

# Il mesotelioma

La ricerca attiva  
delle malattie  
lavoro-correlate



**Venerdì 17 novembre 2017**  
**ore 8.45/17.00**

**Sala di Rappresentanza**  
**ATS Brescia**

**Viale Duca degli Abruzzi, 15**

Evento accreditato ECM per le professioni sanitarie.

Sistema Socio Sanitario



ATS Brescia

## LA DIAGNOSI CITO- ISTOLOGICA DI MESOTELIOMA: MORFOLOGIA E IMMUNOISTOCHEMICA

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# **PRESENTAZIONI PIU' FREQUENTI DEL MESOTELIOMA MALIGNO PLEURICO**

- ✓ **Versamento**
- ✓ **Noduli / ispessimento della sierosa parietale**
- ✓ **Massa**
- ✓ **Pneumotorace**
- ✓ **Linfoadenopatia**

**In ciascuna situazione il campione che perviene all'Anatomia Patologica è diverso e le diagnosi differenziali cliniche possono essere diverse**

# **PROCEDURE DI PRELIEVO PER LA DIAGNOSI DI MESOTELIOMA MALIGNO PLEURICO**

- ✓ **Toracentesi**
- ✓ **Agobiopsia transtoracica (ECO-/ TC-guidata)**
- ✓ **Toracosopia medica / chirurgica**
- ✓ **Agoaspirato/agobiopsia transbronchiale (eco-guidata, e.g. TBNA-EBUS)**

# **MESOTELIOMA: principali problematiche diagnostiche**

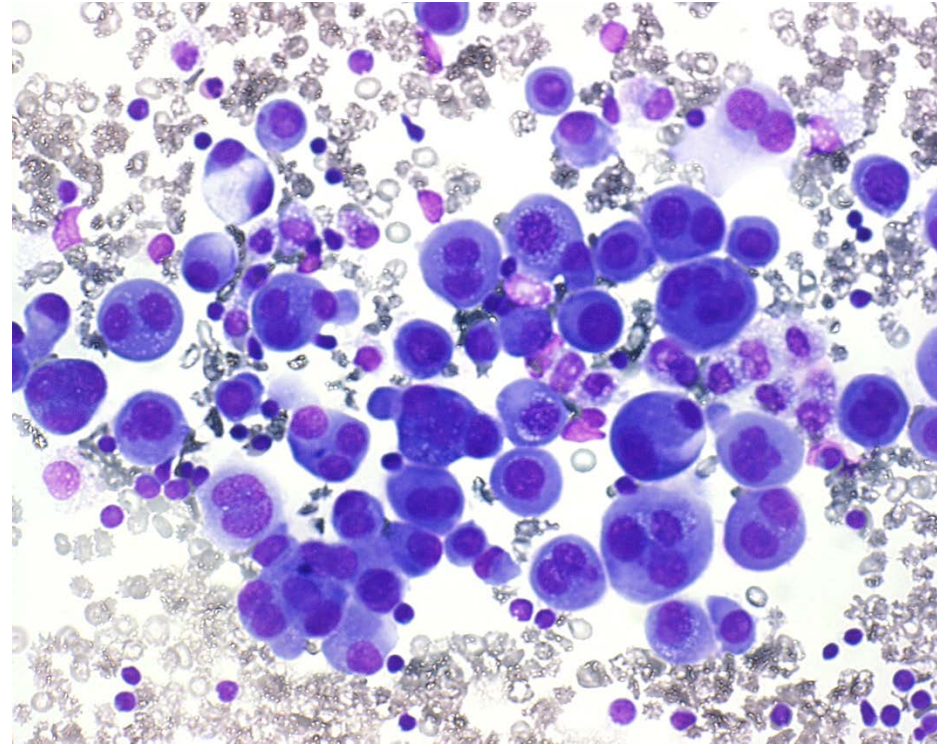
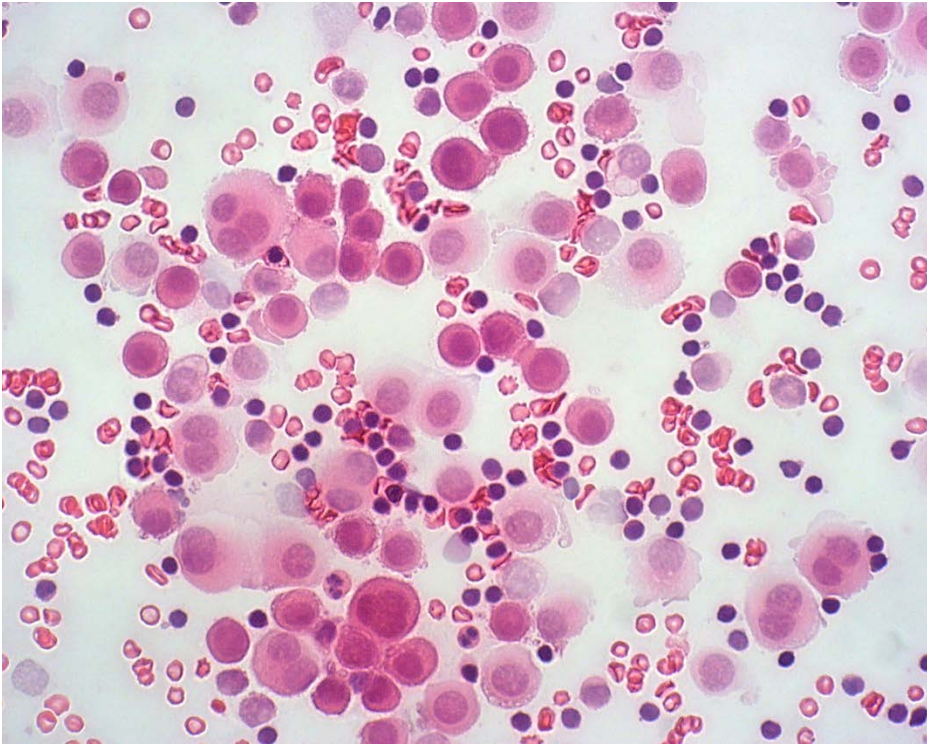
- **Differenziare una popolazione mesoteliale reattiva da una neoplastica (versamenti e biopsie in assenza di invasione)**
- **Classificare un mesotelioma con citologia / piccole biopsie (epitelioide, bifasico, sarcomatoide)**
- **Identificare l'origine mesoteliale di una neoplasia morfologicamente non differenziata (> sarcomatoide)**

# **Guidelines for the Cytopathologic Diagnosis of Epithelioid and Mixed- Type Malignant Mesothelioma**

**Complementary Statement from the  
International Mesothelioma Interest Group,  
Also Endorsed by the International  
Academy of Cytology and the Papanicolaou  
Society of Cytopathology**

Anders Hjerpe,<sup>1\*</sup> Valeria Ascoli,<sup>2</sup> Carlos W.M. Bedrossian,<sup>3</sup>  
Mathilde E. Boon,<sup>4</sup> Jenette Creaney,<sup>5</sup> Ben Davidson,<sup>6</sup> Annika Dejmek,<sup>7</sup>  
Katalin Dobra,<sup>1</sup> Ambrogio Fassina,<sup>8</sup> Andrew Field,<sup>9</sup> Pinar Firat,<sup>10</sup>  
Toshiaki Kamei,<sup>11</sup> Tadao Kobayashi,<sup>12</sup> Claire W. Michael,<sup>13</sup>  
Sevgen Onder,<sup>14</sup> Amanda Segal,<sup>15</sup> and Philippe Vielh<sup>16</sup>

# LE CELLULE MESOTELIALI

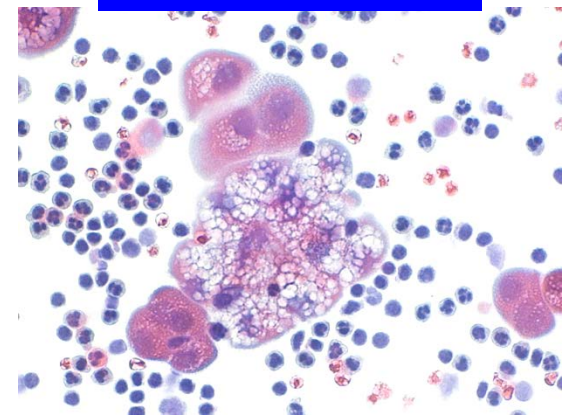
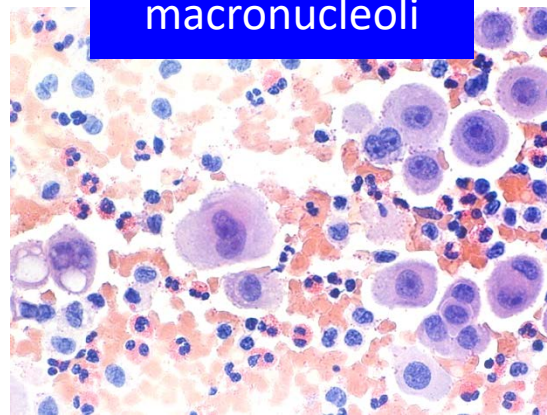
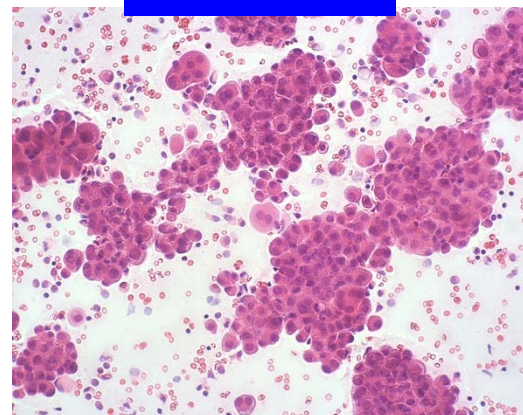
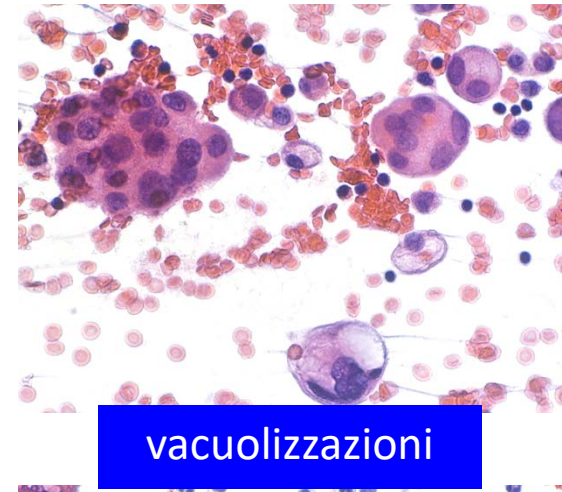
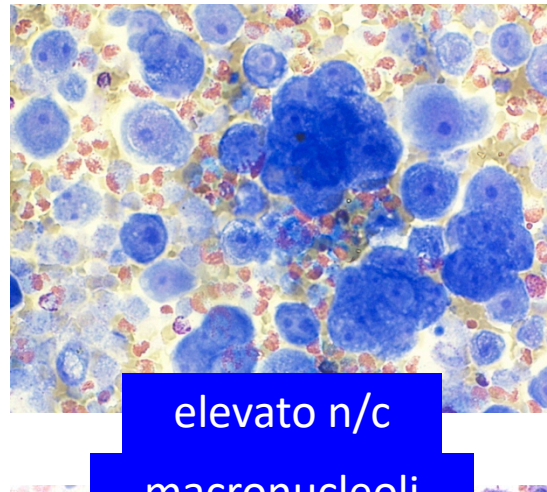
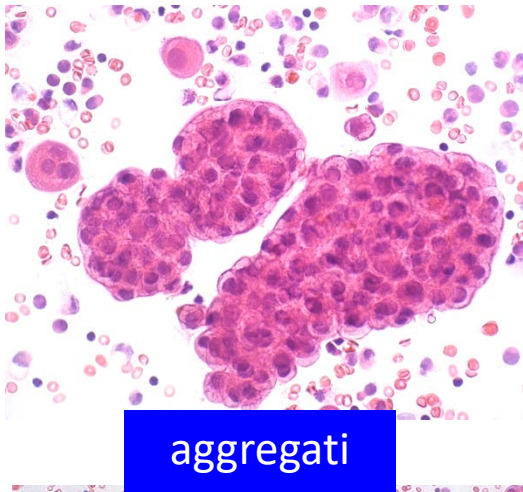
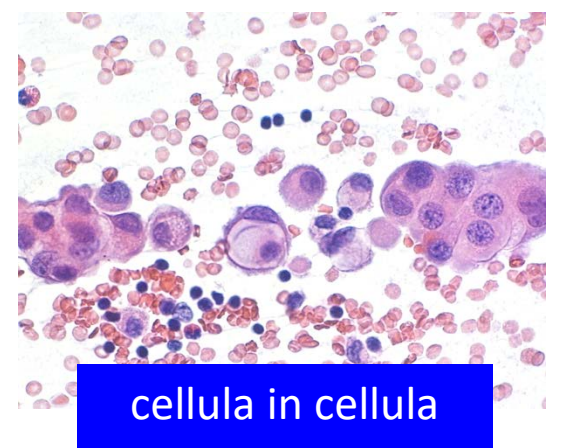
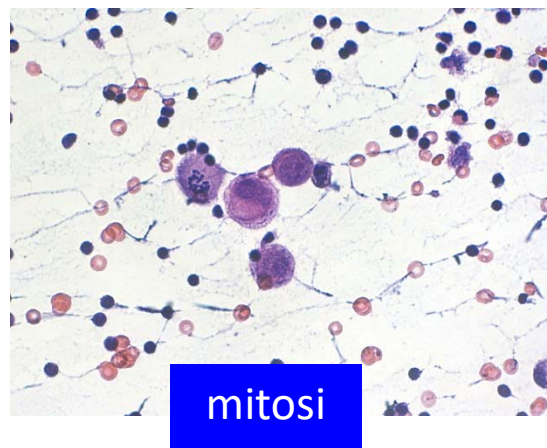


## Caratteri distintivi principali:

- nucleo centrale o eccentrico con rima di citoplasma
- bicromatismo del citoplasma
- microvacuolizzazione della periferia del citoplasma
- microvilli

Altri caratteri: bi- o plurinucleazione, nucleoli evidenti, vacuoli citoplasmatici, aggregati





# General Recommendations

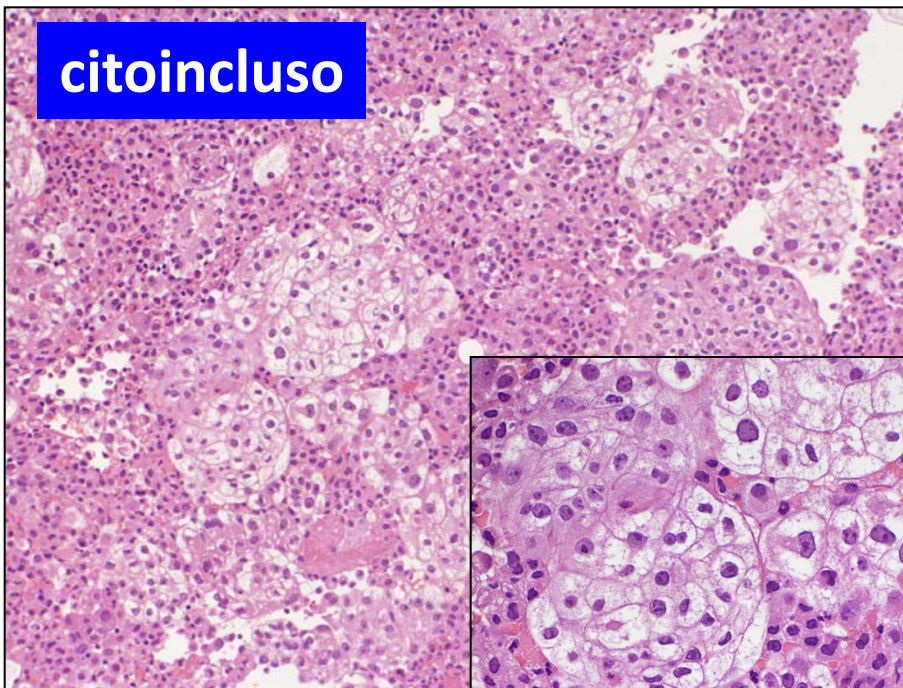
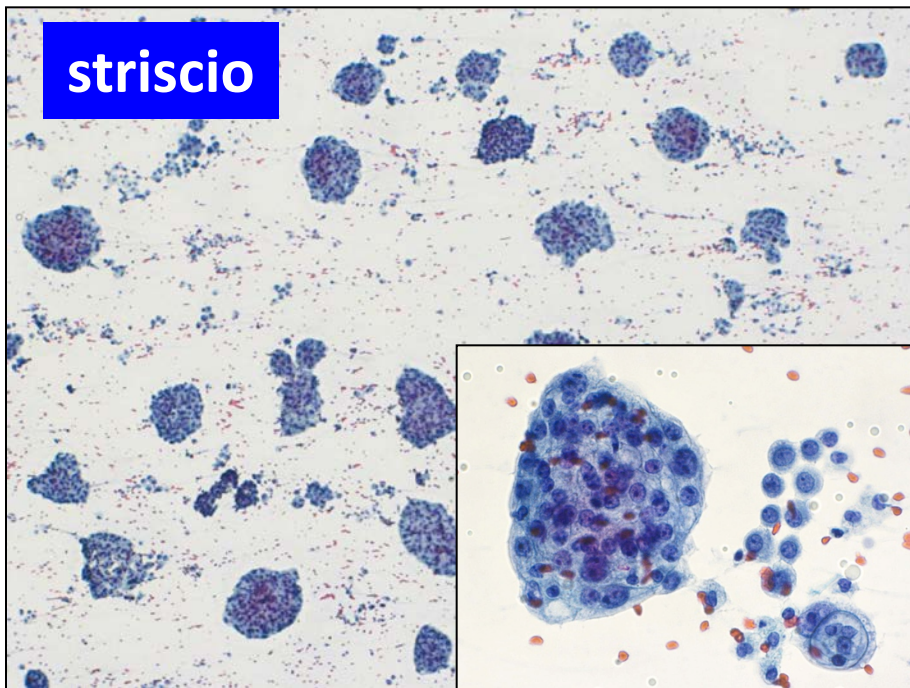
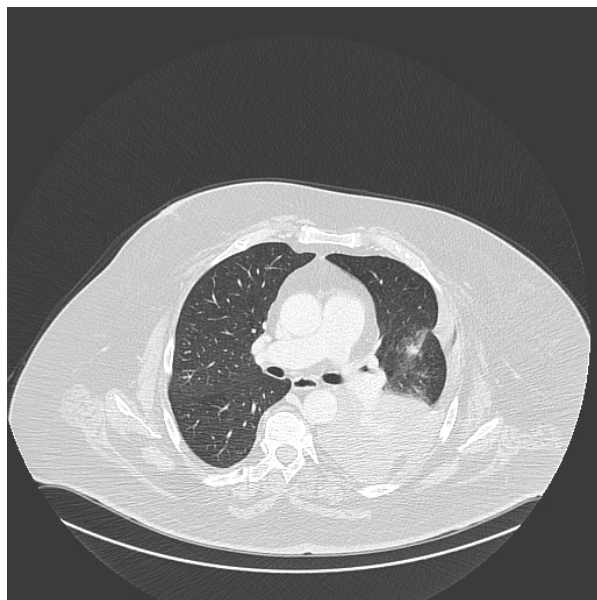
The cytological diagnosis of MM in effusions should fulfil one of the following criteria:

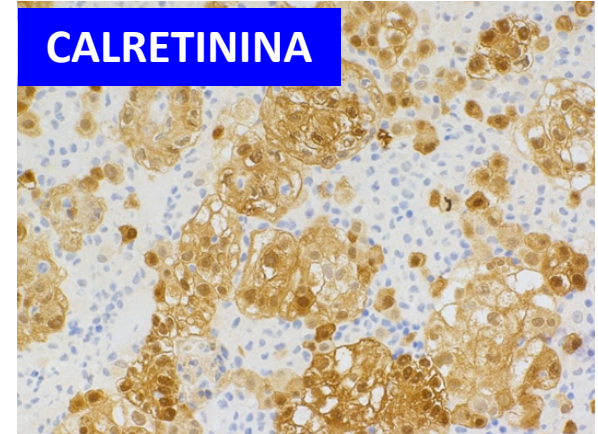
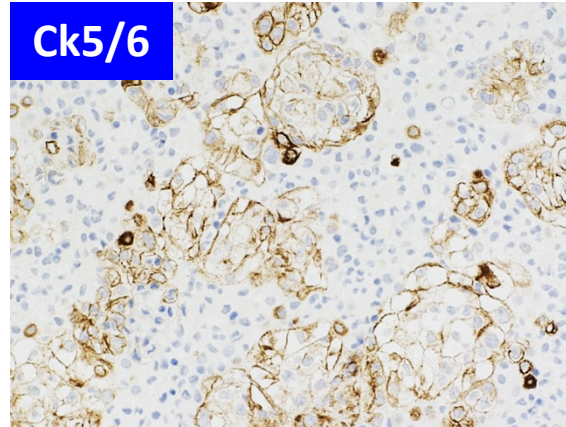
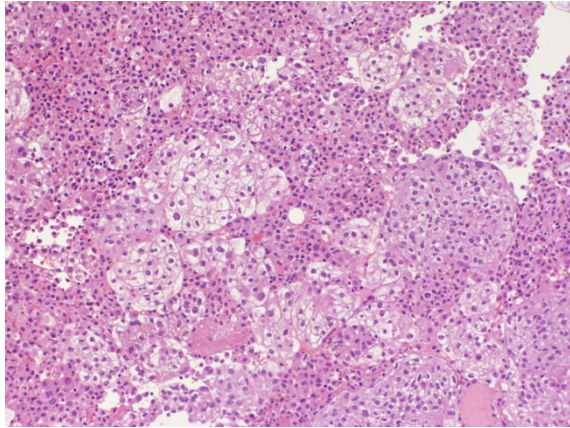
- Indisputable malignant cells on cytomorphological criteria which demonstrate a mesothelial phenotype, which should be verified by ancillary techniques;
- Cytomorphological features which are not unequivocally malignant, but ancillary techniques confirm malignancy and a mesothelial phenotype.

When evaluated in clinical practice, these two options can make the specific diagnosis of MM with a high degree of sensitivity and accuracy<sup>5</sup>, while noting that the diagnosis of sarcomatoid MM can rarely be established by effusion cytology.



**F, 59 anni**  
**Versamento pleurico**  
**Ricoverata per**  
**volvolo intestinale**





**CD10 (-/+)**

**CI4 (-)**

**TTF1 (-)**

**P63 (-)**

**PAX8 (-)**

**mesotelioma maligno diffuso di tipo  
epiteloide con cellule chiare (confermata da  
biopsia pleurica toracoscopica successiva)**

**Table 5. Immunohistochemical Markers Used in the Differential Diagnosis Between Epithelioid Pleural Mesothelioma and Lung Adenocarcinoma**

Marker	Current Value/Comments
<b>Epithelioid mesothelioma (positive mesothelioma markers)</b>	
Calretinin	Very useful. It can be demonstrated in nearly all epithelioid mesotheliomas when antibodies to human recombinant calretinin are used. The staining is often strong and diffuse, and both nuclear and cytoplasmic. Five percent to 10% of lung adenocarcinomas are positive, but the staining is usually focal.
Cytokeratin 5 or 5/6	Very useful. It is expressed in 75% to 100% of the mesotheliomas. Approximately 2% to 20% of lung

**Table 6. Immunohistochemical Markers Used in the Differential Diagnosis Between Epithelioid Pleural Mesothelioma and Squamous Carcinoma of the Lung**

Marker	Current Value/Comments
WT-1	
D2-40 (podoc)	

Lung adenocarcinoma  
MOC-31

**Table 7. Immunohistochemical Markers Used in the Differential Diagnosis Between Epithelioid Pleural Mesothelioma and Renal Cell Carcinomas**

BG8 (Lewis<sup>Y</sup>)

Marker	Current Value/Comments
Epithelioid mesothelioma	
WT-1	
Calretinin	

CEA (monoclonal)

Marker	Current Value/Comments
Epithelioid mesothelioma	
Cytokeratin 5 or 6	

B72.3

**Table 8. Peritoneal Malignant Mesothelioma (PMM) Versus Papillary Serous Carcinoma (PSC) and Nongynecologic Adenocarcinoma (AdCa)**

Ber-EP4

Marker	Current Value/Comments
Epithelioid mesothelioma	
Mesothelin	
Calretinin	

TTF-1

Marker	Current Value/Comments
Epithelioid mesothelioma	
D2-40 (podoplasmic)	
Cytokeratin 5 or 6	

Napsin A

Marker	Current Value/Comments
Epithelioid mesothelioma	
D2-40 (podoplasmic)	
WT-1	

Marker	Current Value/Comments
Epithelioid mesothelioma	
MOC-31	

Marker	Current Value/Comments
Epithelioid mesothelioma	
BG8 (Lewis <sup>Y</sup> )	

Marker	Current Value/Comments
Epithelioid mesothelioma	
Ber-EP4	

Marker	Current Value/Comments
Epithelioid mesothelioma	
Ber-EP4	

Marker	Current Value/Comments
Epithelioid mesothelioma	
Cytokeratin 5 or 6	

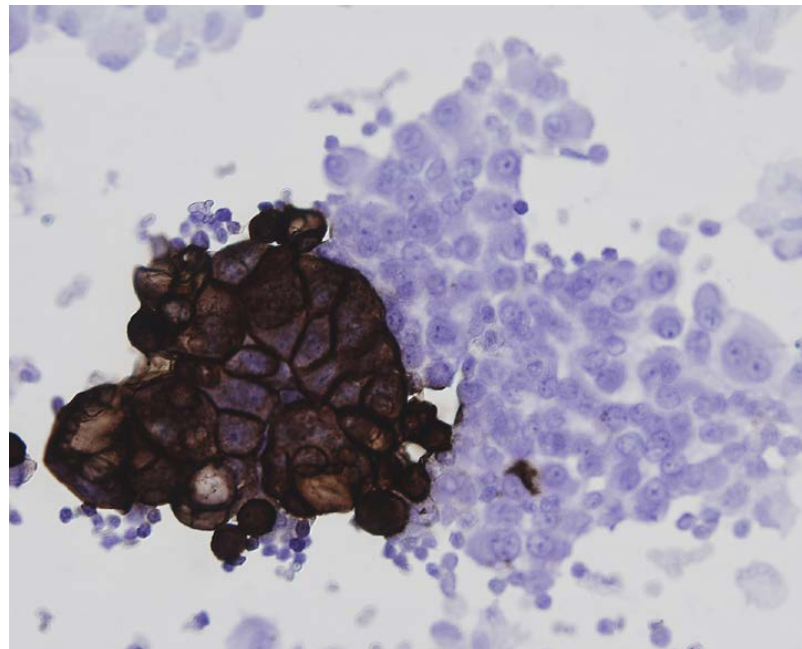
Marker	Current Value/Comments
Epithelioid mesothelioma	
Cytokeratin 5 or 6	

Arch Pathol Lab Med. 2012;136:1–21; doi: 10.5858/ arpa.2012-0214-OA

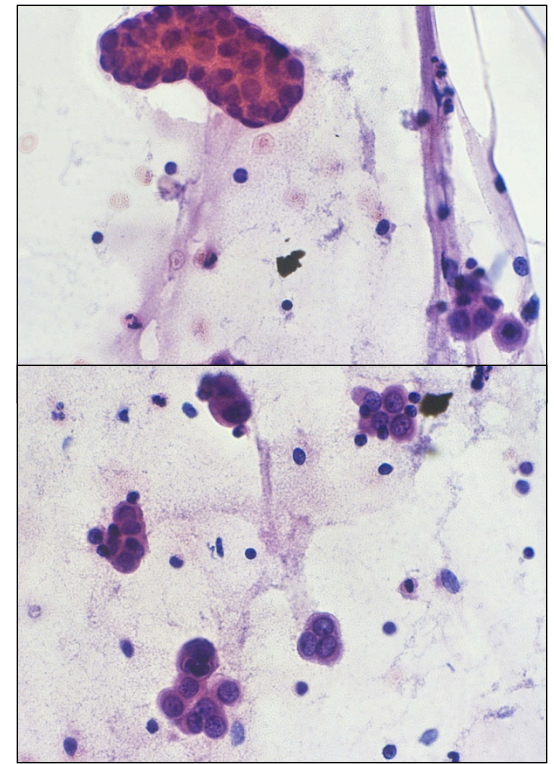
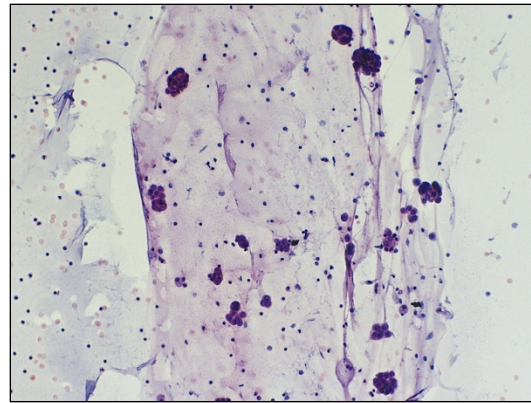
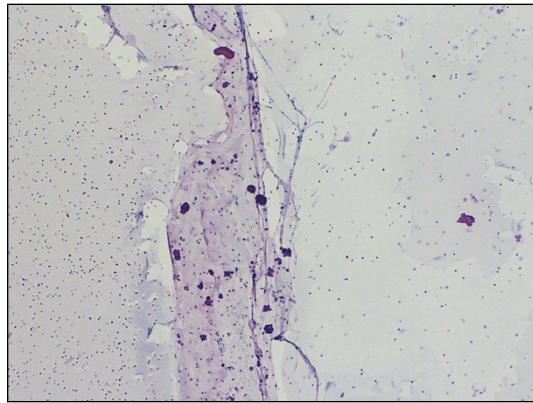
CEA	Very useful. Positivity in 61% of AdCas, negativity in PMM.
B72.3	Very useful. Positivity in 84% of pancreas, 89% of bile duct, 98% of colon AdCas; 0% to 3% of PMM cases.
Ber-EP4	Useful. Positivity in >98% of pancreatic and gastric AdCas, 9% to 13% of PMM cases.
CDX2	Useful. Ninety percent to 100% of colon, 80% of small intestine, and 70% of gastric carcinomas are positive; negativity in PMM.

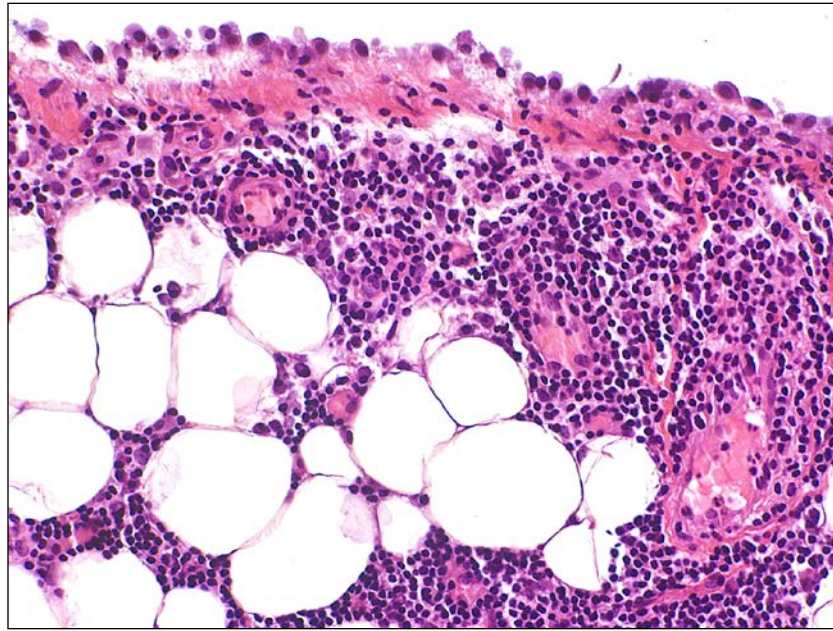
## **Claudin 4 identifies a wide spectrum of epithelial neoplasms and represents a very useful marker for carcinoma versus mesothelioma diagnosis in pleural and peritoneal biopsies and effusions**

**Fabio Facchetti · Silvia Lonardi · Francesca Gentili ·  
Luisa Bercich · Marcella Falchetti · Regina Tardanico ·  
Carla Baronchelli · Laura Lucini · Alessandro Santin ·  
Bruno Murer**



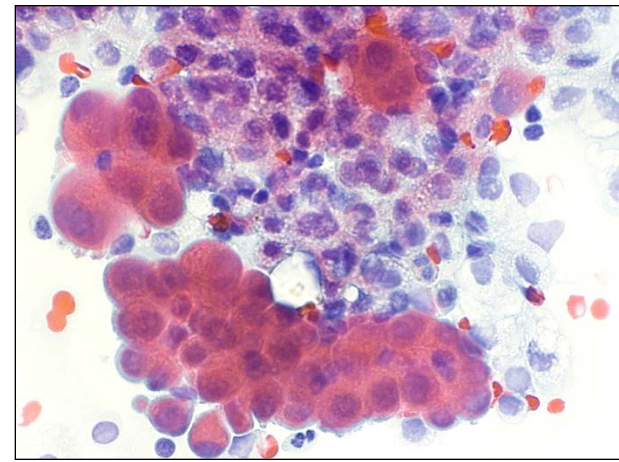
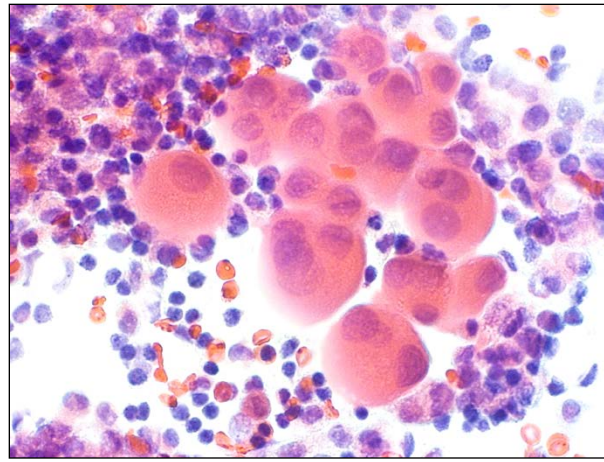
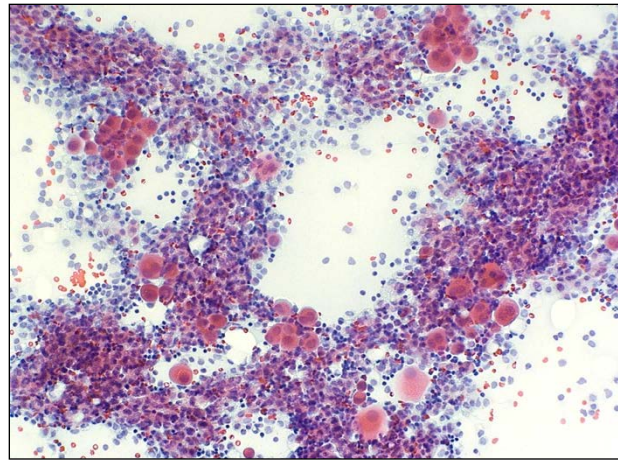
**F, 61 anni con scompenso cardiaco e versamento pleurico inizialmente bilaterale, persistente a sinistra**



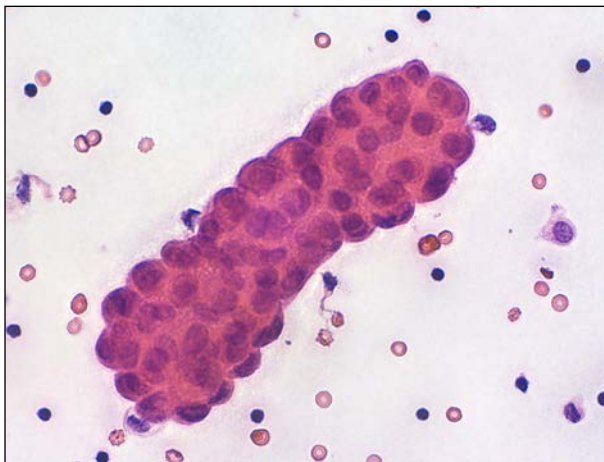
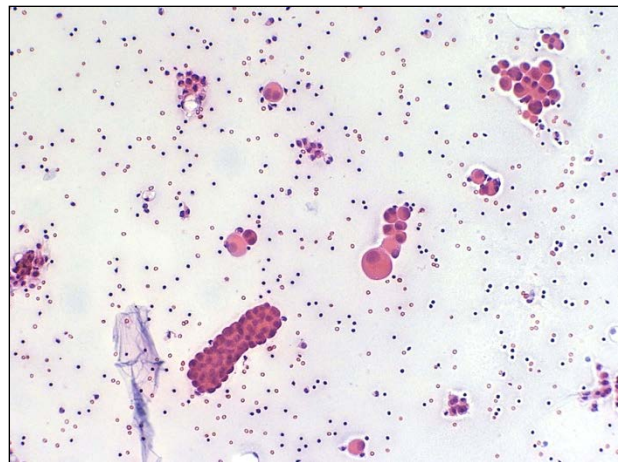


**Biopsia pleurica: *pleurite cronica non specifica***

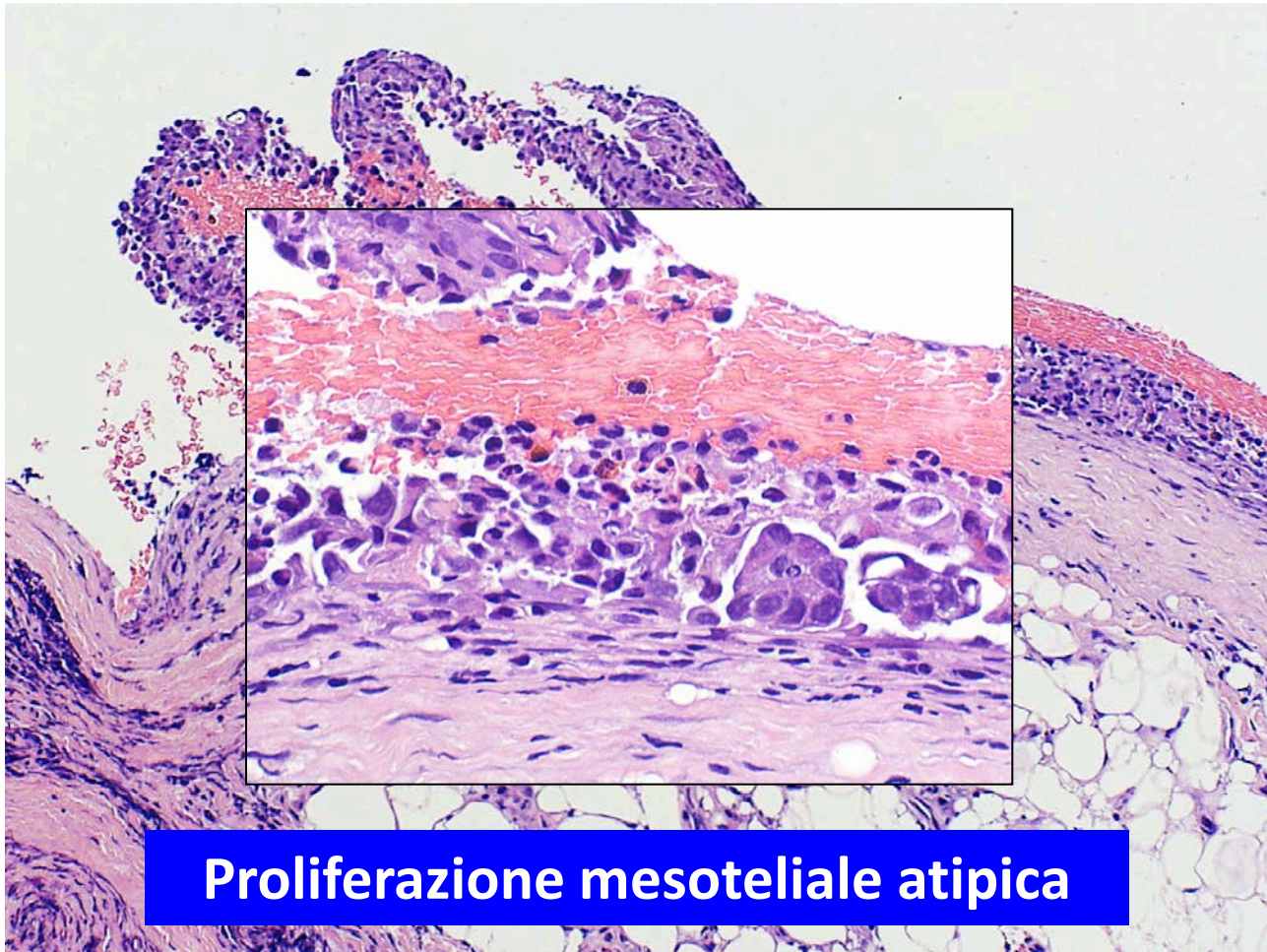
*F, 91 anni, cardiopatica, con versamento pleurico a destra da alcuni mesi, paucisintomatico*



**Proliferazione mesoteliale atipica. Mesotelioma?**



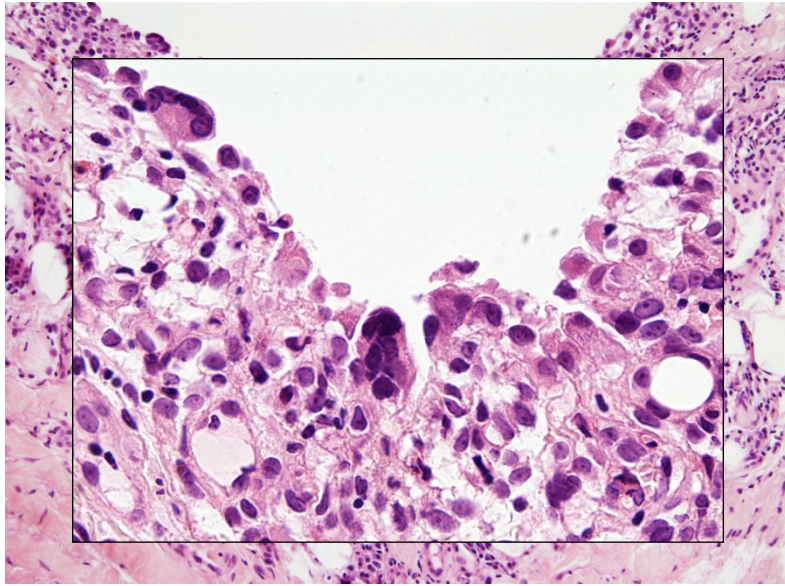
- Uomo di 44 anni con pleuropatia sinistra di n.d.d.
- Non nota esposizione ad asbesto
- Toracoscopia (05.2011): quadro aspecifico
- Biopsia



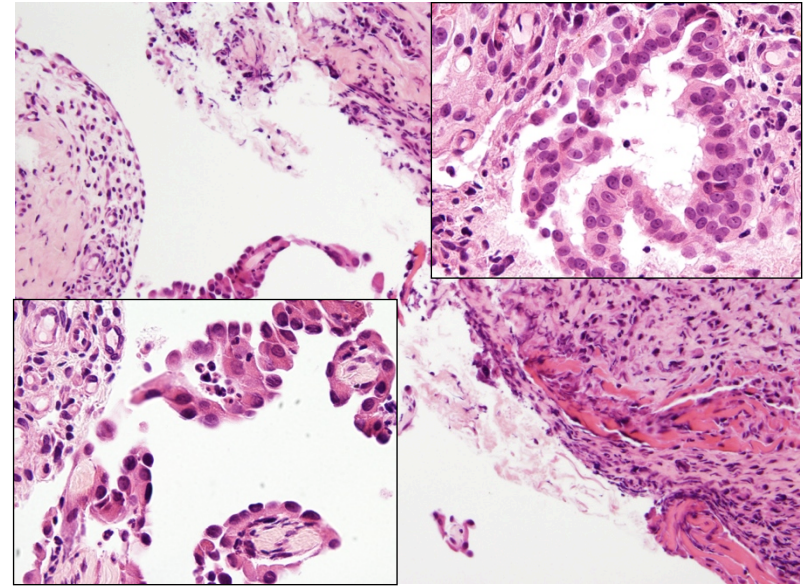
**Proliferazione mesoteliale atipica**



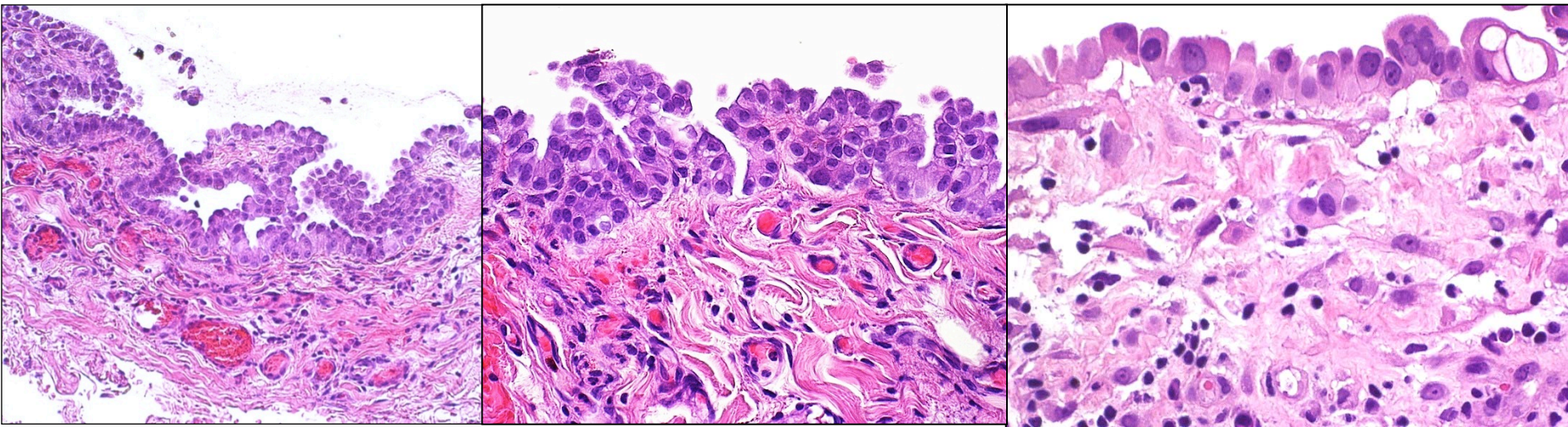
**F 44 aa, pregresso ca mammario operato + RT (1997).  
Versamento pleurico, toracoscopia con biopsia**



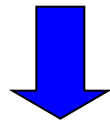
**07.2007**



**PROLIFERAZIONE MESOTELIALE ATIPICA**



- In presenza di elementi morfologici che suggeriscono un mesotelioma (papille, stratificazione, proliferazione continua) ma che non sono sufficienti per una diagnosi di certezza (assenza di invasione e/o noduli)
- In assenza di cause o condizioni riconducibili ad una proliferazione mesoteliale reattiva ancorché esuberante

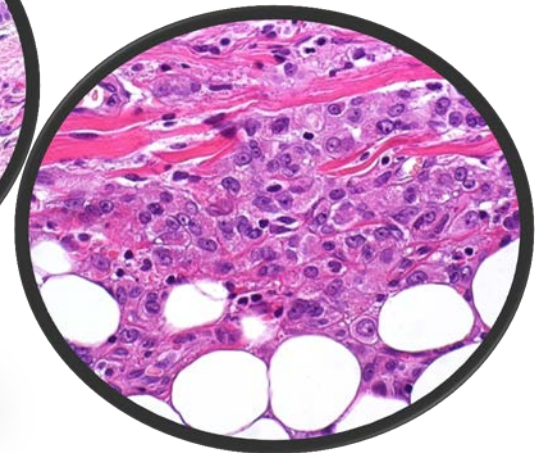
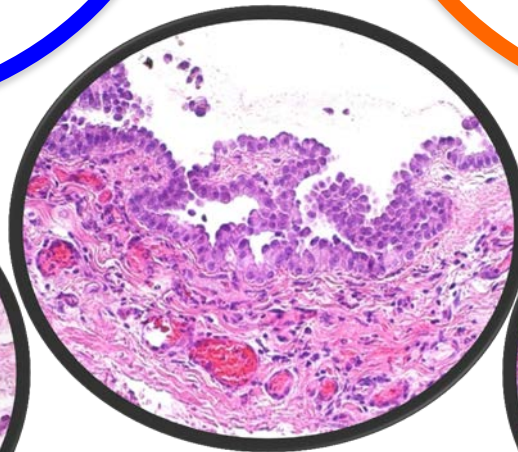
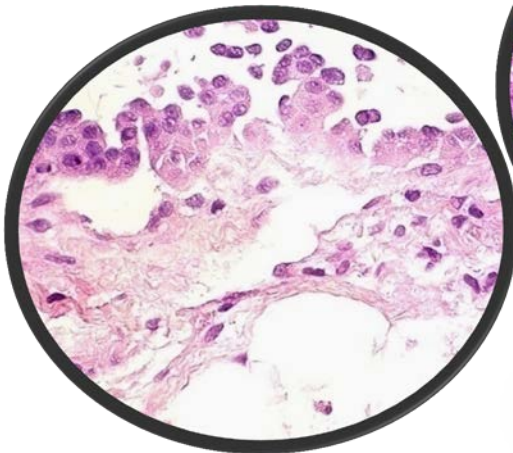


**PROLIFERAZIONE MESOTELIALE ATIPICA**

**PROLIFERAZIONE  
MESOTELIALE  
ATIPICA**

**IPERPLASIA  
MESOTELIALE  
REATTIVA**

**MESOTELIOMA  
MALIGNO**



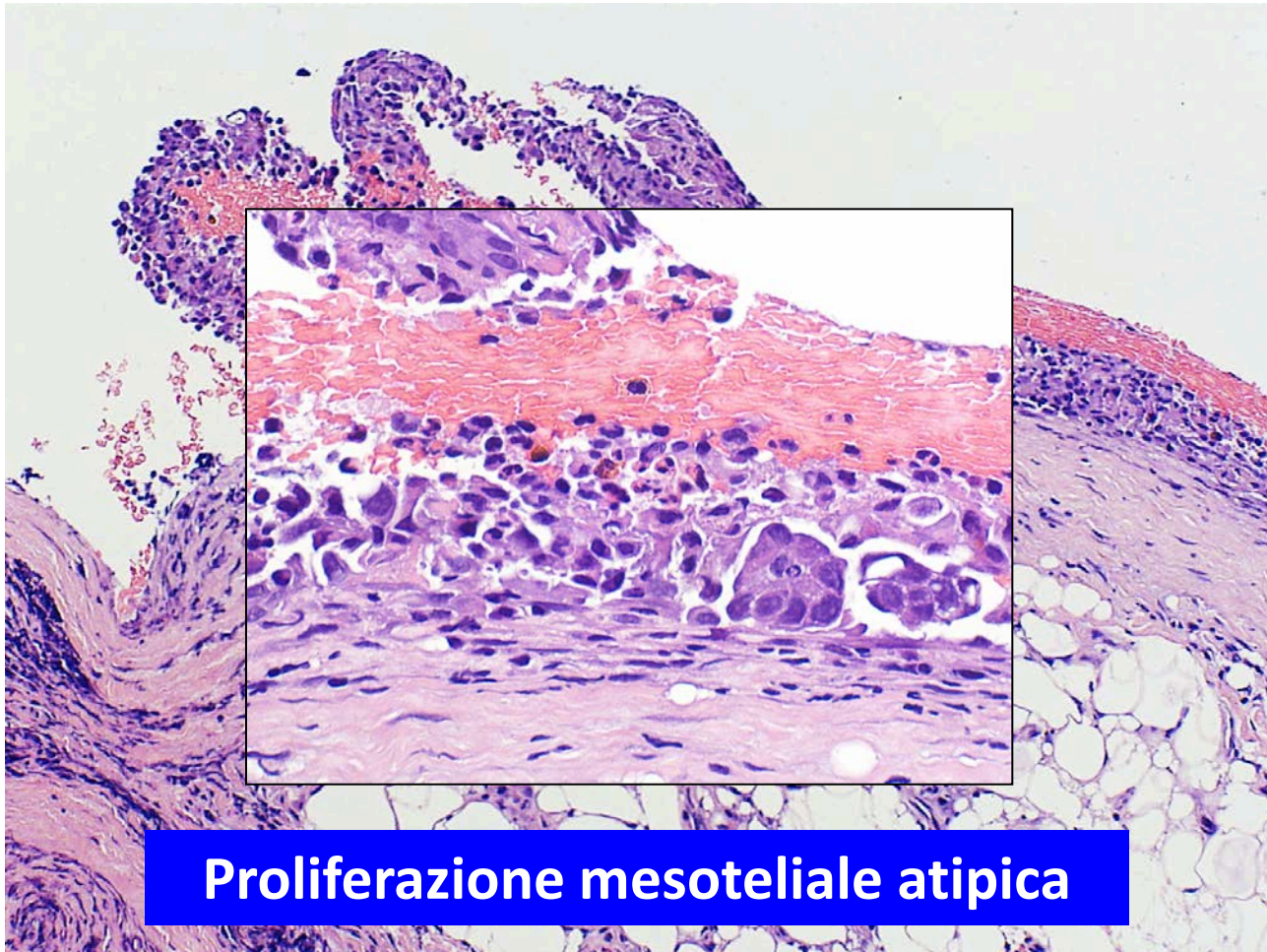
# PROLIFERAZIONE MESOTELIALE ATIPICA

## CLINICA

- Versamento pleurico recidivante in un lasso di tempo imprevedibile (da mesi ad anni)
- Toracosopia iniziale: alterazioni minime non specifiche
- Toracosopia/e di controllo: non specifica/ispessimento/noduli

**Correlazione clinico-radiologica, follow-up, eventuale ripetizione della biopsia con estensivo campionamento**

- Uomo di 44 anni con pleuropatia sinistra di n.d.d.
- Non nota esposizione ad asbesto
- Toracoscopia (05.2011): quadro aspecifico
- Biopsia



**Proliferazione mesoteliale atipica**