

# Cerebrospinal Fluid (CSF)

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## PHYSIOLOGY

### CSF functions:

1. Transport media, maintenance of stable chemical environment.
  - CSF is inside BBB.
  - CSF freely communicates with brain interstitial fluid.
2. Hydraulic shock absorber
  - BUOYANCY reduces **in situ weight of brain** to  $\approx 50$  gm.
  - CSF removal during lumbar puncture  $\rightarrow$  brain weight $\uparrow$   $\rightarrow$  tension on arachnoid trabeculae, nerve roots and blood vessels  $\rightarrow$  headache.

### CSF production

1. Main amount (80%) - CHOROID PLEXUS
2. Small amounts - *secreted* by ependyma and perivascular spaces.

**CHOROID PLEXUS** (derived from neural epithelium) is composed of:

1. **Choroidal epithelium** (folded into microvilli - forms brush border into ventricular lumen):
    - 1) **ependyma** (epithelial lining of ventricular system); cilia are present on apical surfaces of some ependymal cells.
    - 2) highly vascularized **pia mater** (tela choroidea)
  2. **Blood vessels** and interstitial connective tissue; capillaries have gaps between endotheliocytes (vs. choroidal epithelium has tight junctions).
- CHOROID PLEXUS is present in:
    - 1) **4<sup>th</sup> ventricle ependymal roof** – blood supply from *posterior inferior cerebellar artery*.
    - 2) **3<sup>rd</sup> ventricle ependymal roof** – blood supply from *branches of posterior cerebral artery*.
    - 3) **medial wall of lateral ventricles** (continuous with choroid plexus in roof of 3<sup>rd</sup> ventricle) – main mass! – blood supply from *anterior and posterior choroidal arteries*.
  - **TOTAL CSF VOLUME** 90-150 ml (25-30 ml in ventricles\*);  $\approx 50$  ml in infants.  
\* according to other sources – ventricles contain 80% of total CSF volume.
  - CSF flows from ventricles into subarachnoid space.
  - CSF production rate  $\approx 500$  ml/d = 20 ml/hr = 0.35-0.40 ml/min.
  - entire CSF volume is turned over 3-4 times each day.
  - CSF volume removed at lumbar puncture is regenerated in 1 hour.

**CSF production mechanism** – *ultrafiltration* due to hydrostatic pressure within plexus capillaries  $\rightarrow$  water and electrolytes move into interstitial space  $\rightarrow$  choroidal epithelium  $\rightarrow$  transfer into ventricular cavity (by traversing tight apical junctions or plasma membrane of apical villus).

- **ion pumps** are involved in this transfer (Na-K-ATPase in brush border and intercellular clefts, basolateral Na-H antiport, apical and basal Cl-bicarbonate antiport).
- net secretion of Na, Cl, and bicarbonate occurs *from plasma to CSF*.
- strong correlation between rate of Na exchange and rate of CSF formation.
- Na exchange is regulated by bicarbonate permeability (*CARBONIC ANHYDRASE* is important).
- **ACETAZOLAMIDE** (carbonic anhydrase inhibitor) can reduce CSF production significantly.

**Active neurogenic control of CSF formation** - choroid plexus is innervated by adrenergic and cholinergic nerves:

- adrenergic** stimulation  $\rightarrow$  diminished CSF production;
- cholinergic** stimulation may double normal CSF production rate.

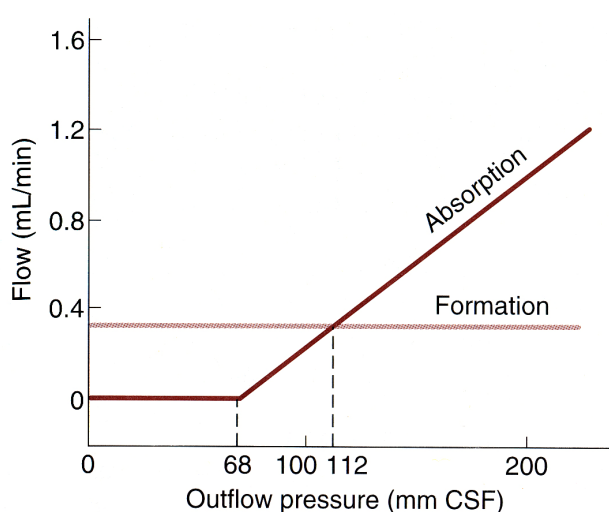
**CSF flow** results from **pressure gradient** (intraventricular pressure  $\approx 180$  mmH<sub>2</sub>O, pressure in superior sagittal sinus  $\approx 90$  mmH<sub>2</sub>O).

### CSF reabsorption

- into venous blood by **ARACHNOID VILLI** – collagenous trabecular core with associated channels and cap of arachnoid cells on apex (serves as **one-way valve** – prevent blood reflux into CSF; opens at  $\Delta p = 5$  mmHg).

- **arachnoid (s. pacchionian) granulations** – arachnoid outpouchings with collections of ARACHNOID VILLI - penetrate gaps of dura mater into **SINUS SAGITTALIS SUPERIOR** (into lateral outpouchings – *lateral venous lacunae*).
- arachnoid villi are also present at veins surrounding spinal nerve roots – drain CSF into **EPIDURAL VEINS**.
- with age $\uparrow$ , arachnoid granulations become more numerous and calcify.
- other routes of CSF absorption (via diffusion into veins) - **VENTRICULAR EPENDYMA, ARACHNOID MEMBRANE**.

**CSF production** is **independent** of intraventricular pressure;  
**CSF absorption** is **proportionate** to intraventricular pressure;



**Figure 32-3.** CSF formation and absorption in humans at various CSF pressures. Note that at 112 mm CSF, formation and absorption are equal, and at 68 mm CSF, absorption is zero.

**PARAMETERS**

**NORMAL**

- Opening pressure** 65-200 mmH<sub>2</sub>O\* (5-15 mmHg) with patient lying down (or at level of foramen magnum in sitting position).
  - \*50 mmH<sub>2</sub>O in neonates, 85 mmH<sub>2</sub>O in young children, 250 mmH<sub>2</sub>O in extremely obese subjects
  - not affected by systemic BP.
  - accurate measurement requires patient cooperation. see p. Op3 >>
  - exquisitely sensitive to blood CO<sub>2</sub> (hyperventilation lowers ICP) and venous pressure.

**Clear & colorless** (> 99% water) – indistinguishable from water.

**Few cellular components** (≤ 5 lymphocytes or mononuclears / mm<sup>3</sup>); *polymorphonuclear (PMN) cells & RBCs* are always abnormal (1 PMN is still normal if total cell count ≤ 5).  
 N.B. *normal newborn* may have up to 19 lymphocytes/mm<sup>3</sup> (up to 60% cells may be PMNs); normal in *infants 1-2 months old* – up to 9 mononuclears/mm<sup>3</sup>.

**Protein** < 60 mg/dL (0-50\*); mainly *albumin*.  
 \*lower in children 6 months ÷ 2 yrs; up to 150-170 mg/dL in neonates, esp. prematures (immature leaky BBB)

CSF albumin : serum albumin = 1:200

- majority of CSF protein (esp. **albumins**) is *derived from serum*.
  - CSF proteins that *arise within intrathecal compartment*:
    - immunoglobulin G** (produced by CNS lymphocytes):  
 adults: < 15% of total CSF protein  
 children < 14 yrs: < 8% of total CSF protein
    - transthyretin** (produced by choroid plexus)
    - structural proteins (**glial fibrillary acidic, tau, myelin basic protein**) found in brain tissue.
  - CSF protein concentration increases from cephalad to caudal levels (reflecting different permeability of capillary endothelial cells).
- Glucose** (> 60% of plasma amount\*, i.e. 50-100 mg/dl or 2.8-4.2 mmol/L); values < 50% (40-45 mg/dl) are usually abnormal, and values < 40% (40 mg/dl) are invariably so.  
 \*ratio is higher in infants.
    - ratio *changes proportionately* in response to rising or falling plasma glucose with 4-hour lag time (obtain concomitant\*\* serum glucose level at time of CSF sample!).
      - hyperglycemia during 4 hours prior to LP results in CSF glucose↑
      - when CSF glucose is of diagnostic importance, CSF and blood samples ideally should be obtained *after 4-hour fast*.  
 \*\*phlebotomy should precede lumbar puncture (stress of LP may increase serum glucose, thereby reducing ratio of CSF/serum glucose)
    - linear ratio (CSF : plasma) decreases as plasma glucose exceeds 500 mg/dl.
    - ventricular CSF* glucose is 6-8 mg/dL higher than in *lumbar CSF*.

- Ions**:
  - concentration same or greater than in serum - Na, Cl, Mg.
  - concentrations lower than in serum - K, Ca, bicarbonate, phosphate.

N.B. CSF chloride as diagnostic aid for tbc meningitis is no longer clinically relevant!

- Acid-base status**:
  - higher pCO<sub>2</sub> → slightly lower pH (than arterial blood).
    - pCO<sub>2</sub> is higher and pH lower in lumbar than in cisternal CSF.
  - bicarbonate levels are equal to arterial blood.

Substance	Plasma	CSF
Na (mEq/l)	140	144
K (mEq /l)	4.6	2.9
Mg (mEq/l)	1.6	2.2
Ca (mg/dl)	8.9	4.6
Cl (mEq/l)	99	113
Bicarbonate (mEq/l)	23.3-26.8	
Phosphate, inorganic (mg/dl)	4.7	3.4
Protein (g/dl)	6.8	0.028 (28 mg/dl)
Glucose (mg/dl)	110	50-80
Osmolality	0.29-0.3	
pH	7.4	7.33
PCO <sub>2</sub> (mmHg)	41.1	50.5
Urea (mg/dl)	15	12
Creatinine (mg/dl)	1.2	1.5
Uric acid (mg/dl)	5	1.5
Lactate (mg/dl)	20	18
Cholesterol (mg/dl)	175	0.2

Six common CSF studies:

- 1) direct observation for color
- 2) direct observation for viscosity & turbidity.
- 3) cell count and differential
- 4) Gram's stain and culture
- 5) glucose
- 6) protein

If **cell count**, **protein**, and **glucose** are all normal, it is highly unlikely that additional studies will be useful (unless special considerations exist).

**OPENING PRESSURE****ELEVATED PRESSURE:**

- A. **ICP**↑ (herniating cerebellar tonsils may occlude foramen magnum and prevent increased ICP transmission to lumbar puncture site!):
1. **Acute meningitis** (bacterial, fungal, viral).
  2. **Mass lesions** (tumors\*, abscess) – **LP is dangerous!!!**  
\*N.B. pressure may be normal despite large tumor!
  3. **Intracerebral bleeding, SAH**
  4. **Brain edema**
  5. **Hydrocephalus - CSF overproduction** (choroid plexus papilloma), **absorption defect, flow obstruction**
  6. **Pseudotumor cerebri**
  7. **Any coma** (slight ICP↑ due to hypoventilation and CO<sub>2</sub> retention)
- B. **Systemic causes** - congestive heart failure, chronic obstructive pulmonary disease (hypercapnia), superior vena cava or jugular venous obstruction, pericardial effusion.

Falsely elevated pressure:

- 1) marked obesity
- 2) tense patient (pressure is not usually measured in struggling or crying child)
- 3) head elevated above plane of needle  
N.B. opening pressure is artificially elevated with patient in sitting position!

**LOW PRESSURE:**

- 1) **needle obstruction** by meninges
- 2) **spinal block** (may be verified with **QUECKENSTEDT test**) see p. Op3 >>
- 3) **CSF leakage:**
  - CSF fistula
  - dural nerve sheath tear
  - post-LP drainage
  - post-CNS surgery
- 4) **idiopathic** low-pressure syndrome
- 5) subdural hematomas in elderly patients
- 6) dehydration-hypovolemia
- 7) barbiturate intoxication.

**COLOR**

Color is observed only in pathological circumstances!

- **XANTHOCHROMIA** (literally, yellow color) = presence of any color; so state actual color and its magnitude (from 1+ to 4+).

**Yellowish** - any cause of **increased protein** (> 100-200 mg/dl).

**Yellow** / **pink** - **hemoglobin**:

- 1) **oxyhemoglobin** (released with lysis of red cells) becomes pink or yellow when diluted.
  - first detected 2 hours after SAH.
  - maximal within first 24-48 hours.
  - disappears over next 7-14 days.
- 2) **bilirubin** (produced by leptomeningeal cells) is yellow.
  - first detected 10-12 hours after SAH.
  - maximal at 48 hours.
  - may persist for 2-4 weeks.
- 3) **methemoglobin** (produced in old hematomas) is brown but seen only spectrophotometrically!

**Yellow** - severe jaundice (> 10-15 mg/dl of total bilirubin), carotenemia, rifampin therapy.

**Brownish** / **gray** - CNS melanoma.

**Greenish** - leukemic meningeal infiltration, pseudomonas meningitis.

**BLOODY CSF**

- bloody CSF should be collected in at least **three separate tubes** (“**THREE-TUBE TEST**”).
- sample of bloody CSF should be **centrifuged** immediately (within 1 hour) and supernatant fluid **compared with tap water\*** (to exclude xanthochromia).  
\*viewing down long axis of tube or holding both tubes against white background

**TRAUMATIC TAP**

- 1) **CSF clears** as sequential amounts are collected (should be **confirmed by cell count** in first and last tubes);
- 2) **no xanthochromia**; causes of xanthochromia in traumatic tap:
  - a) severely traumatic tap (RBC > 150,000-200,000/mm<sup>3</sup>) - xanthochromia is due to serum **protein**.
  - b) **oxyhemoglobin** - starts to appear if tube is tested > 1-2 hour after tap (RBCs lysis).
- 3) presence of **clot** in one of tubes strongly favors traumatic tap!
- 4) immediate\* repeat puncture at higher interspace yields clear CSF.  
\*N.B. any lumbar puncture performed several days after especially traumatic puncture, may find some RBCs and xanthochromia!

**SAH**

- 1) **CSF does not clear** with sequentially collected tubes;  
N.B. occasional declining cell count may represent layering of cells in recumbent patient!
  - 2) **xanthochromia** (only if bleeding occurred before ≥ 2-4 hours); if ≥ 12 hours passed, virtually all patients' CSF will demonstrate xanthochromia!
  - 3) blood **does not clot** (blood is defibrinated at site of hemorrhage).
  - 4) **positive D-dimer test** on CSF (local fibrinolysis); other conditions may produce false-positive test results (e.g. DIC, previous traumatic tap, prior thrombolytic therapy).
- **crenated RBCs** (had been used as indication of SAH) are of no distinguishing value - appear both with true bleeding and after traumatic taps.

Entered blood adds cells and protein to CSF - for every 700-1000 RBCs:

1) add 1 **WBC**

e.g. if bloody CSF contains 10,000 RBC/mm<sup>3</sup> and 100 WBC/mm<sup>3</sup>, 10 WBC would be accounted for by added blood and corrected WBC count would be 90 WBC/mm<sup>3</sup>; if patient's hemogram reveals significant anemia or leukocytosis, formula is used to determine number of WBC in CSF before blood was added:

$$\text{CSF WBC} = \text{blood WBC} \times \text{CSF RBC} \times 100 / \text{blood RBC}$$

2) raise **protein** by 1 mg/dl.

e.g. if RBC count is 10,000/mm<sup>3</sup> and protein 110 mg/dl, corrected protein level - 100 mg/dl; corrections are reliable only if cell count and total protein are made on same CSF tube!

## VISCOSITY & TURBIDITY

- **viscosity**↑ - most likely explanation is **protein**↑↑↑.
- **turbidity** (detected when tube is twirled in beam of bright light) - due to presence of:
  - a) **leukocytes** > 200-300/mm<sup>3</sup>.
  - b) **erythrocytes** > 400/mm<sup>3</sup> (because RBCs are smaller cells than WBCs)
  - c) microscopic **fat globules** (traveled to brain as emboli).

## CELLS

Cell counts should be performed on **every CSF specimen within 1 hour!**

**PLEOCYTOSIS** occurs with gamut of **inflammatory disorders**:

N.B. **many organic CNS diseases produce mild pleocytosis!**

- 1) infections
- 2) autoimmune (cerebral vasculitis, demyelination, etc)
- 3) infarction
- 4) subarachnoid bleeding, thrombosis
  - subarachnoid blood produces secondary inflammatory response (WBC count is most marked ≈ 48 hours after SAH, when meningeal signs are most striking).
- 5) tumors
- 6) generalized or focal seizure (30% cases – many have serious intracranial pathologic processes - subdural hematoma, subarachnoid hemorrhage, stroke, etc)

General rule:

> 100 WBC = **infectious** cause  
< 100 WBC = **noninfectious** cause (carcinomatosis, sarcoid, etc)

After **total cell count** is done, **stain smear of sediment** for **DIFFERENTIAL CELL COUNT**:

**RBC vs. WBC** – add **acetic acid** (rinse capillary tube with acetic acid and then draw CSF into tube) – lyses RBC but leaves WBC intact.

**PMN vs. Lymphocytes** – add **methylene blue**.

- **PMN** - bacterial infection (or onset of viral infection).  
**Neutrophilic pleocytosis** is indication for thorough **BACTERIOLOGIC INVESTIGATION**.
- **mononuclears** – viral, tbc, fungal, immunologic or chronic inflammation, tumor, chemical irritation (e.g. myelogram, intrathecal methotrexate).
- **eosinophils** – parasites.

**Tumor Cells** (neoplasms of brain or meninges) → Millipore, cytocentrifuge, or cytologic examination.

- cytopathological identification requires **large CSF volumes** (> 20 ml).  
N.B. initial tap may be negative → serial LPs  
At least 3 negative cytologic evaluations (i.e. 3 separate samplings) are required to rule out leptomeningeal malignancy!
- sample should be brought **immediately** to laboratory to minimize cell lysis and morphological changes.
- **other CSF markers** may be useful:
  - 1) astroprotein (glioblastoma)
  - 2) carcinoembryonic antigen, ferritin (carcinomas)
  - 3) β2-microglobulin (lymphoblastic leukemia and lymphoma)
  - 4) α-fetoprotein (germ cell tumors), chorionic gonadotropin (choriocarcinoma and testicular tumors).

## PROTEIN

**CSF protein**↑ - sensitive but nonspecific indicator of CNS disease:

- a) increase in endothelial cell permeability (i.e. leaky BBB)
- b) increased intrathecal synthesis
- c) release from destroyed neural tissue

Look for unrecognized **diabetes** when there is unexpected protein elevation!

- **very high CSF protein** (> 500 mg/dl):
  - a) bacterial meningitis (vs. aseptic meningitis < 100)
  - b) blood in CSF
  - c) spinal (s. dynamic) block  
**FROIN'S SYNDROME** (s. loculation syndrome) – yellowish CSF **coagulates spontaneously** in few seconds after withdrawal – due to **protein**↑↑↑; such CSF forms in loculated portions of subarachnoid space isolated from spinal fluid circulation by obstruction.
  - d) meningeal carcinomatosis
- **lower than normal CSF protein**:
  - a) young children (6 months ÷ 2 years)
  - b) pseudotumor cerebri
  - c) unintended CSF loss (frequent LPs, lumbar drain, lumbar dural CSF leak).

**Immunoglobulins** are explored most frequently to support diagnosis of **multiple sclerosis**.

**Intrathecal immunoglobulin synthesis** is determined by:

- a) **IgG index** - intrathecal IgG synthesis rate↑ (vs. serum IgG that entered CNS passively across disrupted BBB):

$$\text{IgG index} = \frac{[\text{IgG}_{\text{CSF}} / \text{albumin}_{\text{CSF}}]}{[\text{IgG}_{\text{serum}} / \text{albumin}_{\text{serum}}]}$$

- normal IgG index is < 0.65-0.77.
- CSF contamination with blood may significantly elevate IgG index.

- b) **oligoclonal bands**; > 1 oligoclonal band in CSF (and absent in serum) is abnormal.

**GLUCOSE**

**HYPERGLYCORRACHIA** – due to **hyperglycemia** within 4 hours prior to LP.

- if 50 ml ampule of 50% glucose has been given, 30 minutes is required to influence CSF glucose concentration.

**HYPOGLYCORRACHIA:**

- 1) **hypoglycemia**
  - 2) **meningitis:**
    - *bacterial* (incl. tuberculosis, neurosyphilis)  
CSF glucose remains ↓ for 1-2 weeks after start of meningitis treatment.
    - *fungal*
    - *certain viral* (mumps, herpes)  
N.B. in general, aseptic meningitis has normal [glucose]
    - *chemical* (that follows intrathecal injections)
  - 3) **parasites** (cysticercosis, trichinosis, amebiasis).
  - 4) **SAH** (4-8 days after onset)
  - 5) meningeal carcinomatosis
  - 6) vasculitis
  - 7) sarcoid
- **HYPOGLYCORRACHIA** reflects:
    - a) mainly - increased **anaerobic glycolysis** in adjacent neural tissues\*
    - b) to lesser degree - increased **PMN leukocytes**\*
    - c) ↓**transfer of glucose** across BBB\*\*

\*invariably accompanied by CSF lactate↑  
\*\*CSF lactate↓

**LACTATE**

- concentration is dependent on CNS glycolysis.

- helpful in diagnosis of **bacterial meningitis** – [lactate] increases proportionally to **number of PMN cells** in CSF.
- **lactate > 4.2 mmol/L** accurately predicts bacterial meningitis vs. viral meningitis.
- CSF [lactate] *remains elevated for significant time* after appropriate therapy is initiated (vs. [glucose]) - helpful in bacterial meningitis diagnosis when antibiotics had been given before CSF acquisition.
- other causes of [lactate]↑ - cerebral hemorrhage, malignant hypertension, hepatic encephalopathy, diabetes mellitus, hypoglycemic coma.

**LDH**

- elevation occurs in:

- 1) bacterial, fungal **meningitis** (LDH remains elevated for 1-2 days after antibiotic start);  
vs. viral meningitis – LDH normal.
- 2) cortical (vs. lacunar) **strokes**.

**pH**

- unreliable indicator of **metabolic CNS state**.

- brain injury (and its complications) can alter CSF pH.  
N.B. CSF pH influences *pulmonary drive* and *cerebral blood flow*!

**Bacteriologic exam**

Larger amounts of CSF (≥ 10 mL) improve chances of detecting pathogens (esp. tbc, fungi).

**Gram stain** is performed in **all cases** when CSF WBC count is elevated!

CSF analysis is essential in establishing provisional diagnosis of acute **bacterial meningitis**

- CSF must be transported to laboratory immediately (CSF cells begin to lyse\* within 1 hour of collection; may be slowed by refrigeration).  
\*esp. meningococci.
- use centrifuged sediment.

1. **Gram stain** dictates initial choice of antibiotic!;

causes of **false-negative Gram stains**:

- a) **early meningococcal meningitis** or **severe leukopenia** - CSF protein insufficiently elevated for bacterial adherence to glass slide; H: mix drop of aseptic serum with CSF sediment.
  - b) **too few organisms** are present.
  - c) **ongoing a/b therapy** – 25-33% positive tests are lost per day in setting of appropriate antimicrobial therapy (it does not significantly affect WBC counts, glucose, protein values)  
Measures to improve yield - *acridine orange stain, repeat lumbar puncture*.
2. **CSF cultures** - bacteria that commonly cause meningitis grow well on standard preparations:
- a) *aerobic* - blood and chocolate agar.
  - b) *anaerobic* - thioglycolate medium.
- cultures are examined at 24-48 hours, but plates should be kept for at least 7 days.

3. **Antigen tests:**

Bacterial antigens persist in CSF for several days after antibiotic therapy.

- 1) **CSF counterimmunoelectrophoresis (CIE)** - wells in two rows of agarose gel; different antiserum is placed in each well; current is passed through gel with reactants then moving toward each other by electrophoretic mobilization of antigen; line of precipitation visualized in 1-4 hours represents positive reaction between antiserum and antigen.
  - 2) **CSF latex agglutination (LA)** - 10 times more sensitive than CIE - antibody on colloid surface combines with antigen binding sites to cross-link colloid-forming antigen bridges (matrix forms and appears as macroscopic agglutination).
  - 3) **enzyme-linked immunosorbent assay (ELISA)** – 100-1000 times more sensitive than LA.
  - 4) **coagglutination counterimmunoelectrophoresis**.
  - 5) **PCR** - rapid test with high degree of sensitivity and specificity!!!
- antigen tests may be **falsely-positive** for up to 10 days after vaccination (e.g. *H. influenzae* polysaccharide vaccine).
  - **blood** and **urine** should also be examined for antigen (e.g. often antigen may be found only in urine).
4. **Additional tests:**
- 1) **blood cultures** (50-80% positive for etiologic agent)
  - 2) **CSF Ig titers** - important in diseases in which peripheral manifestations fade while CNS symptoms persist (e.g. syphilis, Lyme disease).

If **tuberculous** meningitis is diagnostic possibility: see p. Inf3 >>

- 1) **Ziehl-Neelsen acid-fast stain**
- 2) **CSF cultures** onto Lowenstein-Jensen medium (wait at least for 8 weeks)
- 3) **PCR tests** - likely will replace many of current tests for mycobacteria.

If **fungal** meningitis is diagnostic possibility:

- 1) **India ink preparation** (place coverslip over one drop of CSF on slide; place drop of India ink next to coverslip and allow it to seep under; check at interface for *Cryptococcus*).
- 2) cryptococcal polysaccharide capsular **antigen testing**
- 3) **CSF cultures**.

**Viral** meningitis

- 1) **CSF cultures**.
  - most commonly isolated viruses are *enteroviruses* (coxsackieviruses, echoviruses) and *mumps* virus; other viruses are seldom isolated from CSF.  
In known viral CNS disease, **stool** is more rewarding (85% positive) than CSF (10% positive)!
  - cultures in most hospitals are not available and play little role in acute decisions.
  - if CSF cannot be delivered to laboratory in 24-48 hours → refrigerate at 4 °C.
- 2) **CSF antibody titers** (panels are commercially available) - serial rise (intrathecal production of organ-specific antibodies) - useful only as retrospective diagnostic confirmation.
- 3) **PCR** (already diagnostic test of choice for herpes simplex meningoencephalitis).

## CSF in various disorders

Disorder	Pressure (mmH <sub>2</sub> O)	Cells/mm <sup>3</sup>	Protein (mg/dl)	Glucose (mg/dl)	Additional tests
<b>Norma</b>	65-200; clear & colorless	≤ 5 <b>mononuclears</b>	< 60	≥ 50 mg/dl (> 60% of plasma [glu])	
<b>INFECTIONS</b>					
<b>Acute bacterial meningitis</b>	↑ (cloudy, straw-colored)	↑↑↑ 500-20,000; occasionally < 100 (esp. meningococcal or early in disease or immunocompromised); <b>PMN</b> predominate (in partially treated cases - <b>mononuclears</b> )	↑↑↑ 100-500 (occasionally > 1,000)	↓↓↓ 5-40	Gram stain, bacterial Ag, lactate↑, LDH↑
<b>Viral (aseptic) meningitis</b>	N ÷ ↑ (clear or cloudy, colorless)	↑ 5-1000; occasionally > 1,000 (esp. lymphocytic choriomeningitis!); <b>lymphocytes</b> predominate (at onset may be > 80% <b>PMN</b> ; repeat tap in 12-24 hours)	↑ < 100 (vs. bacterial meningitis > 100)	N or ↓ (mumps, lymphocytic choriomeningitis virus, herpes, CMV)	PCR
<b>Brain abscess</b>	↑	↑ 5-1000 <b>PMN</b> (esp. early in cerebritis stage; later↓)	↑	N	LP contraindicated
<b>Viral encephalitis</b>	N ÷ ↑ (clear or cloudy, straw-colored)	↑ 5-500 <b>lymphocytes</b> ; occasionally > 1000 (Eastern equine encephalitis, California encephalitis, mumps, lymphocytic choriomeningitis); + <b>RBC</b> (herpes)	N ÷ ↑ 50-100	N or ↓ (mumps, lymphocytic choriomeningitis virus, herpes)	PCR
<b>HIV encephalopathy, myelopathy, neuropathy</b>		N (or < 50 <b>lymphocytes</b> )	↑	N	↑ markers of immune activation (neopterin, quinolinic acid, β <sub>2</sub> -microglobulin)
<b>Cryptococcal meningitis</b>	↑ (cloudy, straw-colored)	↑ ≈ 50 (0-500); <b>lymphocytes</b> predominate	↑↑ ≈ 100 (20÷500)	↓↓ ≈ 30	cryptococcal Ag, India ink preparation

Disorder	Pressure (mmH <sub>2</sub> O)	Cells/mm <sup>3</sup>	Protein (mg/dl)	Glucose (mg/dl)	Additional tests
<b>Norma</b>	65-200; clear & colorless	≤ 5 <b>mononuclears</b>	< 60	≥ 50 mg/dl (> 60% of plasma [glu])	
<b>Blastomycotic meningitis</b>		↑↑ up to 5000 <b>PMN</b> (!!!)	↑	↓↓	
<b>Tuberculous meningitis</b>	↑ (cloudy, straw-colored)	↑ 10-500 (rarely > 500); <b>lymphocytes</b> predominate (in early stages may be > 80% <b>PMN</b> )	↑↑ 100÷500	↓↓ < 45	± spinal block; acid fast stain, PCR, culture; adenosine deaminase↑
<b>Neurosyphilis (meningovascular)</b>	↑	↑↑ 25-2000; <b>lymphocytes</b> (rarely <b>PMN</b> )	↑ ≈100	N (rarely ↓)	VDRL test
<b>Neurosyphilis (paretic)</b>	N ÷ ↑	↑ 15-2000; <b>lymphocytes</b>	↑ 50-100	N	CSF abnormalities↓ with disease duration
<b>Neurosyphilis (tabes dorsalis)</b>		N	N		CSF parameters improve with progression
<b>Cysticercosis</b>	↑	↑ <b>mononuclears</b> & <b>PMN</b> (sometimes with 20-75% <b>eosinophils</b> )	↑ 50÷200	N or ↓ (in 20% cases)	
<b>Neuroborreliosis</b>	N ÷ ↑	↑ 5-500 <b>lymphocytes</b>	↑ ≈100	N or ↓	intrathecal Ig production; CSF normalizes in stage III
<b>Tetanus</b>		N!!!	↑ 90-150	N	
<b>Poliomyelitis</b>		10-1000 <b>lymphocytes</b>	↑ 50÷300	N	
<b>Toxoplasmosis</b>		↑ < 100; <b>lymphocytes</b> predominate	↑	N or ↓	
<b>HTLV-I</b>		↑ < 100; <b>lymphocytes</b> predominate	↑ (up to 90)	N	IgG↑, oligo-clonal bands
OTHER					
<b>Sarcoid</b>	N ÷ ↑↑↑	↑ < 100 <b>mononuclears</b>	↑↑ 50-200	↓ 0-30	ACE↑ (in 50% cases)

Disorder	Pressure (mmH <sub>2</sub> O)	Cells/mm <sup>3</sup>	Protein (mg/dl)	Glucose (mg/dl)	Additional tests
Norma	65-200; clear & colorless	≤ 5 <b>mononuclears</b>	< 60	≥ 50 mg/dl (> 60% of plasma [glu])	
Neoplastic meningitis	N ÷ ↑	↑↑ 0÷several hundred <b>mononuclears</b> , <b>PMN</b> + <b>malignant cells</b>	N ÷ ↑↑ 50-200 (up to 1200*)	N or ↓↓↓*	*in meningeal carcinomatosis, spinal block
Pseudotumor cerebri	↑↑↑ 250-600	N	N or ↓	N	CSF removal may be therapeutic
Normal pressure hydrocephalus	N				High volume LP (40-50 cc), improvement after LP
SAH	↑ (cloudy, pink)	↑ RBC, ↑ WBC (blood contamination) → RBC↓, WBC ↑↑ (chemical hemic meningitis)	↑↑↑ (blood contamination)	↑ (early) or ↓ (late)	xanthochromia
Venous thrombosis	↑	↑ RBC; ↑ WBC	N ÷ ↑	N	
Vasculitis	↑	↑ <b>mononuclears</b>	↑	N or ↓	
Guillain-Barré	N ÷ ↑ (clear, yellow)	N!!!	↑↑ 46-400	N	
CIDP		↑ 5-50 <b>mononuclears</b>	↑↑ 100÷200	N	
Kearns-Sayre syndrome			↑↑ 70-400		
Multiple sclerosis		few <b>lymphocytes</b>	↑ < 75-80	N	IgG index↑, oligoclonal bands, MBP
Myxedema coma			↑↑ 100-300		
Diabetic radiculoneuropathy			↑↑ 100-300		
Generalized seizures		few <b>mononuclears</b> and <b>PMN</b>	N ÷ ↑		

Disorder	Pressure (mmH <sub>2</sub> O)	Cells/mm <sup>3</sup>	Protein (mg/dl)	Glucose (mg/dl)	Additional tests
<b>Norma</b>	65-200; clear & colorless	≤ 5 <b>mononuclears</b>	< 60	≥ 50 mg/dl (> 60% of plasma [glu])	
<b>Lead encephalopathy</b>	↑	<b>0-500 lymphocytes</b>	↑	<b>N</b>	

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