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PEARLS OF LABORATORY MEDICINE

Pearl Title: **Body Fluids**

Name of Presenter: **Eirini (Irene) Tsilioni, PhD**

Affiliation: **Tufts University School of Medicine**

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Body fluids

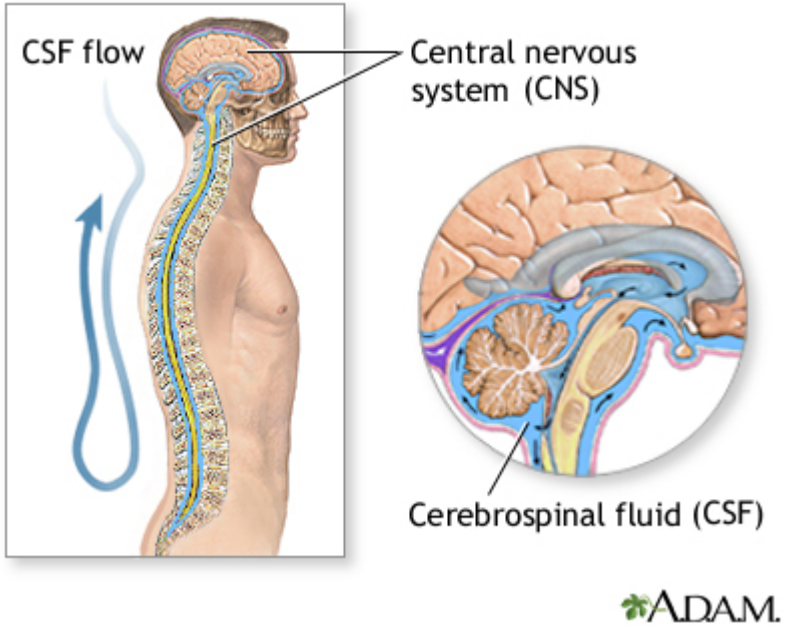
- Ultrafiltrates of blood
  - support the delivery and removal of nutrients and metabolic byproducts
  - may contain biomarkers
  - present in the healthy population or in the disease state
- Pathogenic processes lead to accumulation of body fluids
- Increased volume of fluid in any organ, tissue or 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



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CNS pathologies

Pathologic conditions	Primary findings
Hemorrhage	Subarachnoid hemorrhage (SAH)
Meningitis	Inflammation of the leptomeninges
Malignant tumors (e.g. gliomas)	Shed cells into the fluid
Demyelinating diseases	• Products of demyelination in the fluid • Leukocytes in the fluid • Increased oligoclonal immunoglobulins

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

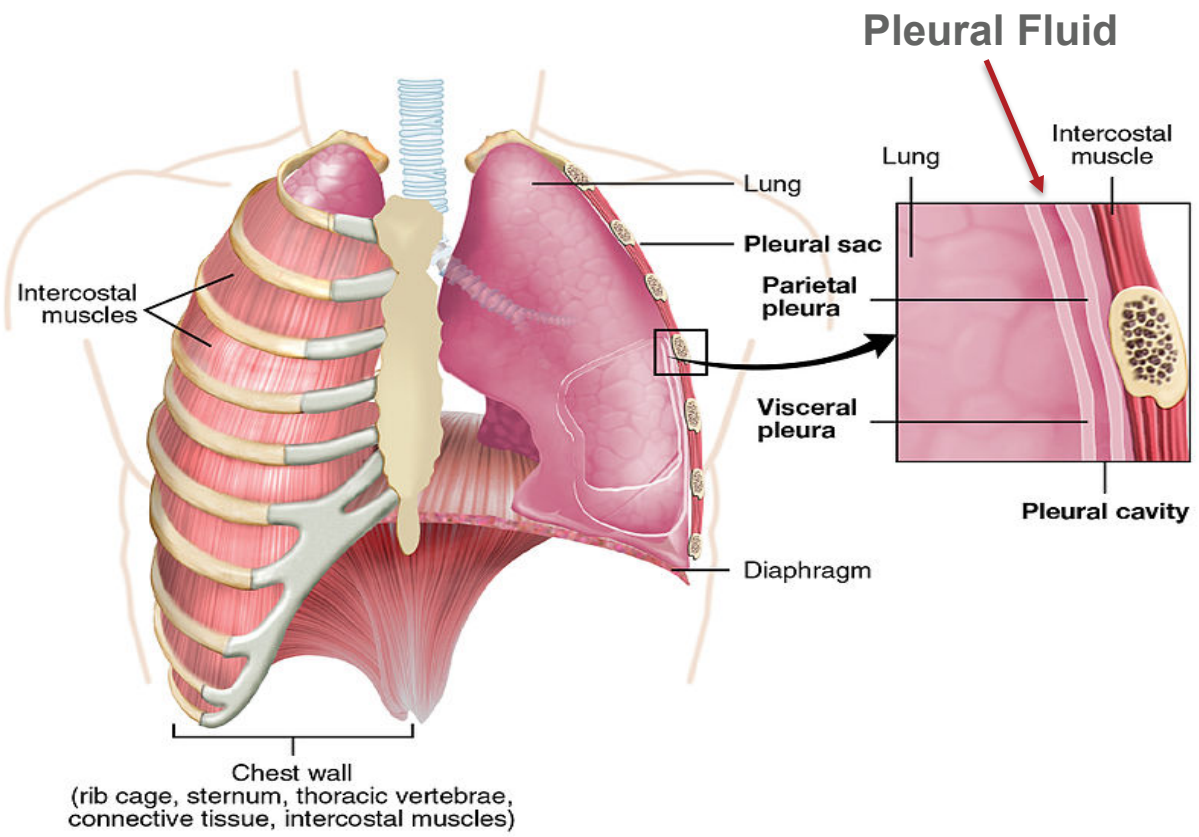
Glucose

- 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

	Bacterial Meningitis	Viral Meningitis
WBC	>1000/μL, neutrophilic predominance	<250/μL, lymphocytic predominance
Protein	>2.5 g/L (0.25 g/dL)	<1.5g/L (0.15 g/dL)
Glucose	<2.5 mmol/L (45 mg/dL)	>50% of serum glucose

Pleural Fluid



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 → **PLEURAL FLUID**

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**

APPEARANCE OF FLUID → **TRANSUDATES VS EXUDATES**

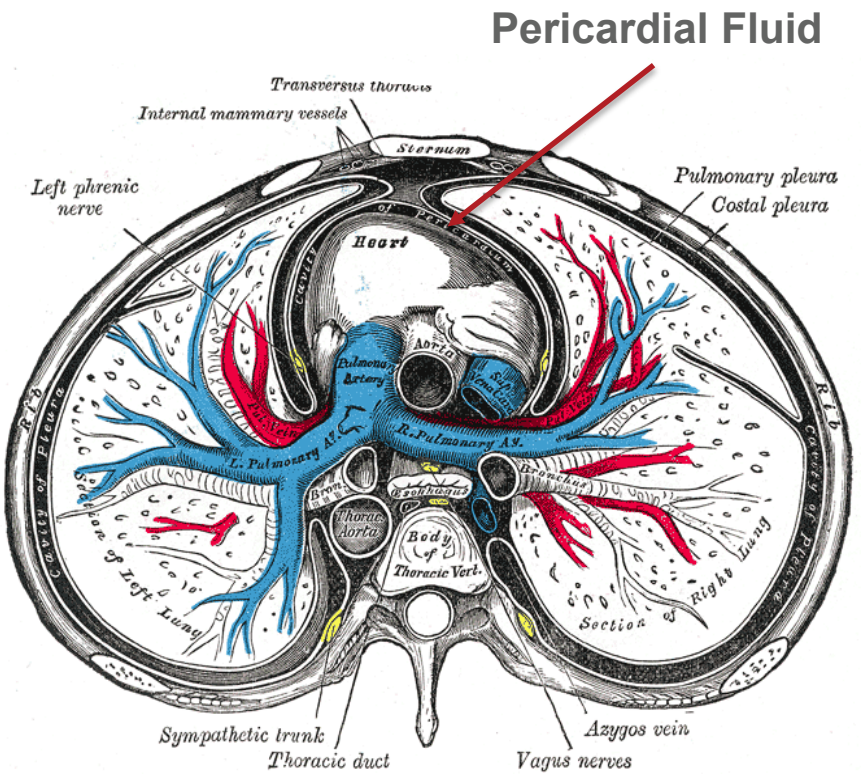
TRANSUDATES VS EXUDATES → **LIGHT'S CRITERIA (one or more):**
(a) Pleural fluid protein/serum protein ratio ≥ 0.5
(b) Pleural fluid LDH/serum LDH ≥ 0.6
(c) Pleural fluid LDH level ≥ 2/3 upper reference limit for serum LDH

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 → **PERICARDIAL FLUID**

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

APPEARANCE OF FLUID

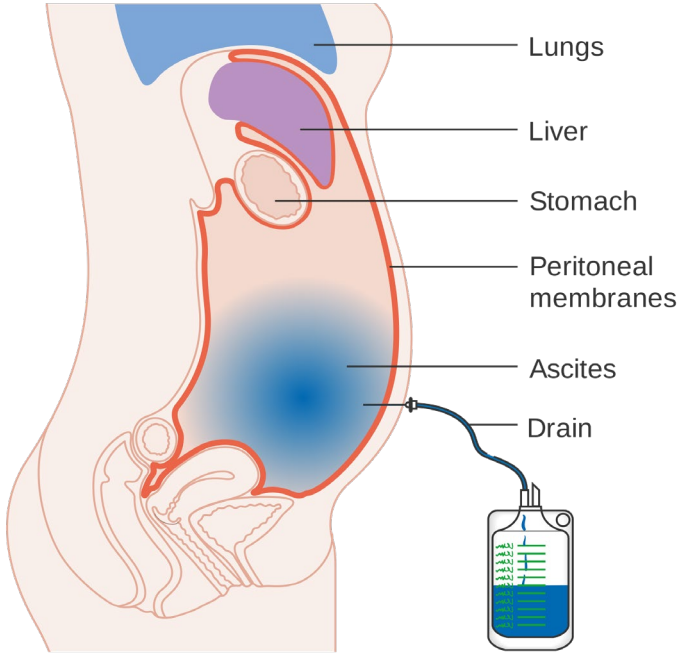
- **TURBID: infection or malignancy**
- **BLOODY: malignancy or tuberculous**
- **MILKY: chylopericardium**

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

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

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

Increased hydrostatic pressure (portal hypertension)	- Cirrhosis - Hepatic venous outflow obstruction - Constrictive pericarditis
Decreased colloid osmotic pressure (hypoalbuminemia)	- Nephrotic syndrome - Malnutrition and protein losing enteropathy
Malignant conditions	- Adenocarcinoma - Epidermoid carcinoma - Melanoma - Mesothelioma
Infection	- TB - Fungal - Parasite - Chlamydia
Miscellaneous	- Chylous ascites - Pancreatic ascites - Bile ascites - Ovarian disease

Biochemical Analysis of Peritoneal / Ascitic fluid

PARACENTESIS → **PERITONEAL FLUID**

- 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**

APPEARANCE OF FLUID → **TRANSUDATES VS EXUDATES**

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

SERUM ASCITES ALBUMIN GRADIENT (SAAG):

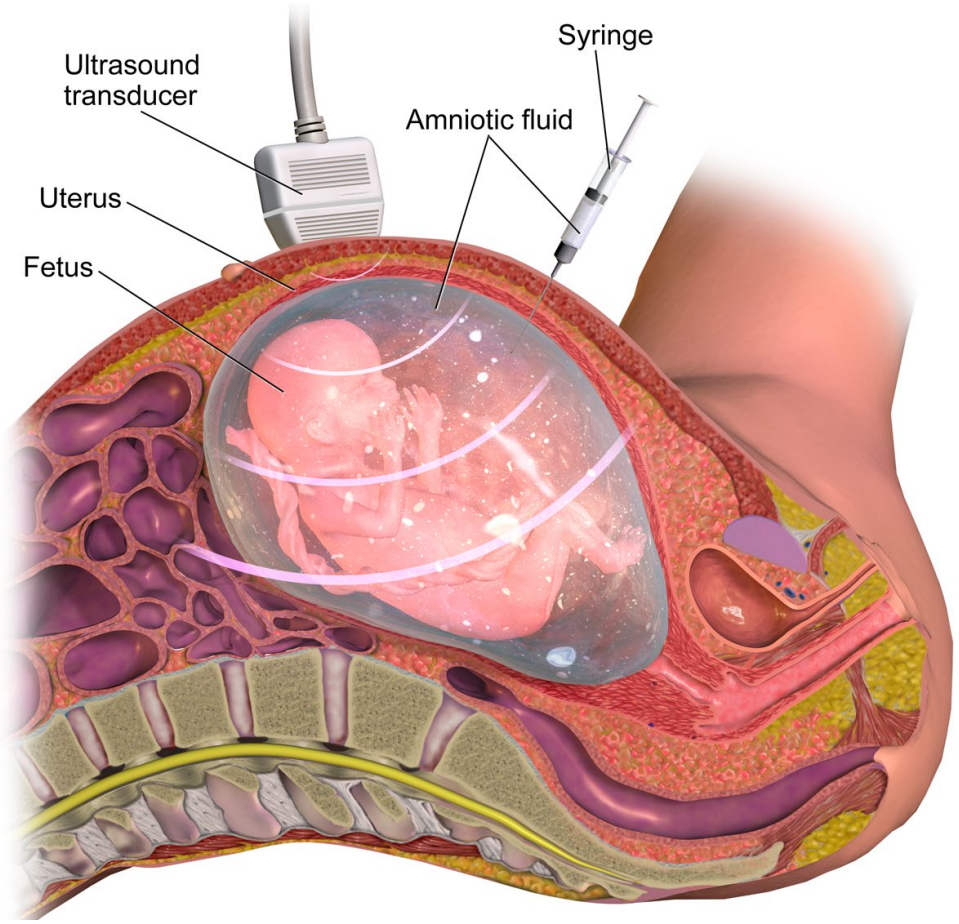
(a) >1.1 g/dL (11 g/L) indicates transudative ascites

(b) <1.1 g/dL (11g/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

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- **Gross Examination**

Appearance	Significance
Colorless with slight to moderate turbidity	Normal
Blood-streaked	Traumatic tap, abdominal trauma, intra-amniotic hemorrhage
Yellow	Rh Disease
Dark green	Meconium
Dark red-brown	Fetal death

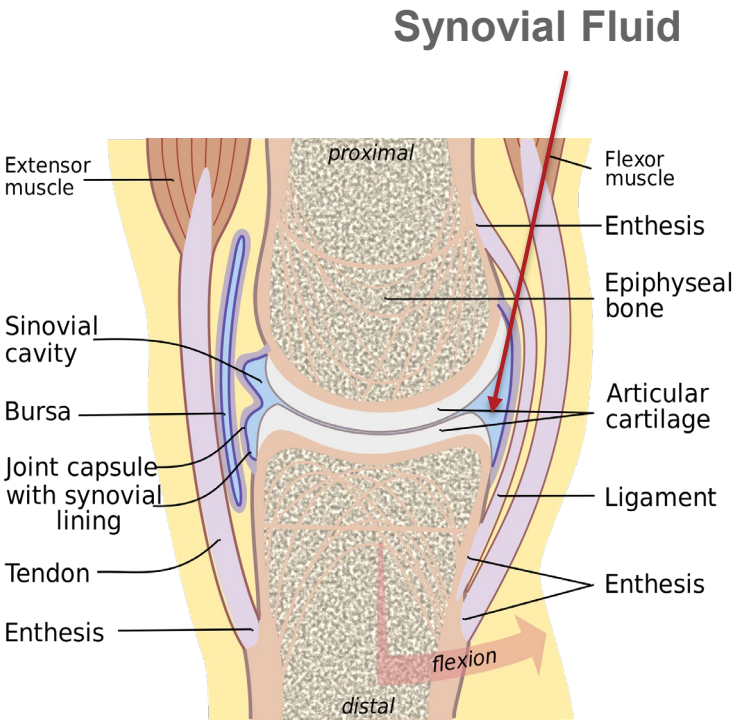
- **Bilirubin**

- 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

Measure	Normal	Non-inflammatory	Inflammatory	Septic	Hemorrhagic
Volume (mL)	<3.5	>3.5	>3.5	>3.5	>3.5
Viscosity	High	High	Low	Mixed	Low
Clarity	Clear	Clear	Cloudy	Cloudy	Cloudy
Color	Colorless to light yellow	Yellow	Yellow/ Green	Yellow/ Green	Red, brown or xanthochromic
WBC/mm^3	<200	<2,000	2,000-50,000	>50,000	Similar to blood level
%PMN	<25	<25	>50	>75	Similar to blood level
Gram stain	Negative	Negative	Negative	Positive	Negative
Crystals	Absent	Absent	Absent	Multiple or Absent	Absent

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

Advantages	Disadvantages
Ease of collection and storage	Low levels of analytes
Non-invasive	Contamination
“Lower stress”	Viscosity

Biochemical Tests in Saliva

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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

1. Johnson M, Rohlfs EM, Lawrence MS, Protein.In:Burtis CA, Ashwood ER, editors. Teitz Fundamentals of Clinical Chemistry. Saunders 5th Ed, 2000:341-342
2. Porcel JM, Light RW. Pleural effusions. Dis Mon. 2013;59:29-57
3. Light RW. Pleural effusions. Med Clin North Am. 2011;95:1055-70
4. Light RW. Pleural effusions. N. Engl. J Med 2002; 346:1971-7
5. Burgess LJ, Reuter H, Talijaard JJF, and Doubell AF. Role of biochemical tests in the diagnosis of large pericardial effusions. Chest 2002; 121;495-9
6. Jenkinson F, Murphy MJ. Biochemical analysis of pleural and ascitic fluid: effect of sample timing on interpretation of results. Ann Clin Biochem. 2007;44:471-473
7. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, 4th Edition Eds. C.A. Burtis, E.R.. Ashwood and D.E. Bruns 2006; 2153-2206
8. Kaufman E. The diagnostic applications of saliva-A review. Crit Rev Oral Biol Med 2002; 13:197-212

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