

Cerebrospinal Fluid (CSF)

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PHYSIOLOGY

CSF functions:

- Transport media, maintenance of stable chemical environment.
 - CSF is inside BBB.
 - CSF freely communicates with brain interstitial fluid.
- Hydraulic shock absorber
 - BUOYANCY reduces **in situ weight of brain** to ≈ 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

- Main amount (70-80%) - CHOROID PLEXUS (vast majority – lateral ventricles).
- Small amounts - *secreted* by EPENDYMA and brain's capillary bed, metabolic water production.

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

- Choroidal epithelium** – specialized **ependyma** (epithelial lining of ventricular system); microvilli (brush border) are present on apical surfaces of cells.
 - Tela choroidea** - highly vascularized **pia mater**.
 - Blood vessels** and interstitial connective tissue; capillaries have gaps between endotheliocytes (vs. choroidal epithelium has tight junctions).
- CHOROID PLEXUS is present in:
 - 4th ventricle ependymal roof** – blood supply from *posterior inferior cerebellar artery*.
 - 3rd ventricle ependymal roof** – blood supply from *branches of posterior cerebral artery*.
 - medial wall of lateral ventricles** (continuous with choroid plexus in roof of 3rd ventricle) – main mass! – blood supply from *anterior and posterior choroidal arteries*.
 - TOTAL CSF VOLUME** **150 ml** (62.2-267); ≈ 50 ml in infants; 7.5-70.5 ml in ventricles.
 - CSF flows from ventricles into subarachnoid space.
 - CSF PRODUCTION RATE** ≈ 500 ml/d = 20 ml/hr = 0.35-0.40 ml/min.
 - CSF production is affected minimally, if at all, by changes in ICP (i.e. **CSF production is independent to ICP**).
 - peak production in late evening and early morning.
 - 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 – combination of:

- 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).
- Energy-dependent ION PUMPS** (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 Mg 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 **hydrostatic pressure gradient** (intraventricular pressure ≈ 180 mmH₂O, pressure in superior sagittal sinus ≈ 90 mmH₂O).

CSF reabsorption

- into venous blood by **ARACHNOID VILLI** – protrude from subarachnoid space into lumen of dural sinuses – 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; **CSF reabsorption ceases at ICP < 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 ICP;

CSF absorption is **proportionate** to ICP and dural venous sinus pressure (CSF reabsorption is especially highly dependent on dural venous sinus pressure);

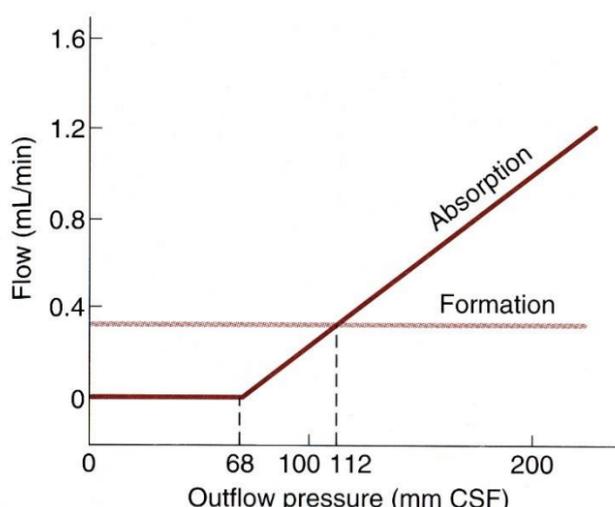


Figure 32-3. CSF formation and absorption in humans at various CSF pressures. Note that at 112 mm CSF, formation and absorption are equal, and at 68 mm CSF, absorption is zero.

PARAMETERS

NORMAL

1. **Opening pressure** 65-200 mmH₂O* (5-15 mmHg) with patient lying down (or at level of foramen magnum in sitting position).
 - *50 mmH₂O in neonates, 85 mmH₂O in young children, 250 mmH₂O in extremely obese subjects
 - not affected by systemic BP.
 - accurate measurement requires patient cooperation. see p. Op3 >>
 - exquisitely sensitive to blood CO₂ (hyperventilation lowers ICP) and venous pressure.
2. **Clear & colorless** (> 99% water) – indistinguishable from water.
3. Few **cellular** components (≤ 5 lymphocytes or mononuclears / mm³); **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/mm³ (up to 60% cells may be PMNs); normal in *infants 1-2 months old* – up to 9 mononuclears/mm³.
4. **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*:
 - 1) **immunoglobulin G** (produced by CNS lymphocytes):
 - adults: < 15% of total CSF protein
 - children < 14 yrs: < 8% of total CSF protein
 - 2) **transthyretin** (produced by choroid plexus)
 - 3) 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).
5. **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*.
6. **Ions**:
 - a) concentration same or greater than in serum - Na, Cl, Mg.
 - b) concentrations lower than in serum - K, Ca, bicarbonate, phosphate.
 - N.B. CSF chloride as diagnostic aid for tbc meningitis is no longer clinically relevant!
7. **Acid-base status**:
 - higher pCO₂ → slightly lower pH (than arterial blood).
 - pCO₂ 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 ₂ (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

CSF has higher levels of Na, Cl, Mg

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 CO₂ 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/mm³) - 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/mm³ and 100 WBC/mm³, 10 WBC would be accounted for by added blood and corrected WBC count would be 90 WBC/mm³; 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/mm³ 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/mm³.
 - b) **erythrocytes** > 400/mm³ (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):

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

- 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.

see p. Dem5 >>

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

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

Disorder	Pressure (mmH ₂ O)	Cells/mm ³	Protein (mg/dl)	Glucose (mg/dl)	Additional tests
Norma	65-200; clear & colorless	≤ 5 mononuclears	< 60	≥ 50 mg/dl (> 60% of plasma [glu])	
Neoplastic meningitis	N ÷ ↑	↑↑ 0÷several hundred mononuclears , PMN + malignant cells	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	↑	↑ mononuclears	↑	N or ↓	
Guillain-Barré	N ÷ ↑ (clear, yellow)	N!!!	↑↑ 46-400	N	
CIDP		↑ 5-50 mononuclears	↑↑ 100÷200	N	
Kearns-Sayre syndrome			↑↑ 70-400		
Multiple sclerosis		few lymphocytes	↑ < 75-80	N	IgG index↑, oligoclonal bands, MBP
Myxedema coma			↑↑ 100-300		
Diabetic radiculo-neuropathy			↑↑ 100-300		
Generalized seizures		few mononuclears and PMN	N ÷ ↑		

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

BIBLIOGRAPHY for “Cerebrospinal Fluid” → follow this [LINK >>](#)