Characteristics of Normal Cerebrospinal fluid

What is being tested?

Cerebrospinal fluid (CSF) is a clear, watery liquid that flows around the brain and spinal cord, surrounding and protecting them. CSF testing is performed to evaluate the level or concentration of different substances and cells in CSF in order to diagnose conditions affecting the brain and spinal cord (central nervous system).

CSF is produced and secreted by the choroid plexus, a special tissue that has many blood vessels and that lines the small cavities or chambers (ventricles) in the brain. The total CSF volume is 3-5 ounces (90-150 mL) in adults and 0.3-2 ounces (10-60 mL) in newborns. CSF is continually produced, circulated, and then absorbed into the blood. About 17 ounces (500 mL) of CSF are produced each day. This rate of production means that all the CSF is replaced every few hours.

A protective, semi-permeable barrier separates the brain from the bloodstream. This blood-brain barrier allows some substances to cross and prevents other substances from crossing. Importantly, it helps keep large molecules, toxins, and most blood cells away from the central nervous system. Any condition that disrupts this protective barrier may result in a change in the normal level or makeup of CSF.

Because CSF surrounds the brain and spinal cord, testing a sample of CSF can be very valuable in diagnosing a variety of conditions affecting the central nervous system.

Although a sample of CSF may be more difficult to obtain than, for example, urine or blood, the results of CSF testing may reveal more directly the cause of central nervous system conditions. The following are some examples:

- **Meningitis**, an infection of the layers that cover the brain and spinal cord (meninges), and **encephalitis**, an infection in the brain
- Autoimmune diseases that affect the central nervous system, such as multiple sclerosis
- Cancers of the central nervous system or cancers that have spread to the central nervous system, such as leukemia
- Alzheimer disease, an irreversible form of dementia

How is the test used?

Cerebrospinal fluid (CSF) testing may be used to help diagnose a wide variety of diseases and conditions affecting the brain and spinal cord (central nervous system). Some examples include:

- Infections, such as meningitis and encephalitis—testing is used to determine if infection is caused by bacteria, viruses or, less commonly, by *Mycobacterium tuberculosis*, fungi or parasites, and to distinguish them from other conditions. CSF testing may also be used to detect infections of or near the spinal cord.
- Bleeding (hemorrhaging) around the brain
- Autoimmune disorders that affect the central nervous system, such as Guillain-Barré

syndrome or multiple sclerosis
- Tumors located within the central nervous system (primary) or cancers that spread to the central nervous system (metastatic cancer)
- Alzheimer disease, an irreversible form of dementia

CSF testing usually involves an initial, basic set of tests performed when CSF analysis is requested:

- CSF color, clarity and pressure during CSF collection
- CSF protein
- CSF glucose
- CSF cell count (total number of cells present)
- CSF differential cell count (numbers of different types of cells present)
- If infection is suspected, CSF Gram stain, routine culture and molecular tests that detect the genetic material of any microbes present

A wide variety of other tests may be ordered as follow-up depending on the results of the first set of tests or the suspected diagnosis. The specific tests that are ordered depend on your signs and symptoms and the disease your healthcare practitioner suspects may be the cause. Each of these tests can be grouped according to the type of exam that is performed.

When is it ordered?

CSF testing may be ordered when your health care practitioner suspects that you have a condition or disease involving your central nervous system. It may be ordered when:

- You have suffered trauma to the brain or spinal cord
- You have been diagnosed with cancer that may have spread into the central nervous system
- Your medical history and/or signs or symptoms suggest a condition affecting your central nervous system. The signs and symptoms of central nervous system conditions can vary widely and many overlap with a variety of diseases and disorders. They may have sudden onset, suggesting an acute condition, such as central nervous system bleeding or infection, or may be slow to develop, indicating a chronic disease, such as multiple sclerosis or Alzheimer disease.

CSF testing may be ordered when you have some combination of the following signs and symptoms, especially when accompanied by flu-like symptoms that intensify over a few hours to a few days and fever:

- Changes in mental status and consciousness
- Sudden, severe or persistent headache or a stiff neck
- Confusion, hallucinations or seizures
- Muscle weakness or lethargy, fatigue
- Nausea (severe or prolonged)
- Sensitivity to light
- Numbness or tremor
- Dizziness
- Difficulties with speech

- Difficulty walking, lack of coordination
- Mood swings, depression
- Infants may be increasingly irritable, cry when they are held, have body stiffness, refuse food, and have bulging fontanels (the soft spots on the top of the head)

What does the test result mean?

CSF usually contains a small amount of protein and glucose and may have a few white blood cells.

Any condition that disrupts the normal pressure or flow of CSF or the protective ability of the blood-brain barrier can result in abnormal results of CSF testing.

What is a lumbar puncture (spinal tap) and how is it performed?

The lumbar puncture is usually performed while you are lying on your side in a curled up fetal position but may sometimes be performed in a sitting position. It is important that you remain still during the procedure. Once you are in the correct position, your back is cleaned with an antiseptic and a local anesthetic is injected under the skin. When the area has become numb, a special needle is inserted through the skin, between two vertebrae, and into your spinal canal. An “opening” or initial pressure reading of the CSF is obtained. The healthcare practitioner then collects a small amount of CSF in multiple sterile vials. A “closing” pressure is obtained, the needle is withdrawn, and a sterile dressing and pressure are applied to the puncture site. You will then be asked to lie quietly in a flat position, without lifting your head, for one or more hours to avoid a potential post-test headache.

The lumbar puncture procedure usually takes less than half an hour. For most patients, it is a moderately uncomfortable procedure. The most common sensation is a feeling of pressure when the needle is introduced.

The lumbar puncture is performed low in the back, well below the end of the spinal cord. There are spinal nerves in the location sampled, but they have room to move away from the needle. There is the potential for the needle to contact a small vein on the way in. This can cause a “traumatic tap,” which just means that a small amount of blood may leak into one or more of the samples collected. While this is not ideal, it does occur a small percentage of the time. The evaluation of your results will take this into account.

Details on CSF Tests

CSF Physical Features (pressure and appearance)

Pressure of the CSF can be measured when opening (starting) and closing (finishing) the collection.

- Increased CSF pressure may be seen with a variety of conditions that increase pressure within the brain or skull and/or obstruct the flow of CSF, such as tumors, infection, abnormal accumulation of CSF within the brain (hydrocephalus), or bleeding.
- Decreased pressure may be due to dehydration, shock, or leakage of CSF through an opening (e.g., another lumbar puncture site or sinus fracture).

The appearance of the sample of CSF is usually compared to a sample of water.

- **Color** of the fluid—normal is clear and colorless. Changes in the color of the CSF are not diagnostic but may point to additional substances in the fluid. Yellow, orange, or pink CSF may indicate the breakdown of blood cells due to bleeding into the CSF or the presence of bilirubin. Green CSF may also sometimes be seen with bilirubin or infection.
- **Turbidity**—cloudy or turbid CSF may indicate the presence of white or red blood cells, microbes, or an increase in protein levels.
- **Viscosity**—normal CSF will have the same consistency as water. CSF that is “thicker” may be seen in people with certain types of cancers or meningitis.

CSF Chemical Tests

Chemical tests detect or measure the chemical substances found in spinal fluid. Many of the substances in CSF are also in blood and the relative amounts in CSF and blood are often compared. Normally, levels of certain substances in CSF, such as protein and glucose, mirror the levels in blood.

- **CSF glucose**—normal is about 2/3 the concentration of blood glucose. Glucose levels may decrease when cells that are not normally present use up (metabolize) the glucose. These may include bacteria, white blood cells, or cells shed by tumors.
- **CSF protein**—only a small amount is normally present in CSF because proteins are large molecules and do not cross the barrier between the blood and brain easily. Decreases in CSF protein are not generally considered significant. Increases in protein are most commonly seen with:
    - Meningitis and brain abscess
    - Brain or spinal cord tumors
    - Multiple sclerosis
    - Guillain-Barré syndrome
    - Syphilis

If any of the initial tests are abnormal or if your healthcare practitioner has reason to suspect a specific condition, then additional testing may be ordered. This may include one or more of the following:

- **CSF protein electrophoresis**—separates different types of protein; oligoclonal bands are often seen with multiple sclerosis and sometimes with other conditions.
- **CSF IgG (Immunoglobulin G)**—increased in some conditions, such as multiple sclerosis, herpes encephalitis, connective tissue diseases
- **Myelin basic protein**—seen when the covering of nerves (myelin) breaks down, such as with multiple sclerosis
- **CSF lactate**—often used to distinguish between viral and bacterial meningitis; the level will usually be increased with bacterial and fungal meningitis while it will remain normal or only slightly elevated with viral meningitis.
- **CSF lactate dehydrogenase (LD, LDH)**—used to differentiate between bacterial and viral meningitis; the level is usually increased with bacterial meningitis and not with viral meningitis; may also be elevated with leukemia or stroke.
- **Tumor markers**—carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), and human chorionic gonadotropin (hCG) may be increased in cancers that have spread from other

sites in the body (metastatic).

- **Amyloid beta 42 (Aß42) and tau protein**—used in the evaluation of Alzheimer disease; in a symptomatic person, a low Aß42 CSF level along with a high tau level reflects an increased likelihood of Alzheimer disease.
- **Beta-2 transferrin**—this is a protein present only in CSF. This test may be done if it is suspected that trauma to the central nervous system has caused a leak of CSF from the central nervous system. A sample of fluid leaking from the nose or ears is collected and tested. A positive test for beta-2 transferrin means the fluid is CSF.

Cell Counts, Differential and Microscopic Exam

Normal CSF has no or very few cells present and appears clear. A small drop of CSF is examined using a microscope, and cells are counted manually (or in some cases counted using an instrument). If the number of white blood cells present is very few (for example, 5 or less in an adult), the laboratory may or may not identify them or perform a cell differential (see below).

If white blood cells are numerous (such as greater than 5), a differential will most likely be done to determine the different kinds of white blood cells that are present. If cancer is suspected or has been previously diagnosed, a differential is always performed.

- **CSF total cell counts**
  - Red blood cell (RBC) count—normally no red blood cells are present in the CSF. The presence of red blood cells may indicate bleeding into the CSF or may indicate a “traumatic tap” – blood that leaked into the CSF sample during collection.
  - White blood cell (WBC) count—normally very few white blood cells are present. A significant increase in white blood cells in the CSF can be caused by infection or inflammation of the central nervous system.

- **CSF white blood cell (WBC) differential**—identifies and counts the different types of WBCs that are present. Small numbers of lymphocytes, monocytes (and, in neonates, neutrophils) are normal in a sample of CSF. There may be:
  - An increase in neutrophils with a bacterial infection
  - An increase in lymphocytes with a viral or fungal infection
  - Sometimes an increase in eosinophils with a parasitic infection
  - A slight increase in lymphocytes with immune disorders of the central nervous system, such as multiple sclerosis
  - Presence of abnormal WBCs with leukemia that has spread to the central nervous system
  - Abnormal cells from cancerous tumors present; if they are seen on a differential, CSF cytology will be performed (see below).

There may be an increase in the different types of WBCs with a variety of other conditions, including brain abscess, following seizures or bleeding around the brain, metastatic tumor, and inflammatory disorders such as sarcoidosis.

- **CSF cytology**—a CSF sample is specially treated so that a microscope can be used to look for abnormal cells. This is often done when a central nervous system tumor or metastatic cancer is suspected. The presence of certain abnormal cells, such as tumor cells or immature blood cells, can indicate the type of cancer present.

Tests for Infections

Normally, CSF does not contain any bacteria, fungi, viruses or parasites.

If meningitis or encephalitis is suspected, select tests may be performed to detect and identify microbes. The selection of testing is frequently done based on signs and symptoms, the health of your immune system, and possible exposure to certain pathogens. Some of the more frequently performed tests are listed below.

- **CSF Gram stain**—this test is always performed on CSF when infection is suspected. A sample of CSF is centrifuged and the concentrated portion is placed on a slide and treated with a special stain. A laboratory professional examines the slide using a microscope to look for bacteria or fungi, which can indicate bacterial or fungal meningitis.
- **CSF culture**—culture is used to detect any bacteria or fungi in the sample. A negative culture does not rule out an infection because the microbes may be present in small numbers or unable to grow in culture due to prior antibiotic therapy.
- **Molecular testing** of the CSF by polymerase chain reaction (PCR) assays can be performed to detect nucleic acid from various pathogens that may be present in the sample. This method detects bacterial, viral, fungal or parasitic genetic material (DNA, RNA) and is particularly helpful if the microbe does not grow in routine culture or if the patient has been on antibiotics.
- **Tests to detect antibodies** produced by the immune system against specific disease-causing microbes may be helpful in infections where culture and molecular testing are insensitive (e.g., West Nile virus, Lyme disease that infects the nervous system, etc.).
- **Testing of CSF to detect proteins or antigens** released by certain microbes, including the fungi *Cryptococcus neoformans/gattii* or *Histoplasma capsulatum*, may also be performed depending on exposure risk and signs and symptoms.