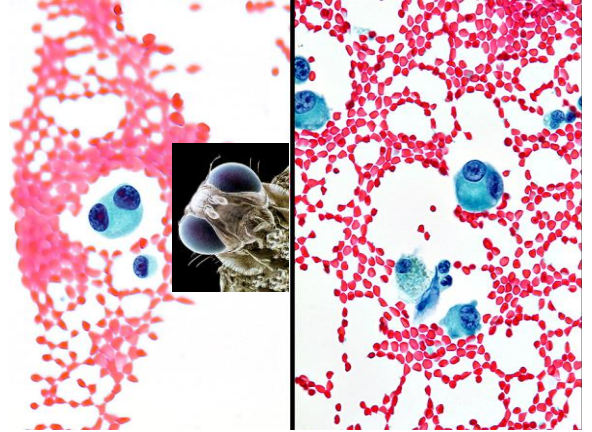
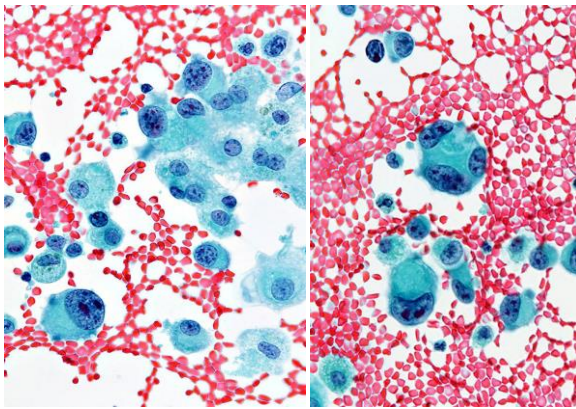




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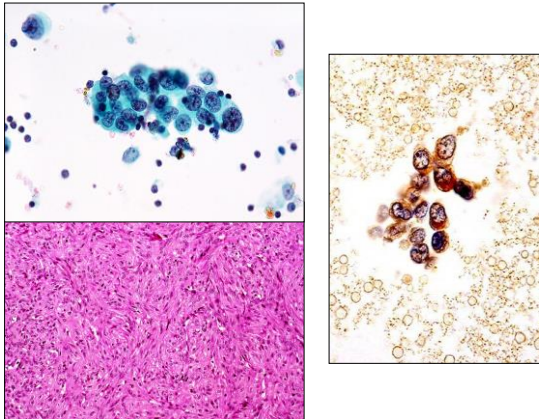
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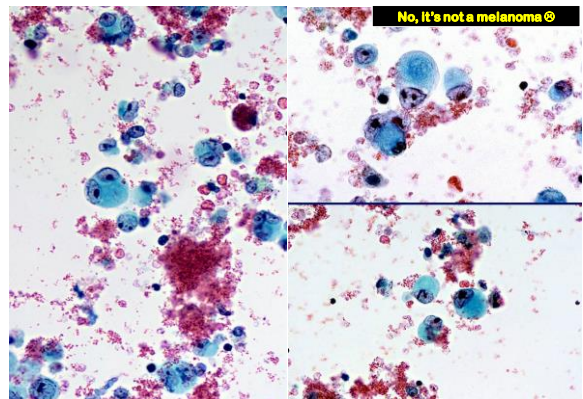
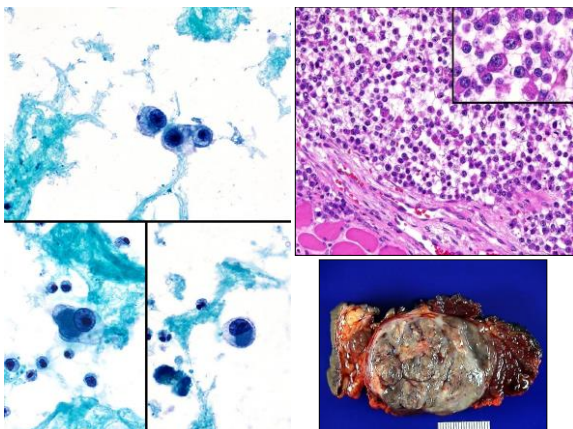
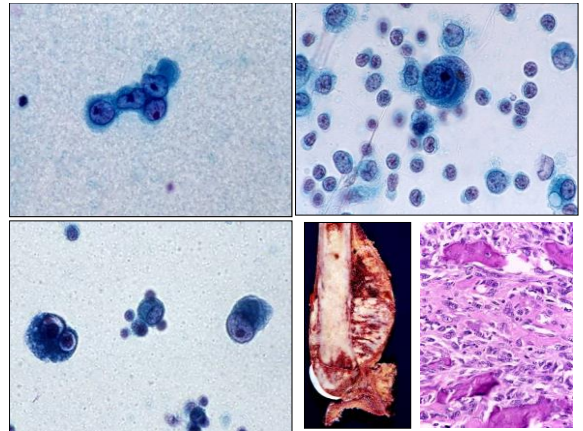
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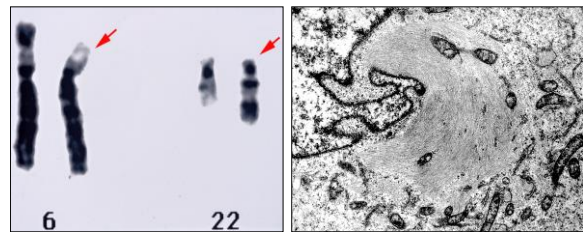
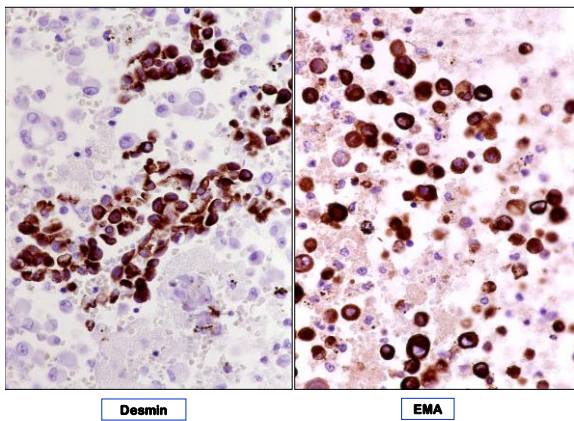
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Sarcomatous Effusions

- **NEVER** Present As Occult Metastases
- Objective Of The Cytologic Examination Is To
 - Document The Presence Or Absence Of Cancer
 - Confirm The Morphologic Resemblance With The Known Primary Sarcoma
- **IMPERATIVE** To Review/Compare With The Original Resection Specimen
- Perform Ancillary Studies



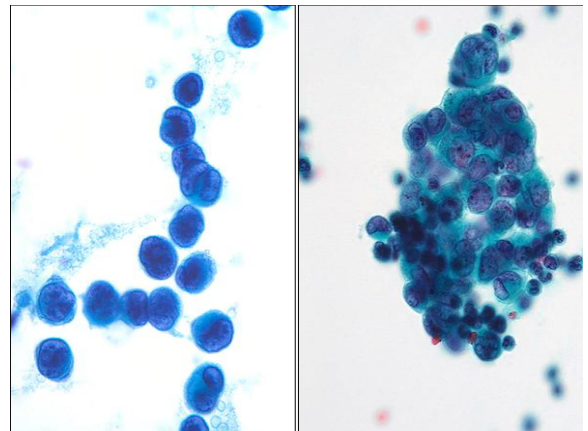
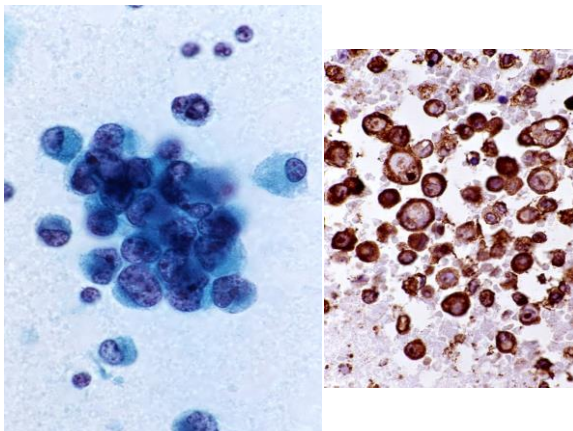


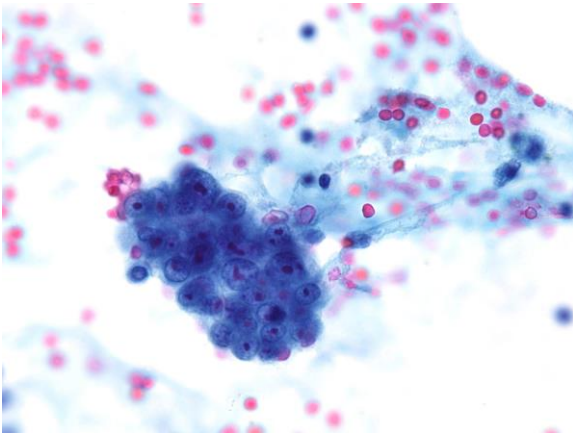
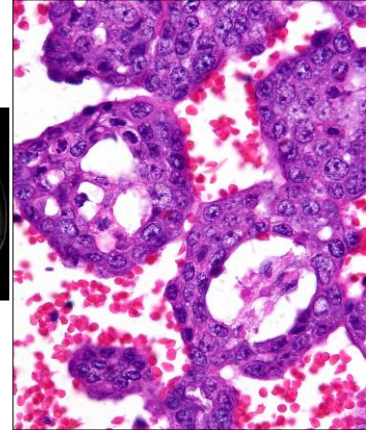
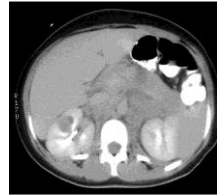
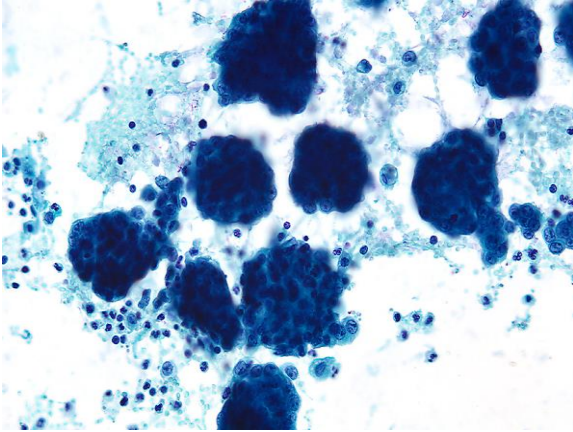
- **Small Round Blue Cell Tumors**
 - Ewing Sarcoma, PNET, Neuroblastoma, Embryonal Rhabdomyosarcoma
- **Hematologic Neoplasm**
 - Lymphomas And Leukemias
- **Other Tumors**
 - Rhabdoid Tumor

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Flow Cytometry in Serous Cavity Effusions

- 17% (16/96) - Significant Modification Of The Pre-Flow Dx*
- Cannot Diagnose Hodgkin Lymphoma

[Czader and Ali, Diagn Cytopathol 2003]

