



SHMU

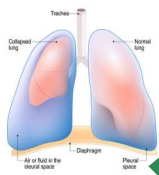
Body Fluids

Mansoure Ajami

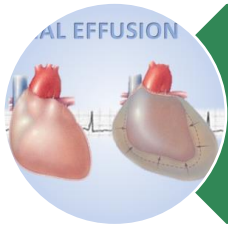
Assistant professor of Hematology
Shahroud University of Medical Sciences

Serous Body Fluid

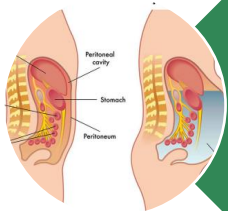
Pleural Effusion



Pleural Fluid

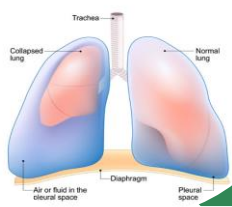


Pericardial Fluid



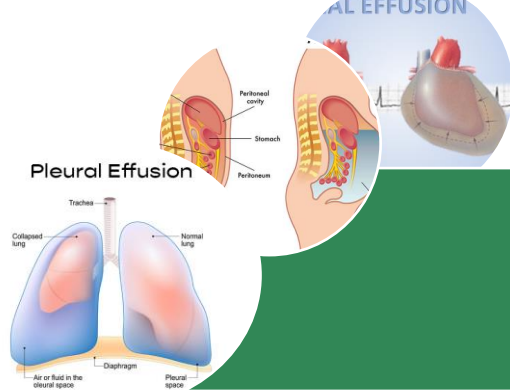
Peritoneal fluid

Pleural Effusion



Pleural Fluid

- Potential space lined by mesothelium of the visceral and parietal pleurae.
- The pleural cavity normally contains a small amount of fluid that facilitates movement of the two membranes against each other
- “Ultra filtrate” of the plasma Closely resembles the plasma.
- Serous fluid is normally Produced at a constant rate by hydrostatic and oncotic / protein pressures in the capillaries lining the membranes
- Production occurs – (▣ parietal membrane) - at the cavity wall
- Re-absorption occurs – (▣ visceral membrane) - at the covering the organs contained within.

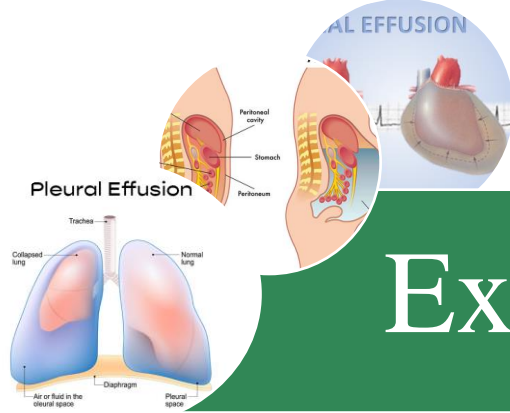


Effusion

An accumulation of fluid results from an imbalance of fluid production and reabsorption.

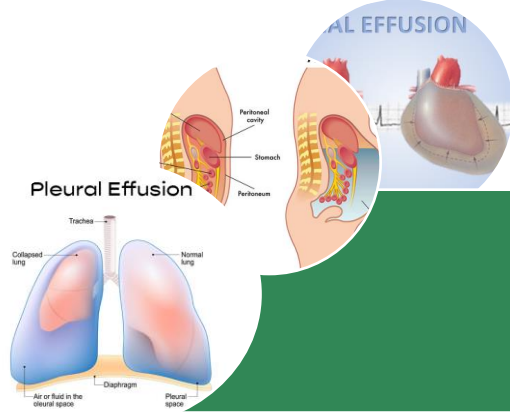
fluid accumulation in the pleural, pericardial, and peritoneal cavities is known as a serous effusion

Determine the reason for the accumulation of the fluid
Infections Hemorrhages malignancies other disorders



Exudates or Transudates

- All effusions are classified as exudates or a transudates
- Classifying help clinicians to determine the disease process responsible for the accumulation of fluid



Transudates

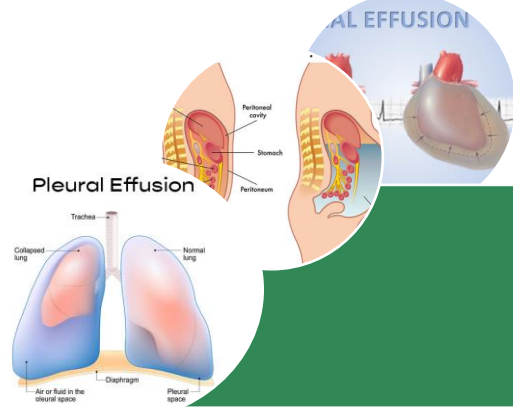
- Transudates are usually owing to systemic conditions
- Malfunctioning membranes causes fluid accumulates in the body cavities.
- Disrupt the balance between the formation and its uptake by the lymphatic system

Transudates: Increased Hydrostatic Pressure or Decreased Plasma Oncotic Pressure

Congestive heart failure

Hepatic cirrhosis

Hypoproteinemia (e.g., nephrotic syndrome)



Exudates

- Exudates are more often associated with localized disorders
- A result of a problem with the membranes themselves.
- Produced by conditions that directly involve the membranes of the particular cavity, ex. infections, inflammation, and malignancies
- An exudate is a fluid with a high content of protein and cellular debris which has escaped from blood vessels and has been deposited in tissues.

Exudates: Increased Capillary Permeability or Decreased Lymphatic Resorption

Infections

- Bacterial pneumonia

- Tuberculosis, other granulomatous diseases (e.g., sarcoidosis, histoplasmosis)

- Viral or mycoplasma pneumonia

Neoplasms

- Bronchogenic carcinoma

- Metastatic carcinoma

- Lymphoma

- Mesothelioma (increased hyaluronate content of effusion fluid)

Noninfectious inflammatory disease involving pleura

- Rheumatoid disease (low pleural fluid glucose in most cases)

- Systemic lupus erythematosus (LE cells are occasionally present)

- Pulmonary infarct (may be associated with hemorrhagic effusion)

Laboratory Criteria for Pleural Fluid Exudate

Pleural fluid/serum protein ratio	≥ 0.50
Pleural fluid/serum LD ratio	≥ 0.60
Pleural fluid LD	$\geq 2/3$ upper limit of normal serum LD

Light's criteria

Sensitivity 98%

Specificity 80%

An effusion with none of these characteristics is classified as a transudate

- Alternative measurements have been proposed to differentiate exudates from transudates

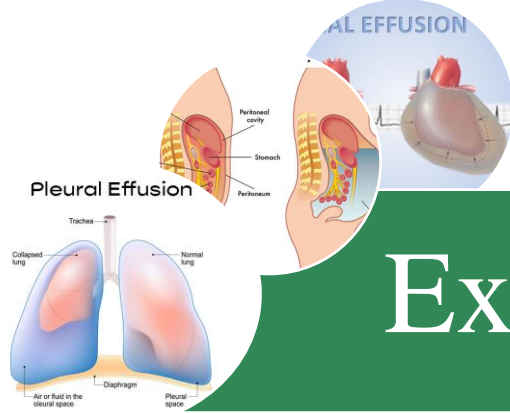
Laboratory Criteria for Pleural Fluid Exudate

Pleural fluid cholesterol	>45 mg/dL
Pleural fluid/serum cholesterol ratio	≥0.30
Serum–pleural fluid albumin gradient	≤1.2 g/dL
Pleural fluid/serum bilirubin ratio	≥0.60

- An effusion with none of these characteristics is classified as a transudate

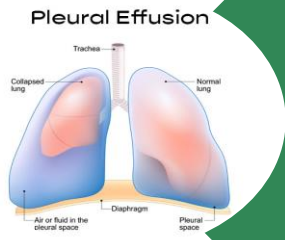
Differentiation Between Transudates and Exudates

CHARACTERISTIC / TEST	TRANSUDATE	EXUDATE
Color	Pale yellow	Any abnormal color
Clarity	Clear	Bloody cloudy, purulent, turbid
Specific gravity	< 1.015	>1.015
Glucose	Equal to serum	Over 30 mg less than serum level
Protein	<3.0 g/dL	>3.0 g/dL
Fluid / serum protein ratio	<0.5	>0.5
Fibrinogen / Spontaneous clotting	No	Possible
Fluid / serum amylase	<2.0	>2.0
Fluid / serum bilirubin ratio	<0.6	>0.6
Lactate dehydrogenase	< 60% of serum	> 60% of serum
Fluid/ serum LD ratio	<0.6	>0.6
Cell counts (total)	<300/L	>1000/L



Exudates or Transudates

- Transudates generally require no further workup
- Further analysis of exudates is directed toward ruling out malignancy and infection. Cytology and appropriate bacterial stains and cultures or PCR-based microbial assays are the most useful tests in this regard



Pleural Fluid

Variety of tests used to aid in determining the cause of the effusion

- **Appearance**
- Evaluation of **clotting ability** whether or not it will form a clot, etc.
- **Cell counts and differential** are performed in the hematology department
- **chemistry**
 - Protein level / Both fluid and current serum level to make comparison: fluid protein / serum protein
 - LDH enzymes / Both fluid and current serum level to make comparison: fluid LDH/ serum LDH
- **Cytology / Pathology** – if malignancy is suspected.
- **Serology** – rarely done on serous fluids as blood testing is adequate

Pleural Effusion: Recommended Tests

Routine Tests

Gross examination

Pleural fluid/serum protein ratio (used for Light's criteria)

Pleural fluid/serum LDH ratio (used for Light's criteria)

Examination of Romanowski-stained smear (malignant cells, LE cells)

Useful Tests in Most Patients

Stains and cultures for microorganisms

Cytology

Useful Tests in Selected Cases

Pleural fluid cholesterol

Pleural fluid/serum cholesterol ratio

Albumin gradient

pH

Lactate

Enzymes (ADA, amylase)

Interferon- γ

C-reactive protein

Lipid analysis

Multiplex PCR assay for bacterial, fungal, viral, and mycobacterial DNA

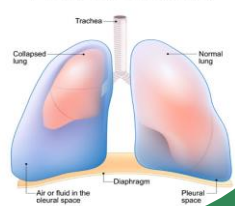
Tumor markers

Immunologic studies

Tuberculostearic acid

Pleural biopsy

Pleural Effusion



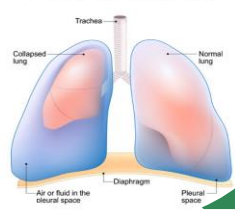
Pleural Fluid

Gross Examination

Transudates:

- Clear
- pale yellow to straw colored
- odorless
- do not clot.
- Approximately 15% of transudates are blood tinged. A bloody pleural effusion (hematocrit $>1\%$) suggests trauma, malignancy, or pulmonary infarction
- A pleural fluid hematocrit greater than 50% of the blood hematocrit is good evidence for a hemothorax

Pleural Effusion



Pleural Fluid

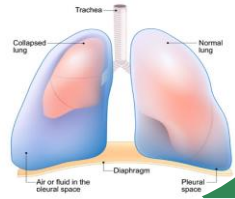
Gross Examination

Exudates:

- may grossly resemble transudates, but most show variable degrees of cloudiness or turbidity, and they often clot if not heparinized.
- A feculent odor- Anaerobic infections.
- Ammonia odour- Urinothorax
- Turbid, milky, and/ or bloody specimens should be centrifuged and the supernatant examined.

If the supernatant is clear, the turbidity is most likely due to cellular elements or debris. If the turbidity persists after centrifugation, a chylous or pseudo-chylous effusion is likely

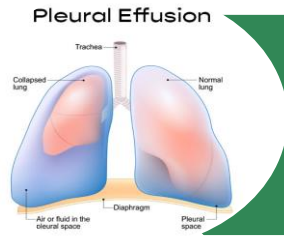
Pleural Effusion



Pleural Fluid

Gross Examination

Appearance	Possible reason / condition
Pale yellow & clear	Normal
White, turbid	WBCs / infection
Bloody	RBCs/ hemorrhage
Milky	Chyle - lymph & emulsified fats
Viscous	Increased hyaluronic acid / malignant mesothelialoma



Pleural Fluid

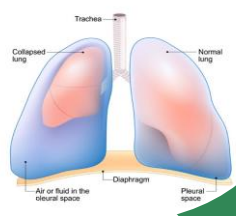
chylous or pseudochylous effusion

- True chylous effusions are produced by leakage from the thoracic duct resulting from obstruction by lymphoma, carcinoma, or traumatic disruption.

Characteristic Features of Chylous and Pseudochylous Effusions

Feature	Chylous	Pseudochylous
Onset	Sudden	Gradual
Appearance	Milky-white, or yellow to bloody	Milky or greenish, metallic sheen
Microscopic examination	Lymphocytosis	Mixed cellular reaction, cholesterol crystals
Triglycerides*†	≥110 mg/dL (≥1.24 mmol/L)	<50 mg/dL (<0.56 mol/L)
Lipoprotein electrophoresis	Chylomicrons present	Chylomicrons absent

Pleural Effusion



Pleural Fluid

Cell counts and differential

Cell count

- Manual hemocytometer methods
- Automated cell counts

Leukocyte counts

transudates $< 1000/\mu\text{L}$

RBC counts

malignancy, trauma, or pulmonary infarction $> 100,000/\mu\text{L}$

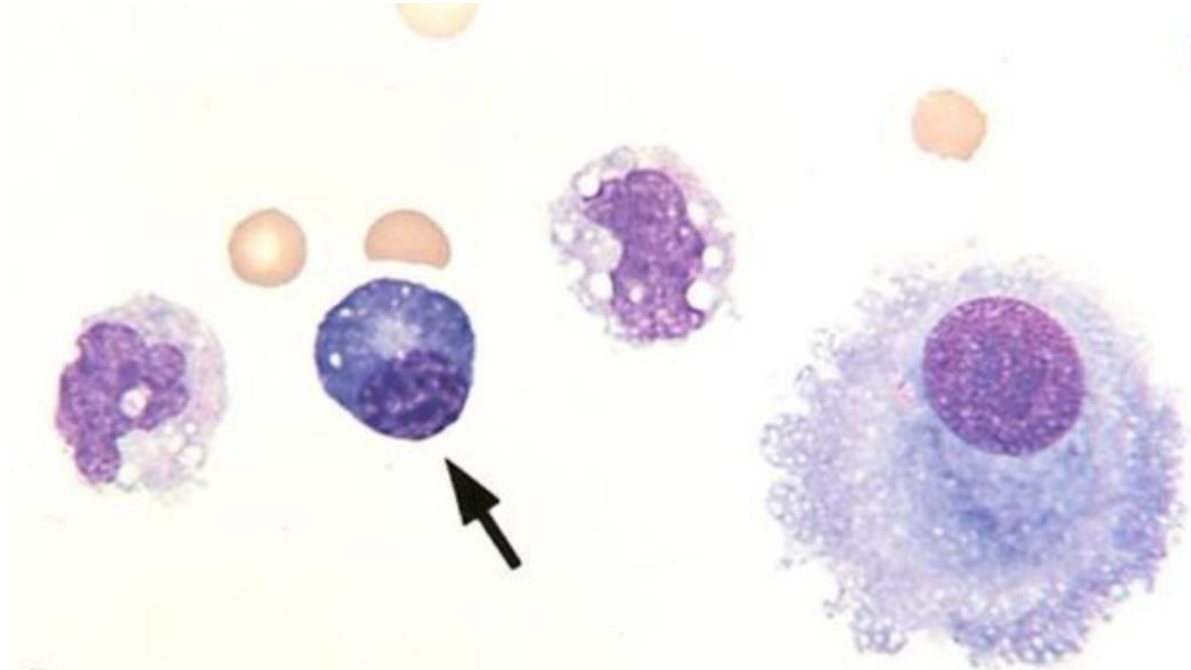
Differential

- any cell in peripheral blood,
- mesothelial cells
- malignant cells

Romanowski stained smear prepared by cytocentrifugation

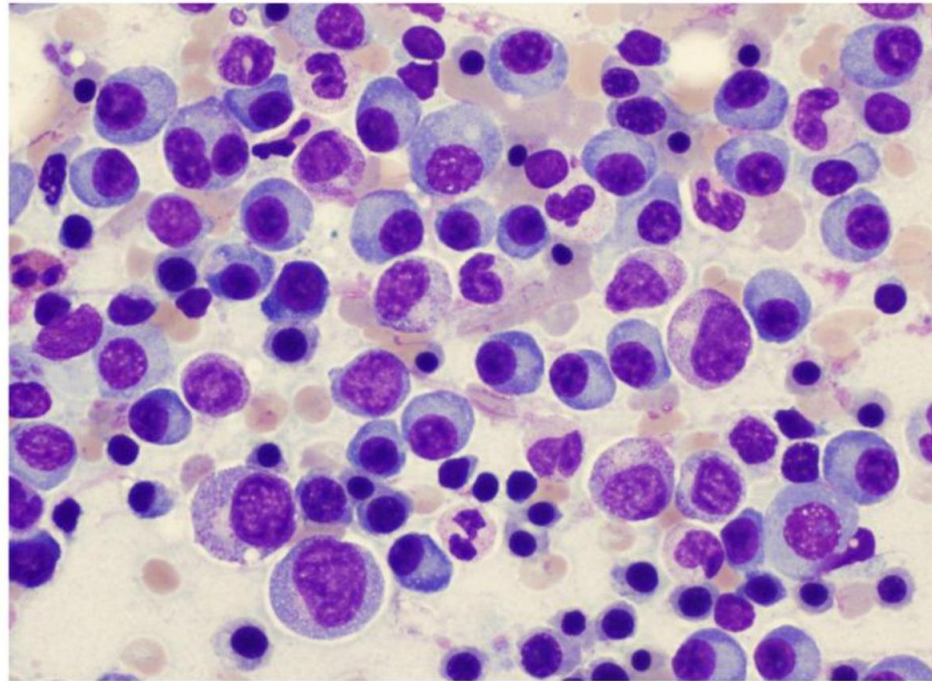
the cells seen in serous fluids..

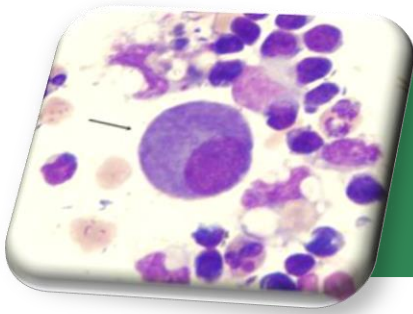
- a mesothelial cell, couple of macrophages / monocytes and a plasma cell at the arrow



Abdominal fluid – plasma cells / multiple myeloma

This acetates fluid is from a multiple myeloma patient and has many other examples of plasma cells

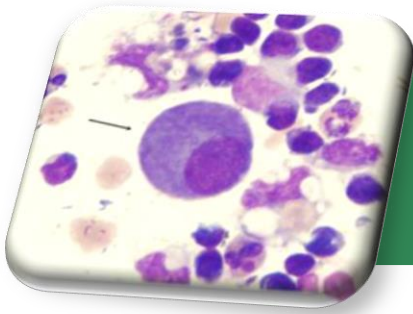




Serous Body Fluids

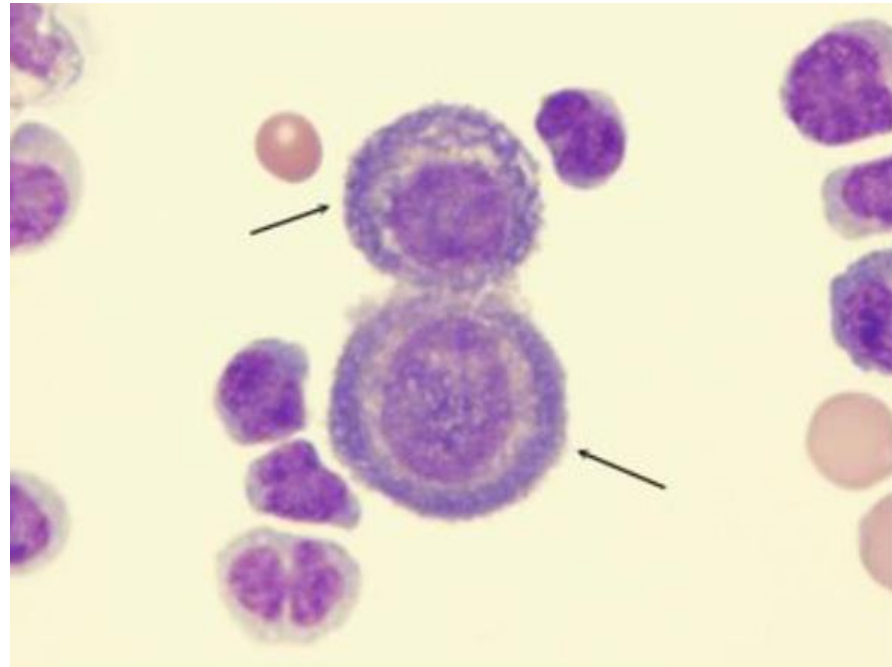
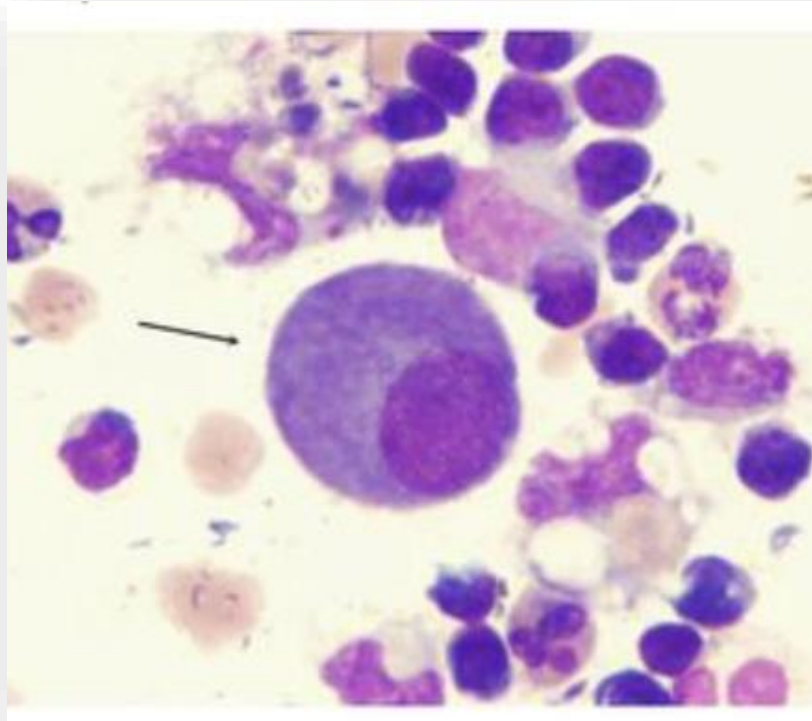
Mesothelial cells

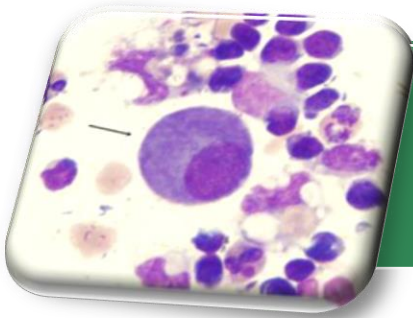
- Unique to serous fluids, originate from lining of peritoneal, pleural, and pericardial cavities.
- Large round cell with abundant blue cytoplasm and purple nucleus which may be eccentric
- sometimes described as having a "fried egg" appearance. - usually are single or may be in sheets
- Nucleus round to oval & has a smooth outline, takes $\frac{1}{3}$ - $\frac{1}{2}$ of the space.



Serous Body Fluids

Mesothelial cells

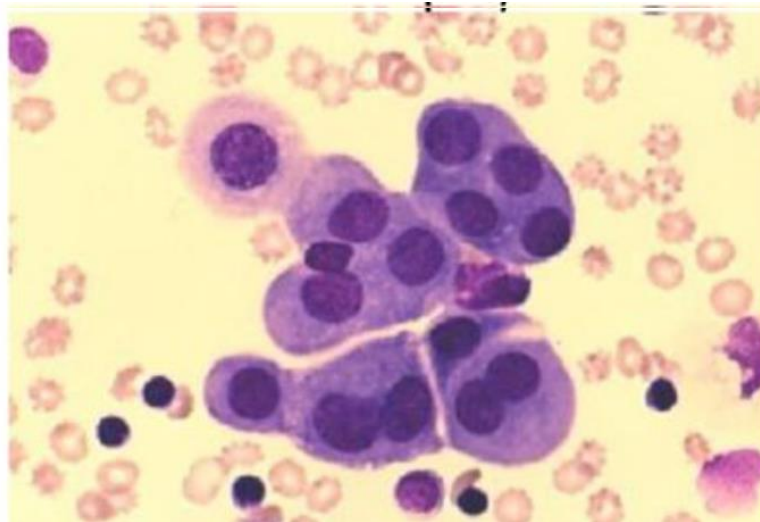




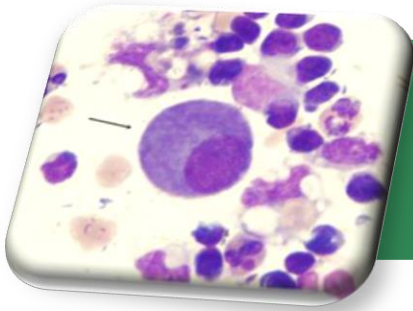
Serous Body Fluids

Mesothelial cells

- If 'reactive' may appear in clusters
- A cluster of reactive mesos may resemble malignant cell clusters, but the mesos display "cell windows."
- have different appearances (Pleomorphic)

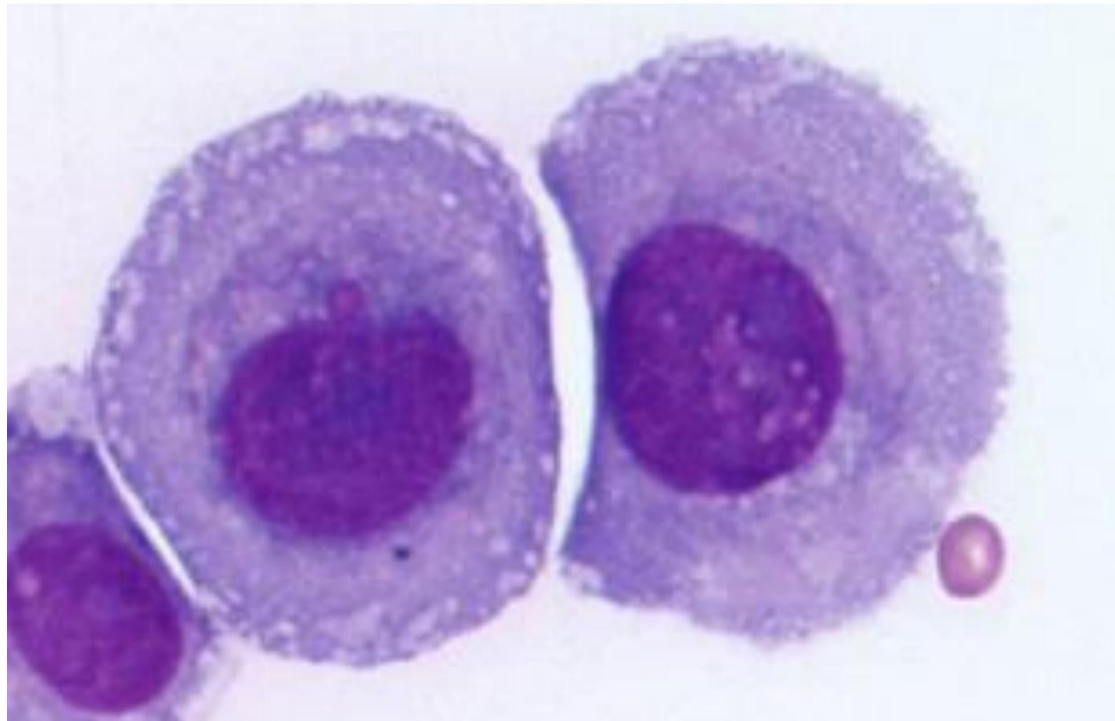


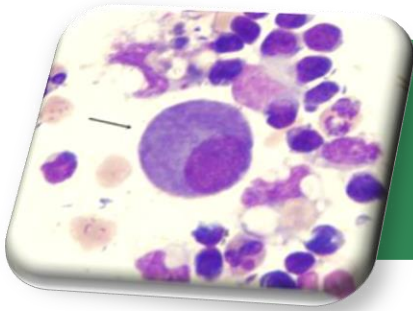
Reactive mesothelial cells



Serous Body Fluids

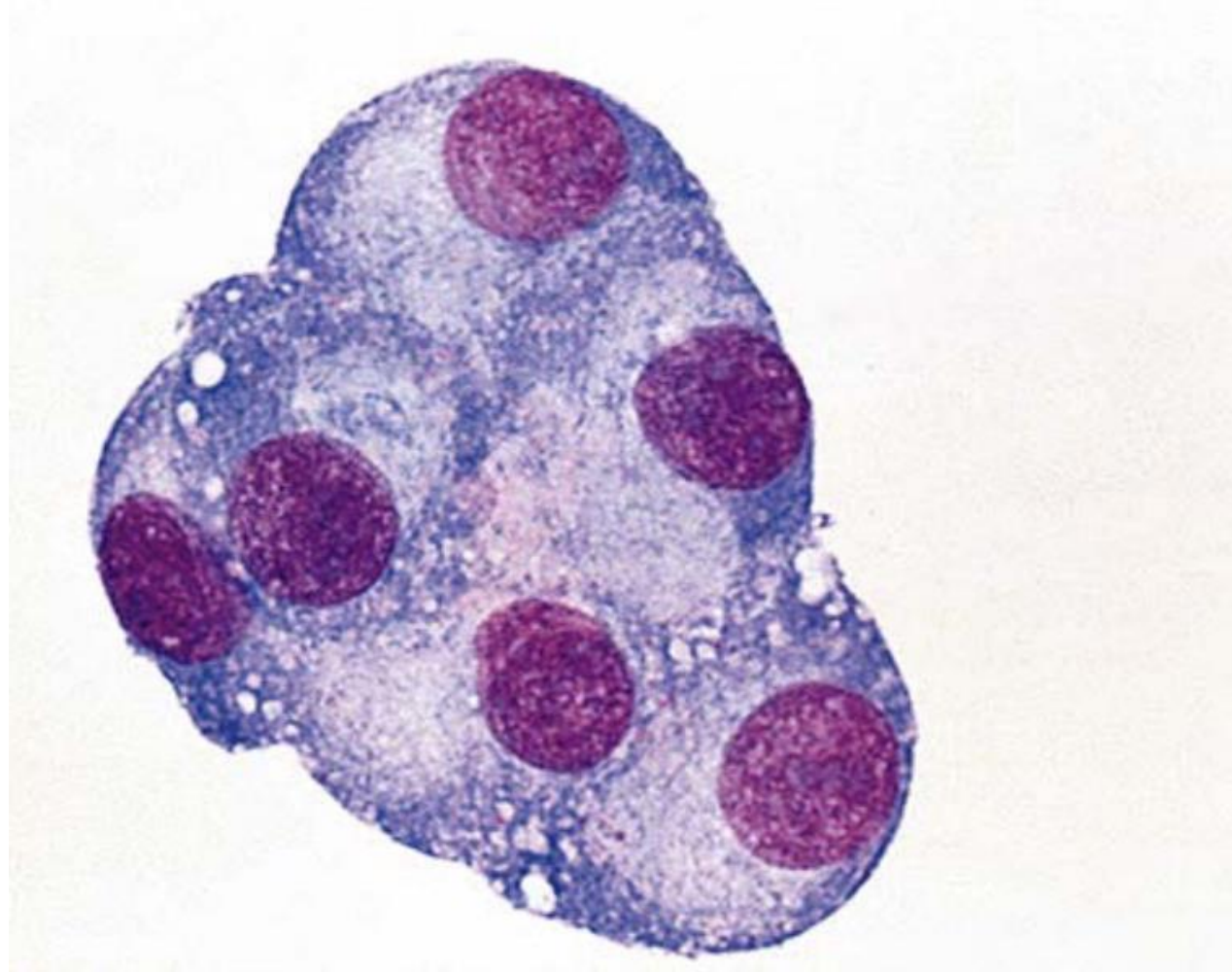
Mesothelial cells

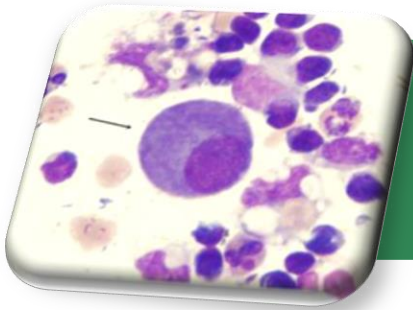




Serous Body Fluids

Mesothelial cells

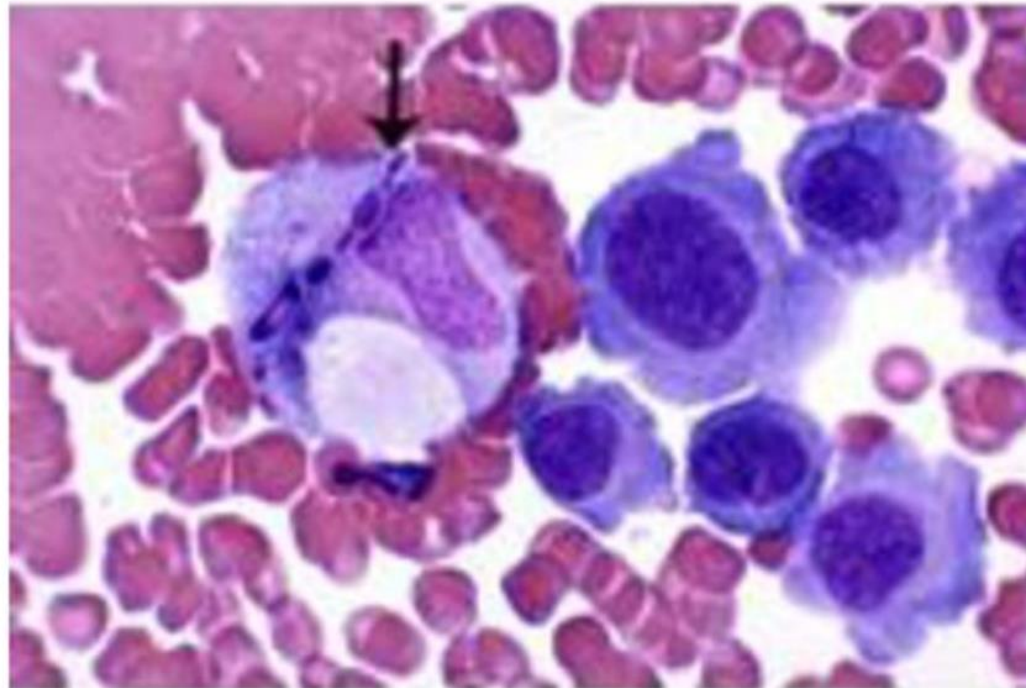


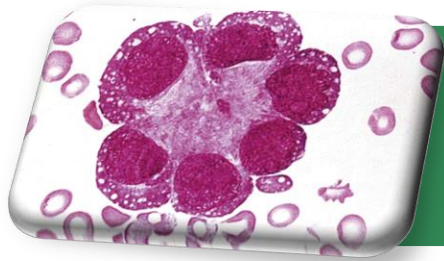


Serous Body Fluids

Mesothelial cells

- Macrophage engulfed *Candidia* species in a pleural fluid, mesothelial cells.

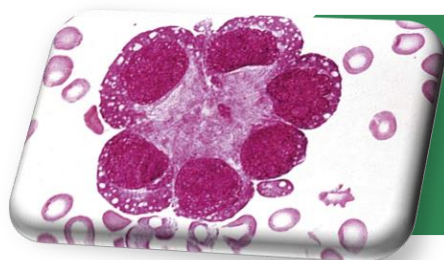




Serous Body Fluids

Malignant cells

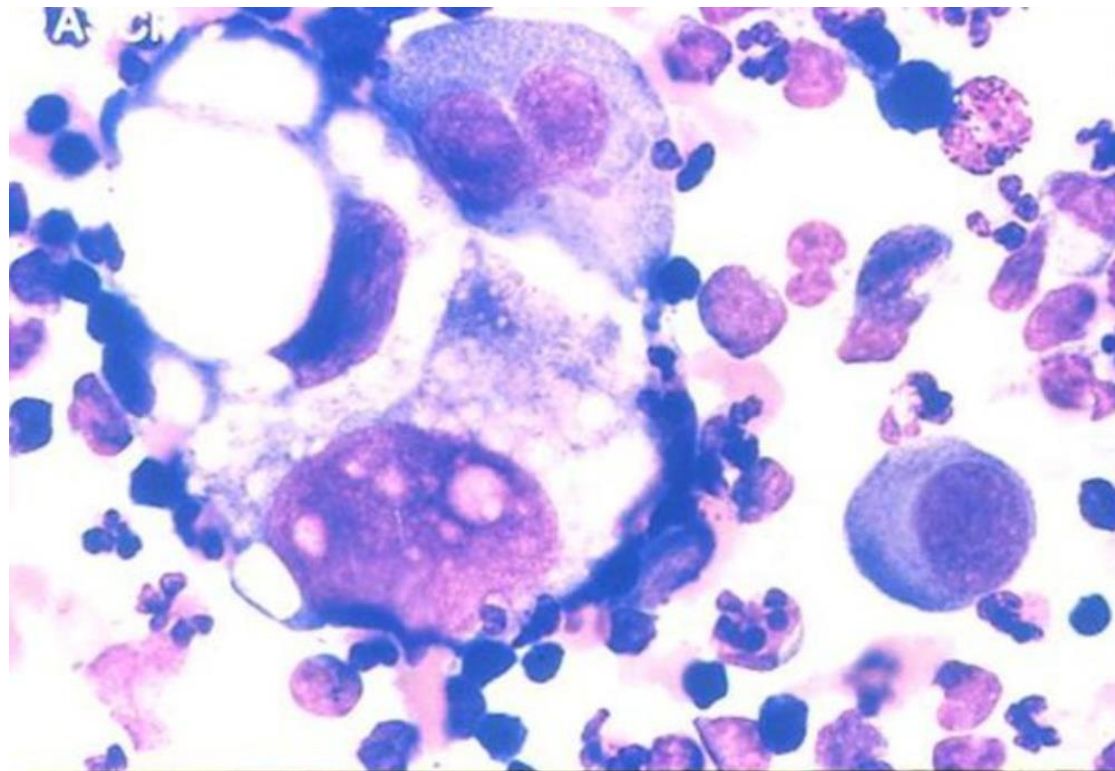
- A frequent concern in any serous fluid due to possibility of cancer of any organ and/or metastasis.
- Cells have irregular size, shape, and staining characteristics of nucleus and cytoplasm. clusters of cells. May be vacuolated.
- There is great variability in the appearance of malignant cells
- Always send suspicious cells to cytology / pathology

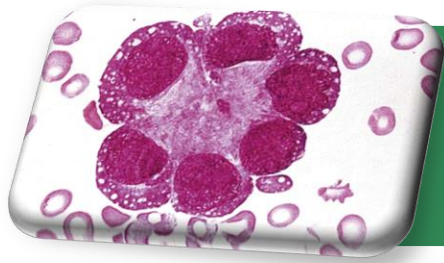


Serous Body Fluids

Malignant cells

Peritoneal fluid, malignancy

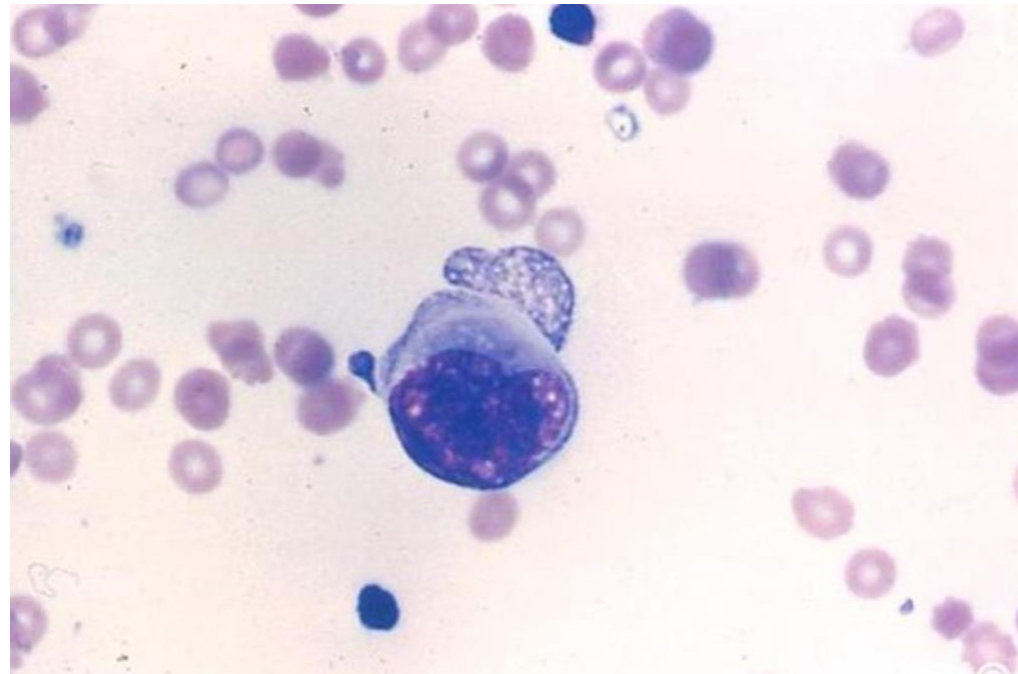


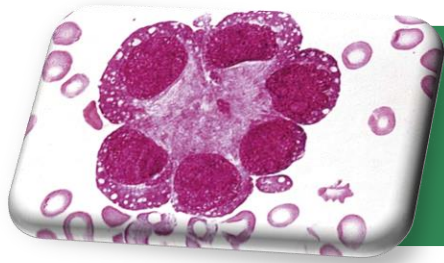


Serous Body Fluids

Malignant cells

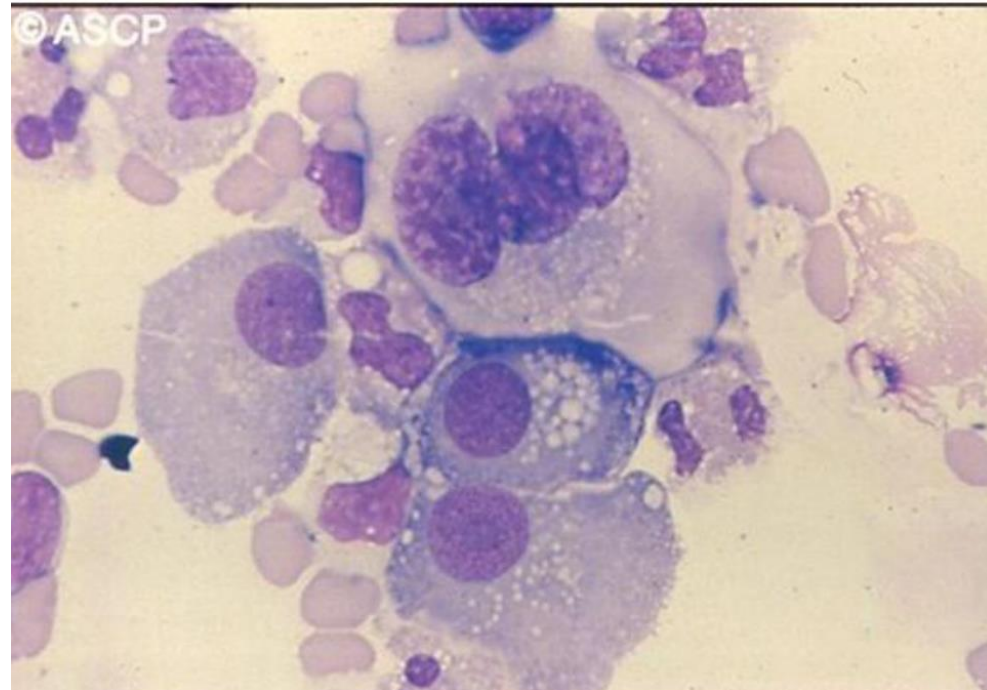
Pleural fluid 42 year old, breast cancer

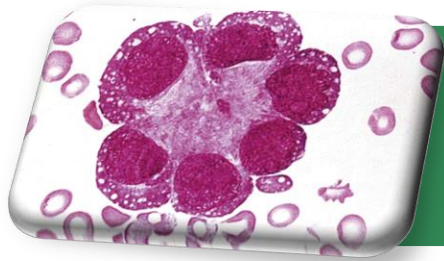




Serous Body Fluids

Malignant cells

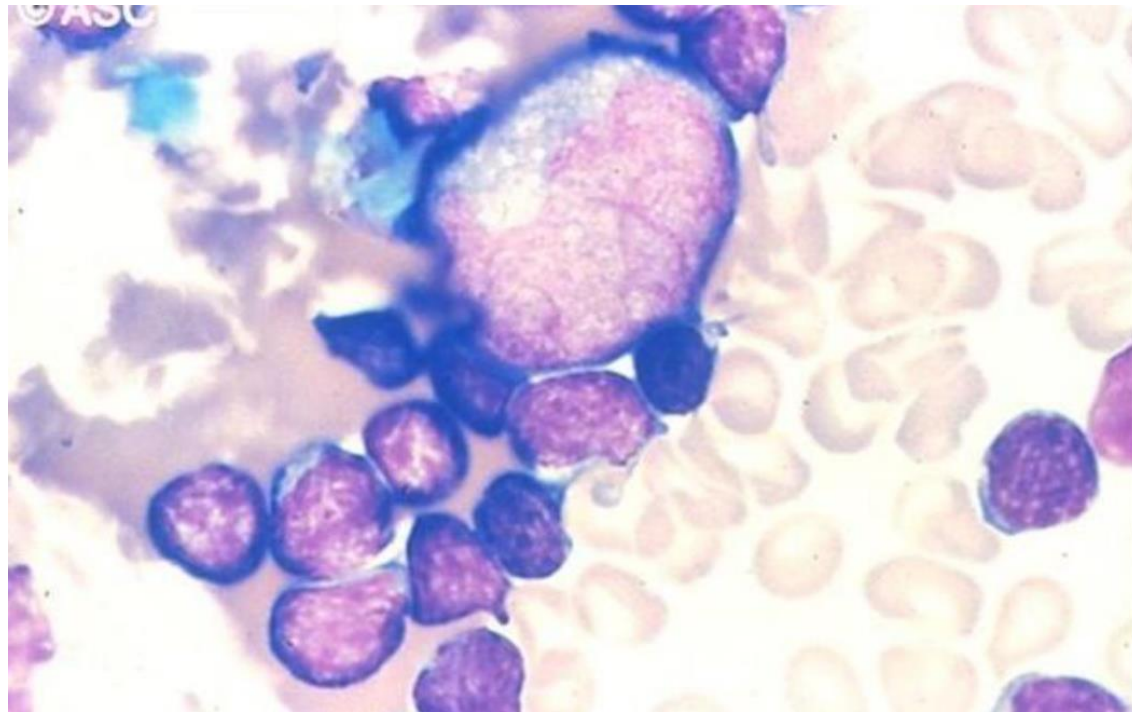


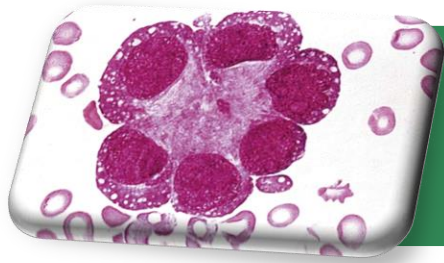


Serous Body Fluids

Malignant cells

- Pleural effusion fluid – malignant tumor on spinal cord

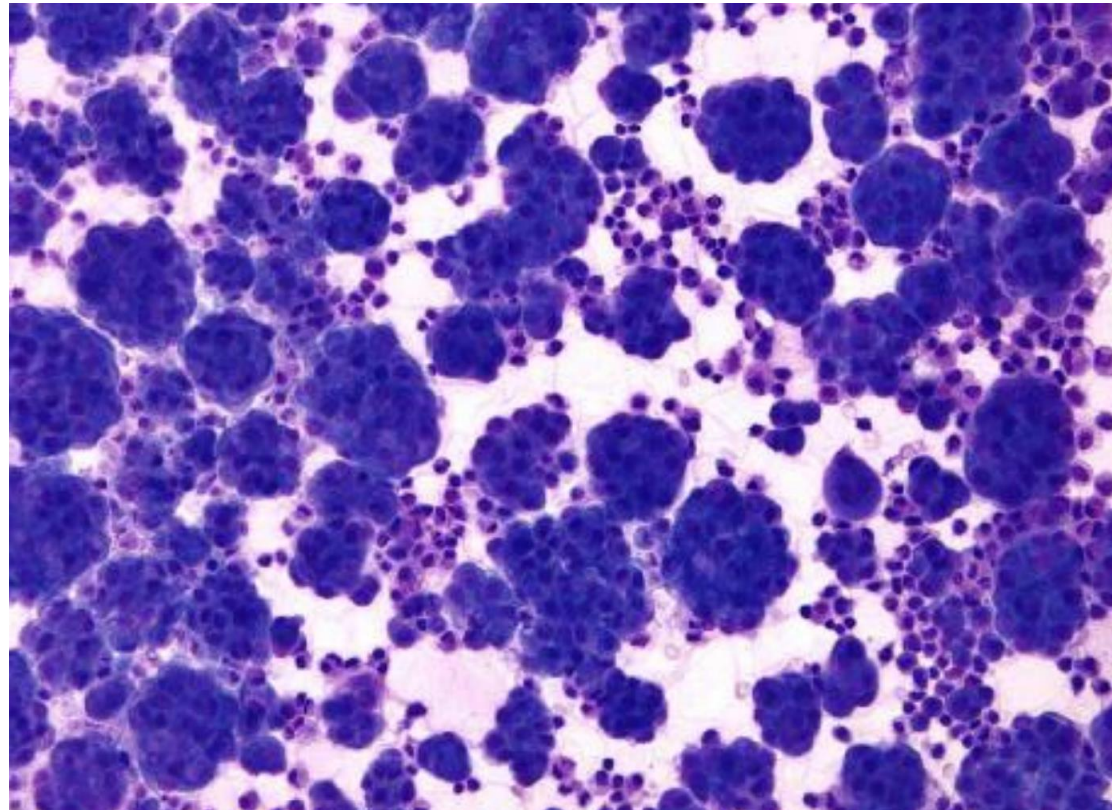


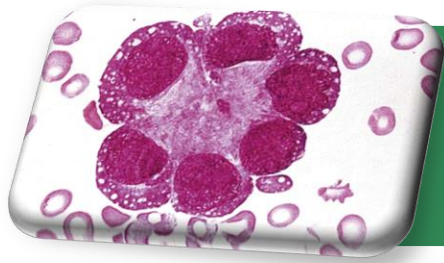


Serous Body Fluids

Malignant cells

- Malignant Mesothelioma

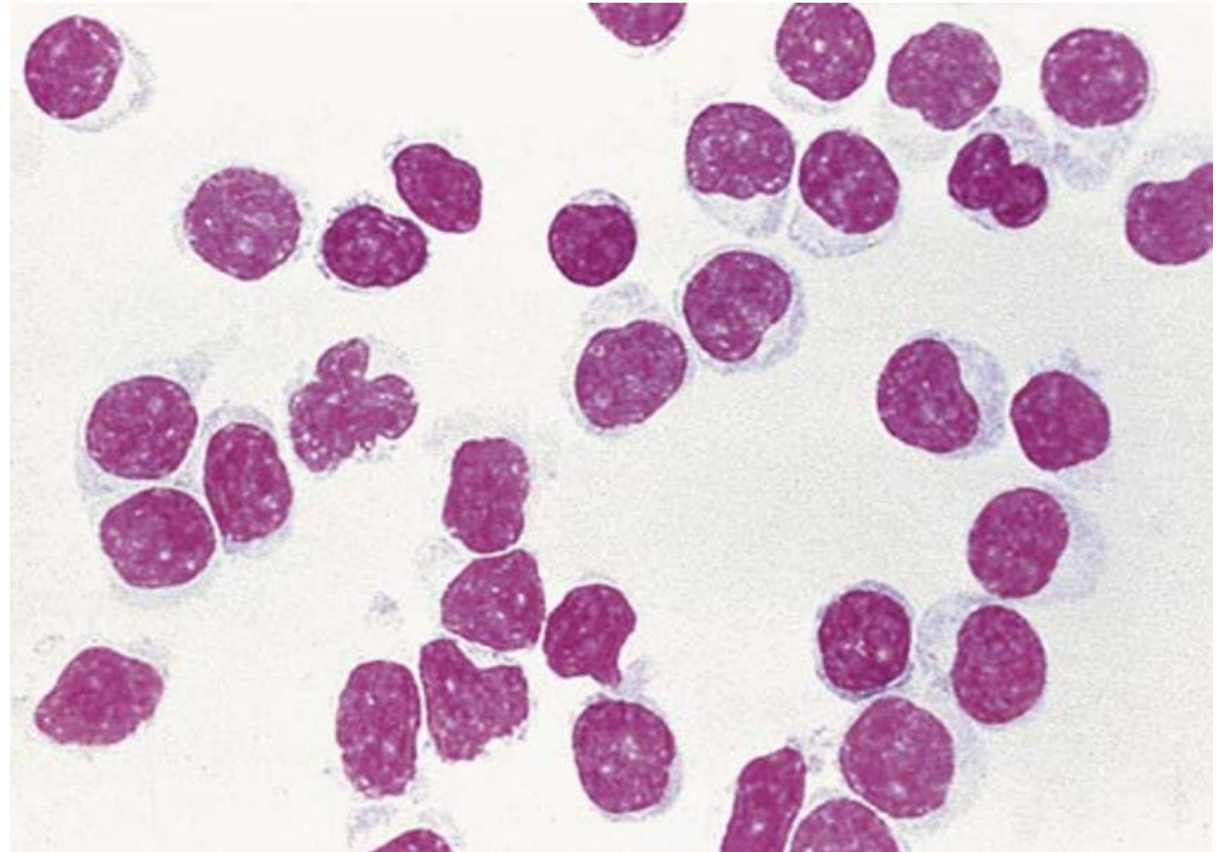


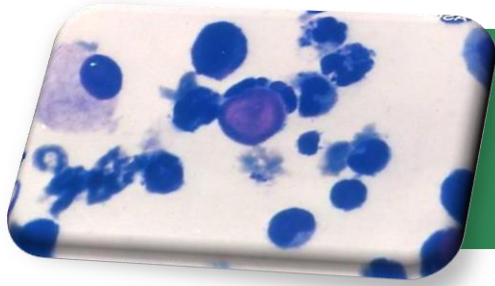


Serous Body Fluids

Malignant cells

- Low-grade non-Hodgkin lymphoma and chronic lymphocytic leukemia (CLL) may be difficult to distinguish from benign lymphocyte-rich serous effusion

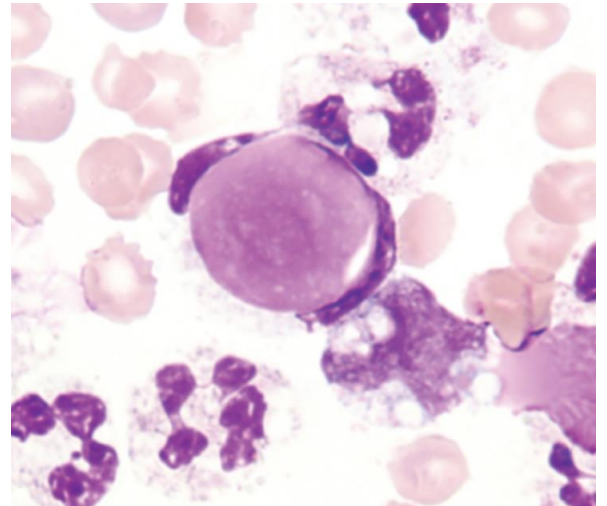


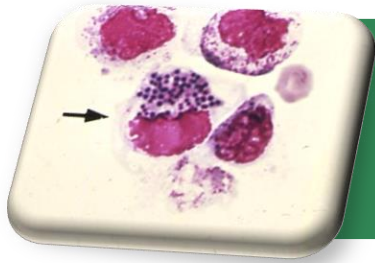


Serous Body Fluids

LE cells

- Seen in patients with Systemic Lupus Erythmatosis (SLE) a systemic disease in which an autoantibody attacks the patients organs and body systems
- LE cell is a neutrophil that has engulfed a homogeneous mass of purple staining nuclear material

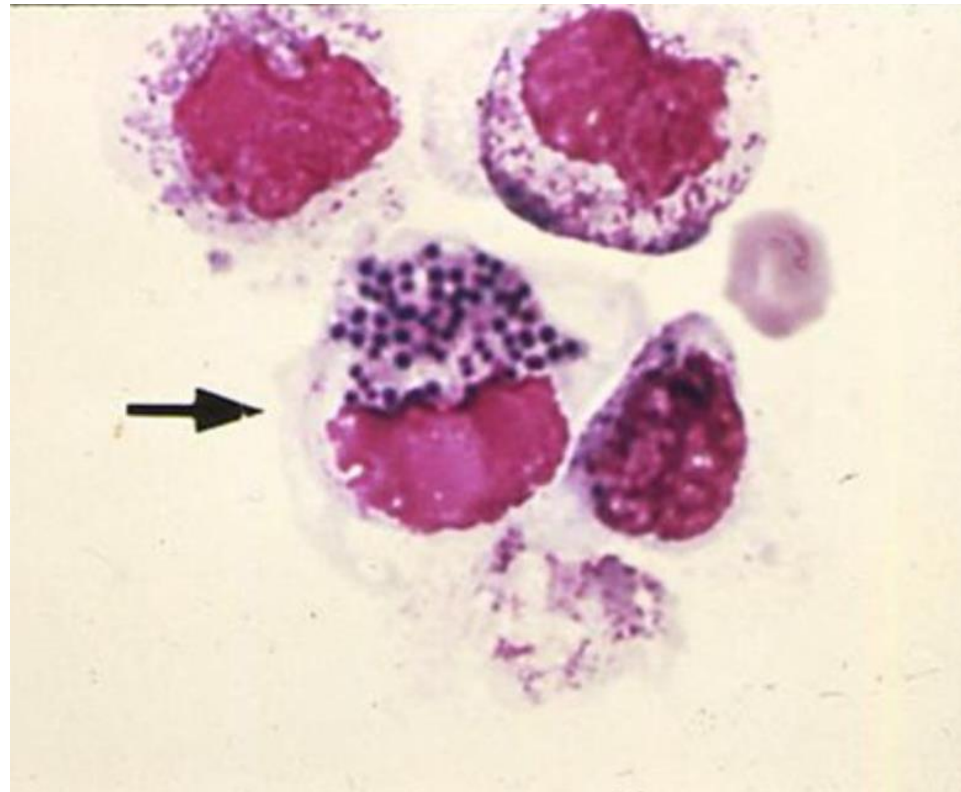


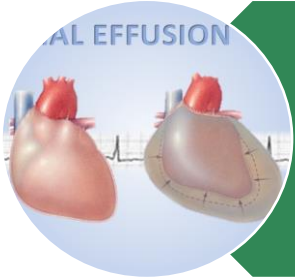


Serous Body Fluids (Pericardial fluid)

Intracellular Bacteria

- At the arrow is a cell with obvious intracellular bacteria





Pericardial Fluid

- From 10 to 50 mL of fluid is normally present in the pericardial space
- Produced by a transudative process similar to pleural fluid.
- Pericardial effusions are most often caused by viral infection; enterovirus is the most common etiologic agent

Causes of Pericardial Effusions

Idiopathic (most often viral)

Infection

Bacteria

Tuberculosis

Fungi

Viruses

AIDS-related (usually viral)

Neoplasm

Metastatic carcinoma

Lymphoma

Drugs

Hydralazine

Procainamide

Phenytoin

Renal failure

Hemorrhage

Trauma

Anticoagulant therapy

Leakage of aortic aneurysm

Autoimmune disorders

Hypothyroidism

Rheumatoid arthritis

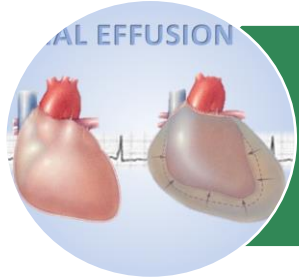
Systemic lupus erythematosus

Inflammatory bowel disease

Wegener's granulomatosis

Acute myocardial infarction

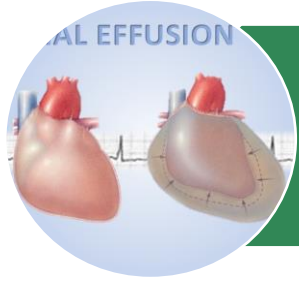
Radiation therapy



Pericardial Fluid

Gross Examination

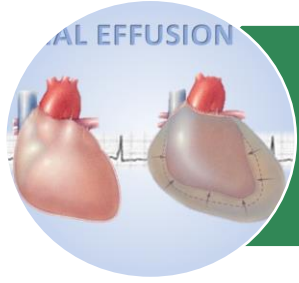
- Normal pericardial fluid is pale yellow and clear. Large effusions (>350 mL)
- are most often caused by malignancy or uremia, or they may be idiopathic.
- Infection or malignancy typically produces turbid effusions, whereas effusions due to uremia are usually clear and straw colored
- several other disorders may produce hemorrhagic effusions



Pericardial Fluid

Gross Examination

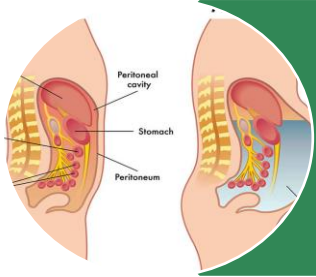
- Blood-like fluid obtained by pericardiocentesis might represent a hemorrhagic effusion or inadvertent aspiration of blood from the heart
- Blood obtained from the heart chamber will have a **hematocrit comparable with that of peripheral blood**, and blood gas analysis yields results similar to venous or arterial blood. In contrast, the **hematocrit of a hemorrhagic effusion is usually lower than that of peripheral blood**.
- Blood from a cardiac puncture clots, but a hemorrhagic effusion usually does not



Pericardial Fluid

Microscopic Examination

- The hematocrit and RBC count document the presence of a hemorrhagic effusion but are of limited value for differential diagnosis.
- Total leukocyte counts over 10,000/ μL suggest bacterial, tuberculous, or malignant pericarditis
- Examination of a stained smear should always be performed to evaluate for atypical or malignant cells
- Metastatic carcinomas of the lung and breast are most frequently observed in malignant pericardial effusion.



Peritoneal fluid

- Ascites is the pathologic accumulation of excess fluid in the peritoneal cavity.
- Up to 50 mL of fluid is normally present in this mesothelial-lined space.
- As with pleural and pericardial fluids, it is produced as an ultrafiltrate of plasma dependent on vascular permeability and on hydrostatic and oncotic pressure.

Causes of Peritoneal Effusions

Transudates: Increased Hydrostatic Pressure or Decreased Plasma Oncotic Pressure

Congestive heart failure

Hepatic cirrhosis

Hypoproteinemia (e.g., nephrotic syndrome)

Exudates: Increased Capillary Permeability or Decreased Lymphatic Resorption

Infections

Primary bacterial peritonitis

Secondary bacterial peritonitis (e.g., appendicitis, bowel rupture)

Tuberculosis

Neoplasms

Hepatoma

Lymphoma

Mesothelioma

Metastatic carcinoma

Ovarian carcinoma

Prostate cancer

Colonic adenocarcinoma

Pancreatic carcinoma

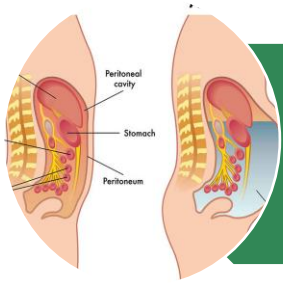
Trauma

Pancreatitis

Bile peritonitis (e.g., ruptured gallbladder)

Chylous Effusion

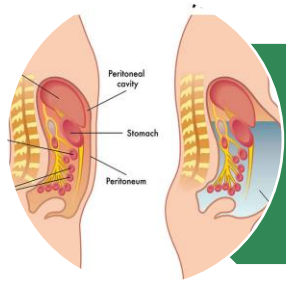
Damage to or obstruction of thoracic duct (e.g., trauma, lymphoma, carcinoma, tuberculosis and other granulomas [e.g., sarcoidosis, histoplasmosis], parasitic infestation)



Peritoneal Fluid

Exudates or Transudates

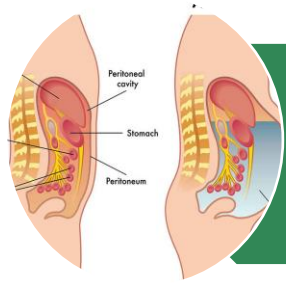
- The laboratory criteria for classifying ascitic fluid as a transudate or an exudate are not as well defined as they are for pleural and pericardial fluids.
- The serum-ascites albumin gradient (SAAG), defined as the serum albumin concentration minus the ascitic fluid albumin concentration, is widely considered to be the most reliable method to differentiate peritoneal transudates from exudates



Peritoneal Fluid

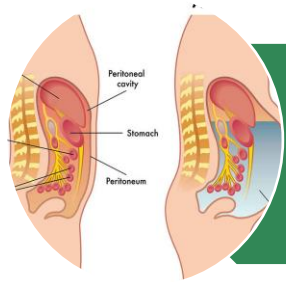
Exudates or Transudates

- Ascites caused by portal hypertension has a gradient of at least 1.1 g/dL (transudate), whereas ascites produced by other causes has a gradient less than 1.1 g/dL (exudate)
- An ascitic fluid/serum bilirubin ratio of 0.6 or greater is also significantly associated with exudate



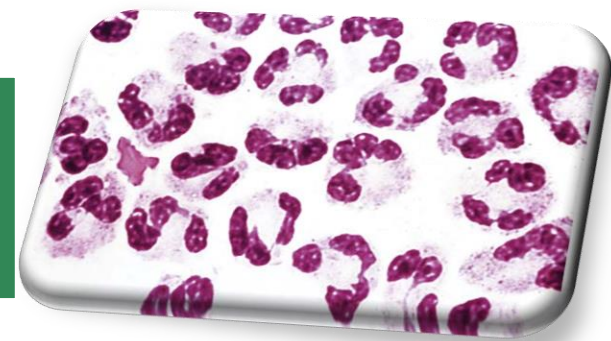
Peritoneal Fluid Gross Examination

- Whereas transudates are generally pale yellow and clear, exudates are cloudy or turbid because of the presence of leukocytes, tumor cells, or increased protein levels.
- The presence of food particles, foreign material, or green-yellow bile staining in a DPL specimen suggests perforation of the gastrointestinal or biliary tract.
- Acute pancreatitis and cholecystitis may also cause greenish discoloration



Peritoneal Fluid

Microscopic Examination



- The total leukocyte count is useful in distinguishing ascites due to uncomplicated cirrhosis from spontaneous bacterial peritonitis (SBP), which is caused by migration of bacteria from the intestine into the ascitic fluid
- Approximately 90% of patients with SBP will have leukocyte counts greater than $500/\mu\text{L}$, more than 50% of which are neutrophils
- The ascitic fluid total neutrophil count is the preferred method for the diagnosis of SBP. Cutoff values of 250 and 500 neutrophils/ μL have been recommended