

Indications

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Larner **ESSENTIALS** Lumbar puncture for cerebrospinal fluid analysis is most often undertaken in cases of suspected central nervous system infection, bleeding, and inflammatory disease. Attention to technical aspects of the procedure is key to successful lumbar puncture, along with prompt analysis of cerebrospinal fluid samples and informed interpretation of laboratory findings.

Introduction Lumbar puncture for examination of the cerebrospinal fluid (CSF) has been an integral part of neurological practice since the pioneering work of Quincke at the end of the 19th century. The proximity of nervous tissue and CSF may afford insights into pathological processes within the nervous system through examination of the CSF, which may not easily be accessed by other investigational modalities. Because of this importance, guidelines on routine CSF analysis have been published. The related procedure of cervical or cisternal puncture may also be used to obtain CSF, but is far less frequently performed. Cerebrospinal fluid samples should always be regarded as precious, and hence every effort made to ensure correct analysis and interpretation; suboptimal performance is not infrequently encountered in day-to-day clinical practice. **Indications** Since lumbar puncture may be associated with morbidity and mortality, it should be undertaken only after careful clinical evaluation of the patient by history, examination and, when necessary, non-invasive investigations, to ascertain the precise potential values and hazards of the procedure. Indications for lumbar puncture may be diagnostic and/or therapeutic. The most common indications for diagnostic lumbar puncture are suspected central nervous system (CNS) infection or intracranial bleeding. CNS infections include meningitis and encephalitis. A variety of organisms, bacterial, viral, fungal, and protozoal can be responsible, and the pattern of findings in the CSF constituents might point to specific diagnoses, as might actual identification of the infecting organism(s) by means of special staining procedures, polymerase chain reaction, or microbial culture. CNS infection may also be suspected in some patients with acute confusional states or status epilepticus and hence these clinical scenarios may be an indication for lumbar puncture. Suspected intracranial bleeding, particularly subarachnoid haemorrhage, for example presenting with thunderclap headache, is an indication for lumbar puncture to look for evidence of bleeding and pigments produced by the breakdown of haemoglobin. Suspected CNS inflammatory disease is an indication for lumbar puncture to look for indices of inflammation (increased cell count, oligoclonal bands). Therapeutic roles for lumbar puncture include the temporary reduction of CSF

pressure, for example, to relieve postural headache with visual obscurations in idiopathic intracranial hypertension. Drainage of 20–30 ml of CSF (the ‘tap test’) may improve gait and 24.3
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of neurological disease

SECTION 24 Neurological disorders 5782 possibly cognition in cases of suspected normal pressure hydrocephalus (NPH), although this is not always a reliable predictor of success with more permanent CSF shunting procedures, perhaps in part because of underlying neurodegenerative brain disorders (Alzheimer’s disease, progressive supranuclear palsy) in patients initially thought to have idiopathic NPH. Lumbar puncture may also permit intrathecal administration of medications. Fatalities related to inadvertent administration of anticancer drugs intrathecally, rather than systemically, have occurred, sometimes leading to high profile legal cases and disciplining of the clinicians at fault. Contraindications It is important to exclude cerebral mass lesions prior to lumbar puncture, since raised intracranial pressure, perhaps evident as papilloedema, may risk brain herniation (coning) through the tentorium or foramen magnum, with potentially fatal consequences. In the presence of papilloedema, brain imaging (CT or MRI) is required before lumbar puncture. Papilloedema without cerebral mass lesion may be due to idiopathic intracranial hypertension, meningeal inflammation, or malignancy, conditions which require lumbar puncture and CSF examination for diagnosis. Therapeutic anticoagulation and other bleeding diatheses such as thrombocytopenia predispose to needle-induced haemorrhage (epidural, subdural, subarachnoid), and hence should be reversed prior to lumbar puncture if the procedure is elective. Patients receiving warfarin should have the medication discontinued at least 4–5 days before lumbar puncture, with international normalized ratio (INR) checked and less than 1.2 before the procedure. If lumbar puncture goes ahead with INR greater than 1.2, close monitoring of sensorimotor function for at least 24 hours is recommended. Urgent lumbar puncture in warfarinized patients requires reversal with fresh frozen plasma and vitamin K. For patients on low molecular weight heparin, lumbar puncture should be delayed for 12–24 hours depending on whether the dose is low or high, and restarted 18–24 hours post lumbar puncture. Antiplatelet medications such as aspirin or other nonsteroidal anti-inflammatory medications present no contraindication, but thienopyridine derivatives such as clopidogrel and ticlopidine should ideally be discontinued 7 and 14 days, respectively, before lumbar puncture. GP IIb/IIIa inhibitors should be discontinued to allow recovery of platelet function before lumbar puncture (8 hours for tirofiban and eptifibatid, 24–48 hours for abciximab). Data are scant for patients requiring lumbar puncture who are receiving thrombolytics or fibrinolytics, but impaired haemostasis persists for beyond 24 hours. For patients with thrombocytopenia less than 20 000/ μ l, platelet transfusion immediately prior to lumbar puncture is required. Local skin sepsis overlying the spine is a contraindication to lumbar puncture. Procedure Patients are often, and not unreasonably, anxious at the prospect of having a needle stuck in their back (perhaps by analogy with being ‘knifed in the back?’); tales of agonizing procedures suffered by others are not uncommon. Careful explanation before and during the procedure may allay many of these anxieties. For elective procedures, signposting to online information may be helpful (e.g. <http://www.clinicspeak.com/lumbar-puncture/>). Key to success is correct patient posture: left lateral decubitus (for a right-handed operator) with the knees drawn up to the chest, supported with a pillow between the legs, to keep the spinal column horizontal and avoid the rolled-over (‘Rokeby Venus’) position. The procedure should be performed under strict asepsis, with all requisite equipment (manometer, sample bottles, fixative) immediately to hand. Anatomical landmarks may be used to guide the operator: a vertical

line down from the anterior superior iliac spine should intersect the vertebral column around the desired L3/4 space. Under local anaesthesia (ensure adequate time is allowed for this to work), the needle is directed slightly cranial, as though aiming for the navel. With luck, the patient may even be unaware when the needle is passed. However, even the most experienced operator may sometimes require more than one pass to succeed, or may fail altogether. Further passes at a lower (L4/5) or higher (L2/3) intervertebral space, safe because the conus normally ends at L1 vertebra, or in the sitting position or under X-ray guidance, may be attempted. Cervical or cisternal puncture may be tried if the clinical indication for CSF analysis is sufficiently compelling, although few clinicians have adequate experience in performing this. Lumbar puncture under ultrasound guidance is becoming an increasingly popular option. All procedures undertaken should be fully documented in the patient record. Cerebrospinal fluid analysis should ideally occur immediately after sample collection, which may necessitate liaison to forewarn specialist laboratories prior to lumbar puncture being performed, and the clinician personally taking the sample to the laboratory if on site. There is always potential for mix-up if acute samples must travel to other sites for analysis. Complications Serious complications of lumbar puncture are thankfully uncommon. The most alarming is coning in the presence of raised intracranial pressure associated with a mass lesion, but this is extremely rare. Some bleeding may be associated with the procedure ('bloody tap') which may affect the interpretation of CSF findings, but infection is rare. Headache is the most common complication of lumbar puncture, as a consequence of CSF leakage and consequent low pressure, so it is sensible to warn patients of this possibility. Use of atraumatic needles may reduce the risk of post lumbar puncture headache. Remaining recumbent post-procedure (advice varies from 30 minutes to 2 hours), adequate hydration, and simple analgesia as required are often recommended. If these measures fail, caffeine may help. Use of a blood patch (epidural injection of autologous blood to produce thrombotic tamponade of the dural breach) is sometimes required, usually undertaken by an anaesthetist. Cerebrospinal fluid Normal ranges for standard CSF parameters are shown in Table 24.3.1.1.

24.3.1 Lumbar puncture 5783 **Opening pressure** The Monro-Kellie doctrine or hypothesis describes the pressure-volume relationship of the cranial compartment: since this is incompressible (in adults), cranial volume is fixed, such that the summed volumes of brain, CSF, and intracranial blood must remain constant, an increase in any one constituent being compensated by a decrease in the others, otherwise intracranial pressure will rise. Raised intracranial pressure may compromise cerebral perfusion pressure, for example, to the retina, resulting in papilloedema and sometimes the symptom of visual obscurations, an alarming clinical finding. In addition to analysis of CSF constituents, the fluid opening pressure should be measured routinely with a manometer. The pressure level in the right atrium is the reference level, with the patient in the lateral decubitus position; opening pressure cannot be measured in the sitting position. Normal CSF pressure reflects the balance between CSF production and resorption, and is generally around 50–200 mmH₂O, sometimes higher in obese individuals (ca. 250 mmH₂O). Disruption of production and/or resorption may lead to abnormal CSF opening pressure. High opening pressure may be seen in CNS infections (meningitis, encephalitis), acute stroke, cerebral venous occlusion, or stenosis, and in idiopathic intracranial hypertension (pseudotumor cerebri). Increased pressure also occurs with intracranial mass lesions but lumbar puncture is usually contraindicated in this situation. Low opening pressure may be technical (incorrect needle placement) or pathological, in conditions such as dehydration, spinal subarachnoid block, CSF leak, spontaneous intracranial hypotension (Schaltenbrand's syndrome) and the related 'frontotemporal brain sagging syndrome'. Blood and

pigments A 'bloody tap' due to needle trauma is a common hazard of lumbar puncture, resulting in the CSF appearing turbid (500–6000 red blood cells (RBC)/ μl) or frankly bloody (>6000 RBC/ μl). In the case of turbid CSF, laboratory RBC counts in successively taken CSF samples may help to differentiate between a bloody tap (reducing RBC count) and intrathecal bleeding (consistent admixed RBC count). Bloody CSF may also contain protein and increased numbers of white cells contributed by the blood, for which correction needs to be made (see next). Normal CSF appears 'crystal clear' to naked eye observation (cell count <400–500/ μl). Xanthochromia describes CSF with a pinkish or yellow pigmentation due to the presence of RBC haemoglobin breakdown compounds such as bilirubin and oxyhaemoglobin. This pigmentation may be evident on visual inspection of CSF at the bedside (e.g. held in front of a white piece of paper, or compared to water), but detection is facilitated by spectrophotometry (which can also detect methaemoglobin), hence this is the preferred assessment method in patients with suspected subarachnoid haemorrhage. Oxyhaemoglobin, released by RBC lysis, may be detected in the supernatant fluid within 2 hours of subarachnoid haemorrhage, reaching a maximum in about the first 36 hours and gradually disappearing over 7–10 days. Bilirubin is produced in vivo by leptomeningeal cells after haemolysis, and is first detected about 10 hours after subarachnoid haemorrhage, reaching a maximum at 48 hours and persisting for between 2 to 4 weeks. Since lumbar puncture may be negative if undertaken in the first 12 hours after the subarachnoid haemorrhage ictus, published recommendations are to delay lumbar puncture until over 12 hours, to send the least blood-stained sample (usually the last) for bilirubin analysis, and to protect the sample from light and avoid vacuum tube transport systems.

Cell count and cytology The consensus is that normal CSF should have ≤ 5 white blood cells (WBC)/ μl . An elevated CSF WBC count suggests disease of the CNS and/or meninges. Since blood in the CSF as a consequence of a bloody tap may increase the WBC count, correction may need to be made. If the patient has a normal peripheral blood count, then the ratio of white cells to red cells is approximately 1:1000. Hence, if the CSF red cell count is 10 000/ μl , the expected CSF white cell count would be 10/ μl . An approximation to the true CSF WBC count can be obtained by subtracting this from the actual count. If the peripheral blood count shows significant anaemia or leucocytosis, CSF WBC count before the blood was added may be determined using the following formula: $\text{True CSF WBC} = \text{blood WBC} \times \text{CSF RBC} / \text{blood RBC} \times 100$

() () □ □ An elevated CSF WBC count, or pleocytosis, may be encountered in various infective, inflammatory, and neoplastic disorders (see Table 24.3.1.2), as well as stroke, subarachnoid haemorrhage, cerebral vasculitis, and acute demyelination. Cerebrospinal fluid eosinophilia is typical of parasitic infections such as neurocysticercosis. Raised WBC count is not typically found in multiple sclerosis or acute inflammatory neuropathies (Guillain-Barré syndrome); if elevated, this should prompt the clinician to question these diagnoses. Cytological staining for cellular morphology is most often undertaken if there is clinical suspicion of leptomeningeal infiltration by neoplastic disease. Sensitivity of CSF cytology is influenced by sample volume and time to fixation. It has been recommended that at least 10 ml of CSF should be taken and that formalin fixative be added to the sample at the bedside or on the ward before it is sent to the laboratory. Repeated CSF studies may sometimes be required to confirm a suspected diagnosis of leptomeningeal metastasis. Protein CSF is an ultrafiltrate of plasma, the integrity of the blood:CSF barrier determining the CSF protein content. This is related to patient age (higher in neonates, and after 60 years of age), site of CSF collection (higher caudally), and possibly posture (higher in the bed-ridden). The CSF:serum albumin concentration quotient, Q_{alb} (normal <0.01), is preferred to total protein by some authorities, since this parameter evaluates blood:CSF barrier integrity, is method-independent, Table 24.3.1.1 Normal cerebrospinal fluid constituents (liaise

with local laboratory for their ranges) Parameter Normal range Opening pressure Lymphocytes or mononuclear cells Red blood cells Total protein CSF:serum glucose ratio Xanthochromia ca. 50–200 mmH₂O (CSF) No more than 5/μl None ca. 0.15–0.5 g/litre 60–80% of blood glucose concentration None

SECTION 24 Neurological disorders 5784 corrects for plasma concentration of albumin, and is not influenced by intrathecal protein synthesis. Marginal elevation of CSF total protein may be a nonspecific finding; clinical context is all important. Protein is elevated in meningitides, more so in bacterial and tuberculous than viral, and encephalitides (although may be normal in herpes simplex encephalitis early in the course), invariably in association with cellular reaction (see Table 24.3.1.2). Noninfectious causes of elevated protein include subarachnoid haemorrhage, CNS vasculitis, leptomeningeal metastases, and sometimes with neoplasms and in Creutzfeldt–Jakob disease. Classically there is elevated protein in the absence of cellular reaction in Guillain–Barré syndrome, the dissociation albumin-cytologique, although this elevation may not be apparent early in the disease course. Very high CSF protein content may cause increased CSF viscosity, with yellowish discolouration, a finding sometimes known as Nonne–Froin sign after the first descriptions in association with spinal tumour (e.g. ependymoma) and meningitis, respectively.

Immunoglobulins Intrathecal immunoglobulin (Ig) synthesis occurs in certain inflammatory CNS disorders. The CSF:serum IgG concentration quotient, Q_{IgG}, is closely correlated with Q_{alb}, their ratio constituting the CSF IgG index (Q_{IgG}/Q_{alb}; normal <0.65). However, the detection of CSF oligoclonal bands using, for example, isoelectric focusing is a superior method of detecting intrathecal IgG synthesis than IgG index. Since some immunoglobulins are passively transferred from plasma to CSF, the production pattern in serum mirrors that in CSF. Hence it is mandatory that paired blood and CSF samples are examined to determine whether immunoglobulin synthesis confined to the CSF compartment is occurring. Although the finding of CSF oligoclonal bands is nonspecific, in the particular clinical situation it may help to support a clinical diagnosis of multiple sclerosis. They may also be found in infective, neoplastic, paraneoplastic, and granulomatous disorders, and even on occasion in neurodegenerative disorders such as Alzheimer’s disease.

Glucose Serum and CSF glucose should be measured concurrently, since the latter is dependent on the former, to provide a CSF:serum glucose ratio which is normally 0.6–0.8. This ratio may be lower (down to 35%) in the presence of hyperglycaemia in the four hours before lumbar puncture in the absence of neurological disease. Low CSF glucose (hypoglycorrhachia) may be a feature of bacterial, fungal, or tuberculous (but generally not viral) meningitides, Table 24.3.1.2 Cerebrospinal fluid findings in neurological conditions in which lumbar puncture is frequently performed

Opening pressure (mmH ₂ O)	WBC/μl	Protein (g/l)	Glucose (mmol/l)*	Acute bacterial meningitis
Usually elevated	Several hundred to more than 60 000; usually a few thousand, but occasionally <100 (especially meningococcal, or early in disease).	Polymorphonuclear cells predominate	Usually 1–5, occasionally >10	0.2–2.2 in most cases (in the absence of hyperglycaemia)
Viral meningitis	Normal to moderately elevated 5 to a few hundred; but may be >1000, particularly with lymphocytic choriomeningitis.	Lymphocytes predominate, but there may be >80% polymorphonuclear cells in the first few days	Frequently normal or slightly elevated; <1; may show greater elevation in severe cases	Normal (may be reduced in some cases of mumps)
Tuberculous meningitis	Usually elevated; may be low with dynamic block in advanced stages	Usually 25–100; rarely more than 500. Lymphocytes predominate except in early stages when polymorphonuclear cells may account for 80%	Nearly always elevated, usually 1–2; may be much higher if dynamic block	Usually reduced; <2.5 in

three-quarters of cases Cryptococcal meningitis Usually elevated 0–800; average 50. Lymphocytes predominate Usually 0.2–5; average 1 Reduced in most cases; average 1.7 (in absence of hyperglycaemia) Herpes simplex encephalitis Usually elevated 10–200; lymphocytes predominate Usually 0.6–6 Normal (rarely reduced) Acute neurosyphilis Usually elevated Average 500. Usually lymphocytes; rarely polymorphonuclear cells Average 1 Normal (rarely reduced) Neurocysticercosis Often increased; low with dynamic block Increased mononuclear and polymorphonuclear cells with 2–7% eosinophilia in about half of cases Usually 0.5–2 Reduced in a fifth of cases Neurosarcoidosis Normal to considerably elevated 0 to fewer than 100 mononuclear cells Slight to moderate elevation Reduced in half of cases CNS tumour† Normal or elevated 0 to several hundred mononuclear cells plus malignant cells on cytology Elevated often to high levels Normal or greatly reduced (low in three-quarters of carcinomatous meningitis cases) Idiopathic intracranial hypertension† Elevated, by definition Normal cell count Usually normal Normal

- Compare with plasma glucose to calculate CSF:serum glucose ratio. † Brain imaging (CT, MRI) mandatory before undertaking lumbar puncture if these diagnoses are suspected on clinical grounds.

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