

Body Fluids I

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Today's Discussion

- ▶ Body Fluid Analysis Tests
- ▶ Common Fluids
 - ▶ Cerebrospinal Fluid
 - ▶ Serous Fluid
 - ▶ Synovial Fluid
- ▶ Malignant Cells in Body Fluids



Why is Body Fluid Analysis Important

- ▶ Provides valuable diagnostic information
- ▶ Results will depend on the fluid type:
 - ▶ Cerebrospinal Fluid (CSF)
 - ▶ Serous Fluids
 - ▶ Pleural, pericardial, and peritoneal
 - ▶ Synovial Fluid
 - ▶ Bronchoalveolar Lavage (BAL) Fluid

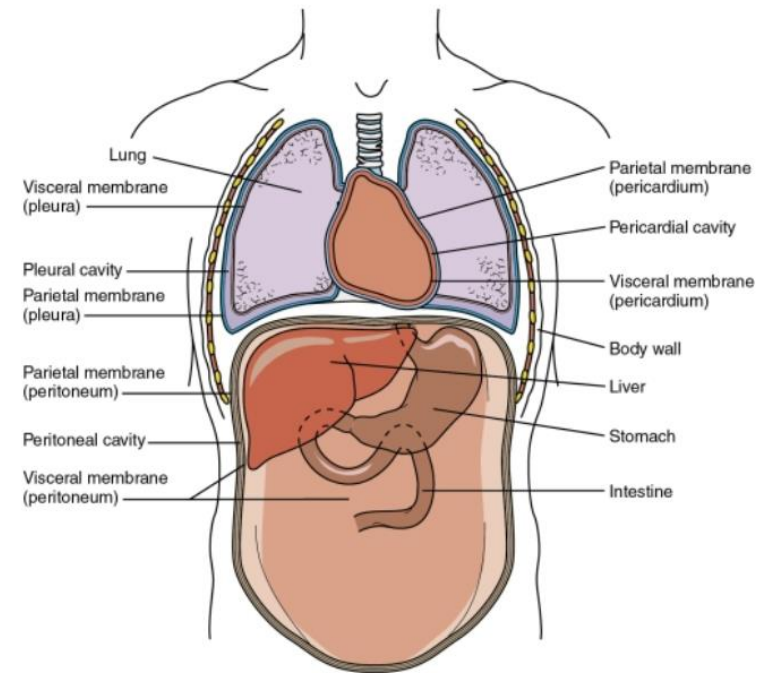
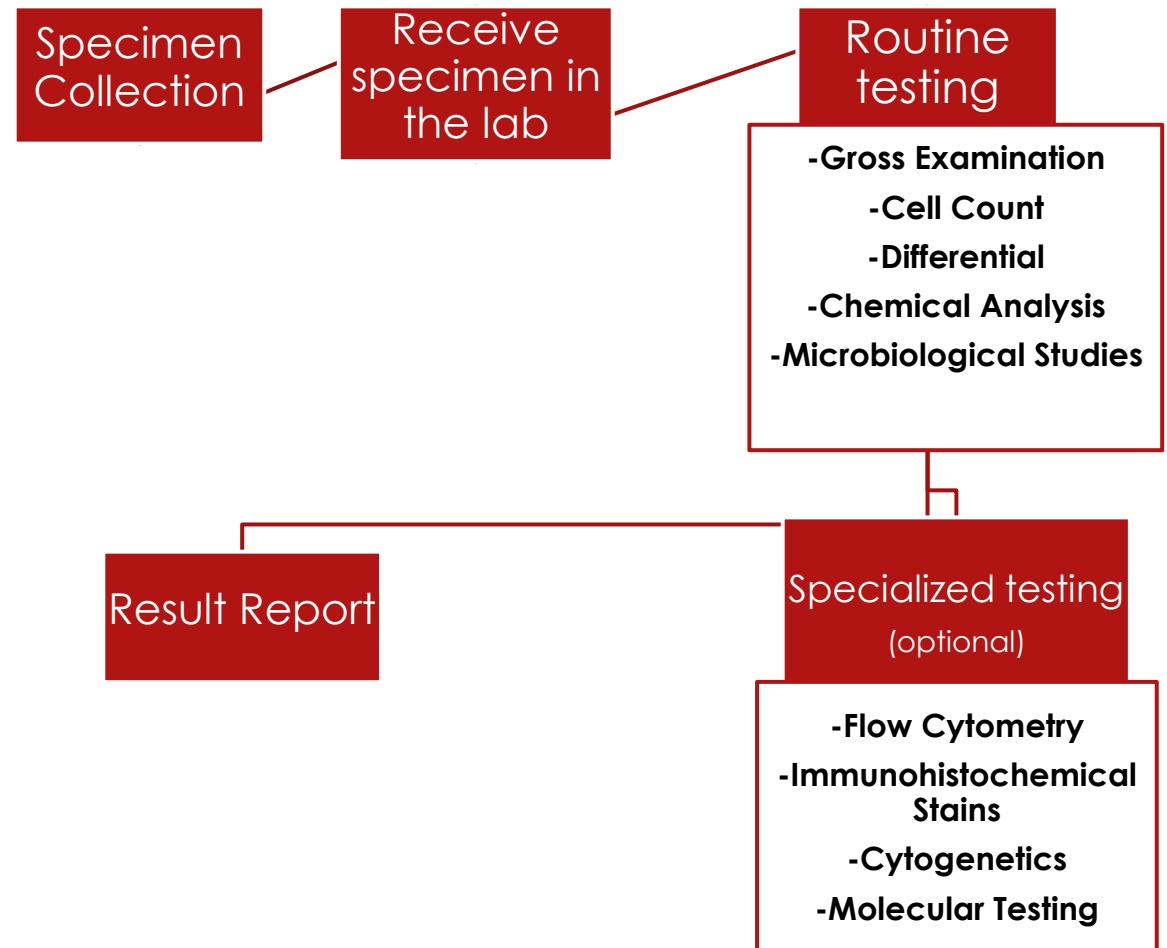


FIGURE 15.13 Parietal and Visceral Membranes of the Pleural, Pericardial, and Peritoneal Cavities. Parietal membranes line the body wall, whereas visceral membranes enclose organs. The two membranes are actually one continuous membrane. The space

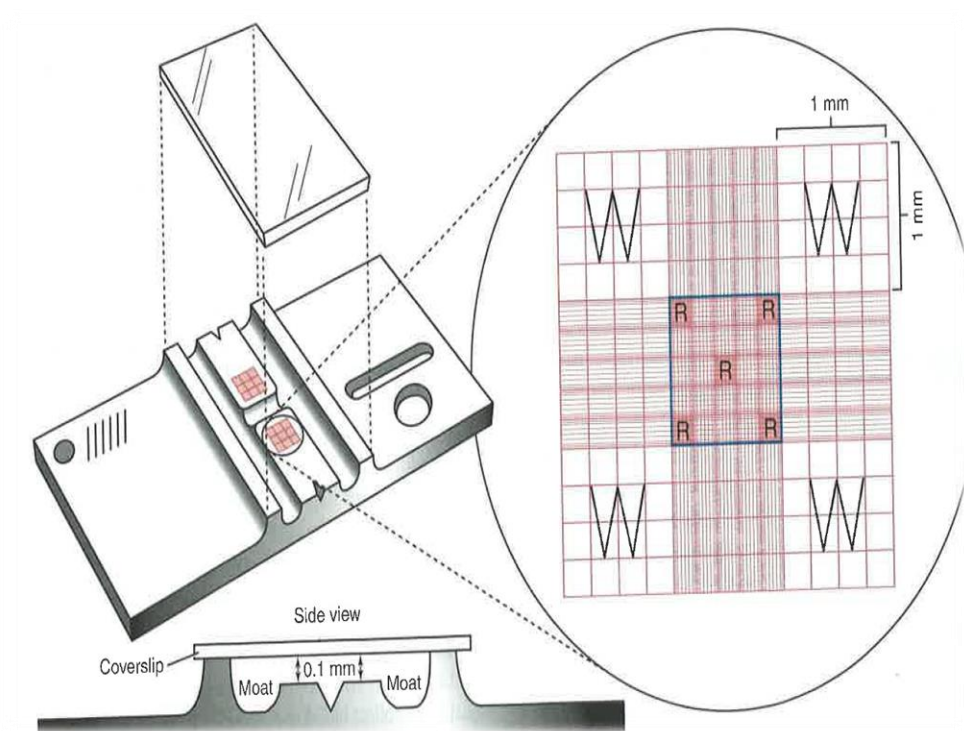


Process and Analysis

- ▶ Gross Appearance
 - ▶ Color and Clarity/ Spin Color and Clarity
 - ▶ Each fluid type is different
 - ▶ Changes during disease states
- ▶ RBC and TNC Counts
 - ▶ Manual or Automated
- ▶ Differential Cell Counts
- ▶ Specific Gravity
- ▶ Body Fluid pH
- ▶ Other Chemistry tests



Manual Cell Counts



- ▶ Hemacytometer (Neubauer Chamber)
- ▶ Total Count = $\frac{\text{Cells counted} \times \text{dilution factor}}{\text{Area} \times \text{Depth (0.1)}}$
- ▶ = Cells/ μL (Cells per mm^3)
- ▶ Diluents Available:
 - ▶ Cell Pack
 - ▶ 1 % HCL
 - ▶ 0.1N HCL
 - ▶ 3% Acetic Acid

Lysis of RBCs



Automated Cell Counts

PROS

- Less time consuming and labor intensive
- Highly reproducible
- Dedicated body fluid “mode” on most analyzers

CONS

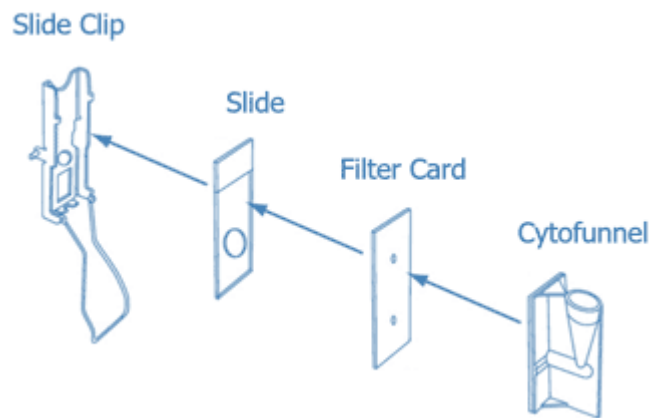
- Only certain fluid types approved
- Not able to analyze
 - Colorless clear CSF
 - Peritoneal dialysis fluid
 - BALs



Sysmex XN-1000



Differential Cell Count: Preparation



<https://www.thermofisher.com/us/en/home/bands/thermo-scientific.html>



<https://www.hettweb.com/cyto-system/>

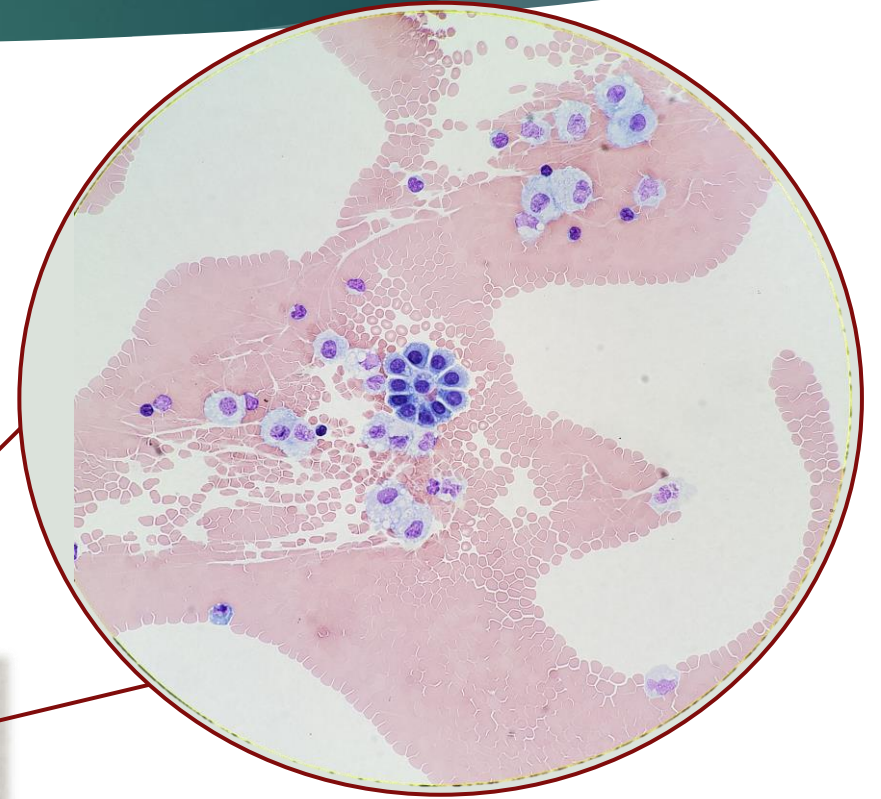
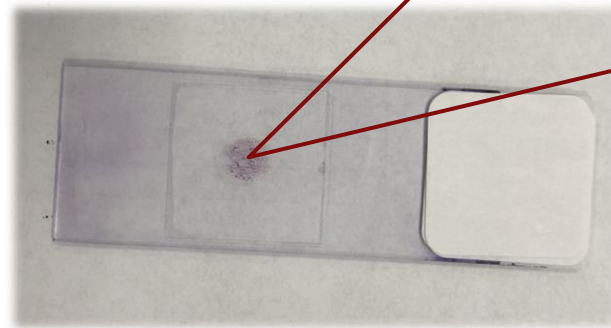


<https://www.hettweb.com/cyto-system/>



Differential Cell Count

- ▶ Two separate slides are prepared for each patient
- ▶ 100 cells counted and the percentage of cells reported
- ▶ Normal cell types and percentages are fluid dependent

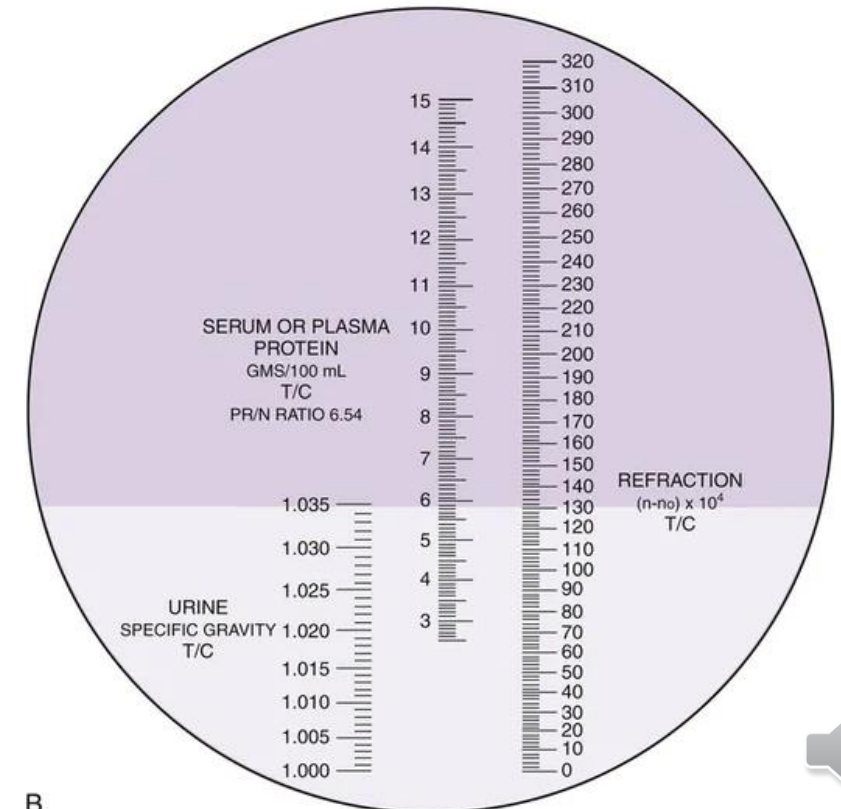


Body Fluid Specific Gravity

- ▶ Definition: Test used to determine the density of a fluid in relation to the density of water
- ▶ Clinical Significance: Helps to determine the number of dissolved substances in a fluid and can help distinguish transudate verses exudate
 - ▶ Transudate= <1.015
 - ▶ Exudate= >1.015



A



B



Body Fluid pH and other Chemistry Tests

- ▶ Fluid pH
 - ▶ Ion-selective glass electrode
 - ▶ Values can provide diagnostic importance
 - ▶ Currently no reference range for body fluids
 - ▶ Dependent on the fluid type
- ▶ Chemistry Tests
 - ▶ Body Fluid: Protein, Glucose, Lactate, Dehydrogenase
 - ▶ Values are diagnostically important, but are different in specific fluid types
 - ▶ Ex) Protein can be low in serous fluid transudates and protein elevation in CSF can indicate a traumatic tap upon collection



<https://www.weberscientific.com/orion-star-a211-series-benchtop-ph-meter-thermo-scientific>



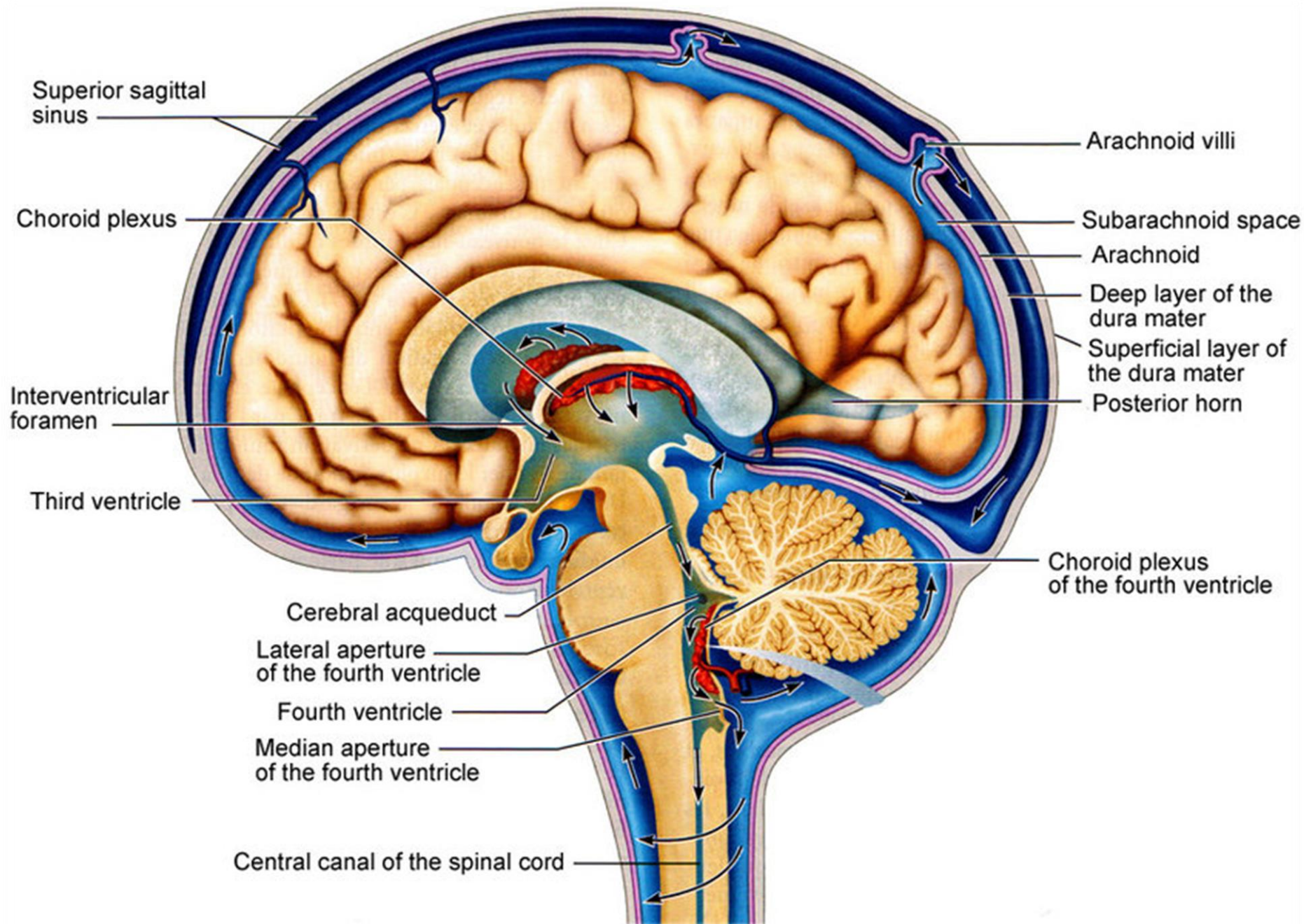
Cerebrospinal Fluid (CSF)



Cerebrospinal Fluid

- ▶ Functions of CSF
 - ▶ Supplies nutrients to nervous tissue
 - ▶ Removes metabolic waste
 - ▶ Mechanical barrier to cushion brain and spinal cord
- ▶ Produced in the Choroid Plexuses
 - ▶ Formed from plasma through selective filtration under hydrostatic pressure and active transport secretion
 - ▶ Endothelial cells surround the capillaries. The cells have very tight-fitting junctures to prevent passage of many cells- “Blood-Brain Barrier”
 - ▶ Approximately 20 mL of CSF produced per hour
- ▶ Reference Range:
 - ▶ 90-150 mL in adults/ 10-60 mL in neonates

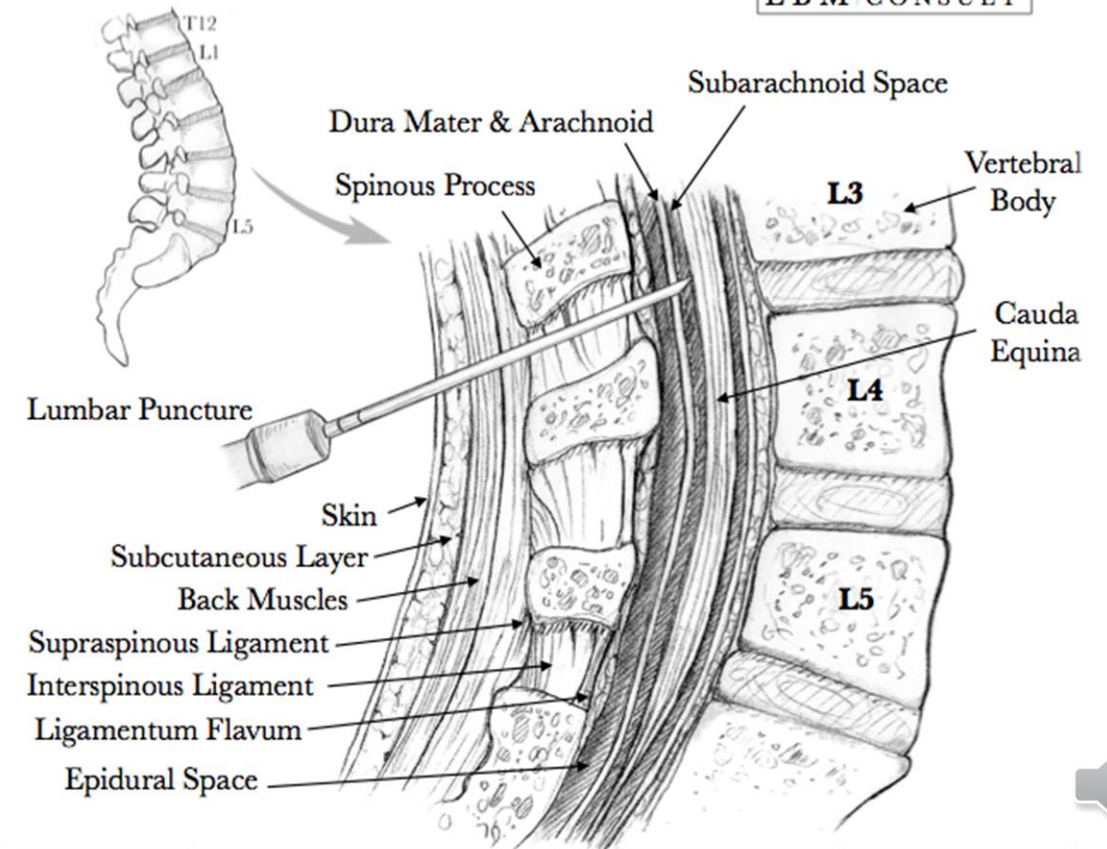




CSF Collection

- ▶ Lumbar puncture between the 3rd, 4th, or 5th lumbar vertebrae
- ▶ Subarachnoid space
 - ▶ Tube 1: Chemistry and serological tests
 - ▶ Least affected by blood or bacteria present due to tap
 - ▶ Tube 2: Microbiology Tests
 - ▶ Tube 3: Cell Count
 - ▶ Least likely to have cells introduced from tap
 - ▶ Tube 4: May be used for microbiology
 - ▶ Cell count usually done on this tube in the hematology lab
 - ▶ Better exclusion of skin contamination
- ▶ Excess Fluid Frozen
- ▶ **STAT testing**
- ▶ If transporting specimen
 - ▶ Refrigerate: Heme tube
 - ▶ Room Temp: Micro tube
 - ▶ Freeze: Chemistry and serology tube

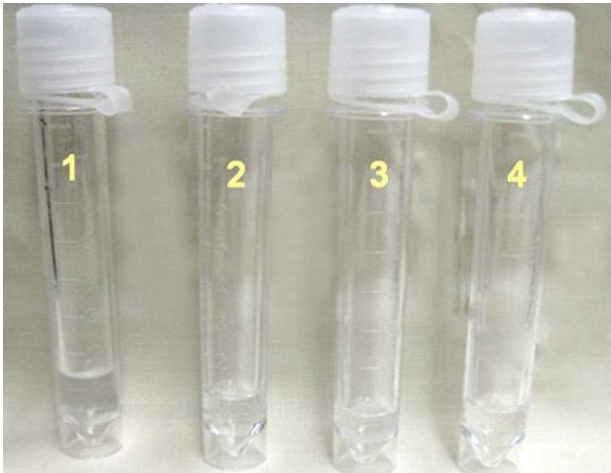
Lumbar Puncture



CSF Appearance

Normal

- Colorless and Clear



<https://spectrumhealth.testcatalog.org/show/LAB268-1>

Abnormal

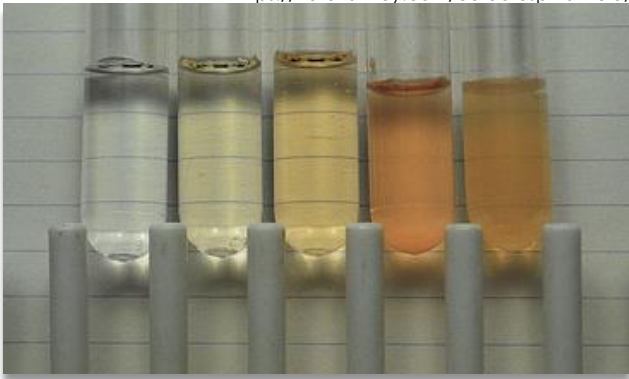
- Cloudy, Turbid, or milky
 - Increased proteins or lipids
 - Infection
 - Presence of WBCs
- Pink, Orange, or yellow supernatant (**Xanthochromia**)
 - Presence of RBC degradation
 - Elevated serum bilirubin
 - Pigment= carotene
 - Increased protein
 - Melanoma pigment
 - Immature liver function in infants (inc. bilirubin)

Pink: Slight oxyhemoglobin
Orange: Heavy hemolysis
Yellow: Unconjugated bilirubin



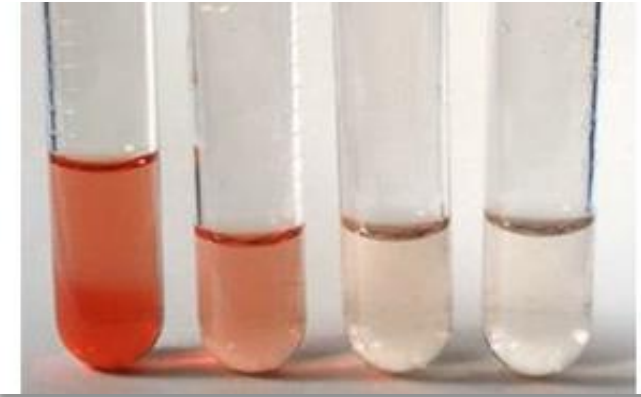
CSF Appearance

<https://veteriankey.com/cerebrospinal-fluid/>



Normal → Abnormal

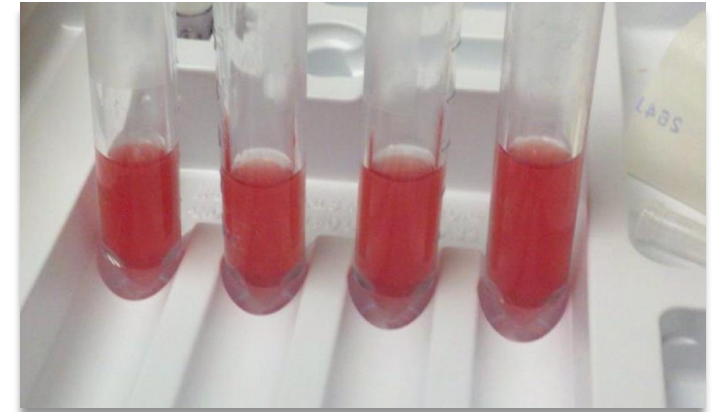
<https://slideplayer.com/slide/10384401/>



Traumatic Tap

- Uneven distribution of blood
- Heaviest concentration of blood in 1st tube

<http://sinaiem.org/wp-content/uploads/2017/10/PositiveLumbarPunctureAfterNegativeBrain.jpg>



Subarachnoid Hemorrhage

- Equal distribution of blood

Important in Emergency Room Patients

- Protocol in the hematology lab is to perform Cell Count and Differential on Tube 1 and Tube 4
- Doctors looking to rule out Subarachnoid Hemorrhages



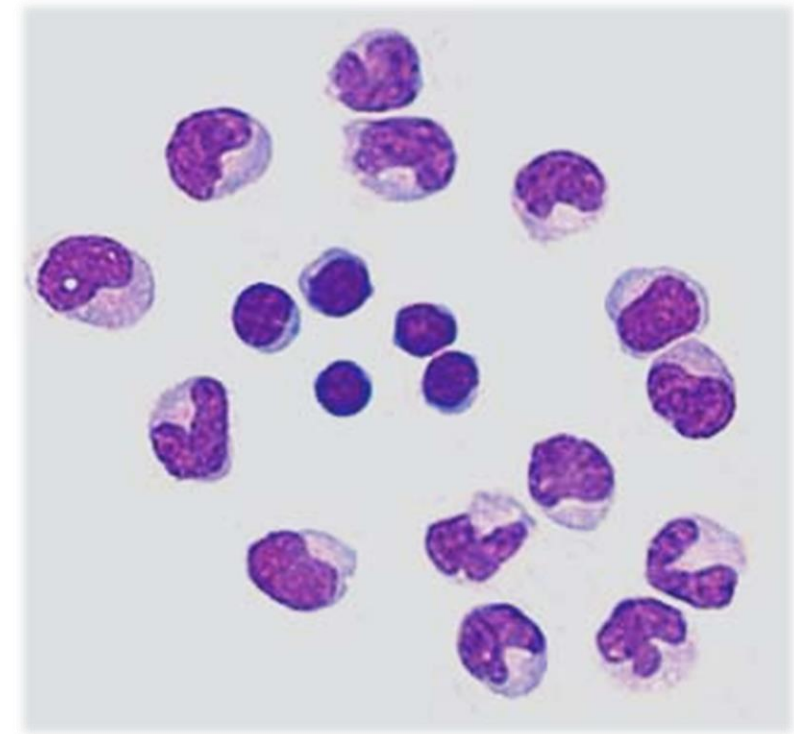
CSF Manual Count

- ▶ Normal adult CSF contains 0-5 WBCs/ μ L
 - ▶ Up to 30 WBCs/ μ L is normal in newborns
- ▶ Should be performed immediately
 - ▶ WBCs and RBCs begin to lyse within 1 hour
 - ▶ 40% leukocytes disintegrates after 2 hours
- ▶ Traumatic tap can cause an increase in WBC and proteins introduced to CSF
 - ▶ To determine # of artificially added WBCs:
 - ▶ $\text{WBC added} = \text{WBC (blood)} \times \text{RBC (CSF)} / \text{RBC (Blood)}$



CSF Differential

- ▶ Normal Cells:
 - ▶ Lymphocytes and Monocytes
 - ▶ 70:30 (Lymphs: Monos) in Adults and 30:70 (Lymphs: Monos) in Neonates
 - ▶ Other normal cells that can be seen
 - ▶ Neutrophils
 - ▶ Eosinophils
 - ▶ Macrophages
 - ▶ Choroidal, Ependymal and Spindle-Shaped Cells
 - ▶ Lining cells
- ▶ Abnormal Cells:
 - ▶ Lymphoblasts, myeloblasts, monoblasts
 - ▶ Lymphoma cells
 - ▶ Cells from CSF tumors
 - ▶ Astrocytomas
 - ▶ Retinoblastomas
 - ▶ Medulloblastomas



<https://neupsykey.com/cell-populations-in-the-normal-cerebrospinal-fluid/>



CSF Chemistry Test: Protein

Normal CSF protein: 15-45 mg/dL

Higher in infants and older adults (over 40)

- ▶ Tau (carbohydrate deficient transferrin fraction)- **not** in serum
- ▶ Abnormally Low values
 - ▶ Leaking fluid from Central Nervous System
- ▶ Elevated Values
 - ▶ Damage to blood-brain barrier, decreased clearance of normal proteins from the fluid, and degeneration of neural tissue
 - ▶ Meningitis (#1)
 - ▶ Hemorrhaging (#1)
 - ▶ Primary CNS tumors
 - ▶ MS
- ▶ MS and neurological disorders cause increased IgG
 - ▶ Must determine if IgG is increased due to production in CNS or if there is a defect in blood brain barrier
 - ▶ Compare serum and CSF albumin and IgG levels
- ▶ CSF/serum albumin index
 - ▶ CSF albumin/ serum albumin
 - ▶ <9; intact blood-brain barrier
- ▶ IgG Index
 - ▶ $(\text{CSF IgG} / \text{Serum IgG}) / (\text{CSF Albumin} / \text{serum albumin})$
 - ▶ >0.7 indicates IgG production in CNS



CSF Chemistry Test: Glucose and Lactate

Glucose

- ▶ Enters CSF by selective transport
- ▶ Normal range: 60-70% of plasma glucose
- ▶ Blood glucose must run for comparison; drawn 2 hours before spinal tap
- ▶ Elevated value
 - ▶ Result of plasma elevation
- ▶ Low value
 - ▶ **Useful for determining causative agent of meningitis**
 - ▶ Decreased glucose + increased WBC and increased Neuts
 - ▶ Bacterial meningitis
 - ▶ Decreased glucose + increased Lymphs
 - ▶ Tubercular meningitis
 - ▶ Normal glucose + increased Lymphs
 - ▶ Viral meningitis

Lactate

- ▶ **Useful for diagnosis and management of meningitis**
- ▶ >25 mg/dL
 - ▶ Bacterial
 - ▶ Tubercular
 - ▶ Fungal
- ▶ >35 mg/dL
 - ▶ Bacterial
- ▶ <25 mg/dL
 - ▶ Viral
- ▶ Hypoxia can increase levels- Tissue destruction- head damage
- ▶ Levels remain but then fall rapidly when treatment successful
- ▶ Increased RBCs will falsely increase levels- contain high amounts of lactate



CSF Chemistry Test: Glutamine

Normal Range: 8-18 mg/dL

- ▶ Produced from ammonia and alpha-ketoglutarate by brain cells
 - ▶ Removes toxic metabolic waste (ammonia) from CNS
- ▶ ↑ Glutamine
 - ▶ Liver disorders → increased ammonia (blood and CSF)
 - ▶ Reyes Syndrome
- ▶ Measurement is based on the amount of ammonia liberated from glutamine
- ▶ Increased glutamine can cause a coma
 - ▶ As the concentration of CSF ammonia ↑, the supply of α-ketoglutarate ↓ → glutamine can no longer be produced → increased ammonia toxicity → coma
- ▶ >35 mg/dL -disturbance of consciousness



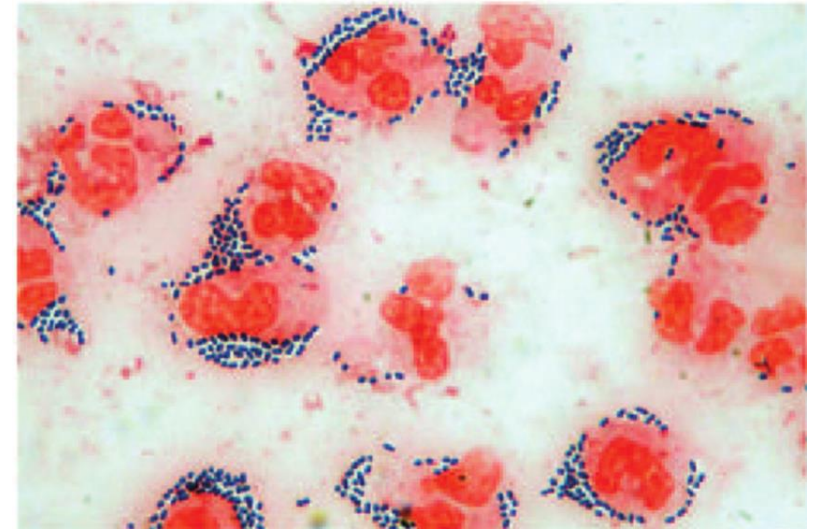
CSF Microbiological Studies

Gram Stain

- Performed on all cases of meningitis; mainly for bacterial and fungal infection
 - Can be extremely difficult to interpret (low # organisms present)
 - False-negative and false-positive results

Organisms Most frequently Found

- *S. pneumonia* (gram-pos cocci)
- *H. influenza* (gram-neg rods)
- *E. coli* (gram-neg rods)
- *N. meningitidis* (gram-neg cocci)
- *Listeria monocytogenes* (gram-pos rods)
- *S. agalactiae* (gram-pos cocci)
- *C. neoformans* (encapsulated fungi)



https://www.researchgate.net/figure/Diagnostic-Gram-stain-of-CSF-from-a-patient-with-pneumococcal-meningitis-Neutrophils_fig1_49704548



Serous Fluid



Serous Fluid

- ▶ Fluid between the two serous membranes of closed cavities
 - ▶ Parietal membrane- lines cavity wall
 - ▶ Visceral membrane- lines the organs within cavity
- ▶ Ultrafiltration of plasma
- ▶ Prevents friction between parietal and visceral membranes because of movement
- ▶ Normally a small amount present
 - ▶ Production and reabsorption take place at constant rate
 - ▶ Subject to hydrostatic and colloidal (oncotic) pressure
 - ▶ Hydrostatic pressure causes fluid to enter between membranes
 - ▶ Increased oncotic pressure from fluid entering causes reabsorption into capillaries
- ▶ The type of serous fluid is dependent on location of fluid
 - ▶ Pleural fluid (lungs)
 - ▶ Pericardial fluid (heart)
 - ▶ Peritoneal fluid (abdomen area)

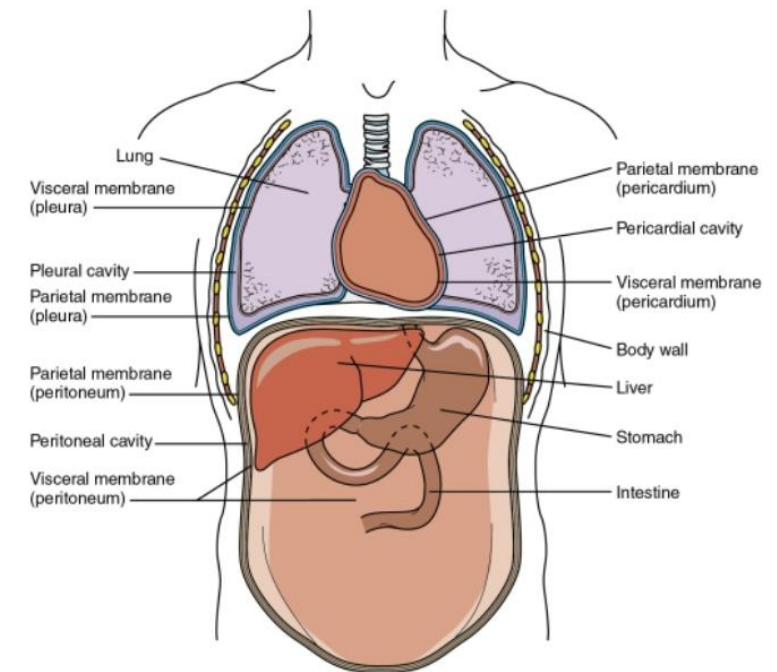


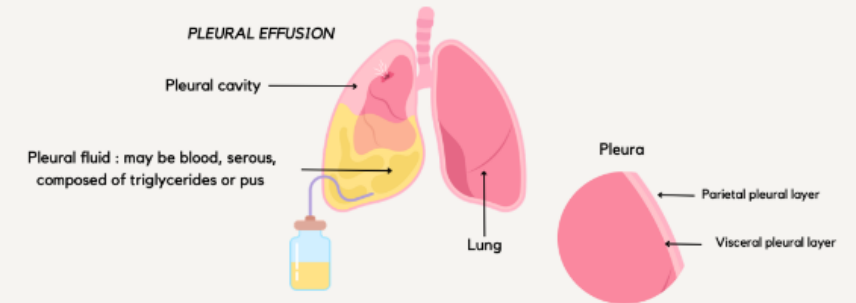
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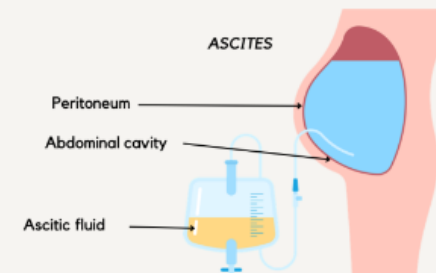
Collection

- ▶ Body fluid collection through needle aspiration
 - ▶ Thoracentesis: pleural collection
 - ▶ Pericardiocentesis: pericardial collection
 - ▶ Paracentesis: peritoneal collection (abdomen)
- ▶ EDTA tube used for cell count and differential
- ▶ Heparin tube or syringe acceptable for microbiology and cytology, but both prefer non-additive containers
- ▶ pH specimens stored anaerobically on ice (sodium heparin syringe)
- ▶ **Blood samples should be obtained at same time as fluid collection**

Thoracentesis



Paracentesis



Effusions

- ▶ An accumulation of fluid between the serous membranes

- ▶ Two Types

- ▶ Transudate
 - ▶ Exudate

- ▶ Cause of Effusion

- ▶ Increased hydrostatic pressure
 - ▶ Congestive heart failure and salt/fluid retention
 - ▶ Decreased oncotic pressure
 - ▶ Hypoproteinemia and nephrotic syndrome
 - ▶ Increased capillary permeability
 - ▶ Inflammation and infection
 - ▶ Lymphatic obstruction
 - ▶ Tumors and lymphoma



Effusions

Transudate

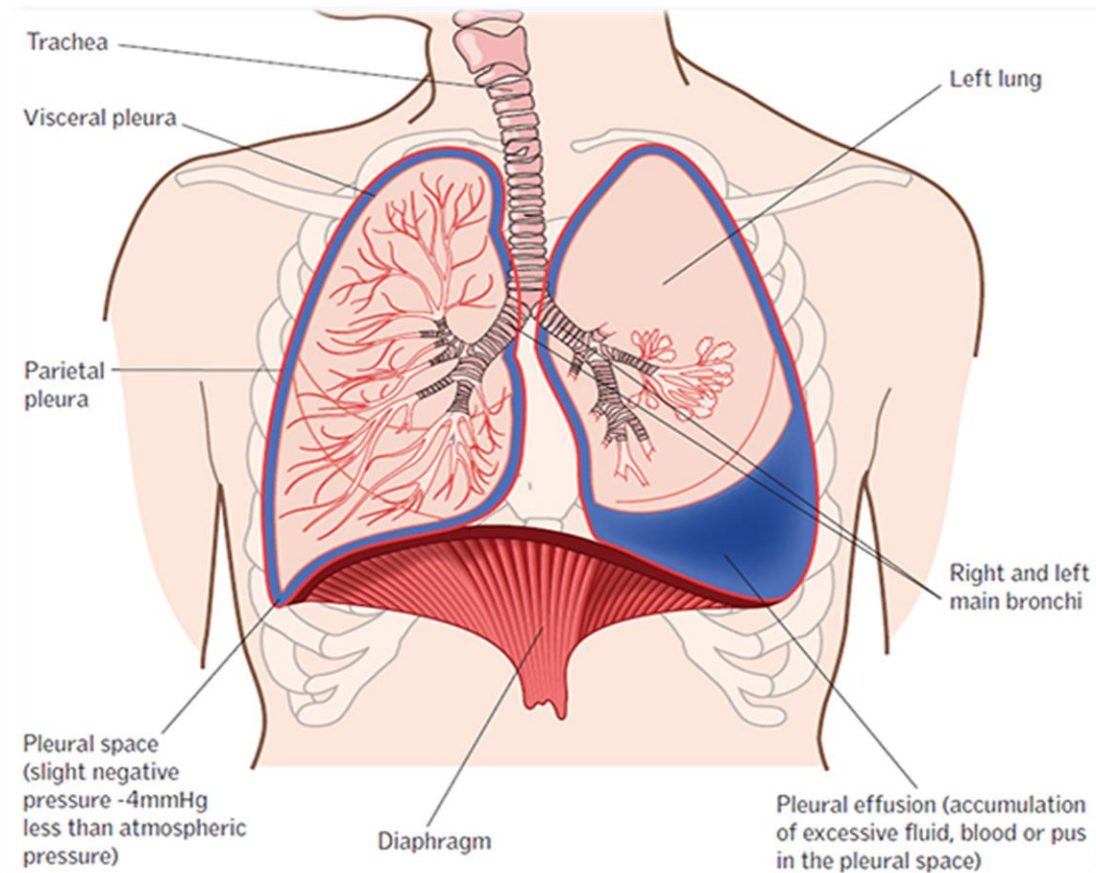
- ▶ Effusions forming due to systemic disorder
 - ▶ Congestive heart failure
 - ▶ Nephrotic syndrome forming hypoproteinemia
- ▶ Disruption balance in regulation of fluid filtration and reabsorption
- ▶ Lab Results
 - ▶ WBC <1000 cells/uL
 - ▶ Fluid: Serum Protein <0.5
 - ▶ Fluid: Serum LD <0.6

Exudate

- ▶ Effusions produced by conditions involving membranes of cavity
 - ▶ Infections
 - ▶ Malignancies
- ▶ Lab Results
 - ▶ WBC >1000 cells/uL
 - ▶ Fluid: Serum Protein > 0.5
 - ▶ Fluid: Serum LD >0.6



Pleural Fluid



Pleural Fluid: Appearance

Normal: Clear to pale yellow

Abnormal Appearance:

▶ **Milky**

- ▶ Chylous material
 - ▶ Thoracic duct leakage
 - ▶ High triglycerides
 - ▶ Strongly (+) Sudan III stain
 - ▶ Predominance of lymphocytes
- ▶ Pseudochylous material
 - ▶ Chronic inflammation
 - ▶ Lower triglycerides
 - ▶ Mixed WBCs with cholesterol crystals present
 - ▶ High cholesterol
 - ▶ Green tinge
 - ▶ Negative/weak (+) Sudan stain

▶ **Bloody**

- ▶ Hemothorax (traumatic injury)
 - ▶ Hct >50% of whole blood
- ▶ Membrane damage (malignancy)
- ▶ Traumatic collection

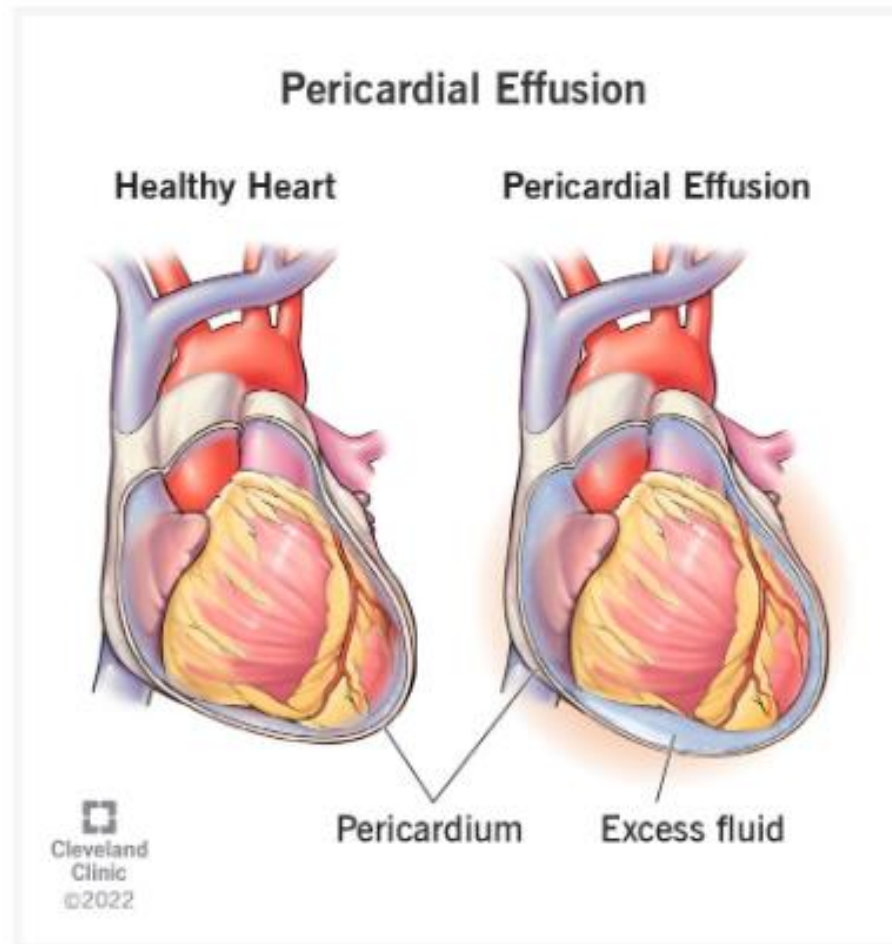


Pleural Fluid: Important Testing

- ▶ Pleural fluid cholesterol
 - ▶ >60 mg/dL: exudate
- ▶ Fluid: serum cholesterol ratio
 - ▶ >0.3: exudate
- ▶ Fluid: serum total bilirubin
 - ▶ >0.6: exudate
- ▶ Glucose
 - ▶ Decreased (<60 mg/dL): in tuberculosis and rheumatoid inflammation
 - ▶ Parallels plasma levels
- ▶ pH
 - ▶ <7.2 indicated need for chest tube drainage
 - ▶ 0.3 lower than blood pH is significant
 - ▶ <0.6: esophageal rupture
- ▶ ADA (adenosine deaminase)
 - ▶ >40 U/L: tuberculosis
- ▶ Amylase
 - ▶ Elevated in pancreatitis

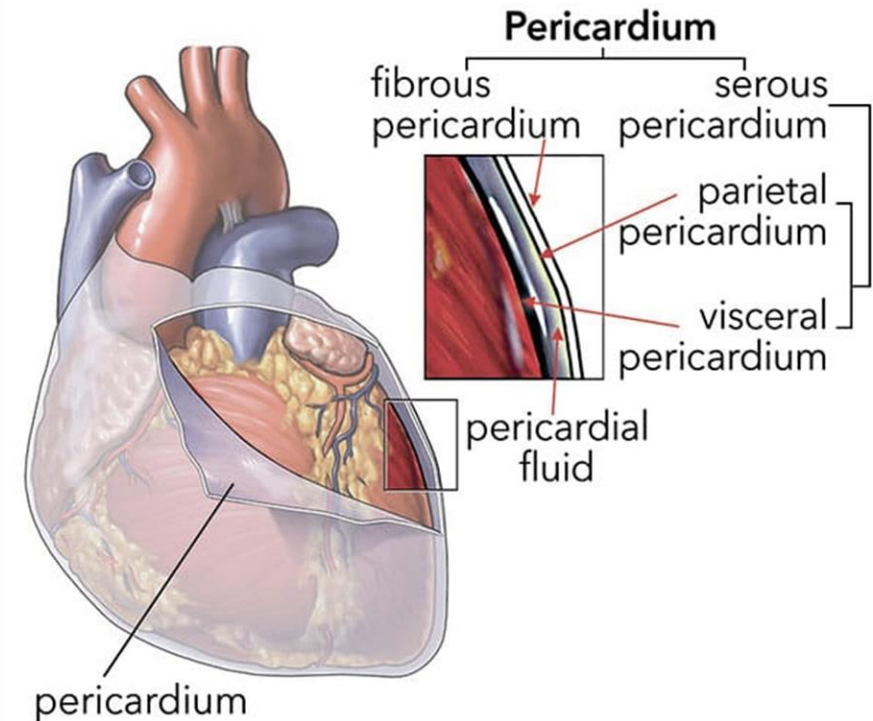


Pericardial Fluid



Pericardial Fluid

- ▶ Fluid surrounding the heart
- ▶ Normal: 10-50 mL between membranes
- ▶ Effusions primarily due to changes in membrane permeability due to infection (pericarditis), malignancy, and trauma producing exudates
- ▶ Metabolic disorders (such as uremia, hypothyroidism) or autoimmune disorders are the primary causes of transudates
- ▶ Effusion suspected when cardiac compression (tamponade) noted during physical examination



Pericardial: Appearance

- ▶ Normal, transudate
 - ▶ Clear/ pale yellow
- ▶ Abnormal
 - ▶ Blood streaked
 - ▶ Infection, malignancy
 - ▶ Grossly Bloody
 - ▶ Cardiac puncture, anticoagulant therapy
 - ▶ Milky
 - ▶ Chylous and pseudochylous material

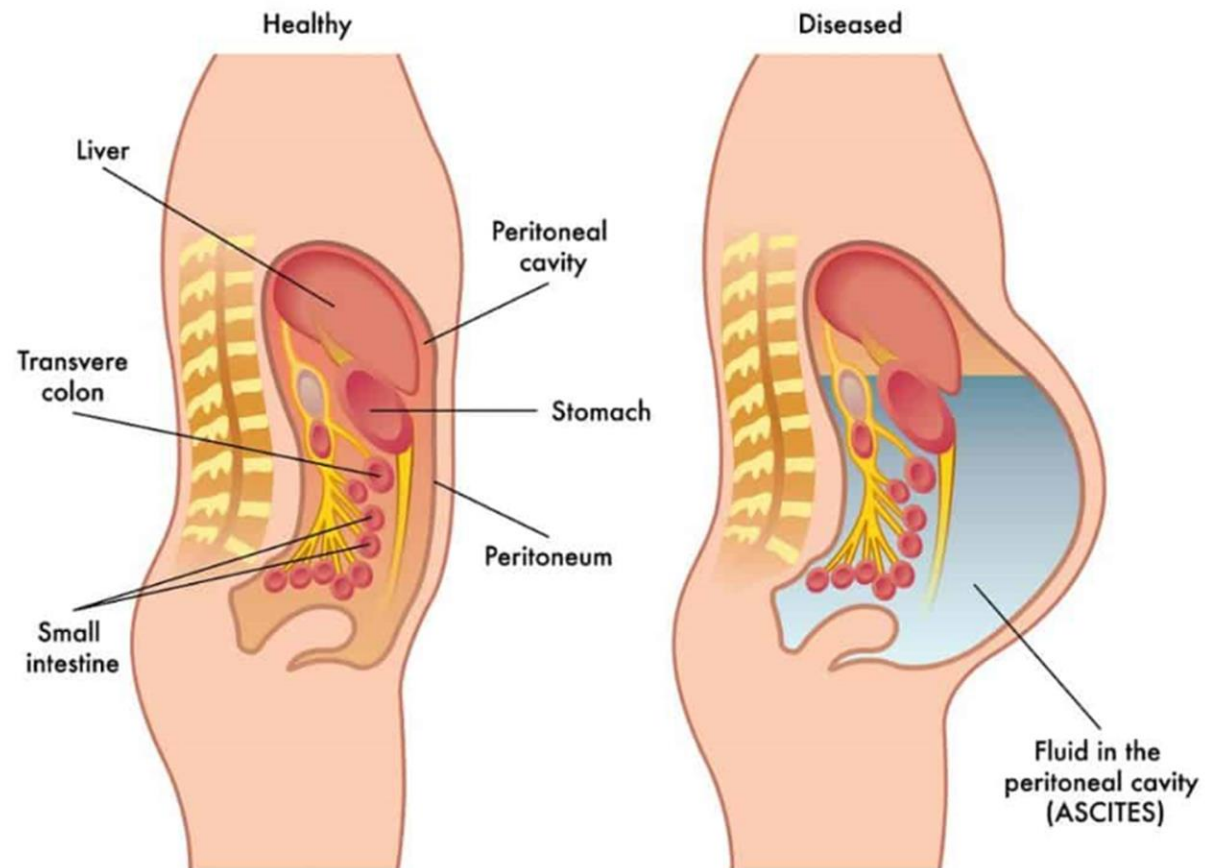


Pericardial: Important Testing

- ▶ Fluid: Serum Protein and Fluid: Serum LD ratios
 - ▶ Transudates vs. exudates
- ▶ WBCs >1000 /uL with high percentage of neutrophils
 - ▶ Bacterial endocarditis
- ▶ Malignant cells or carcinoembryonic antigen
 - ▶ Metastatic Carcinoma
- ▶ Gram stain and culture
 - ▶ Bacterial endocarditis
- ▶ Acid fast stain and ADA
 - ▶ Tubercular effusion



Peritoneal Fluid



Peritoneal Fluid

- ▶ Accumulation of fluid between the peritoneal membrane is termed ascites
 - ▶ Fluid associated with ascites is known as ascetic fluid
- ▶ Cirrhosis is a frequent cause of ascetic transudates
- ▶ Bacterial infections (peritonitis) and malignancy are both common cause of ascetic exudates



Peritoneal Lavage

- ▶ Normal saline is introduced into the peritoneal cavity as a lavage to detect abdominal injuries that have not yet resulted in fluid accumulation
- ▶ Can be used in the detection of intra-abdominal bleeding in blunt trauma case
 - ▶ RBC counts $>100,000/\mu\text{L}$ are indicative of blunt trauma
- ▶ Replaced by focused assessment with sonograph for trauma (FAST) and CT
- ▶ Cell count and differential used to detect infection and allergic reactions to the equipment or introduction of air into the peritoneal cavity



Peritoneal: Transudates vs. Exudates

- ▶ **SAAG (Serum-Ascites Albumin Gradient)**

- ▶ Detection of peritoneal transudates vs exudates of hepatic origin
 - ▶ Recommended over total protein and LD ratios
- ▶ Peritoneal albumin and serum albumin are measured concurrently

- ▶ Equation:

$$\text{SAAG} = \text{Fluid Albumin} - \text{Serum Albumin}$$

- ▶ ≥ 1.1 suggests transudate of hepatic origin
- ▶ < 1.1 associated with exudative effusions



Peritoneal: Appearance, Important Testing, Differential

Appearance

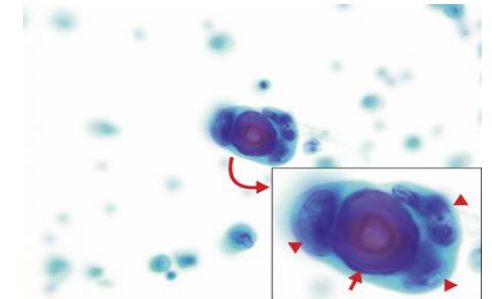
- **Turbid**- microbial infection/green
 - Bile, gall, pancreas disorder
- **Blood streaked**- trauma, infection, malignancy
- **Milky**- lymphatic trauma and blockage

Testing

- WBCs >500 cells/uL
 - bacterial peritonitis or cirrhosis
- Glucose
 - Decreased below serum levels in tubercular peritonitis, malignancy
- Amylase and Alkaline Phosphatase
 - Increased in pancreatitis and gastrointestinal perforations
- Blood Urea Nitrogen (BUN) and Creatinine
 - Ruptured or punctured bladder

Differential

- Common cells:
 - Leukocytes
 - Mesothelial cells
 - Macrophages
- Psammoma bodies: concentric striations of collagen like material seen in benign, ovarian, and thyroid malignancies



Common Cells Seen on Serous Fluid Differentials

- ▶ Macrophages (the most) → Lymphocytes → Neutrophils
 - ▶ Neutrophils-↑ in pancreatitis, pulmonary infarction
 - ▶ Lymphocytes- ↑ in TB, viral infection, autoimmune disorders, and malignancy
 - ▶ Eosinophils
 - ▶ >10% with trauma, causing presence of air or blood in cavity
 - ▶ ↑ in allergic reactions and parasitic infections
 - ▶ Mesothelial Cells
 - ▶ Found in clusters when reactive
 - ▶ ↓ in TB
 - ▶ Plasma cells- can be indicated in TB
 - ▶ Malignant cells- metastatic lung or breast carcinoma



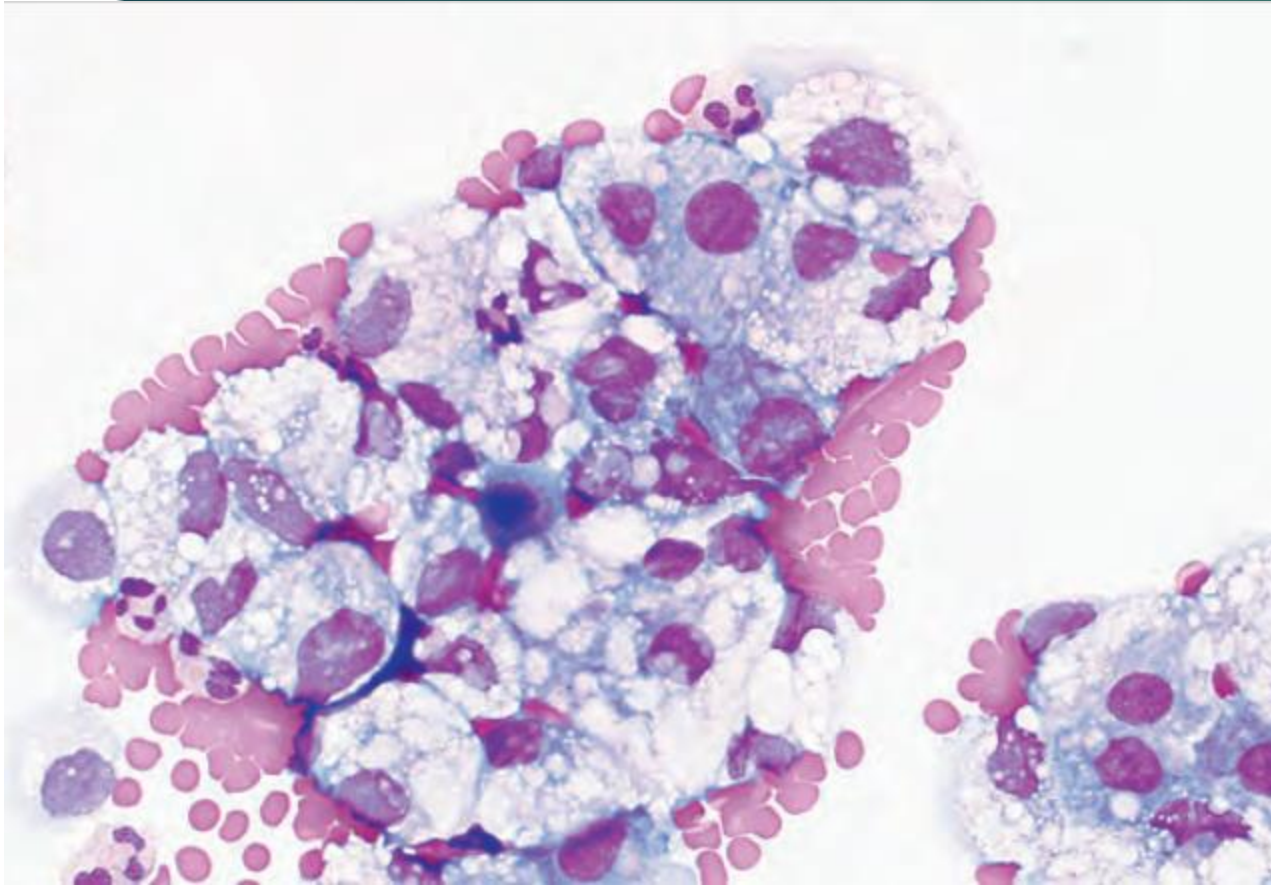
Macrophage vs Mesothelial Cells



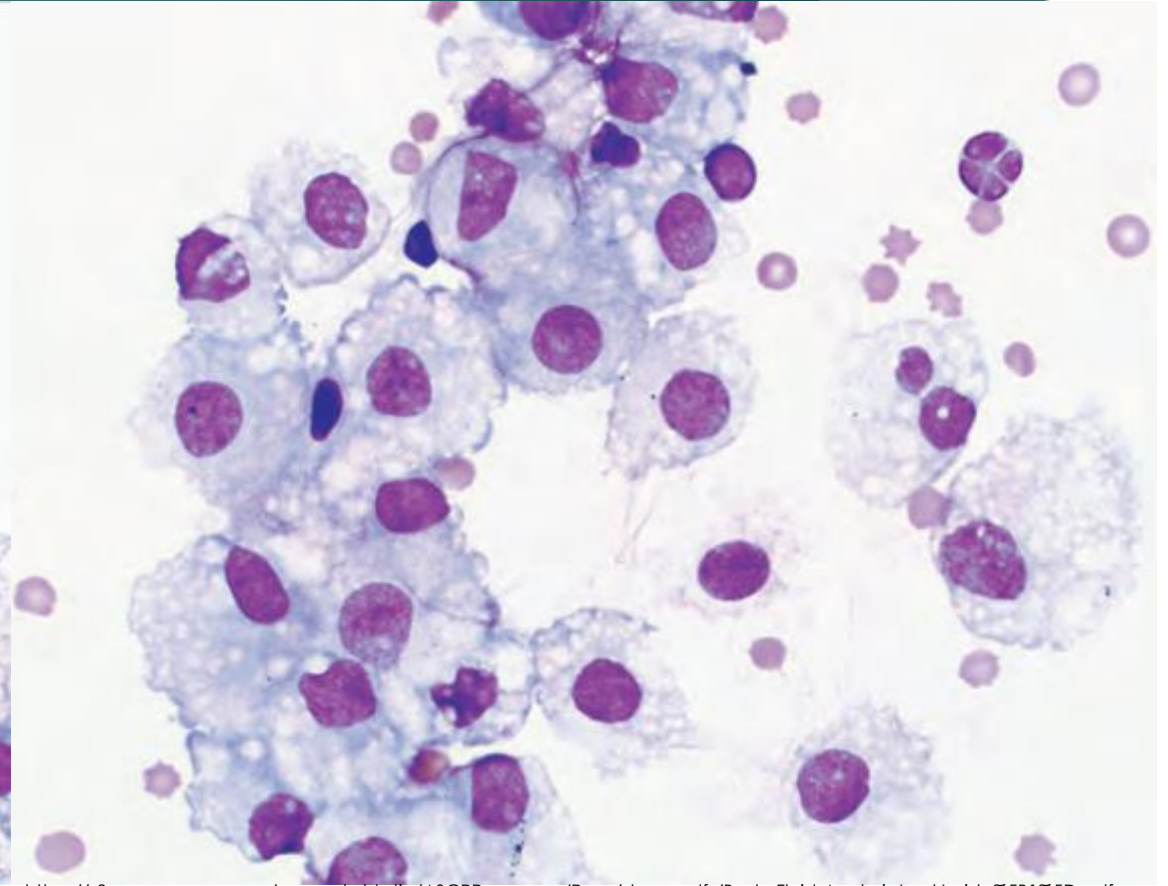
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More Macrophages...



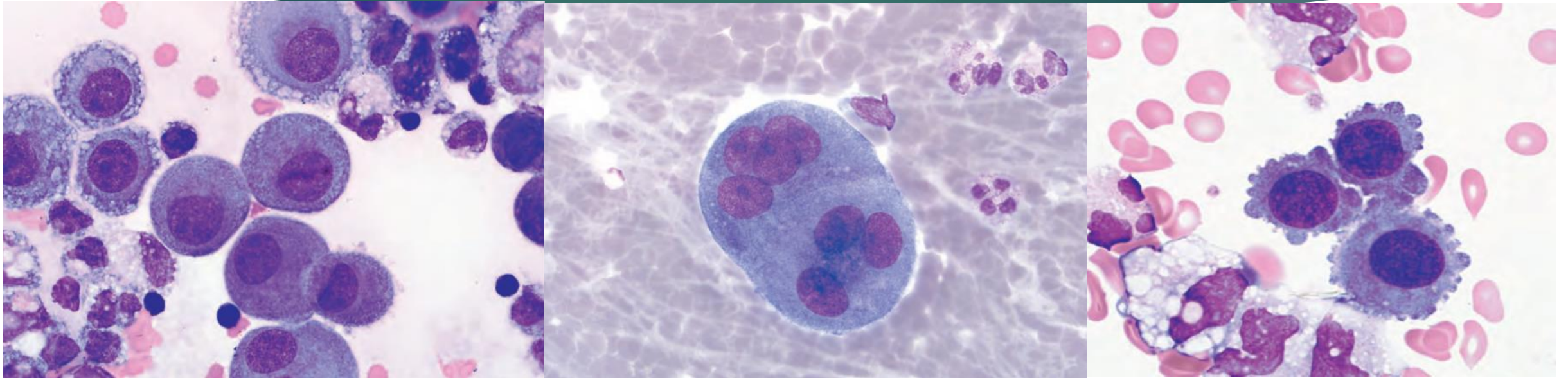
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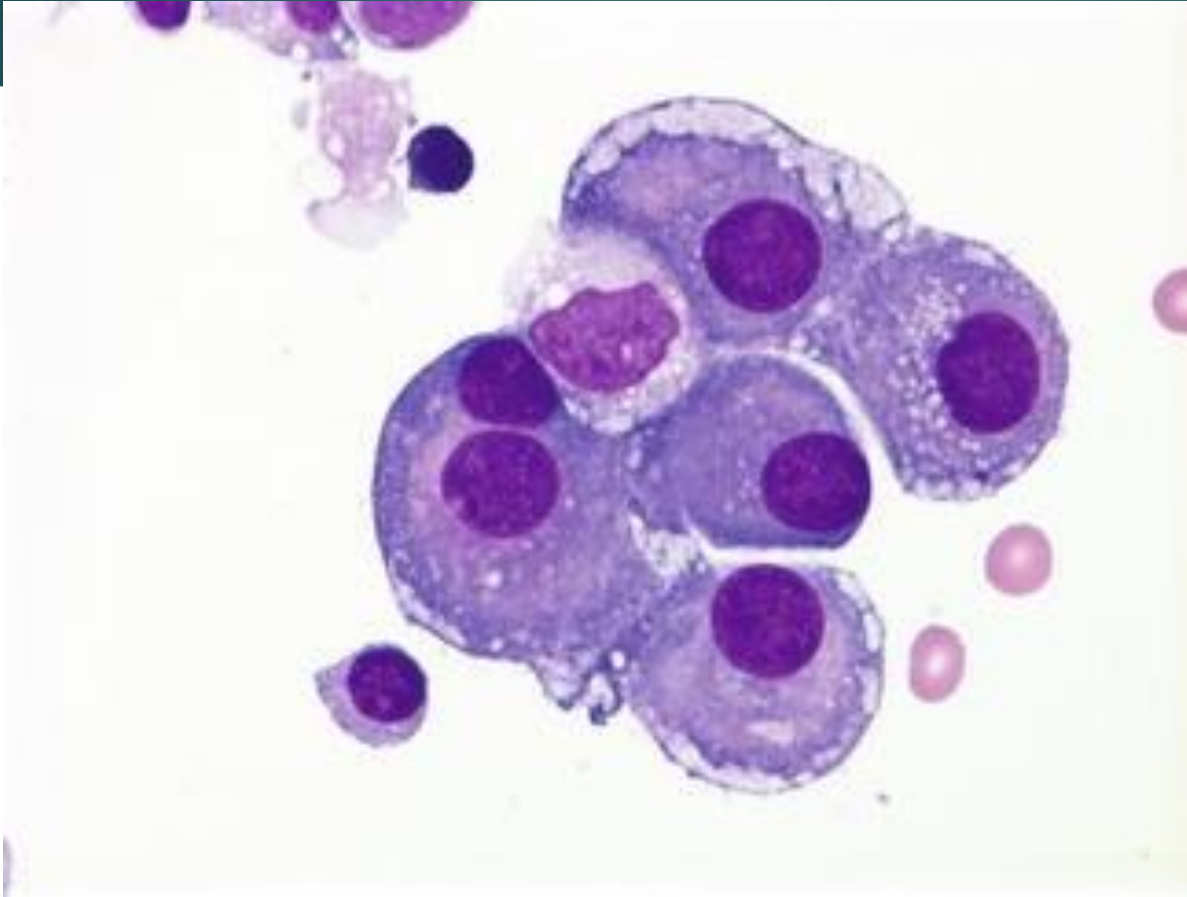
More Mesothelial Cells...



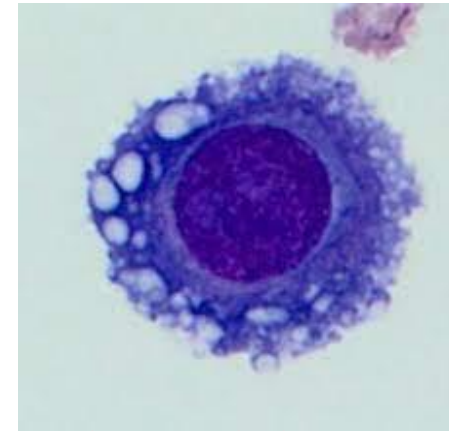
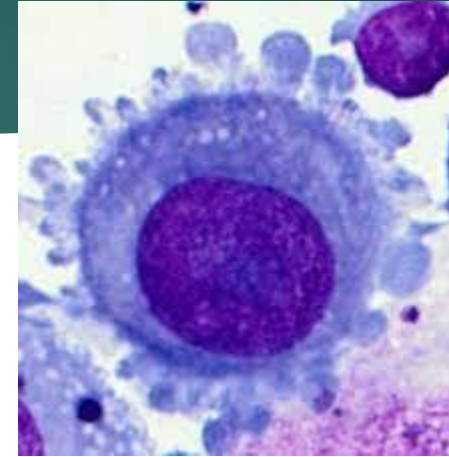
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Reactive Mesothelial Cells



https://link.springer.com/referenceworkentry/10.1007%2F978-3-319-33286-4_920



www.hema-research.or.kr



Synovial Fluid



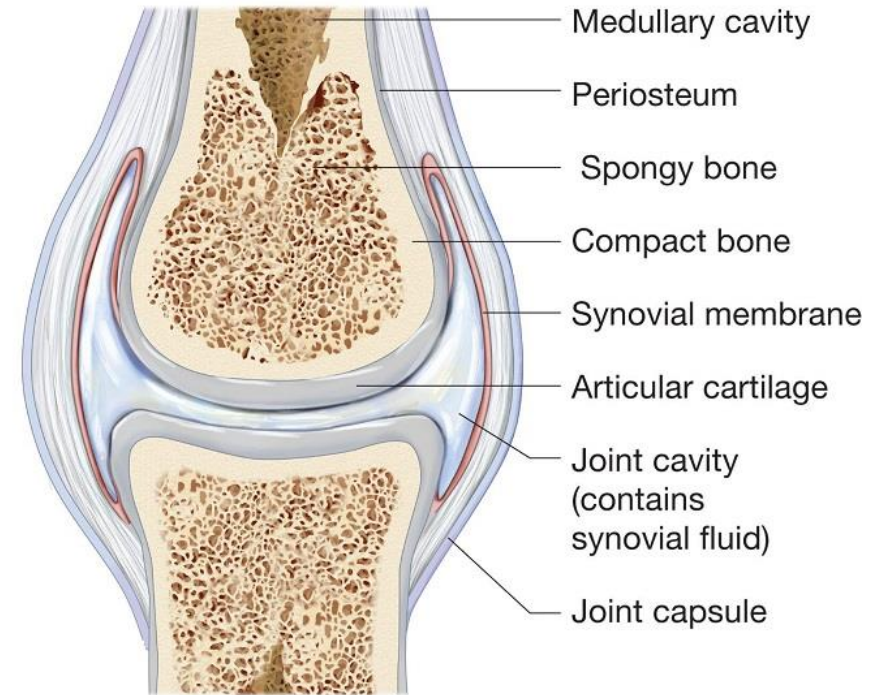
Synovial Fluid

- ▶ Viscous fluid in the cavities of movable joints (diarthroses)
- ▶ Synovial membrane contains specialized cells called synoviocytes
 - ▶ Secrete hyaluronic acid
 - ▶ Contributes to the viscosity of the fluid
- ▶ Formed as an ultra-filtrate of plasma
- ▶ Provides lubrication and nutrients to articular cartilage
- ▶ Lessens shock of joint compression



Collection

- ▶ Needle aspiration called arthrocentesis
- ▶ Normally does not form a clot
 - ▶ Fluid from a diseased joint may contain fibrinogen and form a clot
- ▶ Sodium heparin or EDTA tube used for cell count, differential, and crystal ID
- ▶ Sterile tube, with or without heparin, used for gram stain and cultures



<https://scopeheal.com/synovial-membrane/>



Normal Values and Characteristics

- ▶ Volume: <3.5 mL
- ▶ Appearance: Colorless to pale yellow and clear
- ▶ Viscosity: Highly viscous
 - ▶ Able to form 4-6 cm long strings
- ▶ WBC Count: <200 cells/uL
- ▶ Neutrophils: <25% on the differential
- ▶ Crystals: None present
- ▶ Glucose: <10 mg/dL lower than blood glucose level
- ▶ Total protein: <3 g/dL
- ▶ Lactate: <25.0 mg/dL



Synovial Fluid Viscosity

- ▶ Viscous nature comes from polymerization of hyaluronic acid
 - ▶ Essential for joint lubrication
- ▶ Arthritis can decrease the viscosity of the synovial fluid
- ▶ Ropes (mucin clot) test
 - ▶ Synovial fluid added to 2-5% acetic acid- forms a clot
 - ▶ As ability of hyaluronate to polymerize decreases, the clot becomes less firm
 - ▶ Fluid becomes more turbid
 - ▶ Reported in terms of clot formation: Good, Fair, Low, and Poor
- ▶ In the lab, synovial fluids are treated with hyaluronidase
 - ▶ Breaks down the hyaluronic acid to allow fluid to be more workable



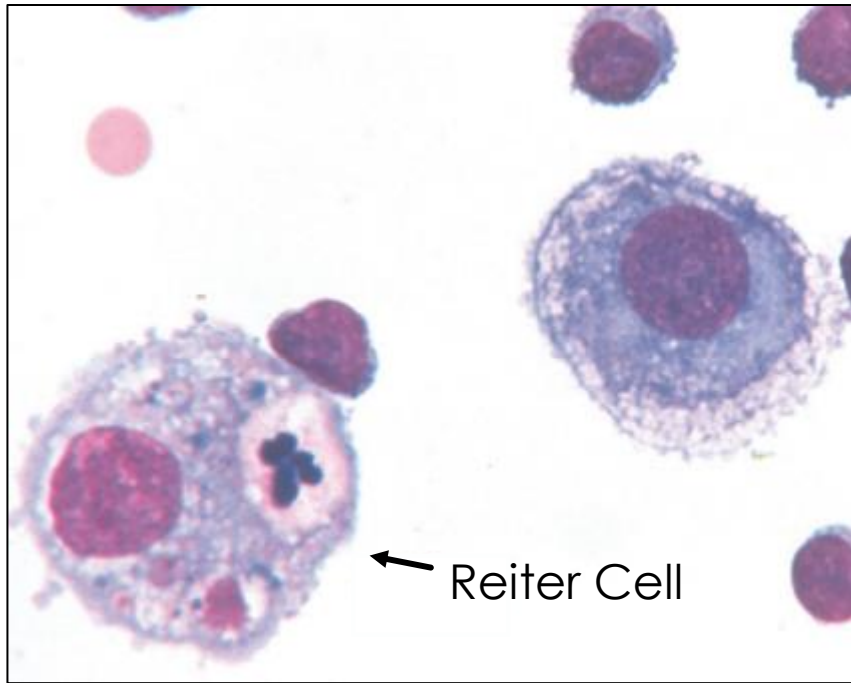
Synovial Fluid: Count and Differential

- ▶ WBC Count is very important
 - ▶ <200 cells/uL is considered normal

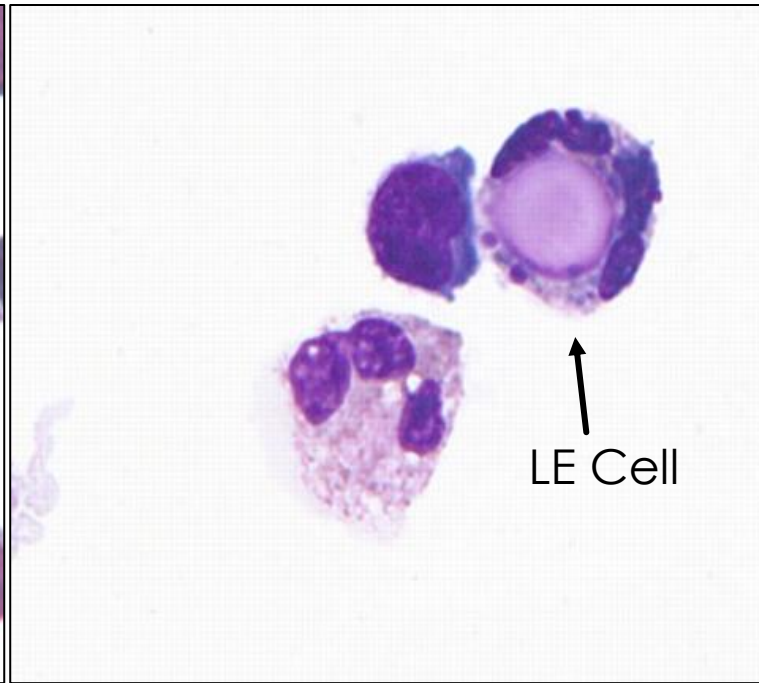
Differential

- ▶ Normal cells seen:
 - ▶ Neutrophils (<25%), Lymphs (<15%), Monos, Macros, and Synoviocytes
- ▶ Cells not typically seen:
 - ▶ Reiter Cells- vacuolated macrophages with ingested neutrophils
 - ▶ LE Cells- Neutrophil containing round body in lupus conditions
 - ▶ RA Cells (ragocytes)- Neutrophil with dark cytoplasmic granules containing immune complexes in rheumatoid arthritis
 - ▶ Rice bodies- collagen and fibrin seen in tuberculosis, septic and R.A.

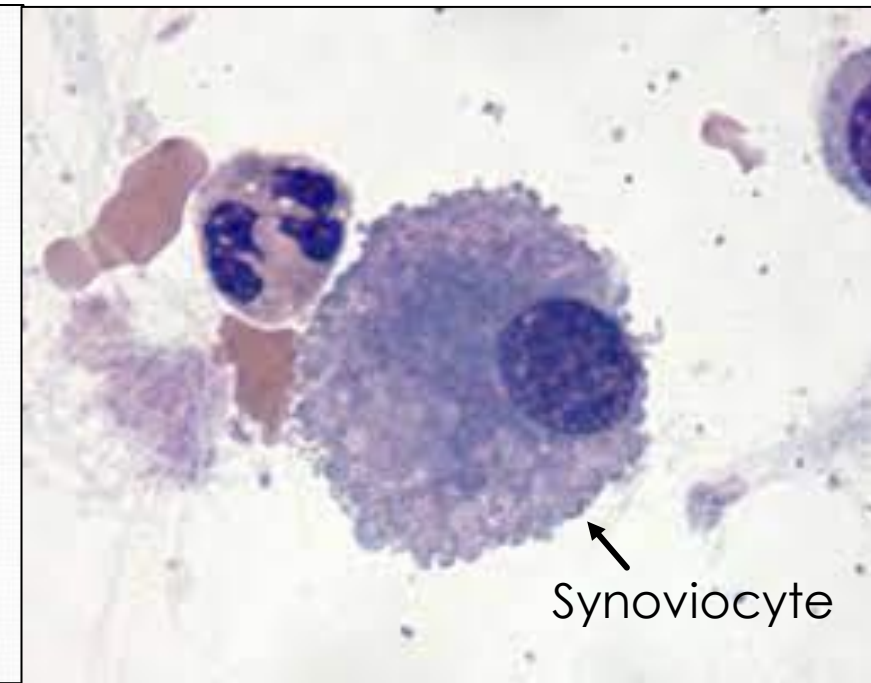




http://www.captodayonline.com/Archives/feature_stories/1006NeutrophageRED.pdf



<https://imagebank.hematology.org/image/3497/le-cell-in-joint-fluid--2>



<http://www.api-pt.com/Reference/Commentary/2016Ascope.pdf>



Crystal Identification

- ▶ Important for evaluation of arthritis
- ▶ Causes:
 - ▶ Metabolic disorders
 - ▶ Decreased renal excretion
 - ▶ Degeneration of cartilage and bone
- ▶ Types:
 - ▶ Monosodium Urate (MSU)
 - ▶ Calcium Pyrophosphate (CPPD) } Primary crystals seen in a synovial fluid
 - ▶ Hydroxyapatite
 - ▶ Cholesterol
 - ▶ Calcium Oxalate



Crystal Identification

- ▶ Identification of crystals is made using a first-order red-compensated polarized light filter
 - ▶ Divides the light entering the microscope into slow-moving and fast-moving vibrations
- ▶ Polarized light is obtained by using 2 polarizing filters
 - ▶ Polarizing filter is rotated to allow only light vibrating in one direction to reach the object
 - ▶ The filters are placed in opposite directions called a “crossed configuration”
 - ▶ Between the cross-polarizing filters, birefringent crystals are visible in characteristic patterns
- ▶ Both MSU and CPPD crystals can polarize light
- ▶ Differences in linear structure of the molecules in the MSU and CPPD crystals create different colors when aligned with the slow vibration

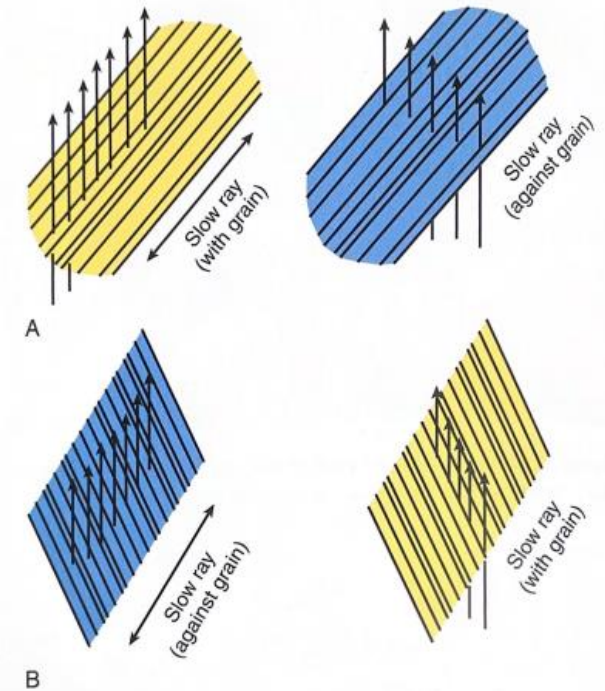


Figure 12-9 Negative and positive birefringence in MSU and CPPD crystals. **A.** MSU crystal with grain running parallel to the long axis. The slow ray passes with the grain, producing negative (yellow) birefringence. **B.** CPPD crystal with grain running perpendicular to the long axis. The slow ray passes against the grain and is retarded, producing positive (blue) birefringence. 🌐

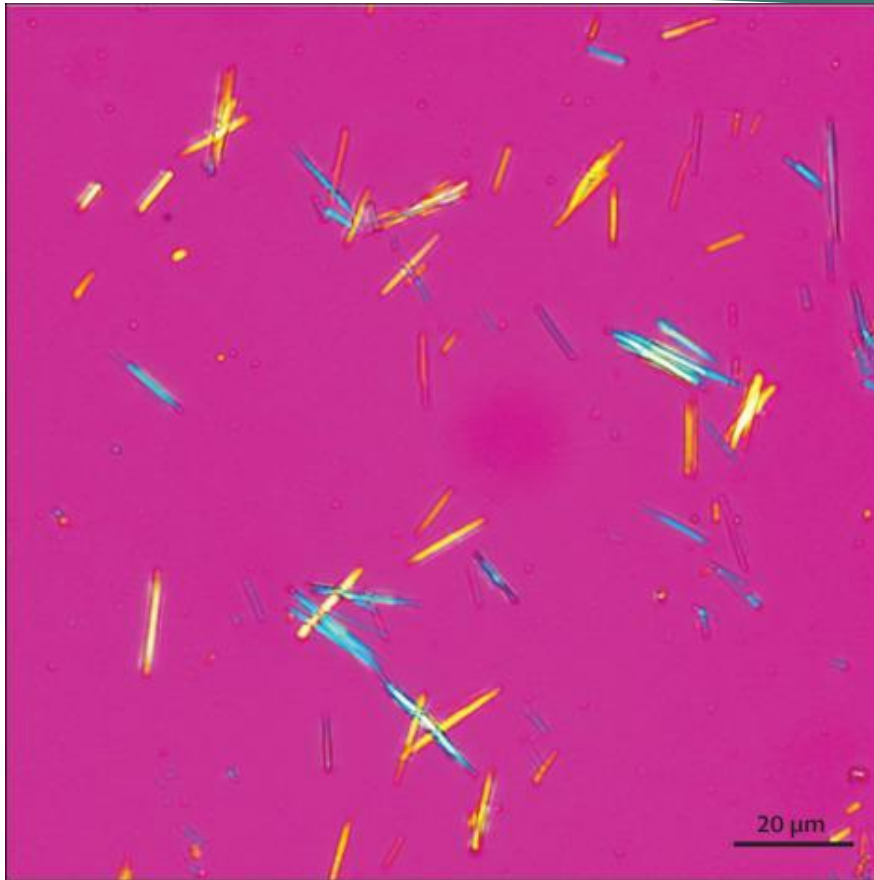


Monosodium Urate (MSU)

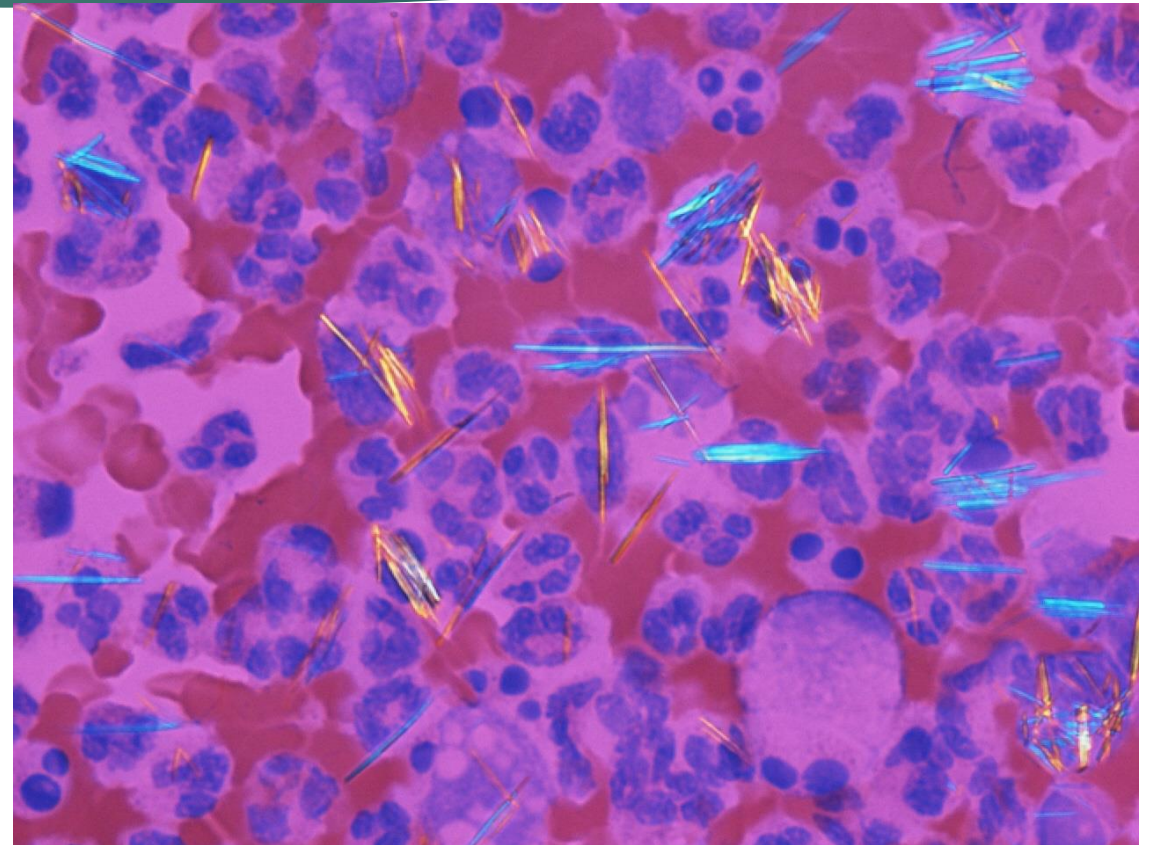
- ▶ Found in cases of **Gout**
- ▶ Causes
 - ▶ Increased serum uric acid resulting from impaired metabolism of purines
 - ▶ Increased consumption of high purine content foods, alcohol, and fructose
 - ▶ Chemotherapy treatment
 - ▶ Decreased renal excretion of uric acid
- ▶ Appearance
 - ▶ Needle appearance and frequently stick through the cytoplasm of phagocytic cells
 - ▶ Can be extracellular or located within the cytoplasm of neutrophils
 - ▶ Lyse phagosome membranes so do not appear in vacuoles of the neutrophil
- ▶ Highly birefringent-appear brighter
- ▶ Produce yellow color under polarization when compensator is parallel to the long axis of the crystal
 - ▶ Slow vibration
 - ▶ Run parallel to long axis (velocity of slow light passing through crystal not impeded as much as fast light, which runs against the grain and produces a yellow color)
- ▶ Negative birefringence



Monosodium Urate (MSU)



[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(16\)00346-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)00346-9/fulltext)



[https://commons.wikimedia.org/wiki/File:Gout_-_monosodium_urate_crystals_\(20X,_polarized,_red_compensator\).jpg](https://commons.wikimedia.org/wiki/File:Gout_-_monosodium_urate_crystals_(20X,_polarized,_red_compensator).jpg)

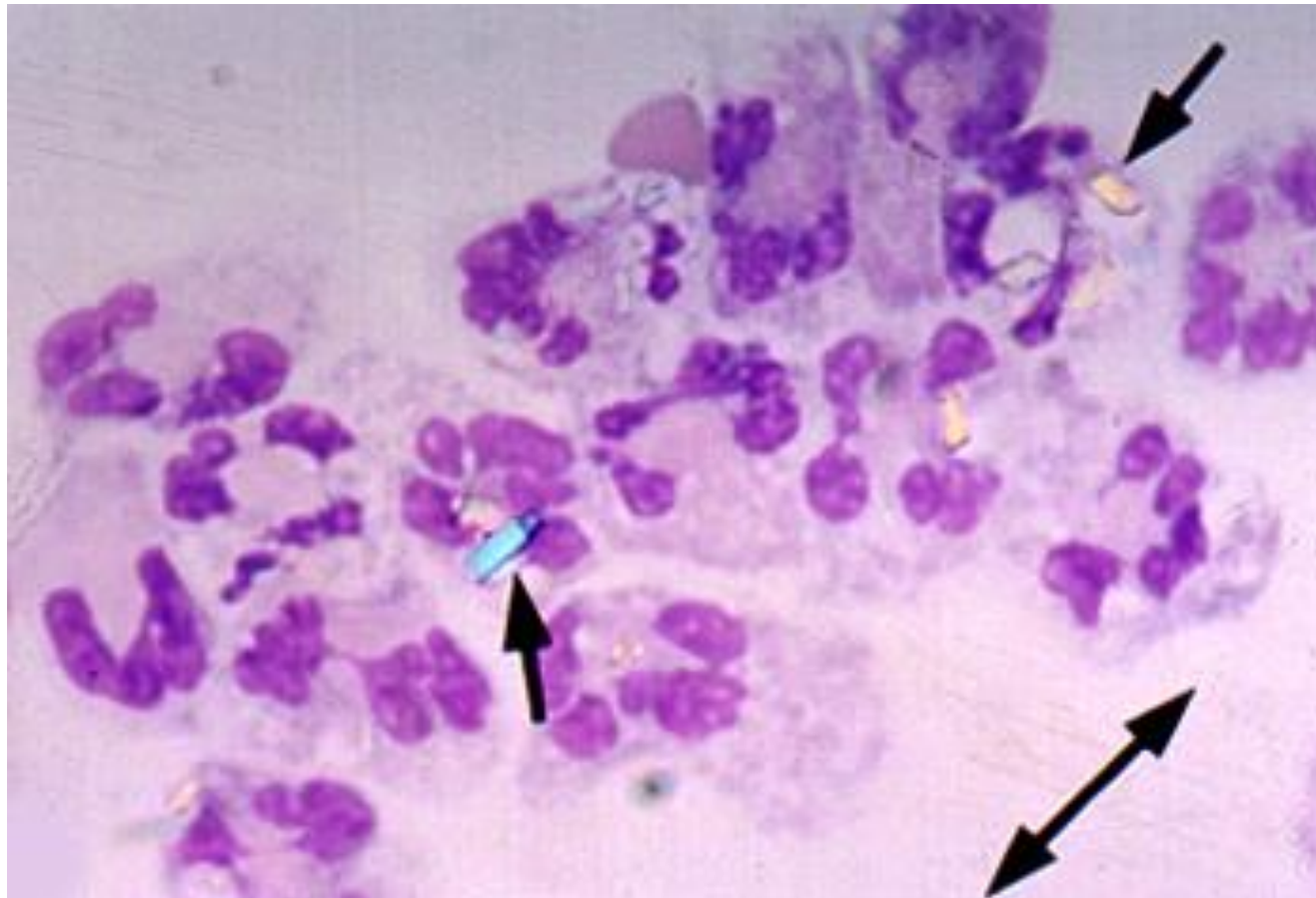


Calcium Pyrophosphate (CPPD)

- ▶ Found in cases of **Pseudogout**
- ▶ Causes
 - ▶ Degenerative arthritis
 - ▶ Cartilage calcification
 - ▶ Endocrine disorders
 - ▶ Produce increased serum calcium levels
- ▶ Appearance
 - ▶ Not as bright as MSU crystals
 - ▶ Produce blue color under polarization
 - ▶ Square rod shape located within vacuoles of neutrophils
- ▶ Perpendicular to long axis of crystal
 - ▶ When aligned with slow axis of compensator, the velocity of fast light is quicker than MSU
 - ▶ Produces a blue color
 - ▶ Positive birefringence



Calcium Pyrophosphate (CPPD)



Joint Disorders

 **I. Non-Inflammatory**

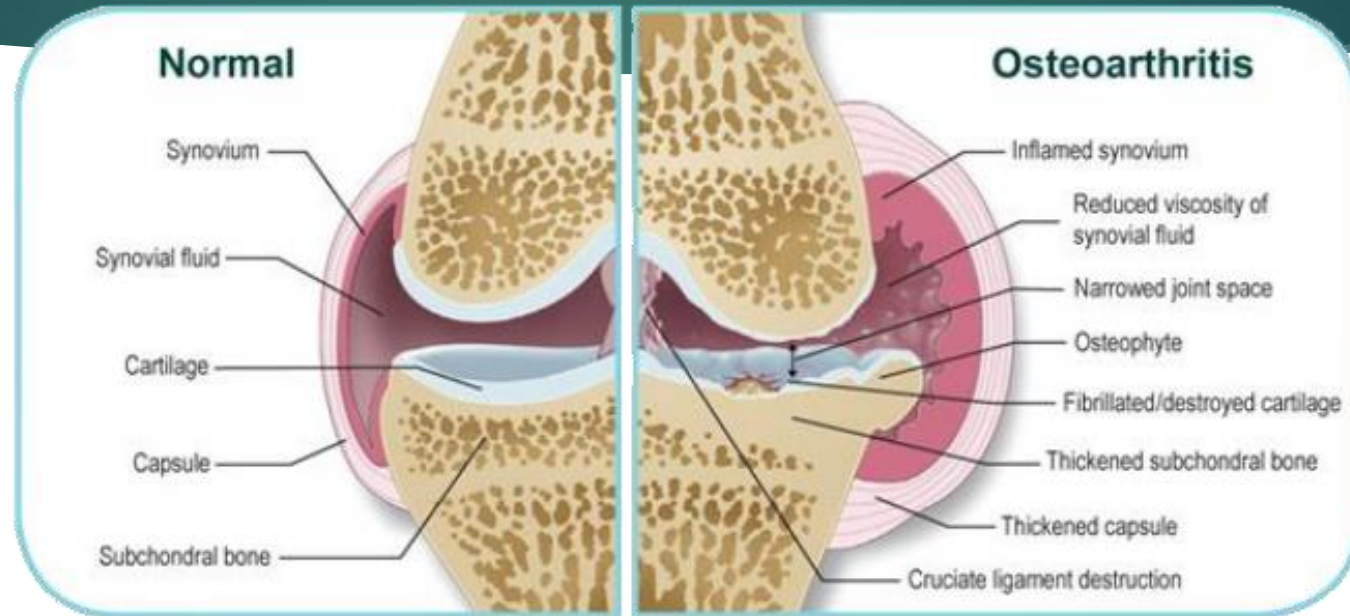
 **II. Inflammatory**

 **III. Septic**

 **IV. Hemorrhagic**



I. Non-Inflammatory



Pathological Significance

- ▶ Degenerative Joint Disorders
- ▶ Osteoarthritis

Laboratory Findings

- ▶ Clear, yellow appearance
- ▶ Good viscosity
- ▶ WBCs <1000/uL and Neutrophils <30%



II. Inflammatory

Immunologic Origins

- ▶ Pathological Significance
 - ▶ Rheumatoid arthritis, systemic lupus, scleroderma, polymyositis, ankylosing spondylitis, rheumatic fever, Lyme disease
- ▶ Laboratory Findings
 - ▶ Cloudy, yellow appearance
 - ▶ Poor viscosity
 - ▶ WBCs 2,000-75,000 /uL
 - ▶ Neutrophils >50%
 - ▶ Decreased glucose level

Crystal-Induced Origins

- ▶ Pathological Significance
 - ▶ Crystal-induced gout
 - ▶ Pseudogout
- ▶ Laboratory Findings
 - ▶ Cloudy or milky appearance
 - ▶ Low viscosity
 - ▶ WBCs up to 100,000 /uL
 - ▶ Neutrophils <70%
 - ▶ Decreased glucose levels
 - ▶ **Crystals present!!!**



III. Septic

Pathological Significance

- ▶ Microbial Infection

Laboratory Findings

- ▶ Cloudy, yellow to green appearance
- ▶ WBCs 50,000-100,000 uL
- ▶ >75% Neutrophils
- ▶ Decreased glucose level
- ▶ Positive culture and gram stain
 - ▶ *Staphylococcus*
 - ▶ *Streptococcus*
 - ▶ *Haemophilus* species
 - ▶ *N. gonorrhoeae*



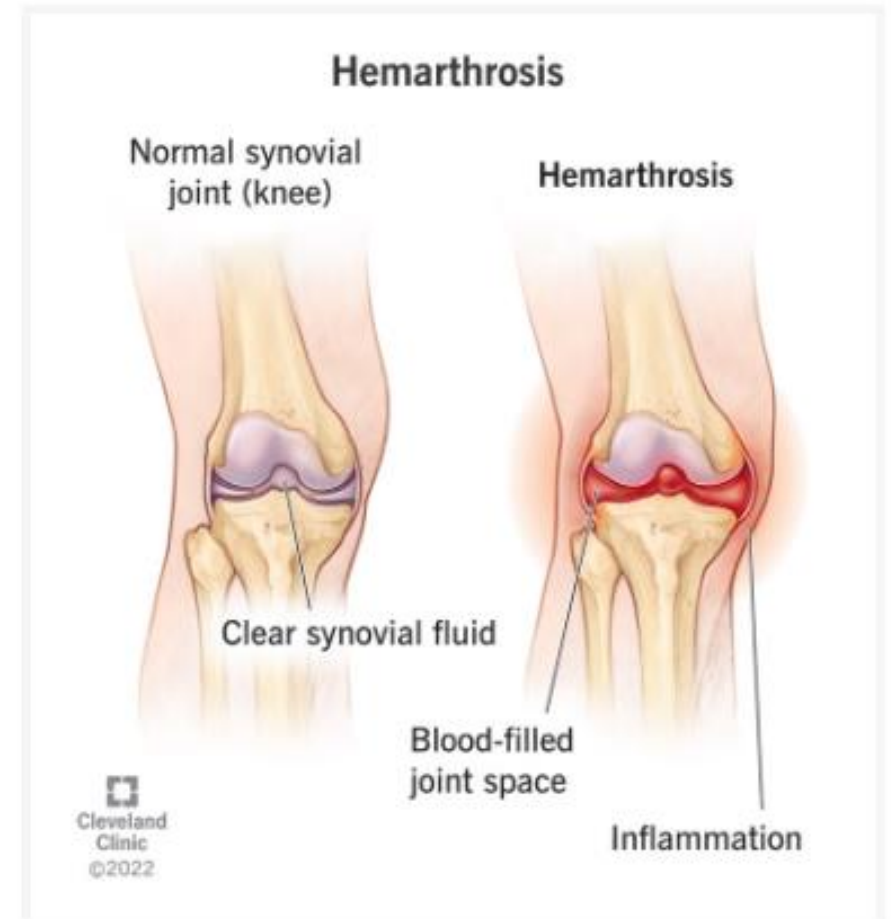
IV. Hemorrhagic

Pathological Significance

- ▶ Trauma injury, tumors, hemophilia, other coagulation disorders, anticoagulant overdose

Laboratory Findings

- ▶ Cloudy, red appearance
- ▶ Low viscosity
- ▶ WBCs equal to peripheral blood
- ▶ Neutrophils equal to peripheral blood
- ▶ Normal glucose level



Malignant Cells in Body Fluids

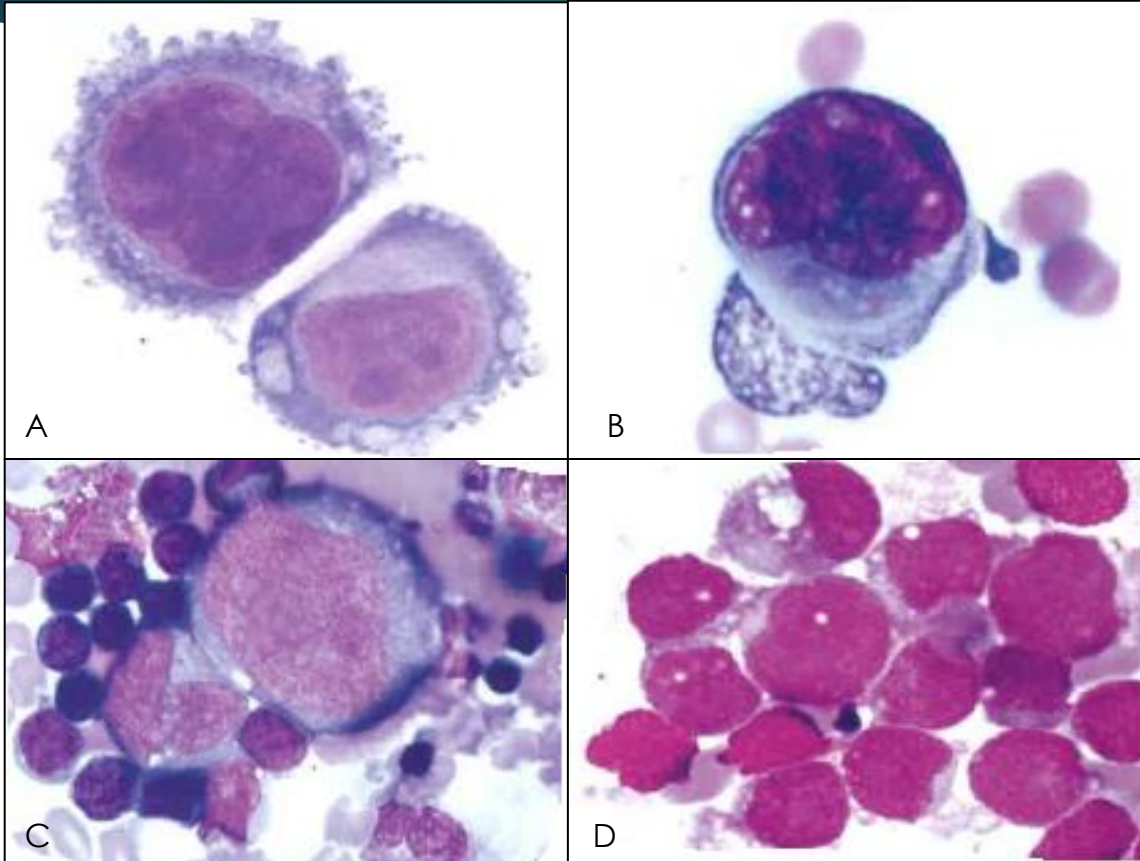


Malignant Cell Characteristics in Body Fluids

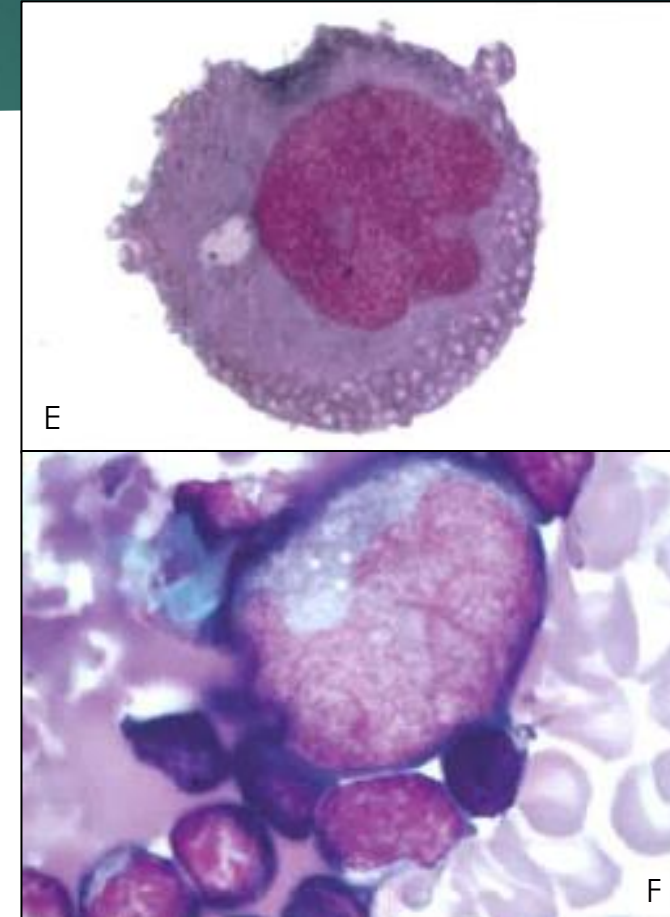
- ▶ Increased N:C ratio
- ▶ Irregular nuclear chromatin
- ▶ Variation in size and shape of nuclei
- ▶ Increased nucleoli shape and number
- ▶ Giant cells and multinucleation
- ▶ Nuclear molding
- ▶ Cytoplasmic molding (community borders)
- ▶ Vacuolated cytoplasm/mucin production
- ▶ Cellular crowding/phagocytosis



Increased N:C Ratio



Irregular Nuclear Chromatin

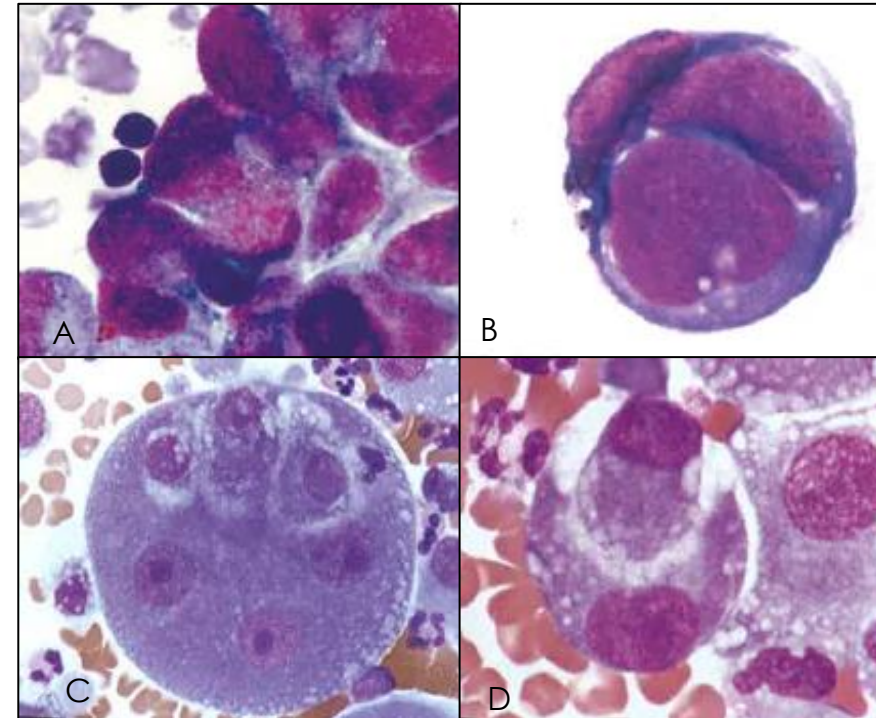
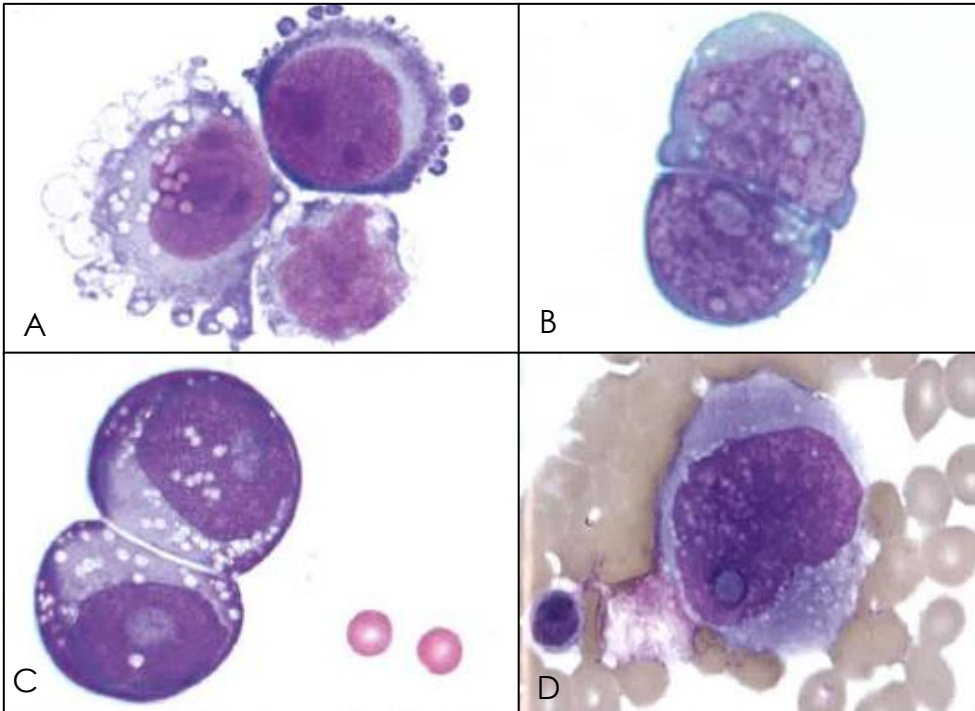


Images Courtesy of: Color Atlas of Body Fluids: An Illustrated Field Guide Based if Proficiency Testing



Increase in Nucleoli Size and Number

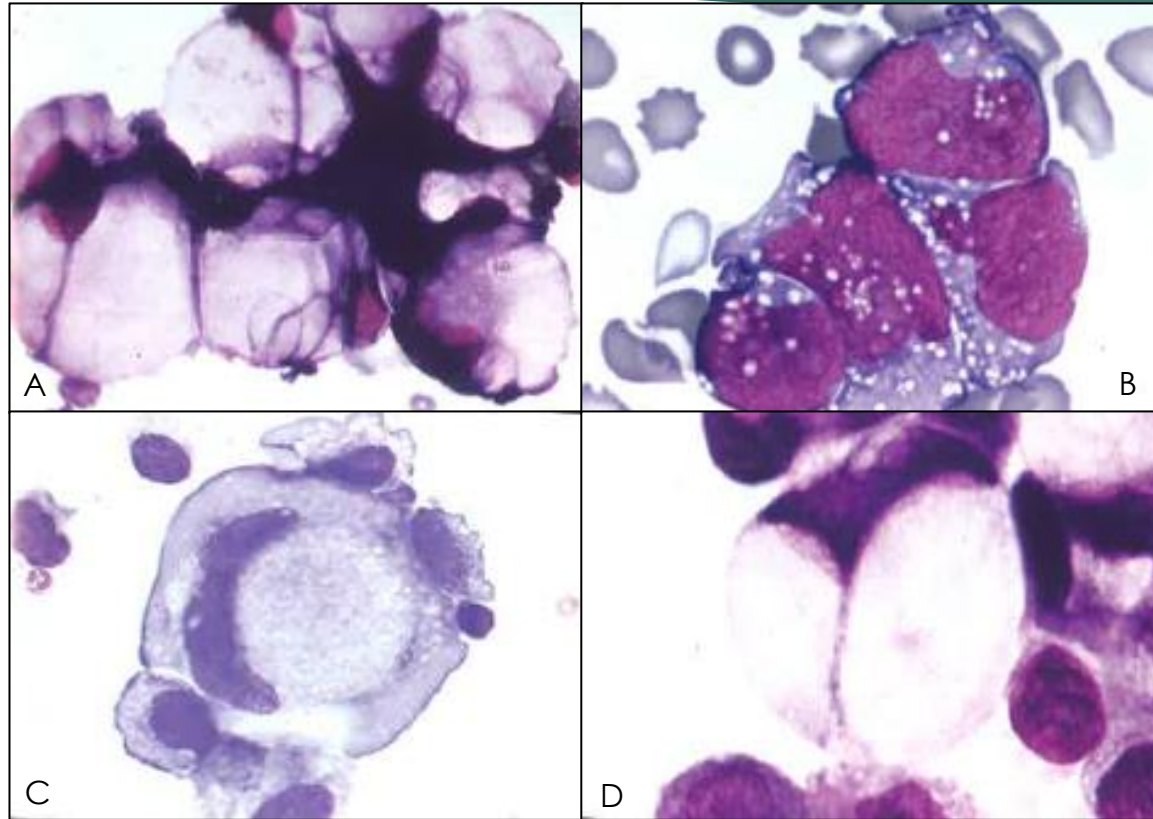
Nuclear Molding and Cannibalism



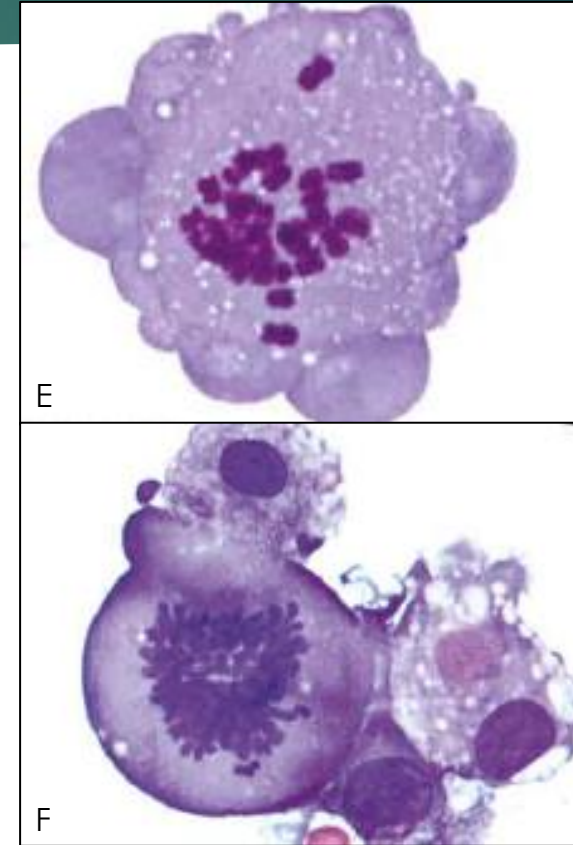
Images Courtesy of: Color Atlas of Body Fluids: An Illustrated Field Guide Based if Proficiency Testing



Abnormal Cytoplasmic Vacuolization/Mucin Production



Abnormal Mitotic Figures



Images Courtesy of: Color Atlas of Body Fluids: An Illustrated Field Guide Based if Proficiency Testing



References

- ▶ Urinalysis and Body Fluids, 7th Edition by Susan King Strasinger and Marjorie Schaub Di Lorenzo
- ▶ Rodak's Hematology Clinical Principles and Applications 6th edition.

