Diagnosing mesothelioma: An ongoing challenge

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Organisers

Partners

Disclosure slide

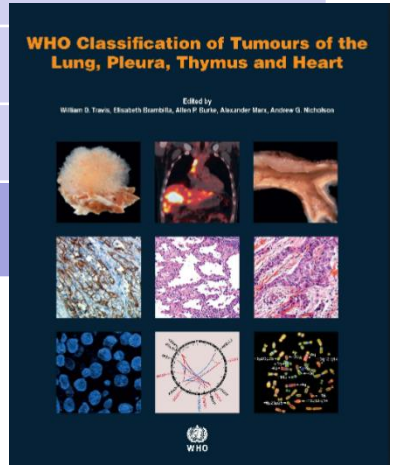
- No disclosures.

GENERAL RULES FOR PATHOLOGISTS WHEN DIAGNOSING MESOTHELIOMA

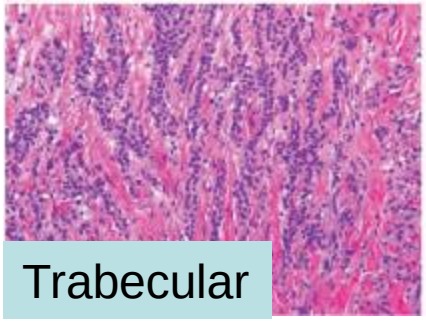
- Adequate tissue
  - large surgical specimens (core biopsies, pleural peel)
- Correlation with radiographic and intraoperative findings
- A history of asbestos exposure should not be taken into consideration
- Perform appropriate immunohistochemistry

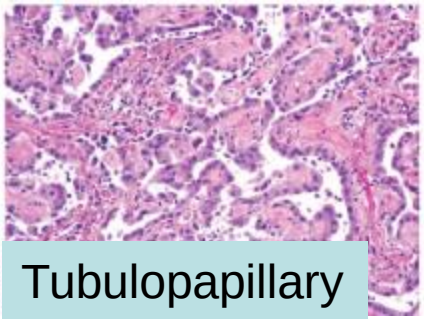
WHO classification of mesothelial tumors

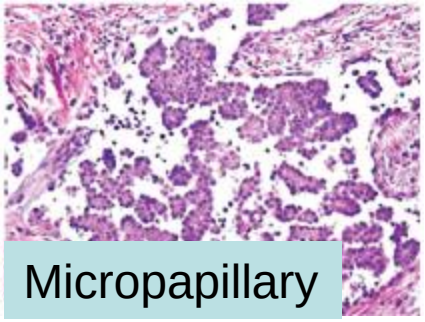
Diffuse Malignant Mesothelioma
Epithelioid
Sarcomatoid
Desmoplastic
Biphasic
Localized Malignant Mesothelioma
Epithelioid
Sarcomatoid
Biphasic
Well-differentiated papillary mesothelioma

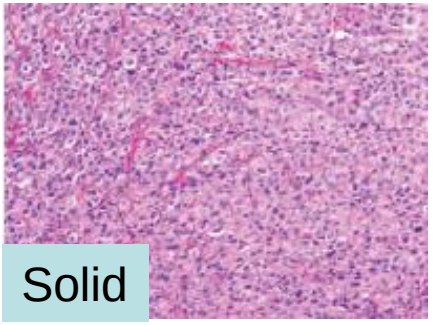


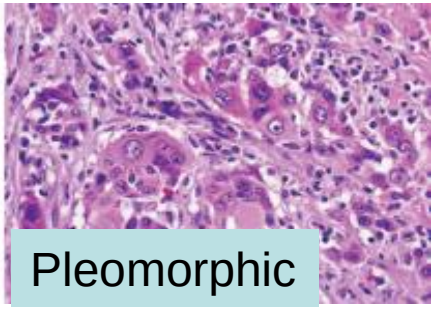
HISTOLOGICAL SUBTYPING OF EPITHELIOD MESOTHELIOMA

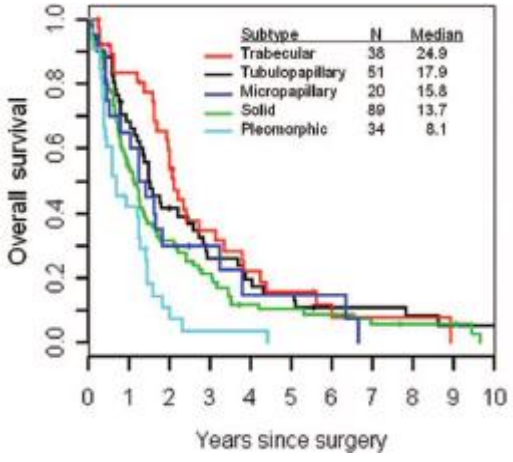

Trabecular

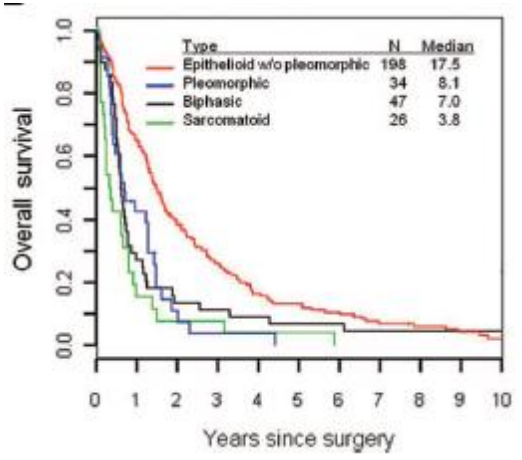

Tubulopapillary


Micropapillary


Solid

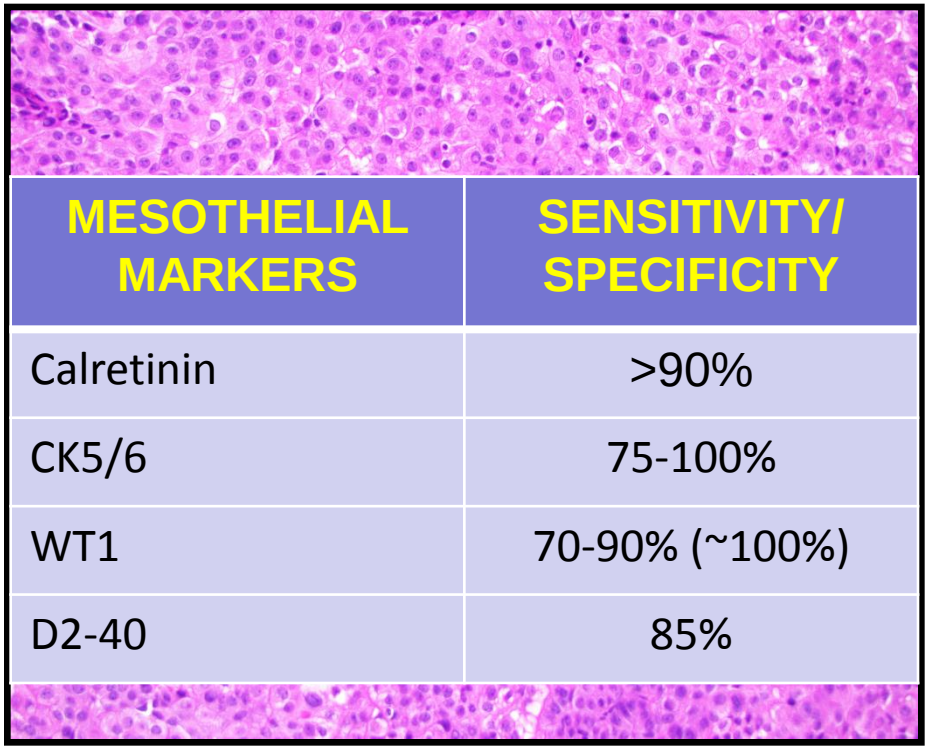

Pleomorphic



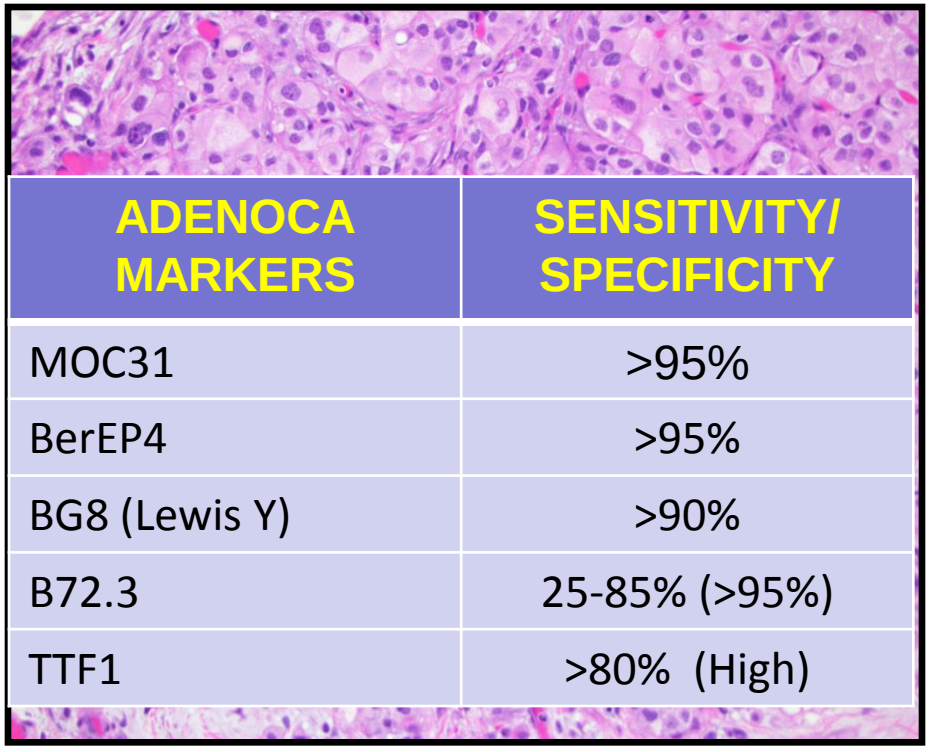


Kadota et al. JTO 2011

MESOTHELIOMA VS. ADENOCARCINOMA

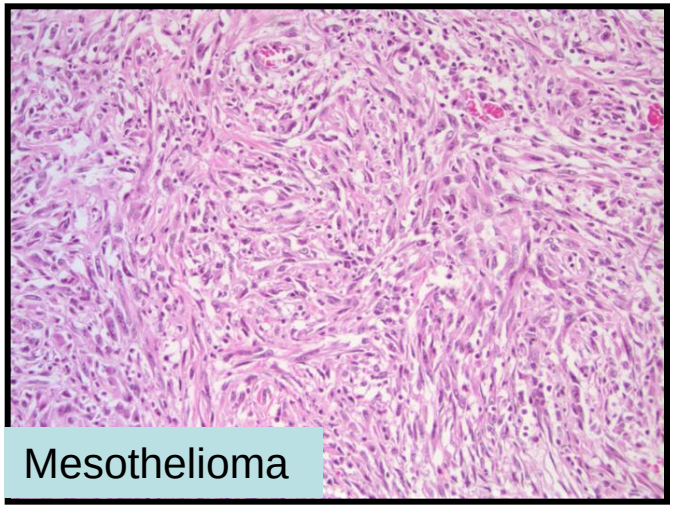


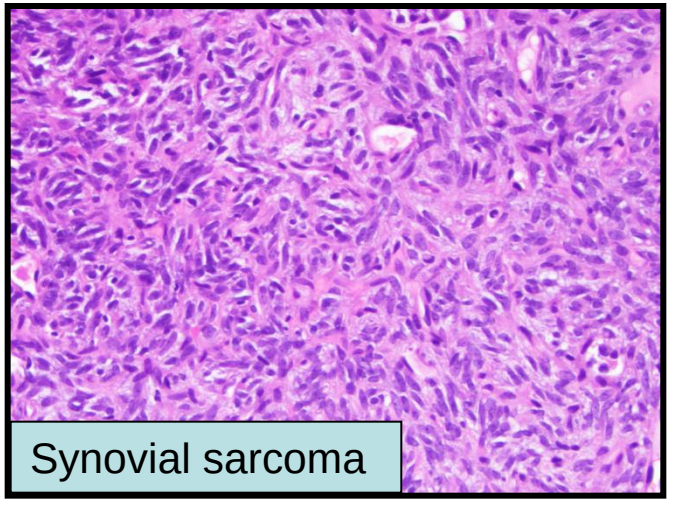
MESOTHELIAL MARKERS	SENSITIVITY/ SPECIFICITY
Calretinin	>90%
CK5/6	75-100%
WT1	70-90% (~100%)
D2-40	85%

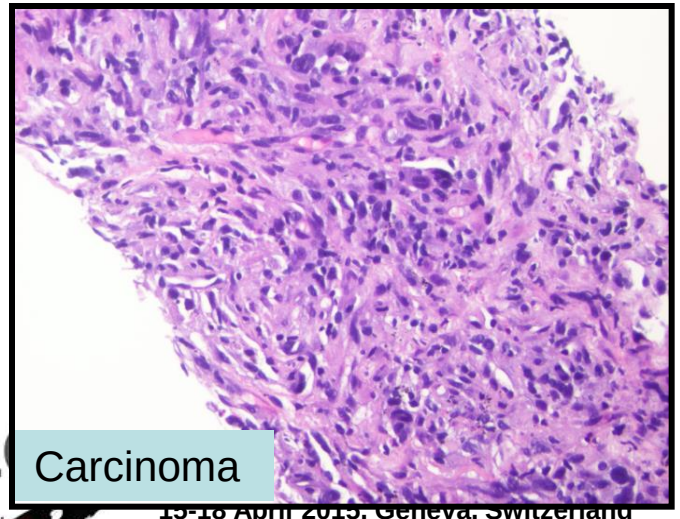


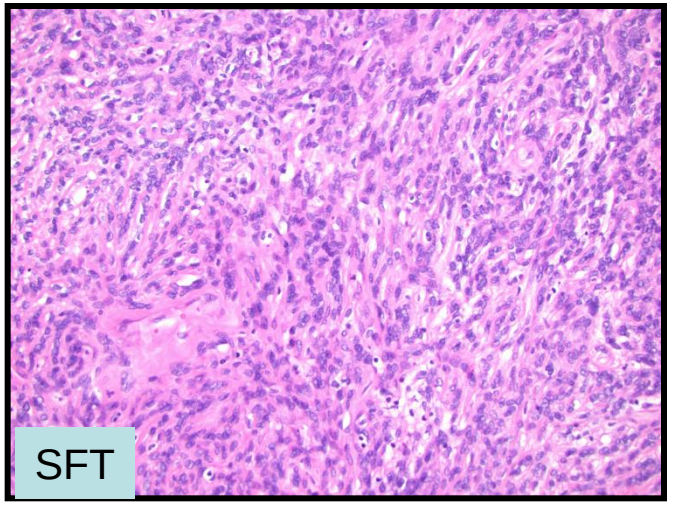
ADENOCA MARKERS	SENSITIVITY/ SPECIFICITY
MOC31	>95%
BerEP4	>95%
BG8 (Lewis Y)	>90%
B72.3	25-85% (>95%)
TTF1	>80% (High)

SARCOMATOID MESOTHELIOMA VS. OTHER SARCOMATOID MALIGNANCIES

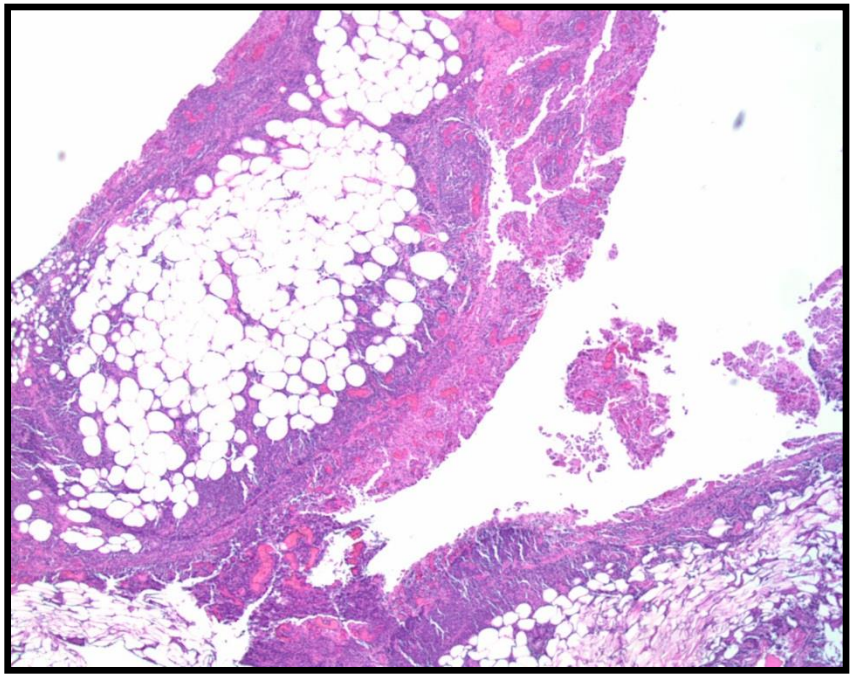


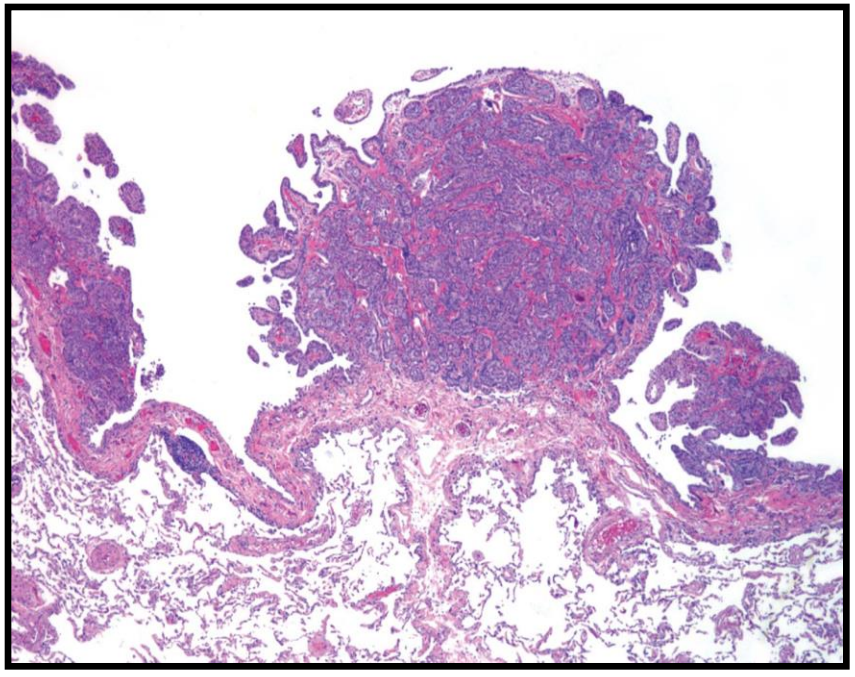




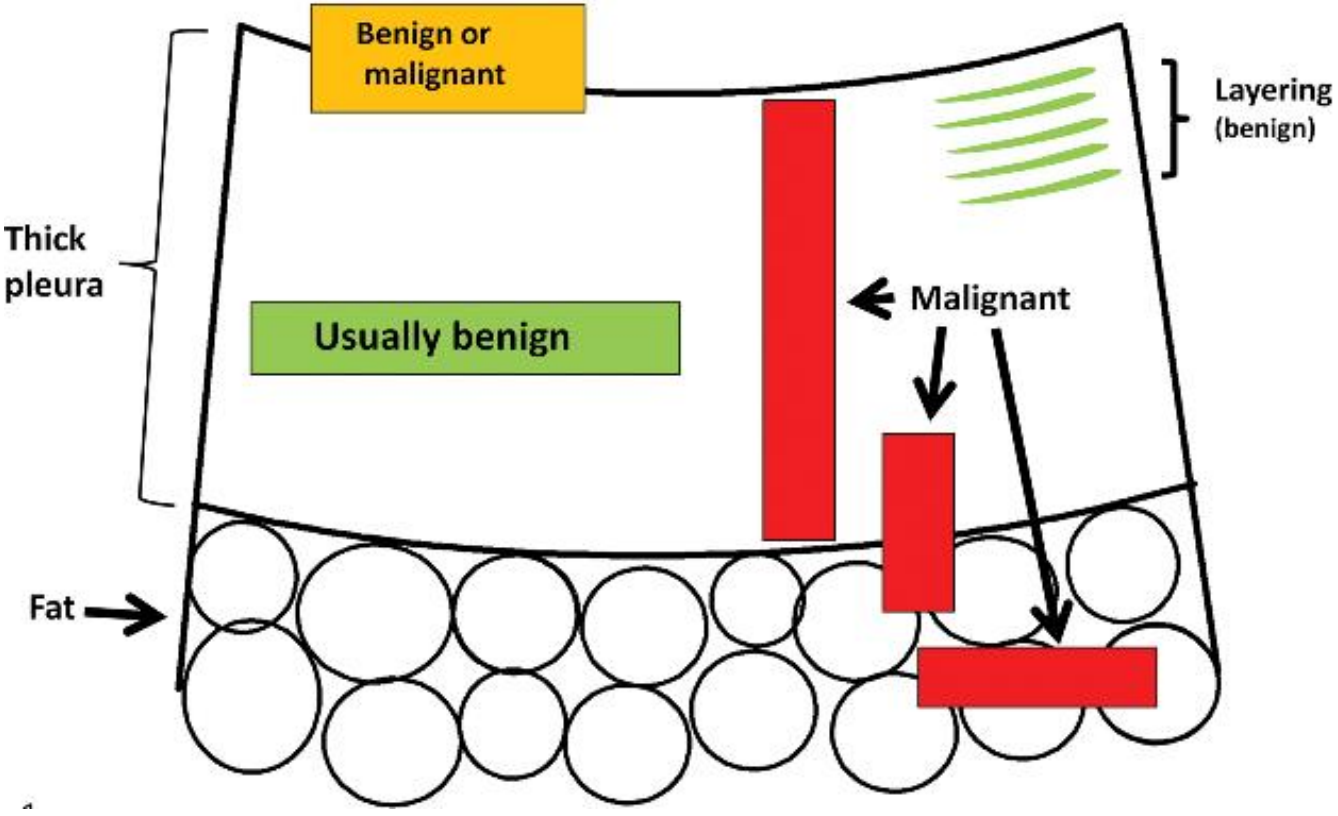


HOW TO SEPARATE MESOTHELIAL HYPERPLASIA FROM MALIGNANT MESOTHELIOMA?





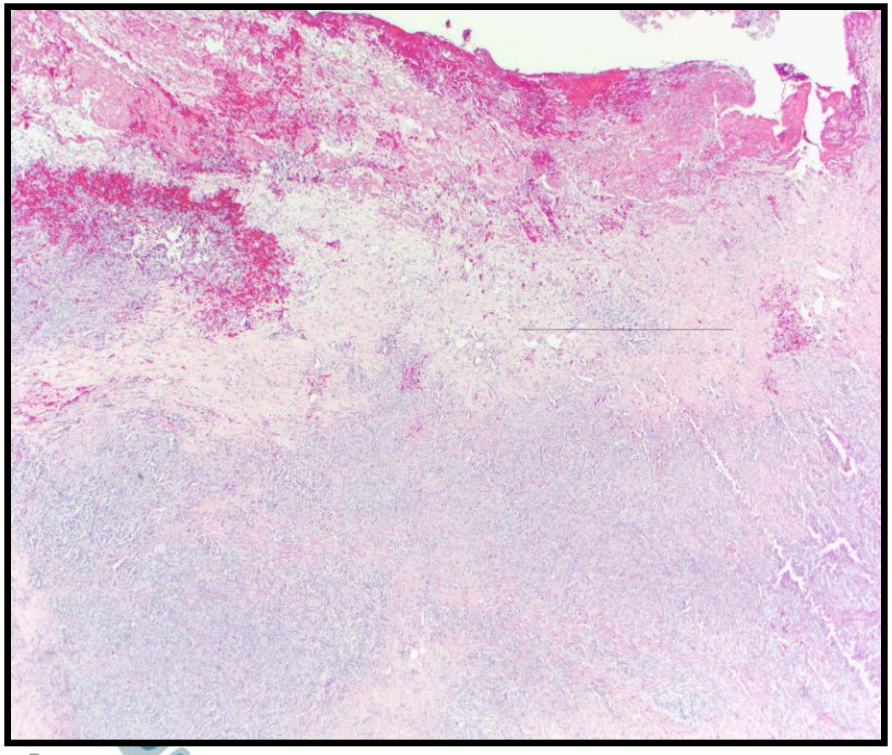
“ZONATION”



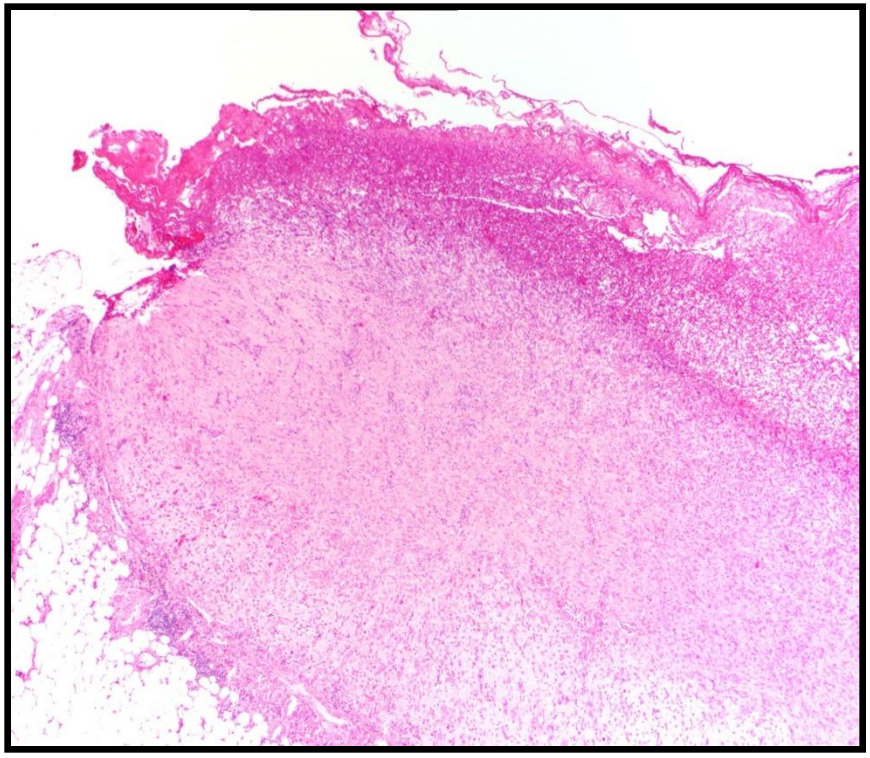
Am J Surg Pathol 2000; 24(9):1183-1200.

ZONATION

MESOTHELIOMA



HYPERPLASIA

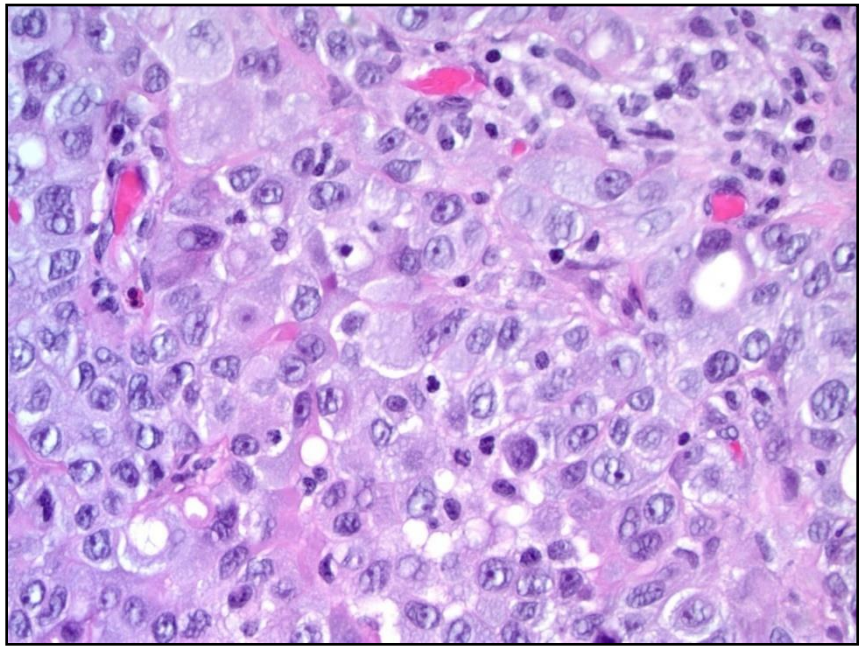


NOT so useful histological criteria

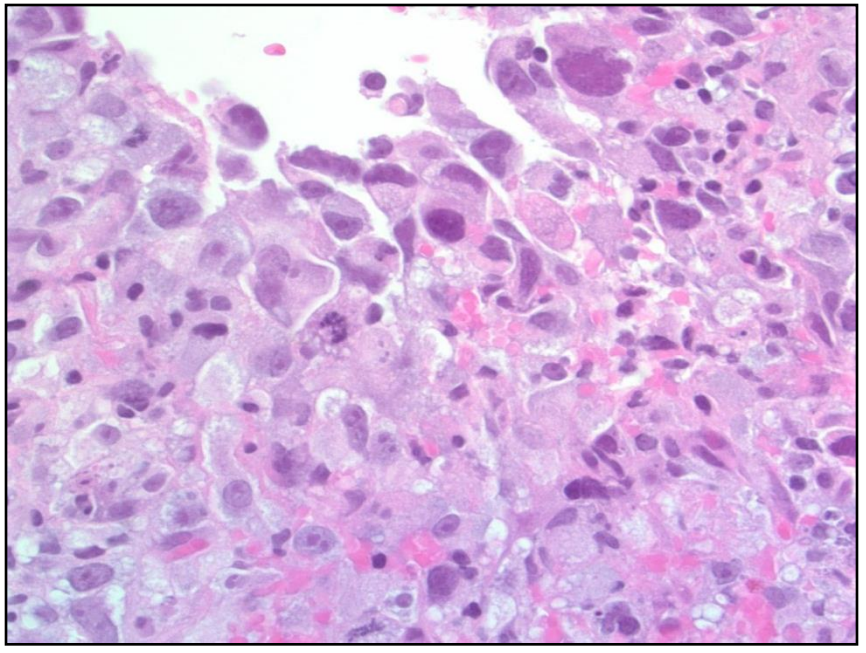
- Cellularity
- Atypia (unless severe)
- Mitoses (unless atypical)

CYTOLOGICAL ATYPIA

MESOTHELIOMA

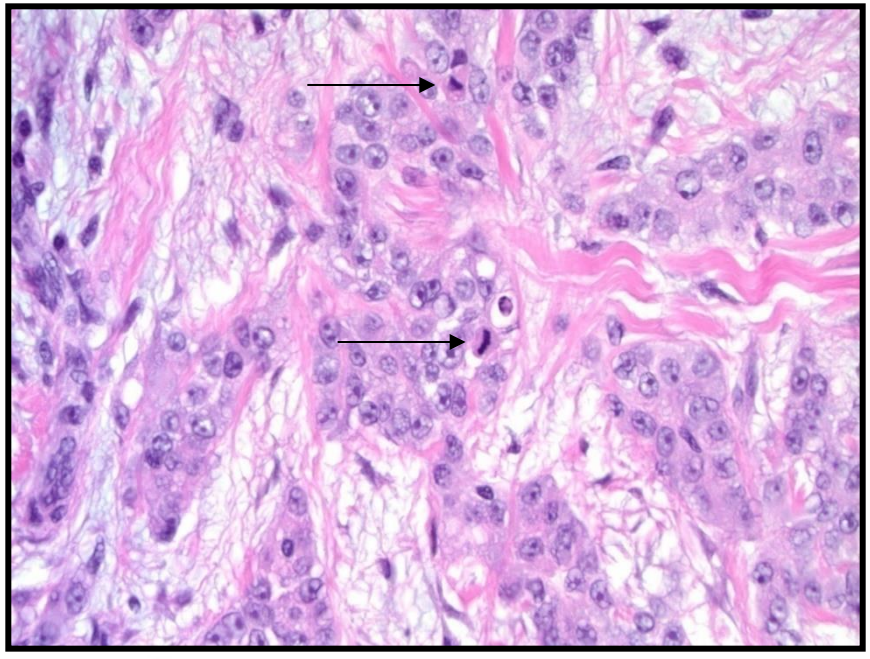


HYPERPLASIA

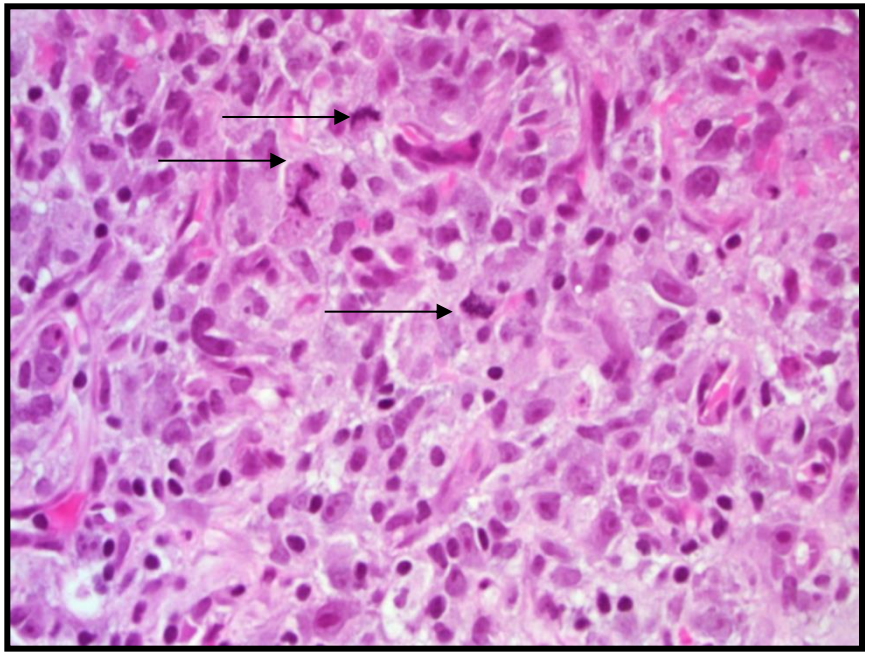


MITOTIC ACTIVITY

MESOTHELIOMA

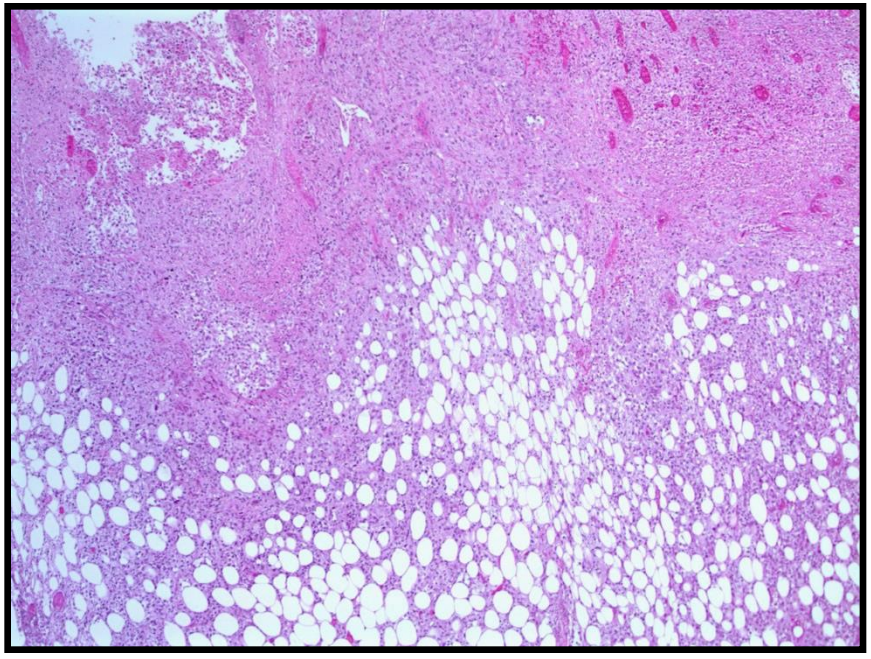


HYPERPLASIA

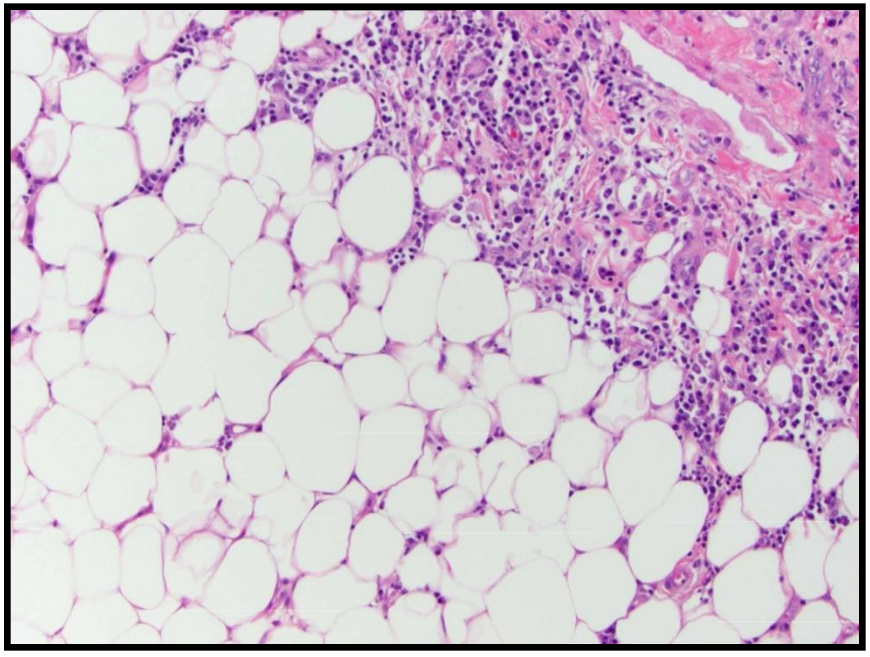


STROMAL INVASION

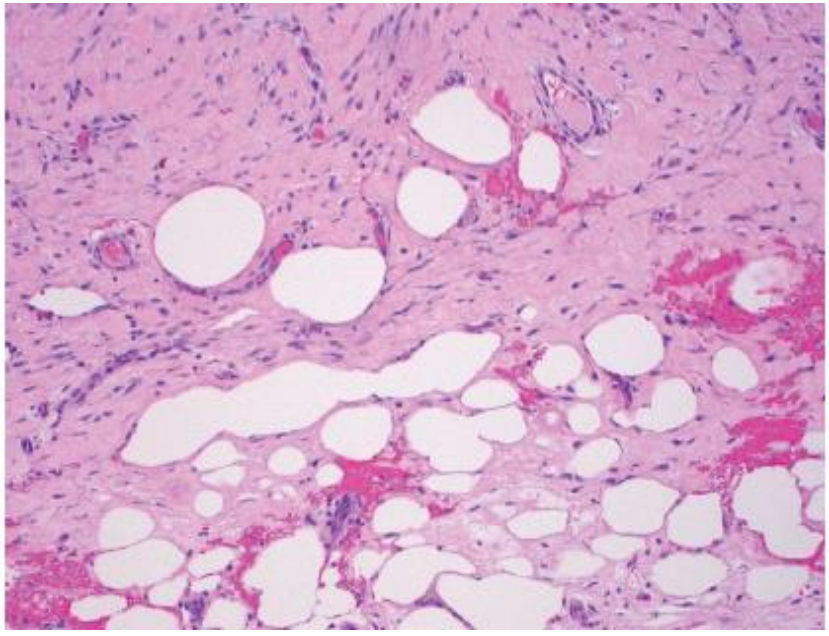
MESOTHELIOMA

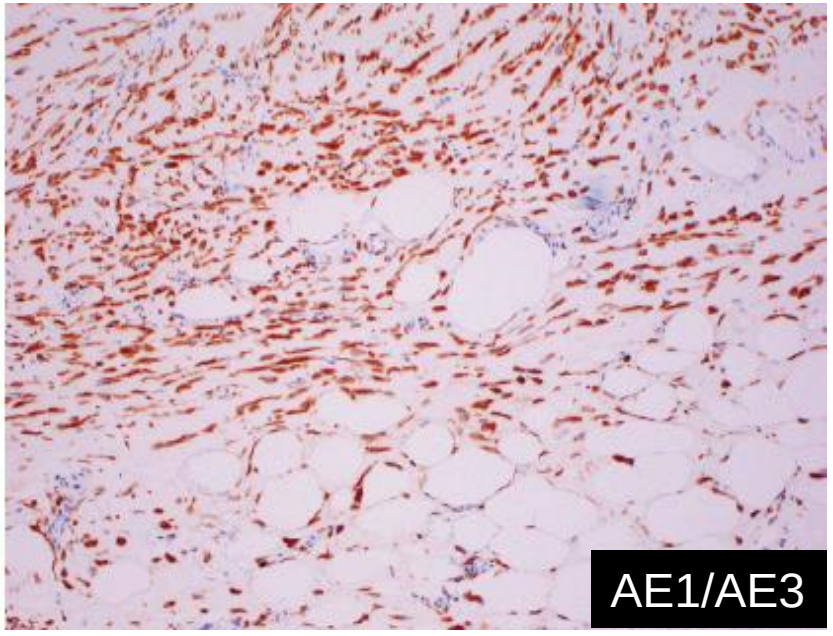


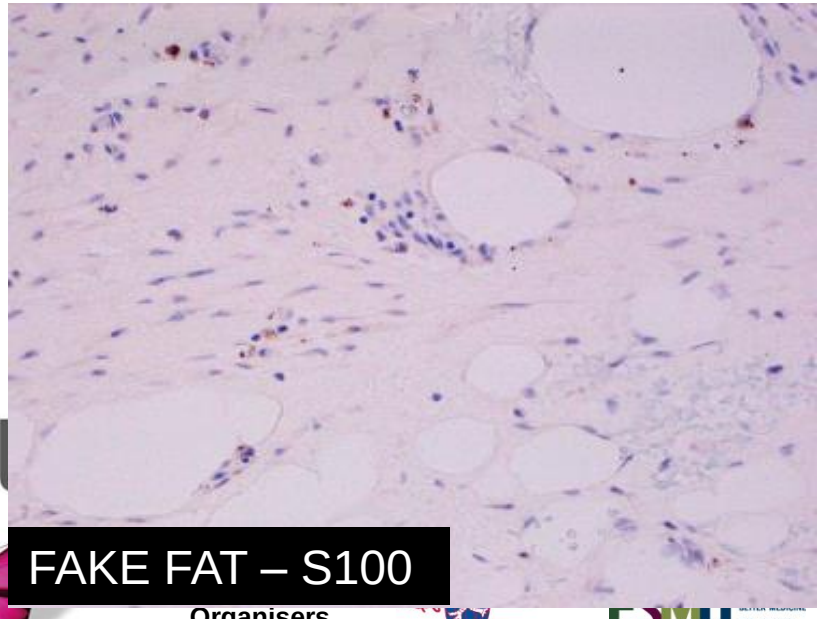
BENIGN PLEURA

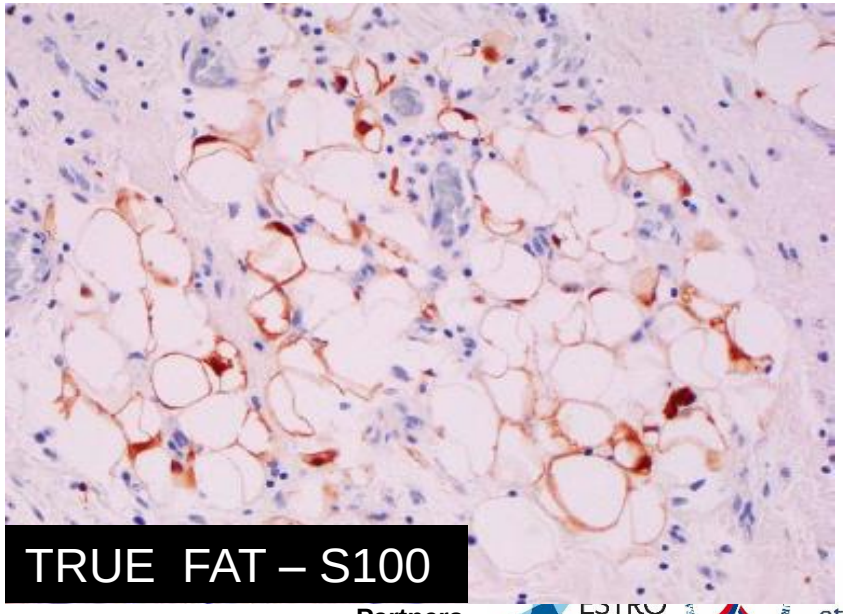


“FAKE FAT”









ANCILLARY STUDIES FOR DISTINCTION BETWEEN BENIGN AND MALIGNANT MESOTHELIAL PROLIFERATIONS

- Immunohistochemistry
- Deletion of *p16* gene by FISH

IMMUNOHISTOCHEMISTRY
MESOTHELIAL HYPERPLASIA VS. MESOTHELIOMA

ANTIBODY	HYPERPLASIA (%)	MESOTHELIOMA (%)
Desmin	85	10
EMA	20	80
p53	0	45
GLUT-1	3	67
IMP3	0	73
BAP-1	0	37

IMMUNOHISTOCHEMISTRY
MESOTHELIAL HYPERPLASIA VS. MESOTHELIOMA

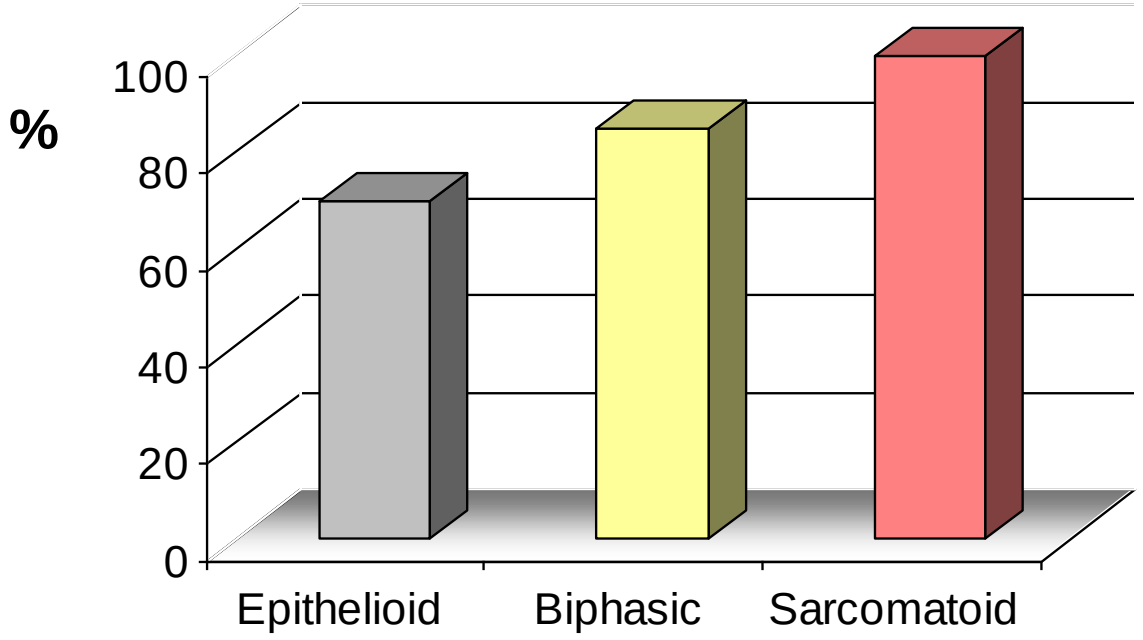
" In the individual case, immunohistochemical staining reactions are simply too variable to be relied upon, and we do not recommend their use."

Churg A, Cagle PT and Roggli VL. Tumors of the serosal membranes, AFIP Atlas of Tumor Pathology Series 4, pg. 100 (2006)

GENETIC ALTERATIONS IN MALIGNANT MESOTHELIOMA

- Loss of *p16* (9p21) is the most common genetic alteration in MM
- Homozygous deletion, point mutation, methylation

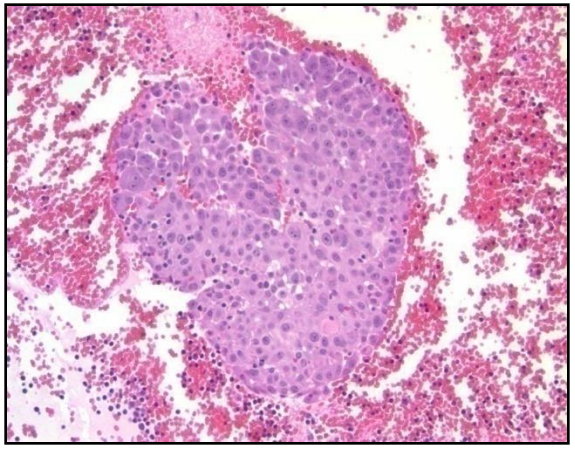
9p21 (*p16*)deletion and histologic type of malignant mesothelioma

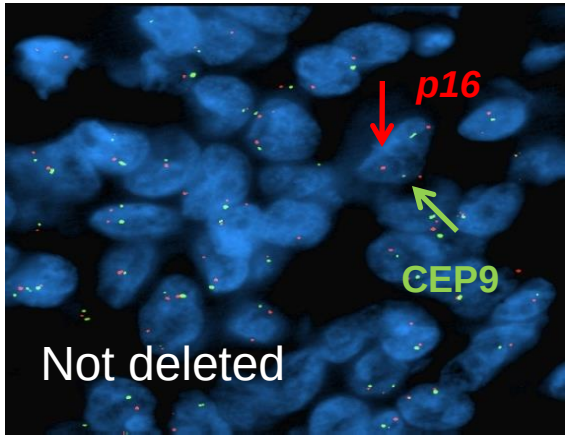


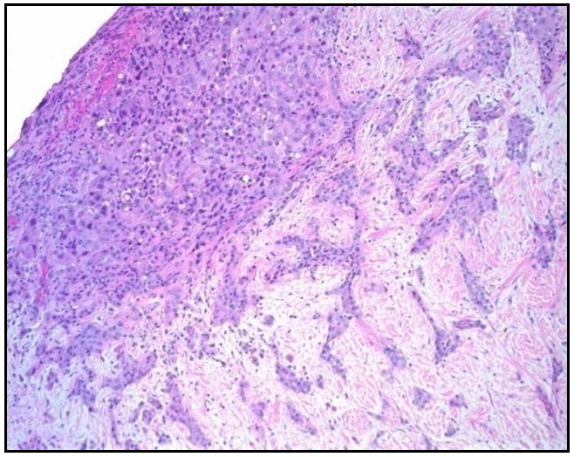
DIAGNOSTIC UTILITY OF *p16* DELETION

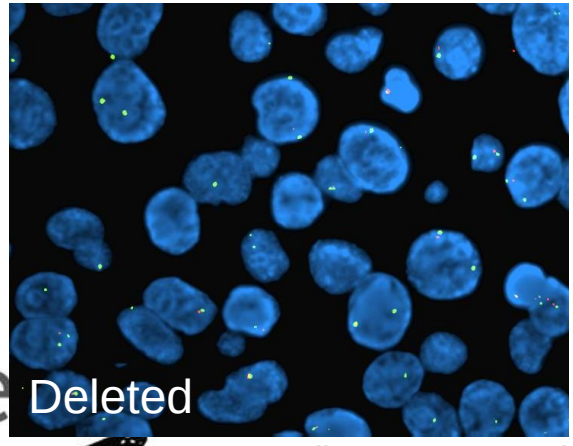
Fluid specimens

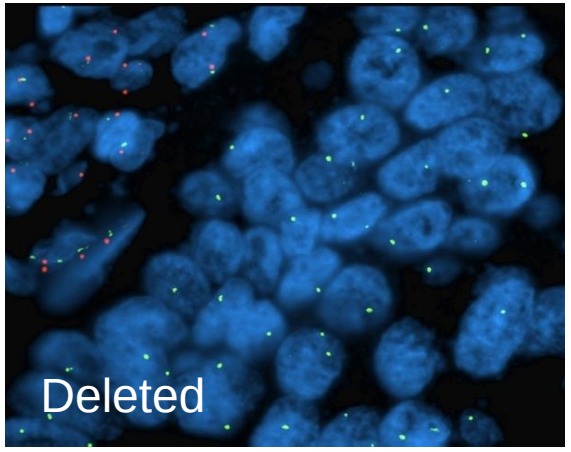
Paraffin embedded tissue









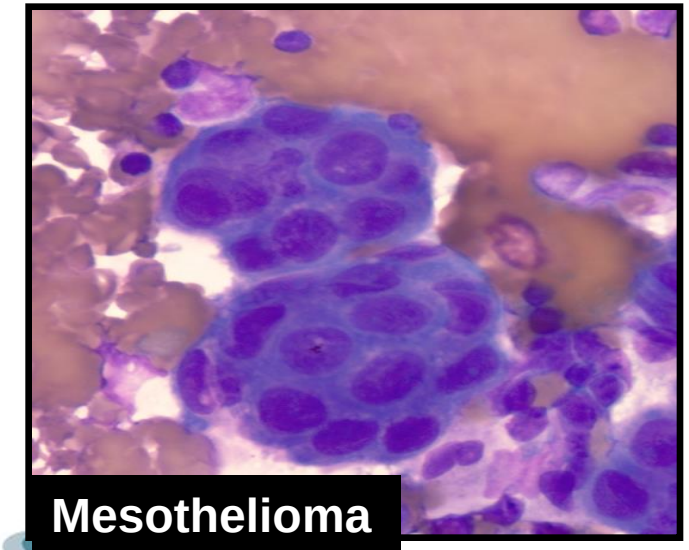


Illei et al. Cancer Ctyopath 2003; 99(1):

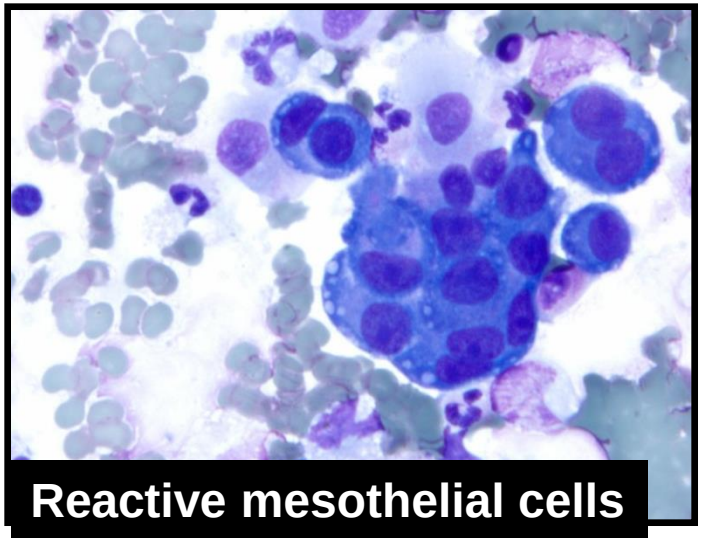
Chiosea et al. Mod Pathol 2008 Jun;21(6):742.

CYTOLOGIC DIAGNOSIS OF MESOTHELIOMA

- High false–negative rate (sensitivity 32% -76%)
- Sarcomatoid mesotheliomas do not shed into the effusion fluid
- FISH for *p16* deletion can be helpful



Mesothelioma



Reactive mesothelial cells

SUMMARY

- Diagnosis of malignant mesothelioma requires multidisciplinary approach
- Sarcomatoid mesotheliomas and distinction from benign mesohtelial prolifeartions are challenging diagnostic areas
- FISH for 9p21 (*p16*) deletion may be diagnostically helpful, although it has a low sensitivity