PEARLS OF LABORATORY MEDICINE

Pearl Title: **Body Fluids**

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Body fluids

- Ultrafiltrates of blood
  - support the delivery and removal of nutrients and metabolic byproducts
  - may contain biomarkers
  - present in the healthy population or in the disease state
- Pathogenic processes lead to accumulation of body fluids
- Increased volume of fluid in any organ, tissue or joint compartment
  necessitates clinical intervention
- Collection may be for diagnostic and/or therapeutic purposes
Body fluids other than serum and urine

- Cerebrospinal Fluid (CSF)
- Pleural Fluid
- Pericardial fluid
- Peritoneal or Ascitic Fluid
- Amniotic fluid
- Synovial Fluid
- Saliva
Cerebrospinal Fluid (CSF)

- Total volume in normal adults: 125mL-150mL
- Normal adults production of CSF: 20mL per hour
- Protects the brain and spinal cord from injury
- Bathes brain and spine in nutrients and eliminates waste products
- CSF is usually collected for testing through a lumbar puncture

https://medlineplus.gov/ency/presentations/100145_1.htm
## CNS pathologies

<table>
<thead>
<tr>
<th>Pathologic conditions</th>
<th>Primary findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhage</td>
<td>Subarachnoid hemorrhage (SAH)</td>
</tr>
<tr>
<td>Meningitis</td>
<td>Inflammation of the leptomeninges</td>
</tr>
<tr>
<td>Malignant tumors (e.g. gliomas)</td>
<td>Shed cells into the fluid</td>
</tr>
<tr>
<td>Demyelinating diseases</td>
<td>• Products of demyelination in the fluid</td>
</tr>
<tr>
<td></td>
<td>• Leukocytes in the fluid</td>
</tr>
<tr>
<td></td>
<td>• Increased oligoclonal immunoglobulins</td>
</tr>
</tbody>
</table>
Routine Biochemical Tests on CSF

**Protein**

- 0.15 to 0.45 g/L (0.015 to 0.045 g/dL) in normal adults
- 0.2 to 1.7 g/L (0.02 to 0.17 g/dL) in normal premature and term neonates
- CSF protein can be falsely elevated due to the presence of RBCs from subarachnoid hemorrhage or traumatic lumbar puncture
- Elevations in the CSF protein concentration can occur in both infectious and non-infectious conditions
Routine Biochemical Tests on CSF

Glucose

- CSF/serum glucose ratio is approximately 0.6 in normal individuals
- CSF glucose concentrations <1.0 mmol/L (18.0 mg/dL) predictive of bacterial meningitis
- CSF glucose concentrations typically normal in viral CNS infections
- Low CSF glucose in bacterial meningitis, mycobacterial and fungal CNS infections as well as malignancies and subarachnoid hemorrhage
Typical CSF findings in Bacterial and Viral Meningitis

<table>
<thead>
<tr>
<th></th>
<th>Bacterial Meningitis</th>
<th>Viral Meningitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WBC</strong></td>
<td>&gt;1000/μL, neutrophilic predominance</td>
<td>&lt;250/μL, lymphocytic predominance</td>
</tr>
<tr>
<td><strong>Protein</strong></td>
<td>&gt;2.5 g/L (0.25 g/dL)</td>
<td>&lt;1.5g/L (0.15 g/dL)</td>
</tr>
<tr>
<td><strong>Glucose</strong></td>
<td>&lt;2.5 mmol/L (45 mg/dL)</td>
<td>&gt;50% of serum glucose</td>
</tr>
</tbody>
</table>
Pleural Fluid

- Intercostal muscles
- Pleural sac
- Parietal pleura
- Visceral pleura
- Diaphragm
- Chest wall (rib cage, sternum, thoracic vertebrae, connective tissue, intercostal muscles)

Pleural Fluid

- Lung
- Intercostal muscle
- Pleural cavity
Causes of Pleural Effusions

- **Transudative Pleural Effusions**
  a. Congestive heart failure (CHF)
  b. Cirrhosis
  c. Nephrotic syndrome
  d. Superior vena caval obstruction
  e. Fontan procedure
  f. Urinothorax
  g. Peritoneal dialysis
  h. Glumerulonephritis
  i. Myxedema
  j. Cerebrospinal leak to pleura
  k. Hypoalbuminaemia

- **Exudative Pleural Effusions**
  a. Neoplastic diseases
  b. Infectious diseases
  c. Pulmonary embolization
  d. Gastrointestinal disease
  e. Heart diseases
  f. Obstetric and gynecological disease
  g. Collagen vascular diseases
  h. Drug-induced pleural disease
  i. Miscellaneous diseases and conditions
  j. Hemothorax
  k. Chylothorax
  l. Pseudochylothorax
Biochemical Analysis of Pleural fluid

THORACENTESIS
- Diagnostic
  Abnormal amount of fluids accumulation in the pleural space
- Therapeutic
  Relief of symptoms due to large pleural effusions

PLEURAL FLUID

APPEARANCE OF FLUID
- CLEAR: transudates
- BLOODY: malignancy, embolism, trauma
- WHITE MILKY: chylothorax, pseudochylothorax
- PUS: empyema
- YELLOW-GREEN: rheumatoid arthritis effusions

TRANSUDATES VS EXUDATES

LIGHT’S CRITERIA (one or more):
(a) Pleural fluid protein/serum protein ratio ≥ 0.5
(b) Pleural fluid LDH/serum LDH ≥ 0.6
(c) Pleural fluid LDH level ≥ 2/3 upper reference limit for serum LDH

IF EXUDATE

- **Total and differential cell count:** total WBC≥ 500 x 10^6 / L, neutrophil predominance in acute inflammatory processes
- **pH:** <7.3 in inflammatory states while <7.2 need for tube drainage in empyema
- **Triglycerides:** > 1.2 mmol/L (106.2 mg/dL) in chylothorax, < 0.6 mmol/L (53.1 mg/dL) in pseudochylothorax
- **Cholesterol:** < 5.2 mmol/L (200.8 mg/dL) in chylothorax, >5.1 mmol/L (196.9 mg/dL) in pseudochylothorax
- **ADA:** > 40 U/L in tuberculous pleuritis
- **Amylase:** pleural fluid/serum ratio >1 in pancreatic pseudocyst, liver cirrhosis and esophageal rupture
Pericardial Fluid

- Normal volume: 15-50 mL
- Originates from the visceral pericardium
- Serves as lubrication to visceral and parietal layers of pericardium
- Pericardial fluid is usually collected for testing through pericardiocentesis
Causes of Pericardial Effusions

- **Transudative Effusions**
  - Congestive heart failure
  - Myxoedema
  - Nephrotic syndrome

- **Exudative Effusions**
  - Tuberculosis
  - Empyema
  - Malignant effusions
Analysis of Pericardial fluid

**PERICARDIOCENTESIS**
- Cardiac Tamponade
- Infection
- Spread of cancer
- Autoimmune disease

**PERICARDIAL FLUID**

**APPEARANCE OF FLUID**
- **TURBID**: infection or malignancy
- **BLOODY**: malignancy or tuberculous
- **MILKY**: chylopericardium

**Parameter** | **Exudate** | **Transudate**
---|---|---
Total protein (g/dL) | >3.0 | <3.0
Pericardial fluid to serum protein ratio | >0.5 | <0.5
Pericardial fluid to serum LDH ratio | >0.6 | <0.6
Pericardial fluid to serum glucose ratio | <1.0 | >1.0

- **Total WBC** >10,000/µl with neutrophil predominance in bacterial, tuberculous or malignant pericarditis
- **Cytological examination, bacteriologic smears and culture**
- **Glucose, Protein and LDH**
Peritoneal/Ascitic Fluid

• Straw-colored liquid

• Originates from the abdominal cavity

• Serves as lubrication to the surface of tissue that lines the abdominal wall and pelvic cavity

• Effusion volume >50mL

• Peritoneal fluid is usually collected for testing through paracentesis
# Causes of peritoneal effusion

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Increased hydrostatic pressure</strong></td>
<td>- Cirrhosis&lt;br&gt;- Hepatic venous outflow obstruction&lt;br&gt;- Constrictive pericarditis</td>
</tr>
<tr>
<td>(portal hypertension)</td>
<td></td>
</tr>
<tr>
<td><strong>Decreased colloid osmotic pressure</strong></td>
<td>- Nephrotic syndrome&lt;br&gt;- Malnutrition and protein losing enteropathy</td>
</tr>
<tr>
<td>(hypoalbuminemia)</td>
<td></td>
</tr>
<tr>
<td><strong>Malignant conditions</strong></td>
<td>- Adenocarcinoma&lt;br&gt;- Epidermoid carcinoma&lt;br&gt;- Melanoma&lt;br&gt;- Mesothelioma</td>
</tr>
<tr>
<td><strong>Infection</strong></td>
<td>- TB&lt;br&gt;- Fungal&lt;br&gt;- Parasite&lt;br&gt;- Chlamydia</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td>- Chylous ascites&lt;br&gt;- Pancreatic ascites&lt;br&gt;- Bile ascites&lt;br&gt;- Ovarian disease</td>
</tr>
</tbody>
</table>
Biochemical Analysis of Peritoneal / Ascitic fluid

PARACENTESIS

- Relieve abdominal pressure from ascites
- Diagnose SBP, metastatic cancer, blood in peritoneal space in trauma

PERITONEAL FLUID

APPEARANCE OF FLUID

- CLOUDINESS due to neutrophils
- MILKY due to triglycerides
- BLOODY due to malignancy, pancreatitis or abdominal trauma
- TEA-COLORED due to pancreatitis

TRANSUDATES VS EXUDATES

TOTAL PROTEIN
25-30 g/L (2.5-3.0 g/dL)

SERUM ASCITES ALBUMIN GRADIENT (SAAG):
(a) >1.1 g/dL (11 g/L) indicates transudative ascites
(b) <1.1 g/dL (11 g/L) indicates exudative ascites

IF EXUDATE

- Total and differential cell count (PMN leukocyte count ≥ 500 x 10⁶ / L in SBP)
- Glucose lower than in serum in tuberculous peritonitis, carcinomatosis and SBP
- Amylase ≥ 2000 U/L in pancreatic ascites, gut perforation, ruptured pseudocyst
- Triglycerides > 2.25 mmol/l (199.1 mg/dL) or higher than in serum in chylous ascites
- Urea higher than serum in urinary bladder rupture
- ADA > 39 U/L in peritoneal tuberculosis
Amniotic Fluid
Amniocentesis

Indications for diagnostic amniocentesis:

• Evaluation of fetal chromosomal anomalies
• Evaluation of fetal lung maturity
• Evaluation of alloimmunization

Indications for therapeutic amniocentesis:

• Direct delivery of medications to the unborn fetus
• Release intrauterine pressure in the presence of polyhydramnios
- **Polyhydramnios**
  - Excessive accumulation of amniotic fluid
  - Indicates fetal distress and often associated with neural tube disorders

- **Oligohydramnios**
  - Decreased amniotic fluid due to increased fetal swallowing urinary tract deformities and membrane leakage

- **Erythroblastosis fetalis/ Rh Disease**
  - Haemolytic disease of the fetus and the newborn
  - Caused by maternal antibodies directed against antigens on fetal erythrocytes
  - Increased bilirubin levels
Biochemical Analysis

### Gross Examination

<table>
<thead>
<tr>
<th>Appearance</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorless with slight to moderate turbidity</td>
<td>Normal</td>
</tr>
<tr>
<td>Blood-streaked</td>
<td>Traumatic tap, abdominal trauma, intra-amniotic hemorrhage</td>
</tr>
<tr>
<td>Yellow</td>
<td>Rh Disease</td>
</tr>
<tr>
<td>Dark green</td>
<td>Meconium</td>
</tr>
<tr>
<td>Dark red-brown</td>
<td>Fetal death</td>
</tr>
</tbody>
</table>

### Bilirubin

- Indirect method for assessing the level of anemia in the fetus
- Normal levels very low (2.7-3.1 µmol/L or 0.16-0.18 mg/dL) peaking at around 19 to 22 weeks
Synovial Fluid

• Colorless to light yellow, highly viscous
• It is found in the cavities of synovial joints
• Normal volume: 3-4 mL
• Reduces friction between articular cartilage of synovial joints during movements
• It is collected for testing through arthrocentesis
Pathological Classification of Synovial Fluid

- **Non-inflammatory**
  - Osteoarthritis
  - Neuroarthropathy

- **Inflammatory**
  - Rheumatoid arthritis

- **Septic**
  - Bacterial or fungal infection

- **Hemorrhagic**
  - Hemophilia
  - Trauma
Arthrocentesis

Indications for diagnostic arthrocentesis:

• Evaluation of suspected septic arthritis
• Evaluation of crystal induced arthritis
• Evaluation of unexplained arthritis with synovial effusion

Indications for therapeutic arthrocentesis:

• Relief of pain by aspirating effusion or blood
• Drainage of septic effusion
• Injection of medications (e.g. corticosteroids, antibiotics, or anesthetics)
# Routine tests of synovial fluid analysis

<table>
<thead>
<tr>
<th>Measure</th>
<th>Normal</th>
<th>Non-inflammatory</th>
<th>Inflammatory</th>
<th>Septic</th>
<th>Hemorrhagic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (mL)</td>
<td>&lt;3.5</td>
<td>&gt;3.5</td>
<td>&gt;3.5</td>
<td>&gt;3.5</td>
<td>&gt;3.5</td>
</tr>
<tr>
<td>Viscosity</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>Mixed</td>
<td>Low</td>
</tr>
<tr>
<td>Clarity</td>
<td>Clear</td>
<td>Clear</td>
<td>Cloudy</td>
<td>Cloudy</td>
<td>Cloudy</td>
</tr>
<tr>
<td>Color</td>
<td>Colorless to light yellow</td>
<td>Yellow</td>
<td>Yellow/Green</td>
<td>Yellow/Green</td>
<td>Red, brown or xanthochromic</td>
</tr>
<tr>
<td>WBC/mm³</td>
<td>&lt;200</td>
<td>&lt;2,000</td>
<td>2,000-50,000</td>
<td>&gt;50,000</td>
<td>Similar to blood level</td>
</tr>
<tr>
<td>%PMN</td>
<td>&lt;25</td>
<td>&lt;25</td>
<td>&gt;50</td>
<td>&gt;75</td>
<td>Similar to blood level</td>
</tr>
<tr>
<td>Gram stain</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Crystals</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Multiple or Absent</td>
<td>Absent</td>
</tr>
</tbody>
</table>
Saliva

- A mixture of oral fluids including
  - salivary gland secretions
  - cellular material
  - food debris
- Contains molecules normally found in serum by several mechanisms:
  - Intra-cellular routes (passive diffusion)
  - Extra-cellular routes (ultrafiltration at tight junctions between the cells)
Pathology & Diagnostic Use of Saliva

- Systemic diseases
- Changes in serum concentrations of certain analytes

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ease of collection and storage</td>
<td>Low levels of analytes</td>
</tr>
<tr>
<td>Non-invasive</td>
<td>Contamination</td>
</tr>
<tr>
<td>“Lower stress”</td>
<td>Viscosity</td>
</tr>
</tbody>
</table>
Biochemical Tests in Saliva

**Endogenous analytes**

**Infectious Disease**
- Helicobacter pylori, Lyme disease, mumps and measles
- HIV-1

**Hormones**
- Free or non-protein-bound hormone concentration
  - Cortisol correlate well with serum concentration
    - May represent 10% of the unbound plasma concentration
  - Testosterone correlate well with serum concentration
    - A useful test in research on male hypogonadism or in sports medicine

**Exogenous analytes**

**Drugs**
- Only the active (unbound) fraction of the drug in serum is available for diffusion into saliva
- Cotinine, cannabinoids, cocaine, opioids, diazepines, amphetamines
References

Disclosures/Potential Conflicts of Interest

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- **Employment or Leadership**: No disclosures
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