Cerebrospinal Fluid (CSF)

What is CSF?

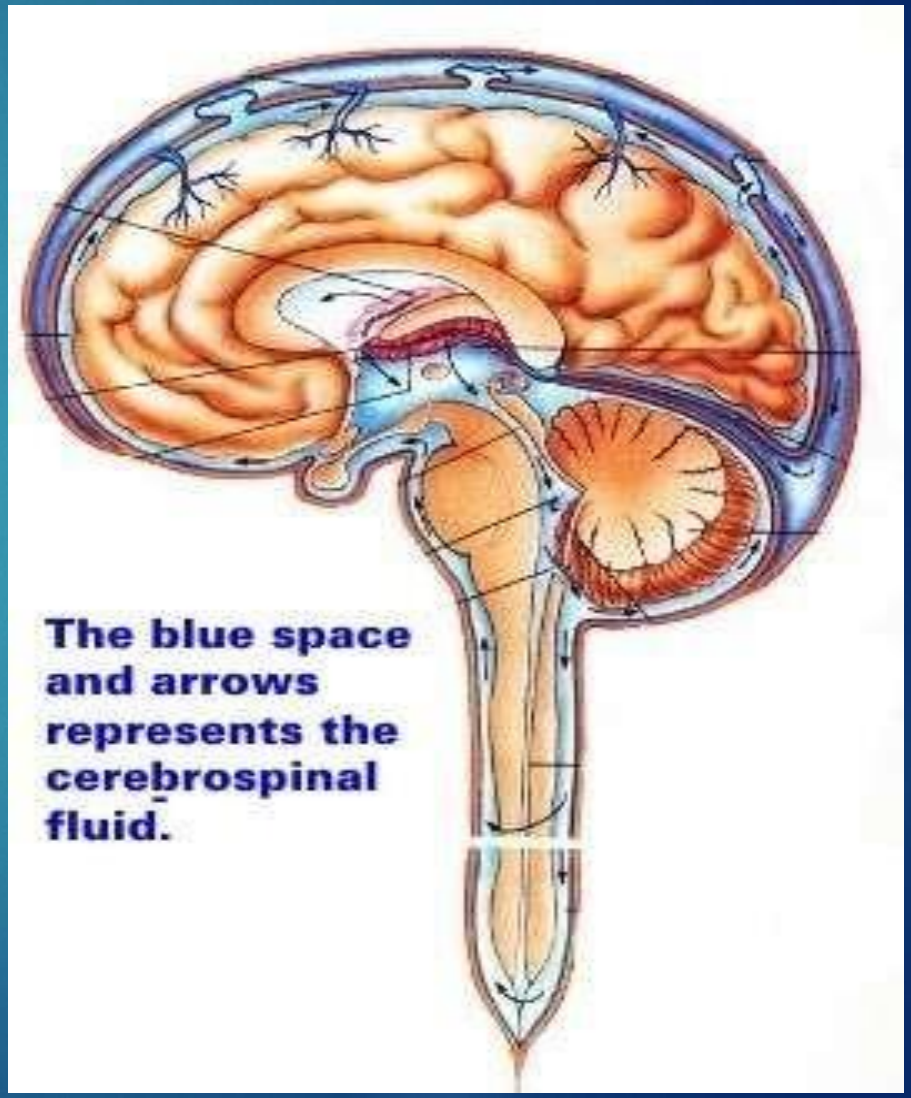
- CSF is a clear, color less fluid that surrounds and permeates the CNS.
- Offers support, protection and nourishment.
- In essence, the brain "floats" in it.
- It is present in the ventricles of the brain, the central canal of the spinal cord, and the subarachnoid space.
- CSF is produced in the brain by modified ependymal cells in the choroid plexus (approx. 50-70%), and the remainder is formed around blood vessels and along ventricular walls.

Functions of CSF

- Protects, lubricates the brain
- Provides nutrients, removes waste 90-150 ml adult &10-60 ml in new born
- Modulates pressure changes (Buoyancy)
- Serves as a chemical buffer to maintain constant ionic environment
- Serves as a transport medium for nutrients and metabolites, endocrine substances and even neurotransmitters

Location of CSF

- Two lateral ventricles
- Third ventricle
- Fourth ventricle
- Spinal cord central canal
- Subarachnoid space
- Continuous with extracellular fluid of brain parenchyma

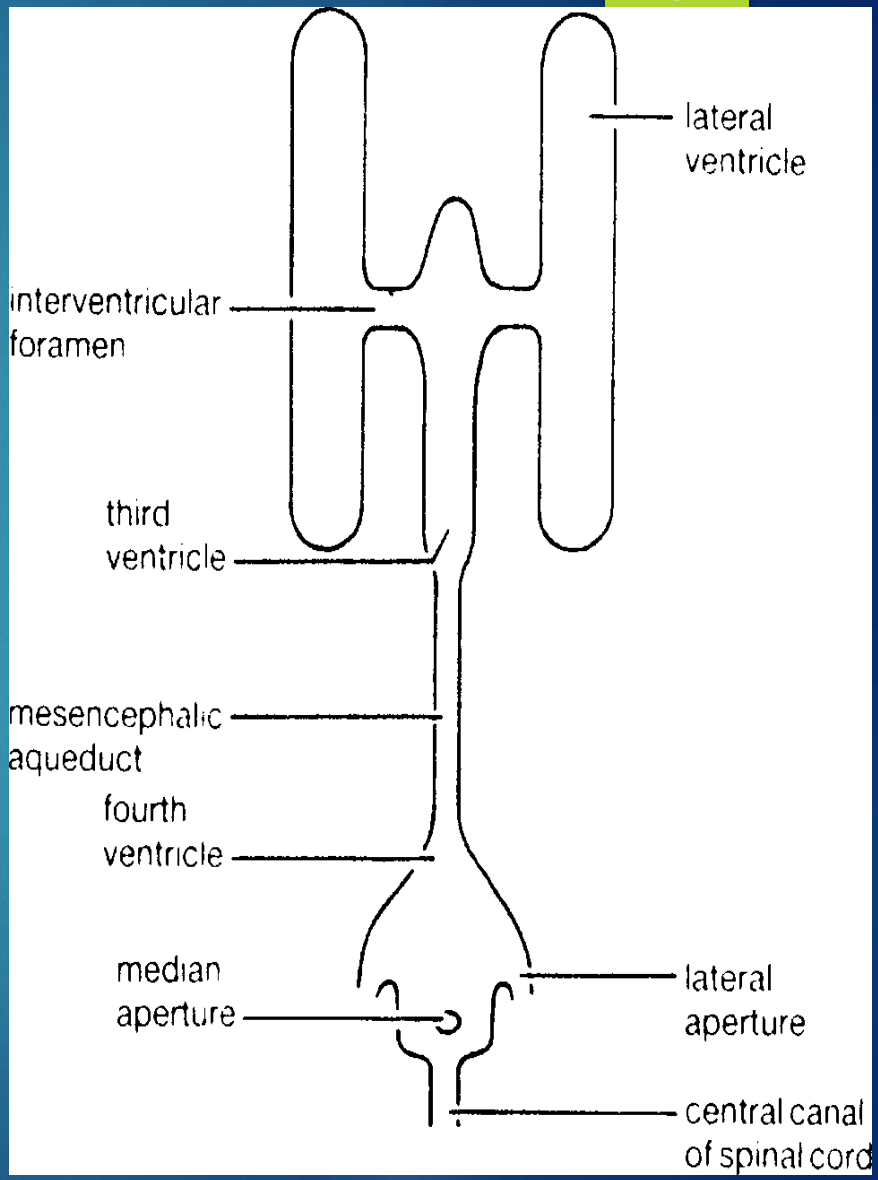


Formation of CSF

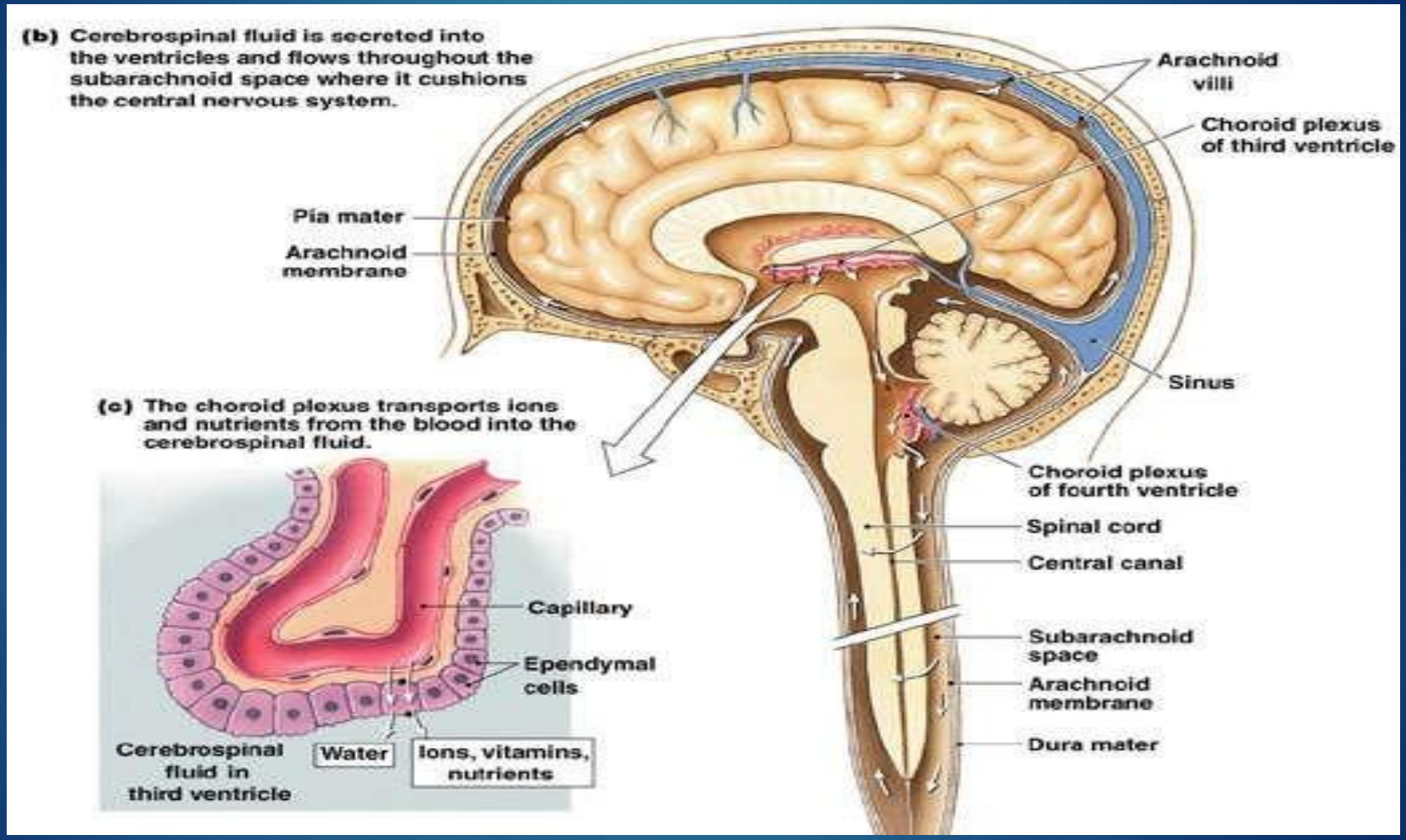
- Average intracranial volume : 1400 to 1700 ml
- CSF occupies about 150 ml : 10 percent approx.
- Rate of formation : 0.35ml/min = ~20ml/hour = ~500ml/day
- Renewed 3 – 4 times a day
- Sites of Production-
  Choroidal plexus : 70-80 percent
  Extra-choroidal : 20-30 percent Ependyma, Capillaries, Brain Interstitial fluid

Circulation of CSF

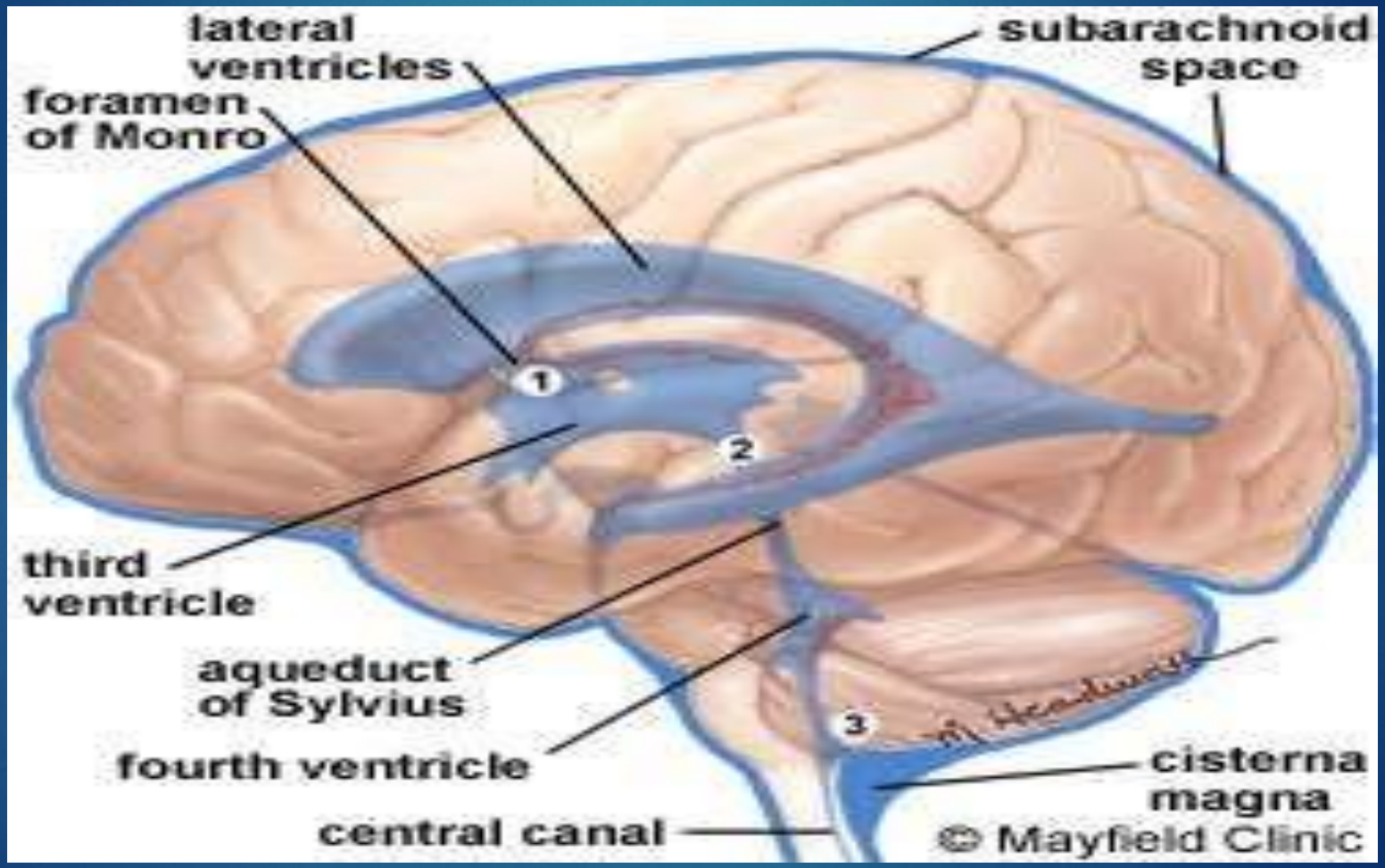
- Lateral ventricles
- Foramen of Monro → Third ventricle
- Aqueduct of Sylvius
- Fourth ventricle
- Foramina of Magendie and Luschka
- Subarachnoid space of brain & spinal cord
- Reabsorption into venous sinus



Circulation of CSF



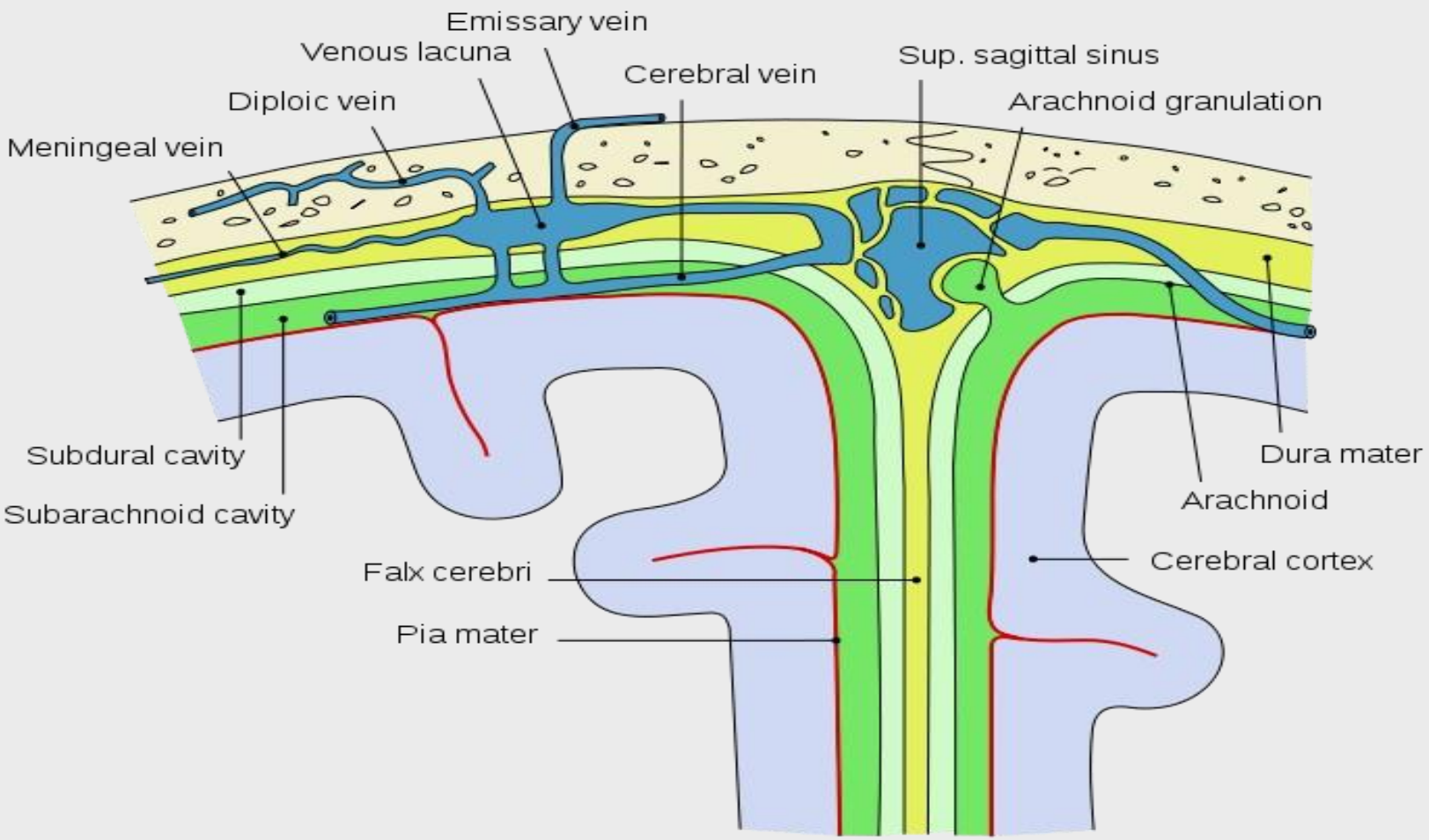
Circulation of CSF



Absorption of CSF

- Through the arachnoid villi, a protrusion of arachnoid membrane into the central venous sinus and other sinuses
- A valve opens when CSF pressure exceeds venous pressure
- Absorption by veins and capillaries of CNS.
- It is suggested that CSF flow along the cranial nerves and spinal nerve roots allow it into the lymphatic channels. It plays a substantial role in CSF reabsorption, in the neonate, where arachnoid granulations are sparsely distributed.

Arachnoid Granulation



CSF ANALYSIS

Why CSF Analysis ?

To diagnose the diseases:

- Bacterial tuberculosis,
- Fungal meningitis,
- Viral meningitis,
- SAH,
- Multiple sclerosis,
- CNS Syphillis,
- Infectious Polyneuritis
- Paraspinal abscess
- Meningeal malignancy
- Intracranial haemorrhage
- Viral encephalitis
- Subdural haematoma

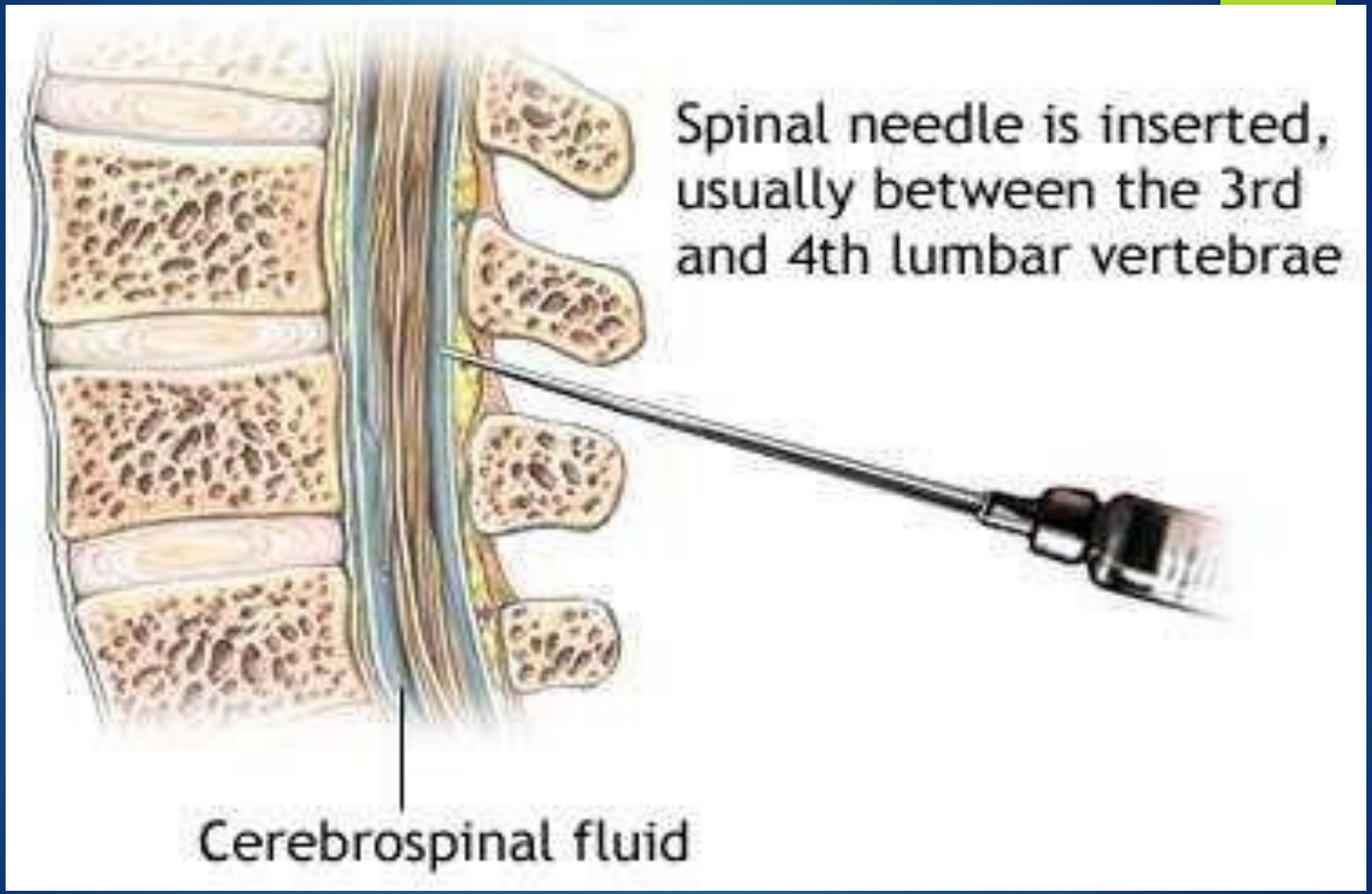
Collection of CSF

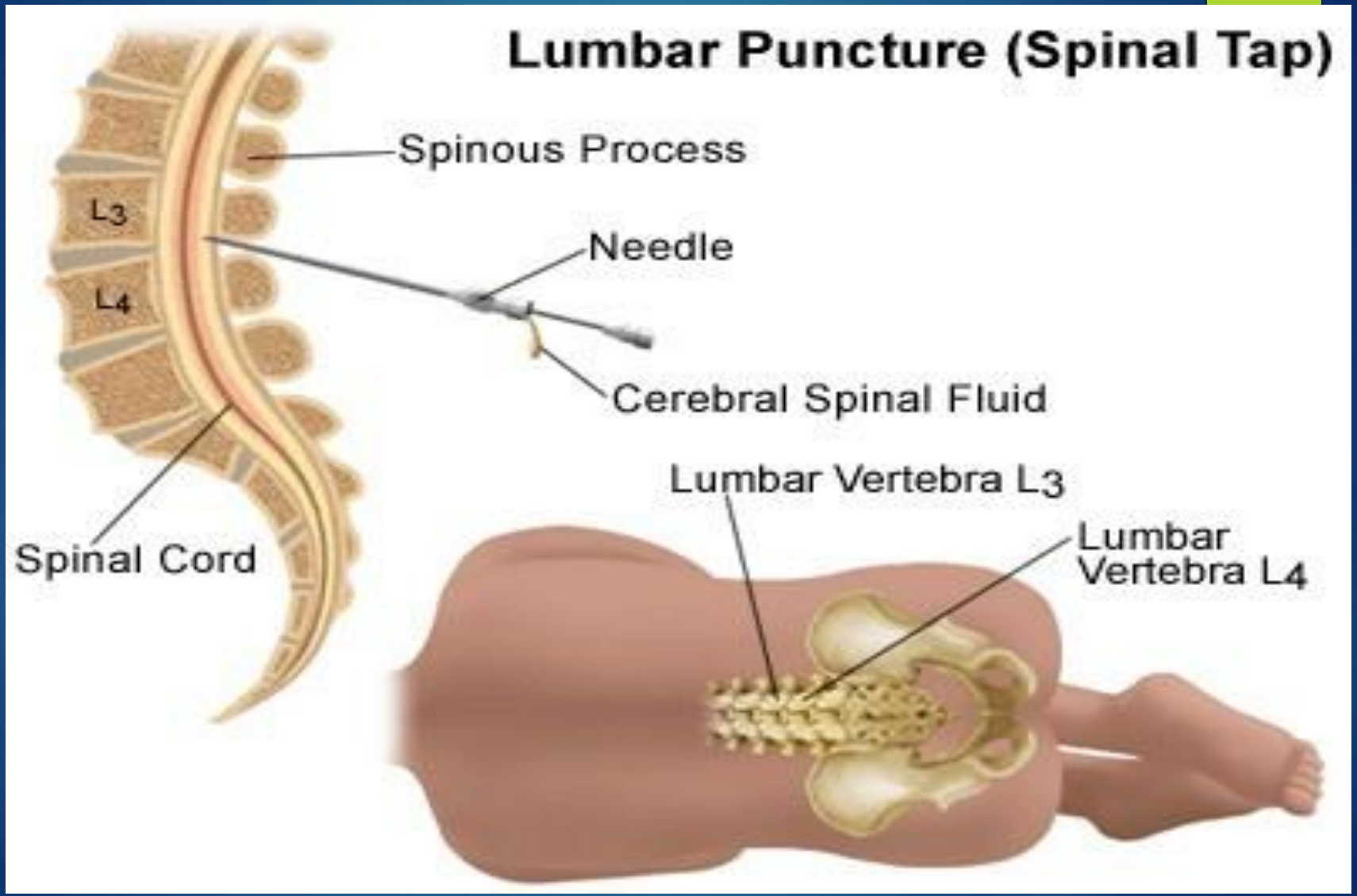
- Most Common way to collect CSF- Lumbar puncture
- Other methods for collecting CSF are rarely used, but may be recommended in some cases. They include:
  - Cisternal puncture
  - Ventricular puncture
  - Removal of CSF from a tube that is already in the CSF, such as a shunt or ventricular drain.
  - Lateral cervical puncture

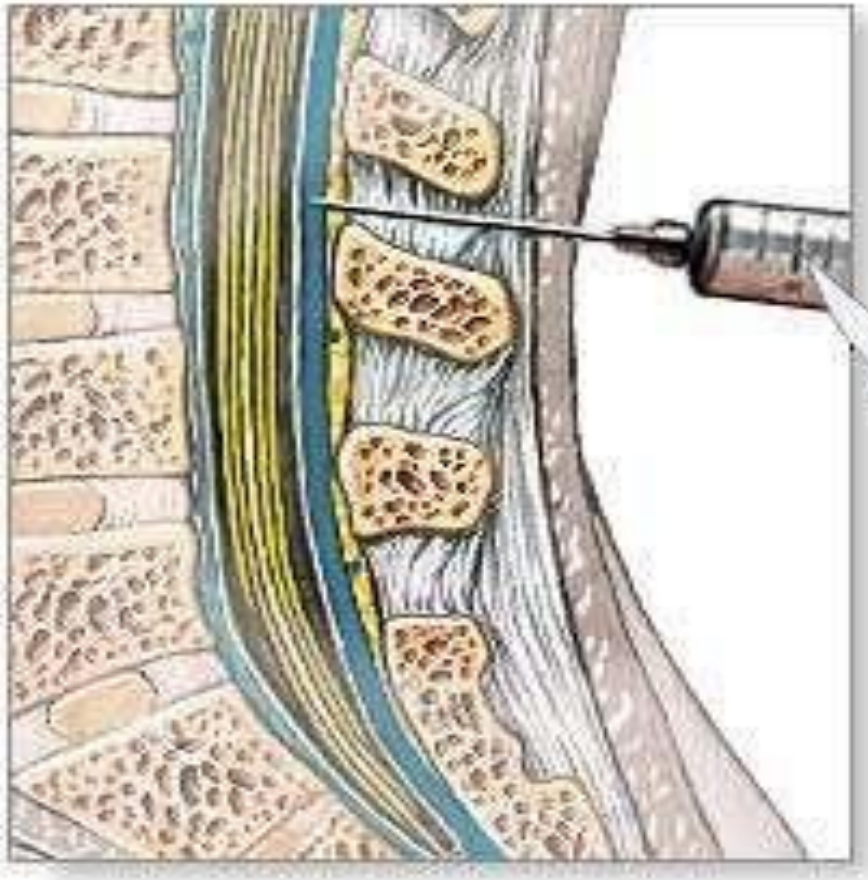
- Opening pressure – 90-180 mm H_2O
- Approximately 15-20 cc fluid is collected

Lumbar puncture

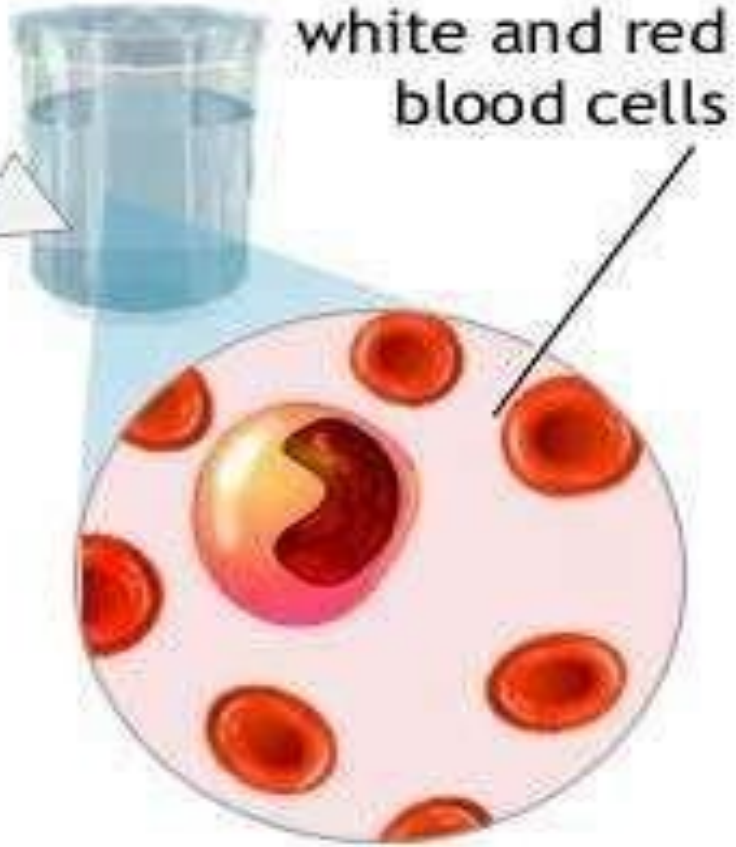
- **Lumbar puncture** or **LP**, colloquially known as a **spinal tap**)
- It is a diagnostic procedure that is performed in order to collect a sample of cerebrospinal fluid (CSF) for biochemical, microbiological, and cytological analysis
- In LP after the area is completely numbed with local anesthetic, a small needle is inserted between the 3rd and 4th Lumbar vertebrae.

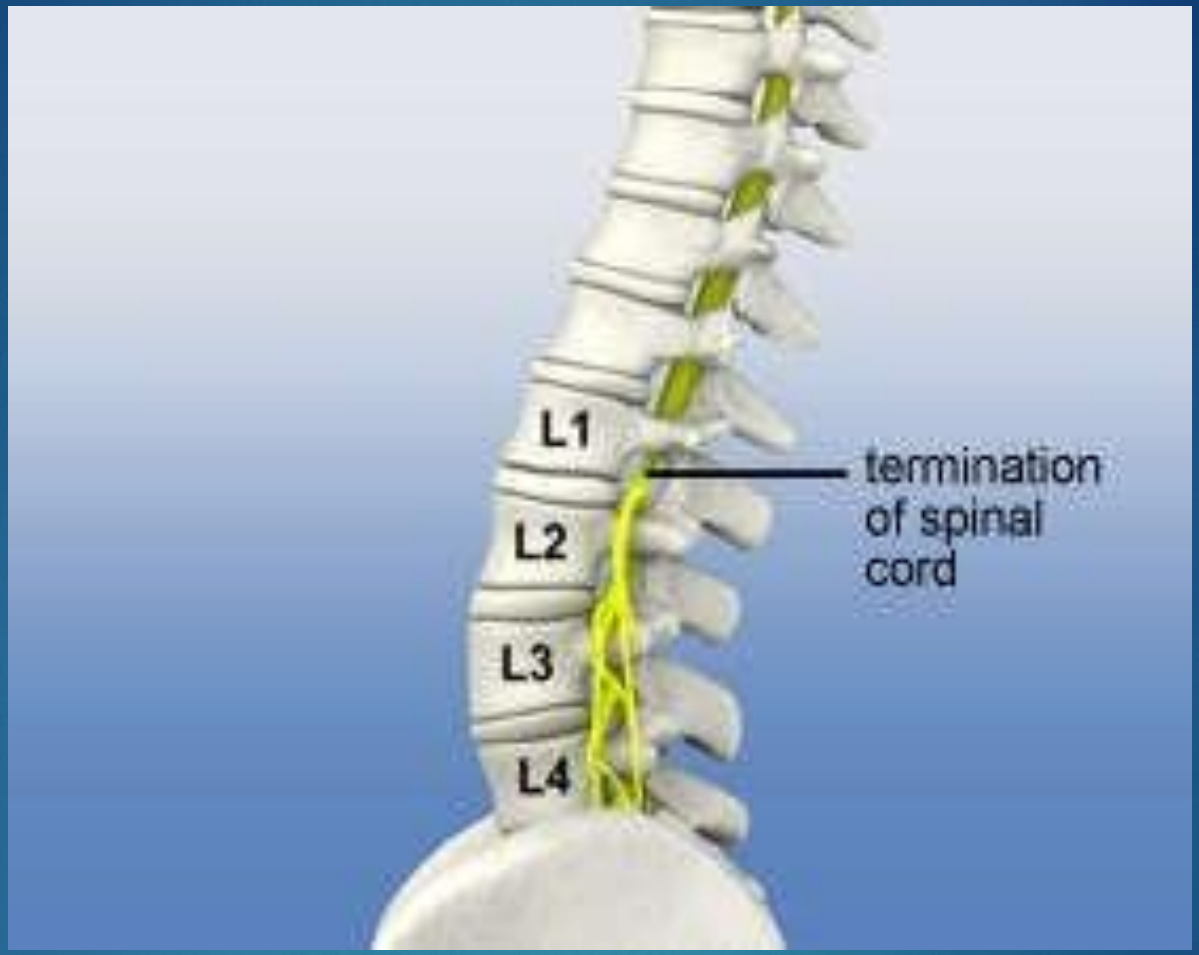

Spinal needle is inserted, usually between the 3rd and 4th lumbar vertebrae
Cerebrospinal fluid


Lumbar Puncture (Spinal Tap)
Spinous Process
L3
L4
Needle
Cerebral Spinal Fluid
Lumbar Vertebra L3
Lumbar Vertebra L4
Spinal Cord



Lumbar puncture performed to obtain cerebrospinal fluid or CSF



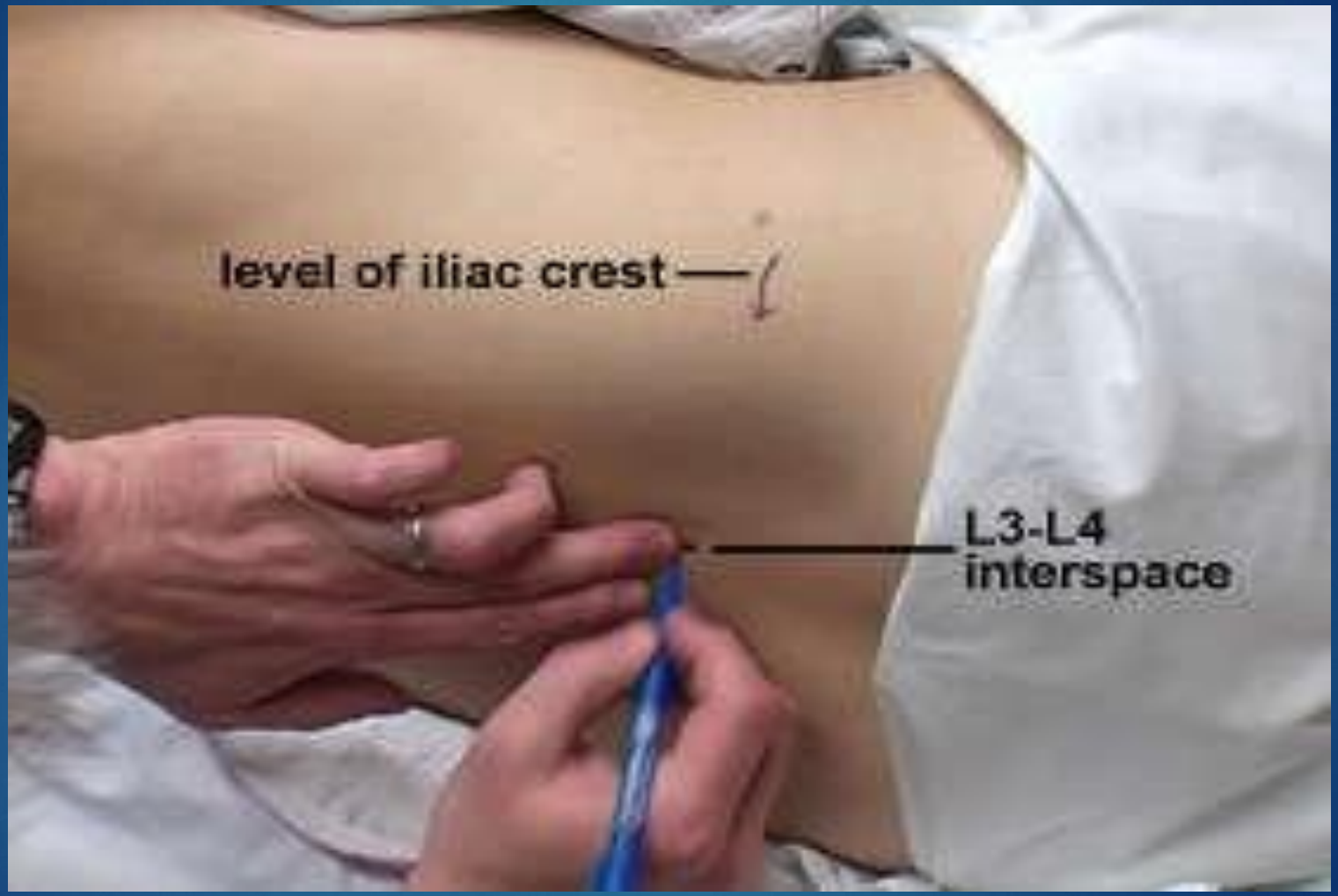


Spinal cord terminates at L1; needle entry must occur distal to this location

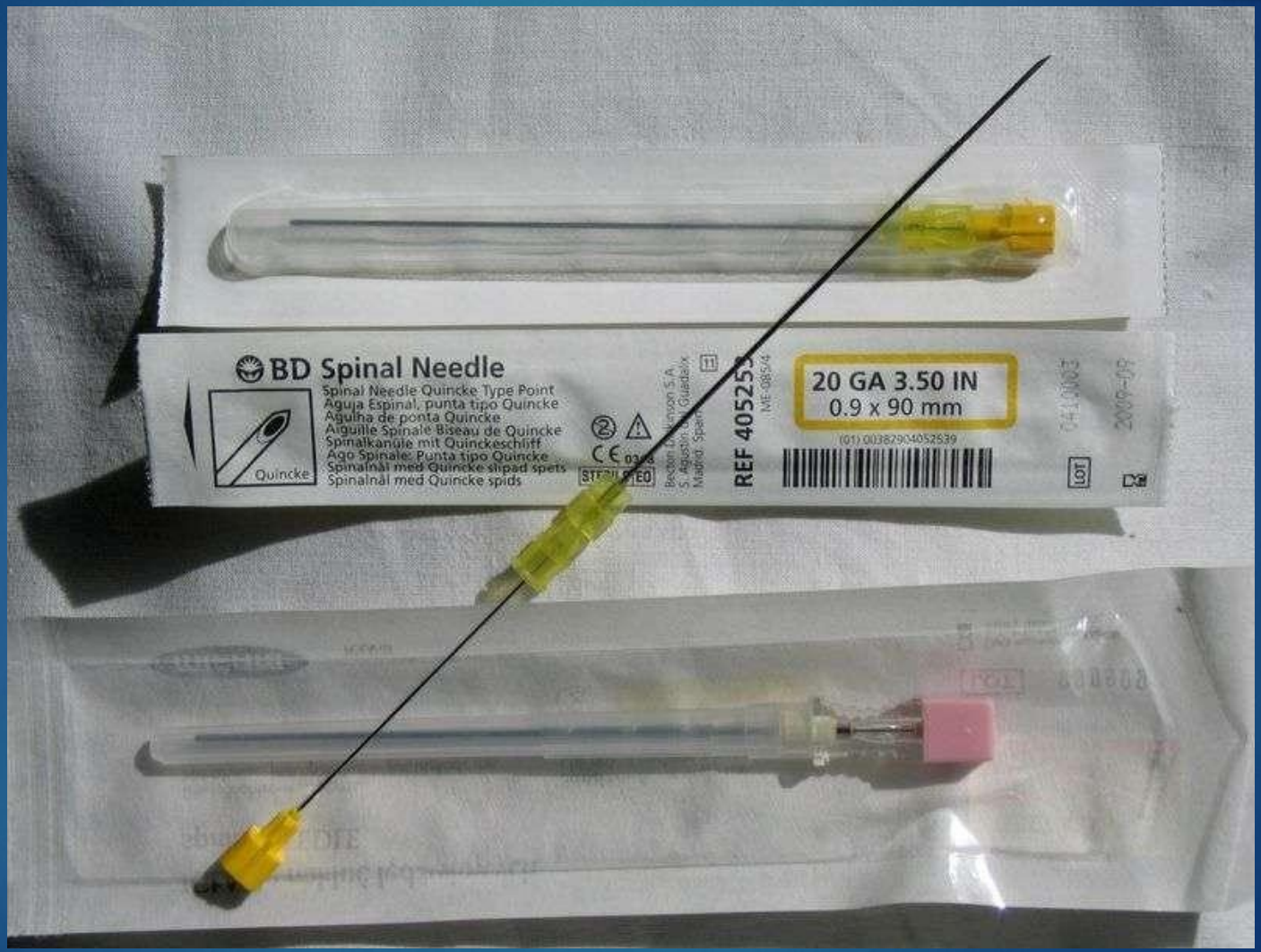
Proper angle of entry through the L3-L4 interspace

Full flexion

Level of entry



Spinal needle



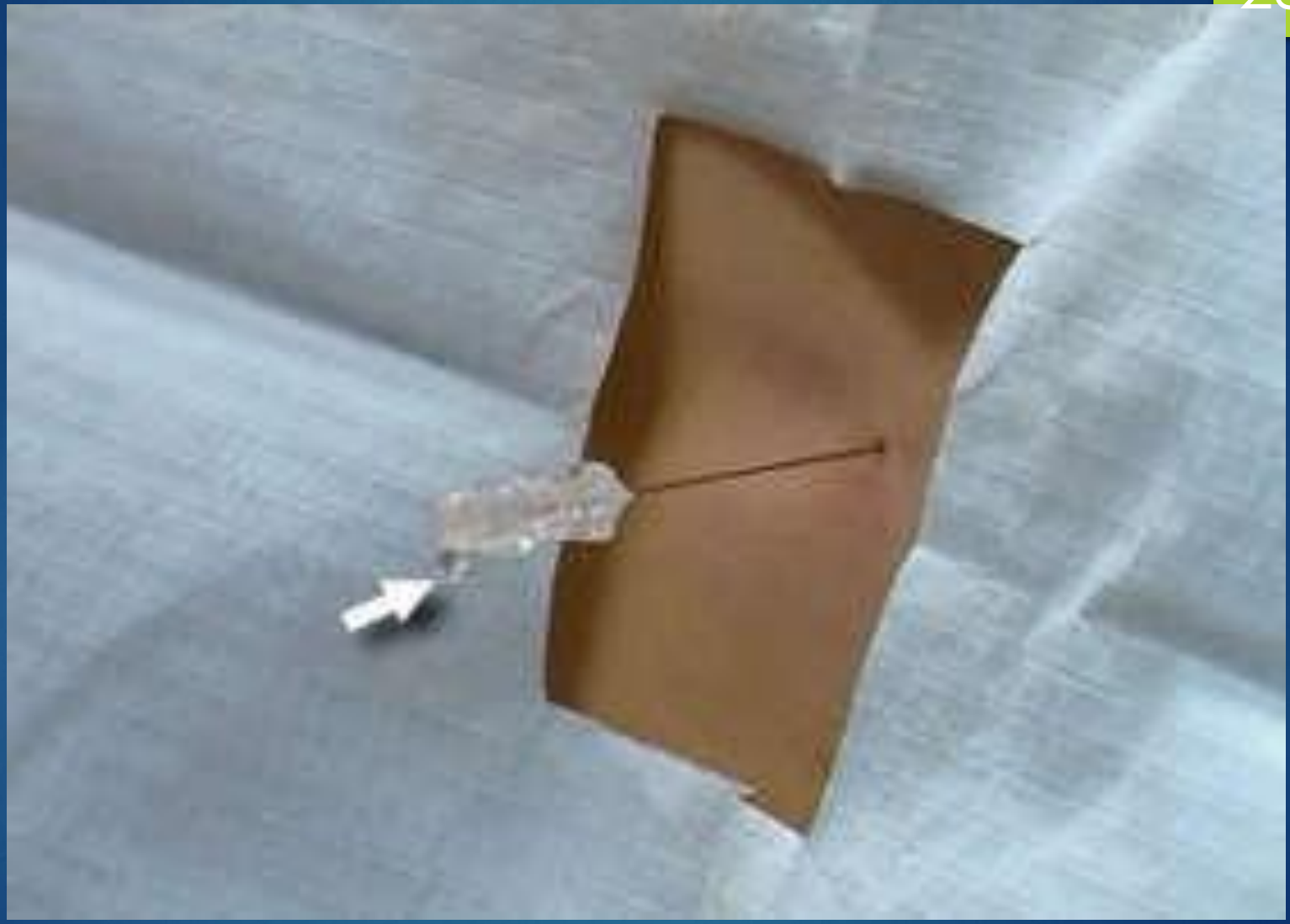
Spinal needle

Under strict aseptic precautions

Lp - layers

- Skin
- Facia and Subcutaneous fat
- Surpaspinous ligament
- Interspinous ligament
- Ligamentum flavum
- Epidural space (epidural anesthesia needle stops here)
- Dura
- Arachnoid
- Right after that the needle pops into the subarachnoid space where the CSF is.


stylet



The opening pressure

Collecting the CSF

Glass tubes should be avoided

- 3 serially collected sterile tubes:

1. Tube 1 for chemistry and immunology studies.
2. Tube 2 for microbiological examination.
3. Tube 3 for cell count & differential/cytology.

- Specimens should be delivered to the laboratory and processed quickly to minimize cellular degradation, which begins **within one hour of collection.**

Routine laboratory CSF tests

- REQUIRED

1. Opening CSF pressure
2. Total cell count
3. Differential cell count
4. Glucose
5. Total protein

- OPTIONAL

  Cultures, Gram stain, AFB, Fungal and bacterial antigens, Enzymes, PCR, Cytology, Electrophoresis, VDRL, D-Dimers

CSF Analysis

Gross Examination

- Quantity
- Colour
- Appearance
- Clot formation
- Viscosity
- Xanthochromia

Microscopic Examination

- Total Cell Count
- Differential Cell Count

Normal CSF

- Thin, colourless, clear fluid
- Pressure 90-180mm WATER (10-100 neonates)
- 0-5 WBC's /mm^3 (neonates 0-30/ mm^3)
  (Lymphocytes & monocytes)
- Occasional ependymal or choroid plexus cells
- Protein 15-45mg/dl
- Glucose 50-80mg/dl
- Chloride 113-130 mEq/L
- Sterile

Normal CSF volumes:

- In Adults: 90 - 150 ml
- In Neonates: 10 - 60 ml

Total CSF volume is replaced every 5-7 hours.

Normal CSF

Characteristic	
Color	Colorless
PH	7.28-7.32
Appearance	Clear
Sp. Gravity	1.003-1.004
Clot formation	No clot on standing
Total solids	0.85-1.70 g/dL
PO2	40-44mmHg

Normal CSF

Protein	15-45 mg/dL
Glucose	50-80 mg/dL
Urea	6-16 mg/dL
Uric acid	0.5-3.0 mg/dL
Creatinine	0.6-1.2 mg/dL
Cholestrol	0.2-0.6 mg/dL
Ammonia	10-35 ug/dL
Cells	0-5 lymphocytes/uL

Gross Examination

COLOUR

- Normal CSF
  - is crystal clear
  - colourless
  - viscosity that of water.
- Abnormal CSF may appear cloudy, frankly purulent or pigment tinged.

Turbidity

- Leucocyte counts over 200 cells/uL
- Red cell counts of 400/uL
- Microorganisms – bacteria, fungi, amoebas.
- Radiographic contrast material
- Aspirated epidural fat
- Protein levels > 150 mg/dL

Clot Formation

Seen in

- Traumatic taps
- Complete spinal block(Froin's Syndrome)
- Suppurative or Tuberculous meningitis

Not seen in patients with Subarachnoid Haemorrhage.

Viscosity

Present in

- Metastatic mucin producing adenocarcinomas
- Cryptococcal meningitis
- Liquid nucleus pulposus

Xanthochromia

- Xanthochromia refers to a pale pink to yellow colour in the supernatant of centrifuged CSF, although other colours may be present.
- Xanthochromic CSF is pink, orange, or yellow owing to RBC lysis and hemoglobin breakdown.
- Pale pink to orange xanthochromia is observed on lumbar puncture performed 2-4 hours after the onset of SAH.
- Yellow xanthochromia is derived from bilirubin. Develops12 hours after a subarachnoid bleed.
- Brown xanthochromia is seen in meningeal metastatic melanoma.

Visible CSF Xanthochromia

Due to

- Oxyhemoglobin resulting from artifactual red cell lysis
- Bilirubin in jaundiced patients
- CSF protein levels > 150 mg/dL
- Carotenoids
- Melanin
- Rifampin thereapy

Bloody CSF

- Usually indicates the presence of blood.
- Grossly bloody when the red blood cell counts exceed 6000/uL.

CAUSES

- SAH (Subarachnoid Haemorrhage)
- Intracerebral haemorrhage
- Cerebral infarct
- Traumatic spinal tap

Differential Diagnosis of bloody CSF:

1. In a traumatic tap the haemorrhagic fluid disappears by third tube, remains uniform in SAH.
2. Xanthochromia, microscopic evidence of erythrophagocytosis, haemosiderin laden macrophages indicate SAH.

CSF Glucose

This test may be done to diagnose:

- Tumors
- Infections
- Inflammation of the central nervous system
- Delirium
- Other neurological and medical conditions

The glucose level in the CSF should be 50 to 80 mg/100 mL (or greater than 2/3 of the blood sugar level)

CSF Glucose

- Abnormal results include higher and lower glucose levels.

  Abnormal results may be due to:
- Infection (bacterial or fungus)
- Inflammation of the central nervous system
- Tumor

- Sample-
- **CSF volume:** Minimum 0.25 mL (6 drops)
- **Sample tube:** 2mL fluoride-oxalate tube (grey top).

CSF Protein

- The spinal fluid normally contains very little protein since serum proteins are large molecules that do not cross the blood-brain barrier.
- Most of the protein that is normally present is albumin.
- CSF protein concentration may rise due to 2 factors: either an increased permeability of the blood brain barrier allowing more protein and higher molecular weight proteins to enter the CSF or proteins may be synthesised within the cerebrospinal canal by inflammatory or other invading cells.

CSF Proteins

- Mild protein elevation may be caused by viral meningitis, neurosyphilis, subdural haematoma, cerebral thrombosis, brain tumour, multiple sclerosis (rarely >1.00 g/L)
- Moderate or pronounced elevation may be caused by acute bacterial meningitis, tuberculous meningitis, spinal cord tumour, cerebral haemorrhage, Guillain-Barre syndrome.
- When CSF protein levels are low it can indicate rapid CSF production.
- Sample-
  CSF volume: Minimum 0.25 mL (6 drops)
  Sample tube: Plain Universal container (tubes containing gel or anticoagulant are not suitable for analysis of CSF protein).

CSF Glutamine

- Glutamine is produced in the CNS by the brain cells from ammonia and alpha-ketoglutarate.
- Removes the toxic metabolic waste product ammonia from the CNS.
- Normal concentration of ammonia is 8-18 mg/dl.
- Elevated levels associated with liver disorders.

CSF Lactate

- Aid in the diagnosis and management of meningitis cases
- Destruction of tissue within the CNS owing to oxygen deprivation (hypoxia) causes the production of increased CSF lactic acid levels.

Microscopic Examination

Total Cell Count-
TLC in CSF can be done by:

I. Manual method
II. Automated method

Manual Method

Diluting fluid has the following composition:

- Crystal violet 0.1gm
- Glacial acetic acid 5ml
- Distilled water 45ml

- Take a RBC pipette, draw diluting fluid upto mark 1 and then draw CSF upto mark 101.
- Charge the Neubauer chamber and count the cells in all 9 squares.
- Cells per uL = number of cells x 1.1

Automated Method

- Precision is poor in the low counts normally encountered in CSF.
- The method employs use of flow cytometry for rapid and reliable WBC and RBC counts.

Normal Leukocyte counts

- In Adults: 0 - 5 cells/cumm
- In Neonates: 0 - 30 cells/cumm
- No RBC's should be present in normal CSF.
- If numerous, one of the following can be considered– traumatic tap, malignancy, infarct, hemorrhage.
- Although red cell counts have limited diagnostic values, they may give a useful approximation of the true CSF WBC counts or total protein in the presence of a traumatic puncture by correcting for leucocytes and proteins introduced by the traumatic puncture.

❖ Corrected WBC count:

- $WBC_{corr} = WBC_{obs} - WBC_{added}$

Where:

- $WBC_{added} = WBC_{BLD} \times RBC_{CSF} / RBC_{BLD}$
- In the presence of normal peripheral blood RBC count, these corrections amount to 1 WBC for every 700 RBC'c

❖ Corrected protein:

- TP added = [TP serum x (1 – HCT)] x RBC_{CSF}/RBC_{BLD}

  In the presence of normal serum protein, these corrections amount to 8mg/dL protein for every 10,000 RBC's/uL.

Differential Cell Count

PREPARATION BY **CENTRIFUGE**

Other techniques:

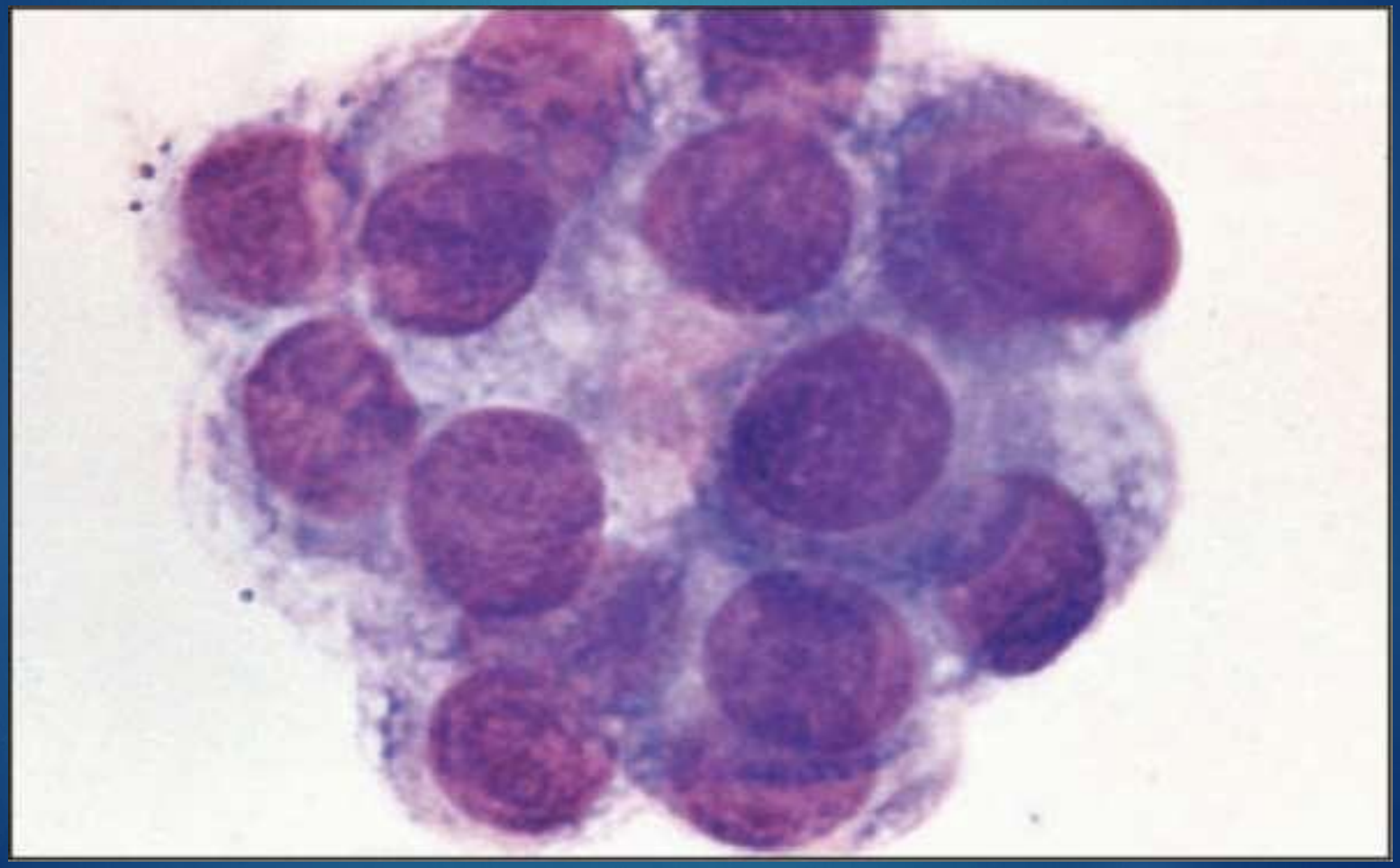
- Cytocentrifuge
- Sedimentation
- Cell catch
- Filtration

- Differential counts performed in a chamber has poor precision.
- Direct smears of the centrifuged smear is also subject to significant error from cellular distortion and fragmentation.
- Filteration and sedimentation methods are too cumbersome for routine use.
- Cytocentrifuge is rapid and is **the recommended method of choice** for differential cell counts in all body fluids.

Normal Cells seen in CSF

- Lymphocytes and monocytes are normally present in small numbers in a ratio of 70:30. Monocytes are more in number in neonates and children.
- Choroid plexus and ependymal cells are rarely seen in hydrocephalus and after intra-thecal chemotherapy
- Cartilage, ganglion cells and artificial admixture of hematopoietic cells.

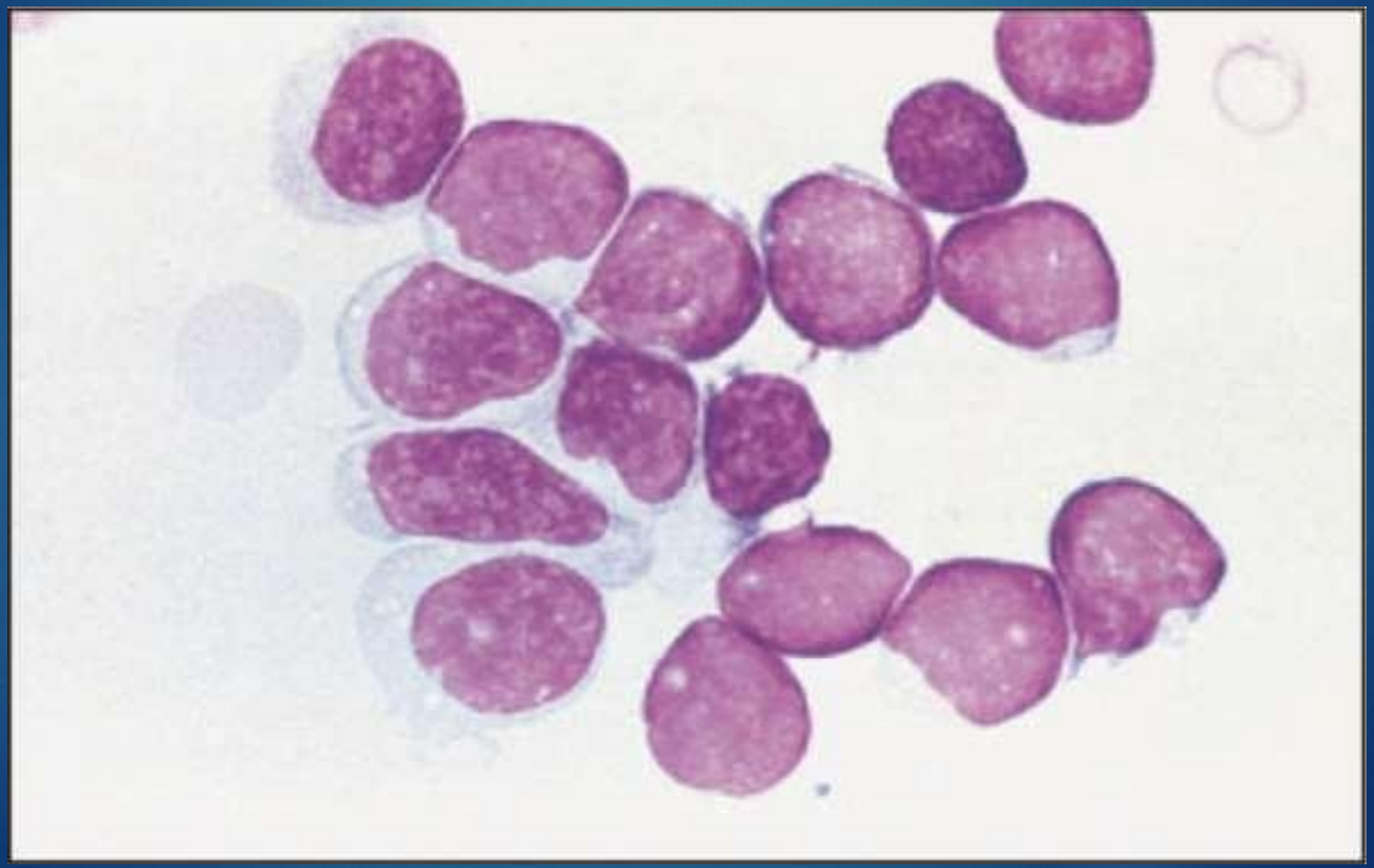
Choroid plexus cells in CSF



- Contaminants : fungus and bacteria.
- Erythrocytes due to minor traumatic bleeeding are commonly seen, specially in infants.
- Small clusters of neutrophils may also be seen in ‘normal’ CSF specimens, most likely as a result of minor hemorrhage.

- Blast like primitive primitive cell clusters, of germinal matrix origin are sometimes found in infants with IVH.
- Corpora amylacea, spherical proteinaceous structure seen commonly in the elderly, is occasionally found in CSF.
- Powder crystals, by starch granules or glove powder can be mistaken for spore of cryptococcus.

Cluster of blast-like cells in CSF from premature newborn

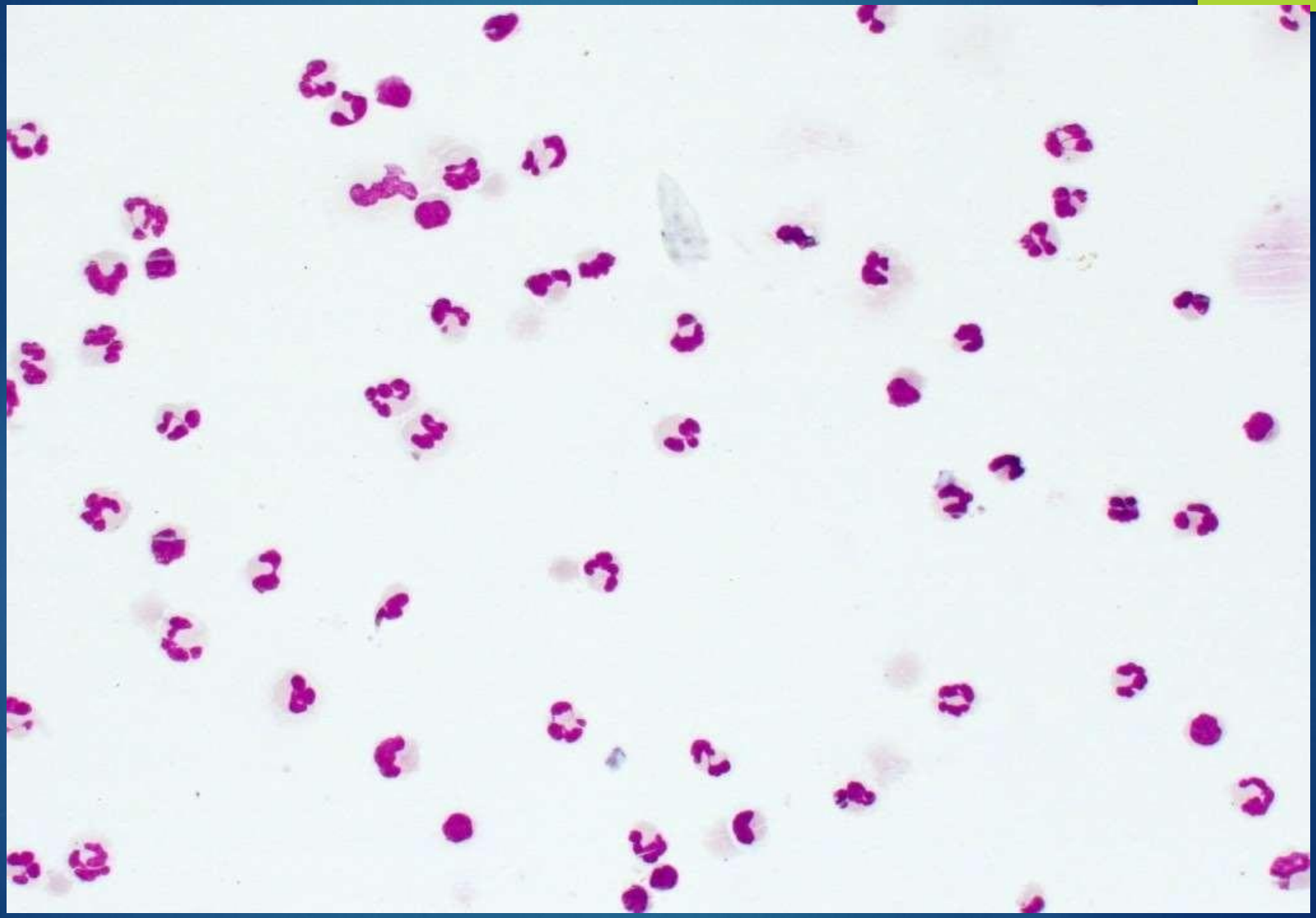


Reference intervals for CSF

Cell type	Adults	Neonates
Lymphocytes	62	20
Monocytes	36	72
Neutrophils	2	3
Histiocytes	Rare	5
Ependymal	Rare	Rare
Eosinophils	Rare	Rare

Increased CSF Neutrophillia

- Meningitis
  Bacterial, viral, tubercular, mycotic and amoebic.
- Other infections
  Cerebral abscess, subdural empyema, AIDS related CMV radiculopathy
- Following seizures
- Following CNS hemorrhage
- CNS infarct
- Repeated lumbar punctures
- Injection of foreign material in subarachnoid space
- Metastatic tumour in contact with CSF



Increased CSF lymphocytosis

- Meningitis

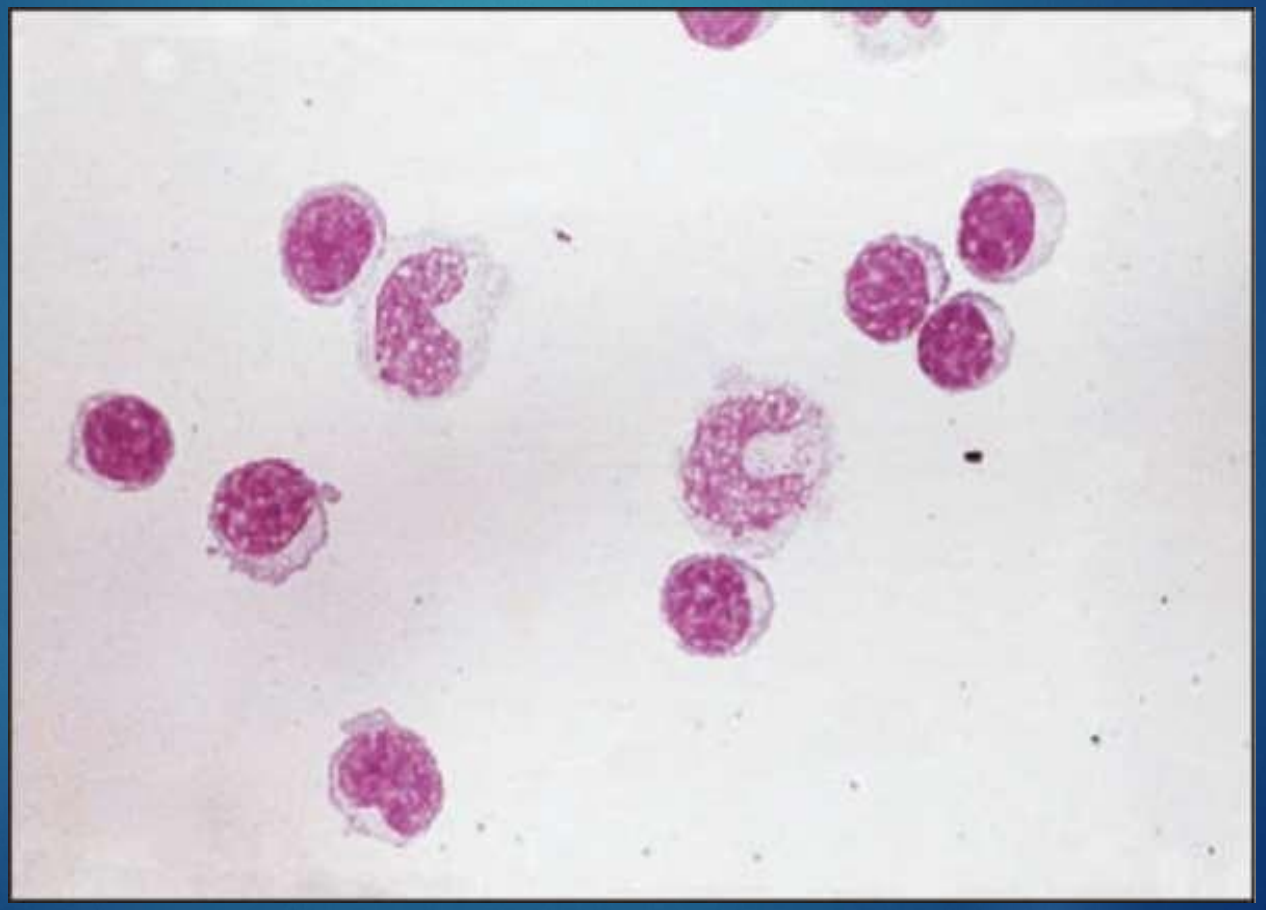
  Viral, tubercular, fungal, syphilitic, leptospiral, parasitic
- Degenerative disorders

  Subacute sclerosing panencephalitis, Multiple sclerosis, Drug abuse encephalopathy, Guillain Barre syndrome, Acute disseminated encephalomyelitis.
- Other inflammatory disorders

  Sarcoidosis, Polyneuritis, CNS periarteritis, Handl syndrome

CSF cytology

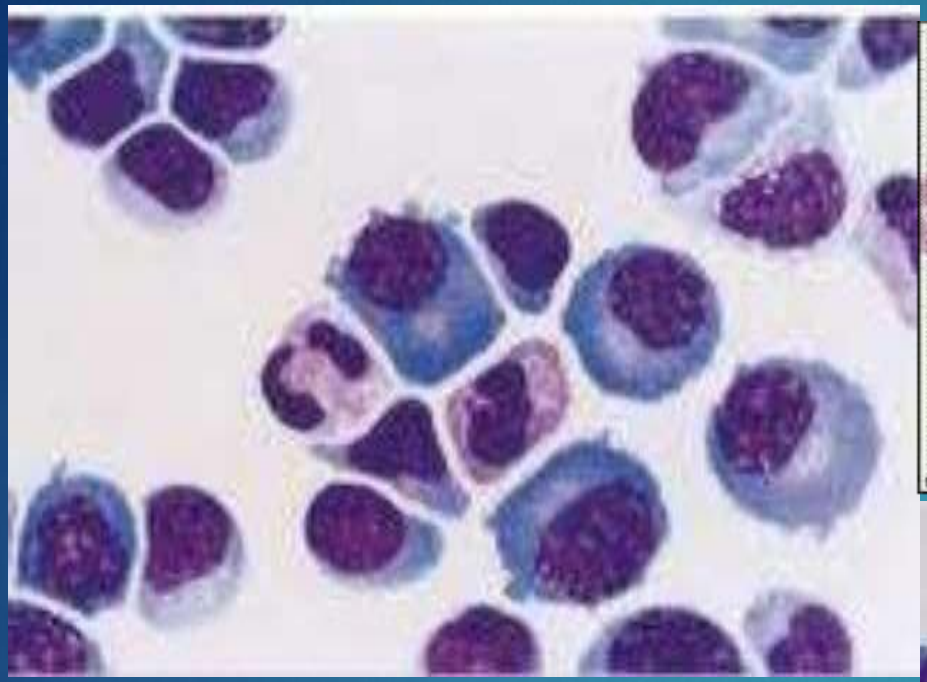
Lymphocyte to monocyte distribution ratio 70:30

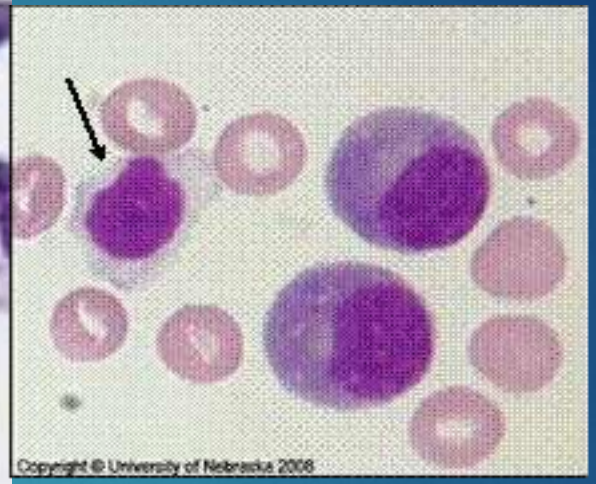


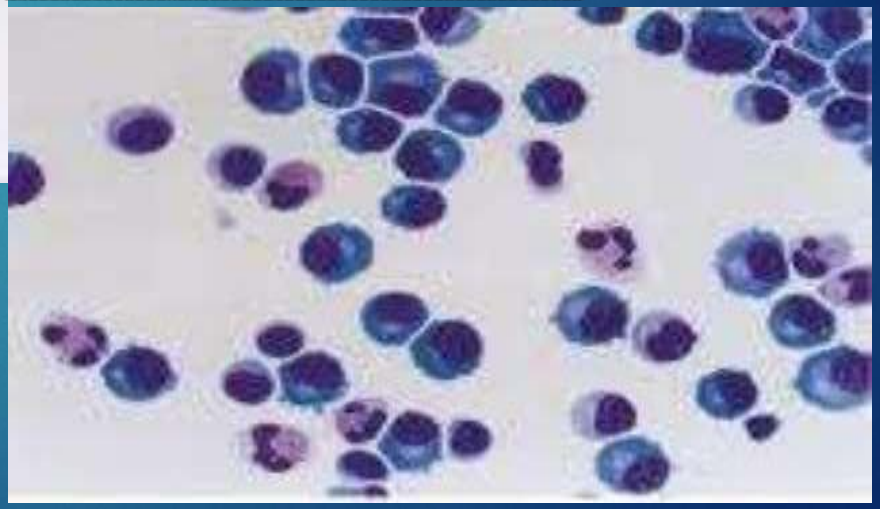
CSF Plasmacytosis

- Acute viral infections
- Guillain Barre syndrome
- Multiple sclerosis
- Parasitic CNS infections
- Sarcoidosis
- Tuberculous meningitis
- Subacute sclerosing panencephalitis
- Syphilitic meningoencephalitis
- Rarely, multiple myeloma

Plasma cells in CSF







CSF Eosinophillia

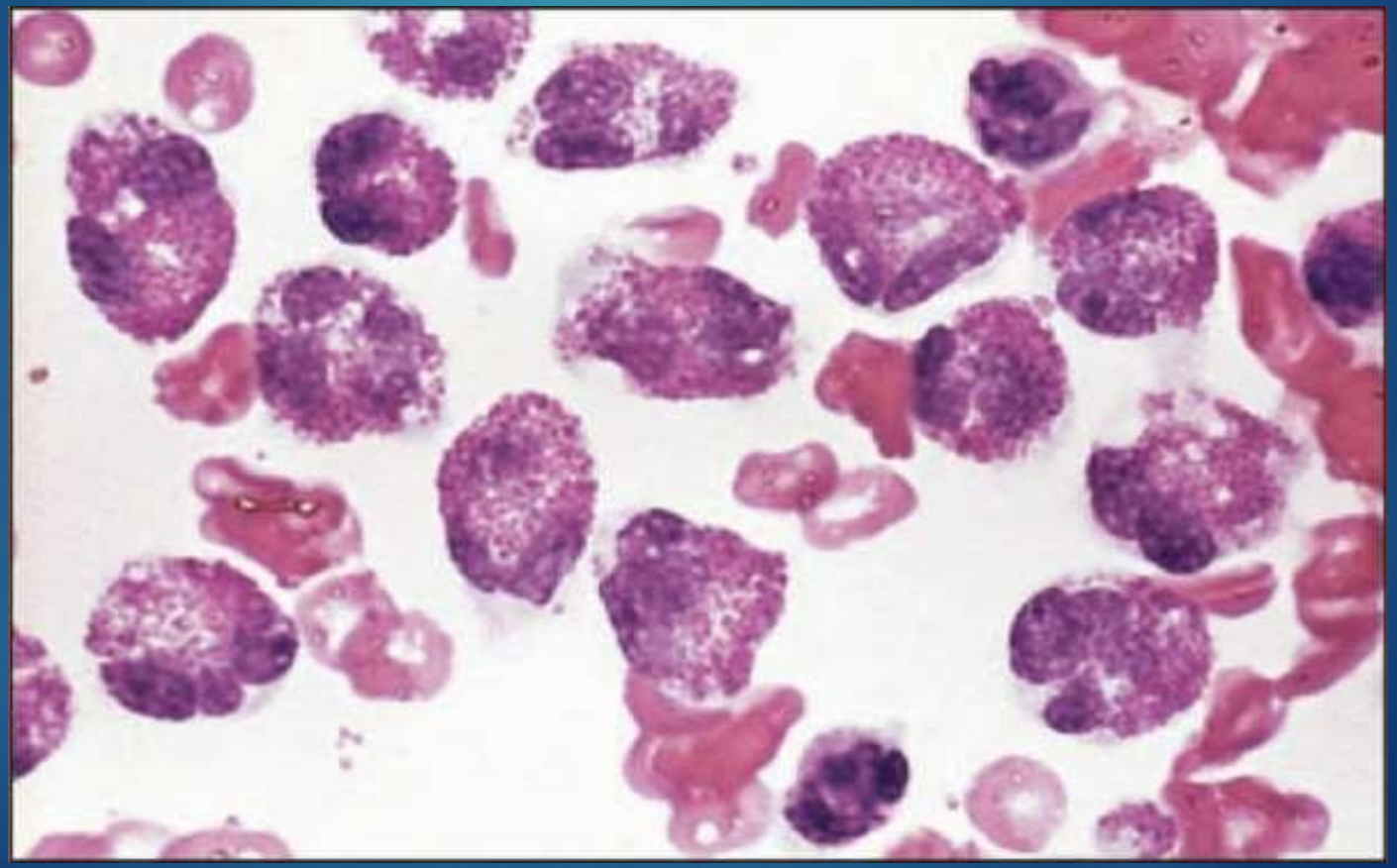
Commonly found in

- Post surgery
- Acute polyneurtis
- CNS reaction to foreign material
- Fungal infections
- Idiopathic hypereosinophillic syndrome
- Parasitic infections

Infrequently found in

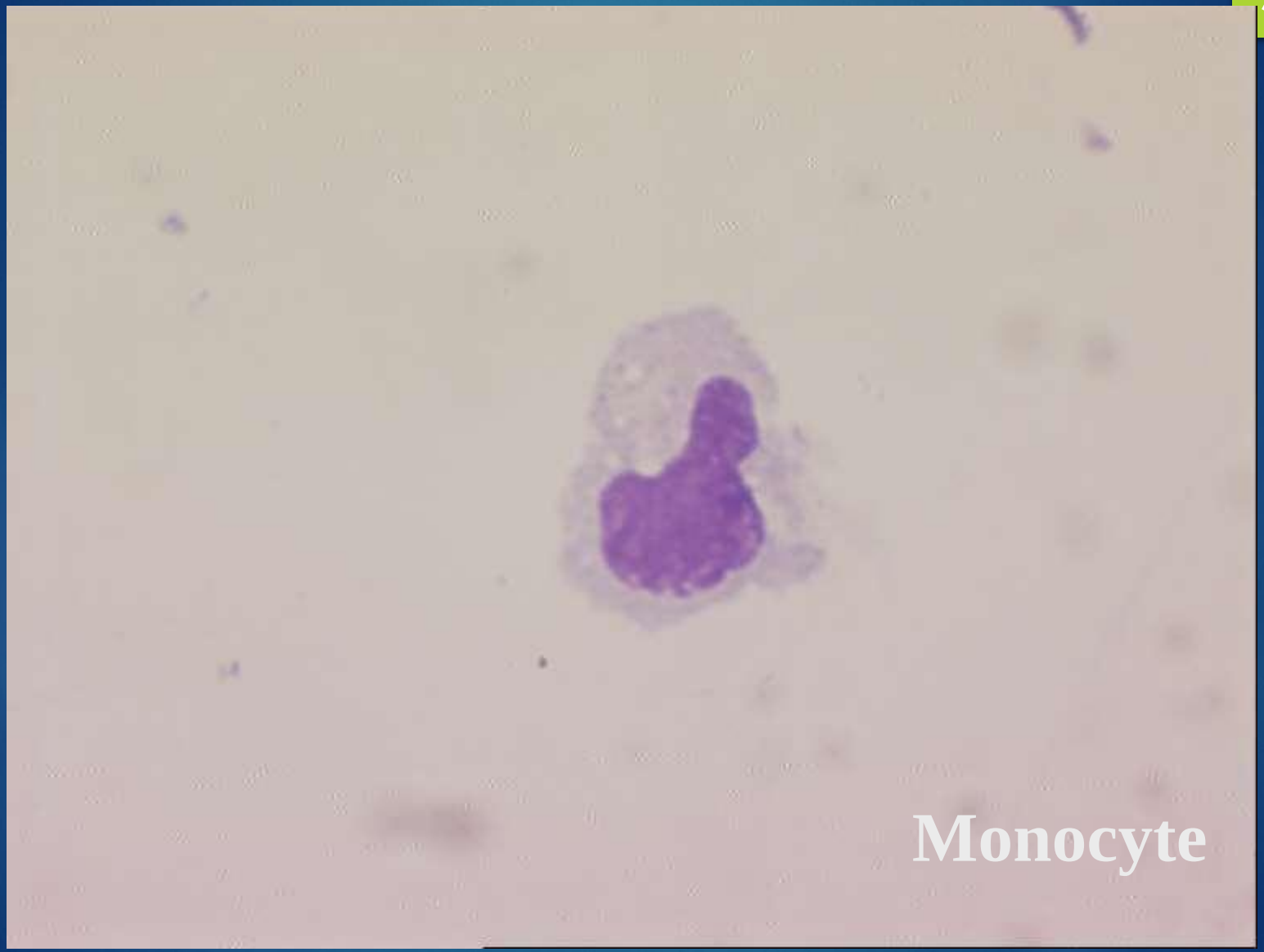
- Bacterial, viral and tubercular meningitis, Leukaemia, Lymphoma, Myeloproliferative disorders, Neurosarcoidosis, Primary brain tumours.

Eosinophils in CSF from a child with malfunctioning ventricular shunt



Increased CSF Monocytes

- They lack diagnostic specificity
- Are usually a part of mixed cell reaction that includes neutrophils, lymphocytes, and plasma cells
- Causes include: tuberculous and fungal meningitis, chronic bacterial meningitis, leptospiral meningitis, ruptured brain abscess, toxoplasma and amebic meningitis.

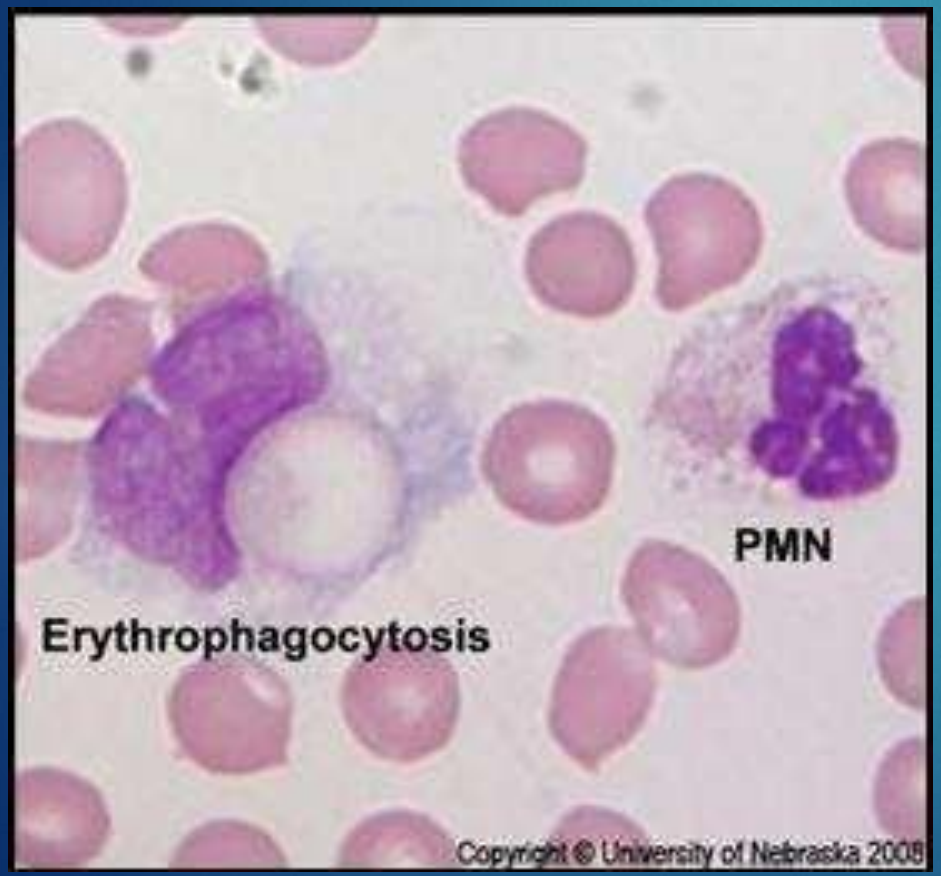


Monocyte

Macrophages

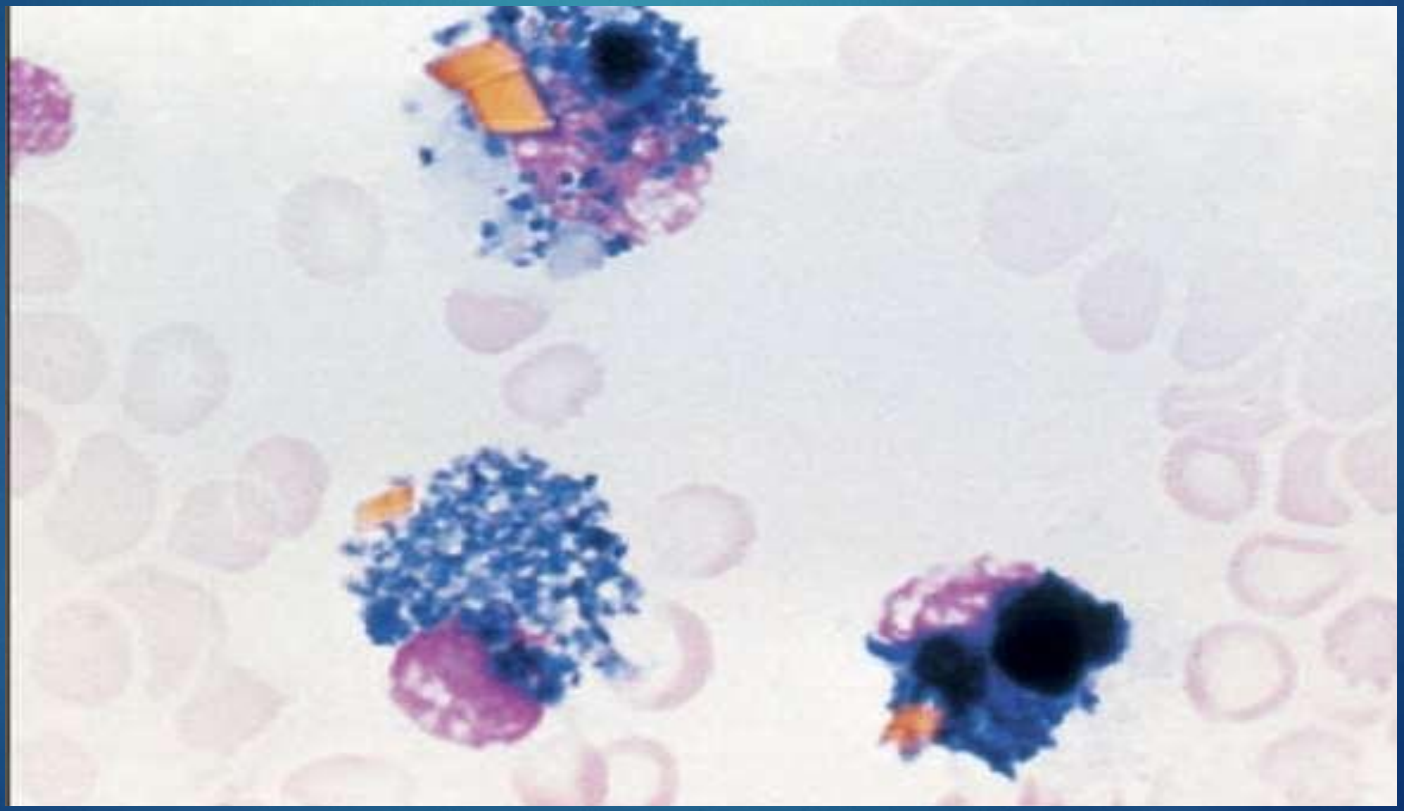
- Macrophages with phagocytosed erythocytes called as "erythrophages" appear from 12-48 hours following a subarachnoid hemorrhage or traumatic tap
- Hemosiderin laden macrophages called as "siderophages" appear after about 48 hours and may persist for weeks.
- Brownish yellow or red hematoidin crytals may form after a few days.

Erythrophagocytosis with a normal neutrophil



- It takes approximately twelve hours for histiocytes to mobilise and phagocytise erythrocytes after a hemorrhage.
- Erythrophagocytosis suggests intracranial hemorrhage, not a traumatic tap.

Hemosiderin laden macrophages (siderophages) from CSF of a patient with SAH Hemosiderin crystals(golden yellow) are also present.



Other Cells

- CSF examination for tumor cells has moderate sensitivity and high specificity.
- Amoebae, fungi (specially cryptococcus neoformans) and Toxoplasma gondii organisms are present in centrifuged specimens, but are difficult to identify without confirmatory stains.

Tumor cells in CSF

- CSF examination for leukemic patients has the highest specificity, followed by metastatic carcinoma and primary CNS malignancies.

Leukemia in CSF

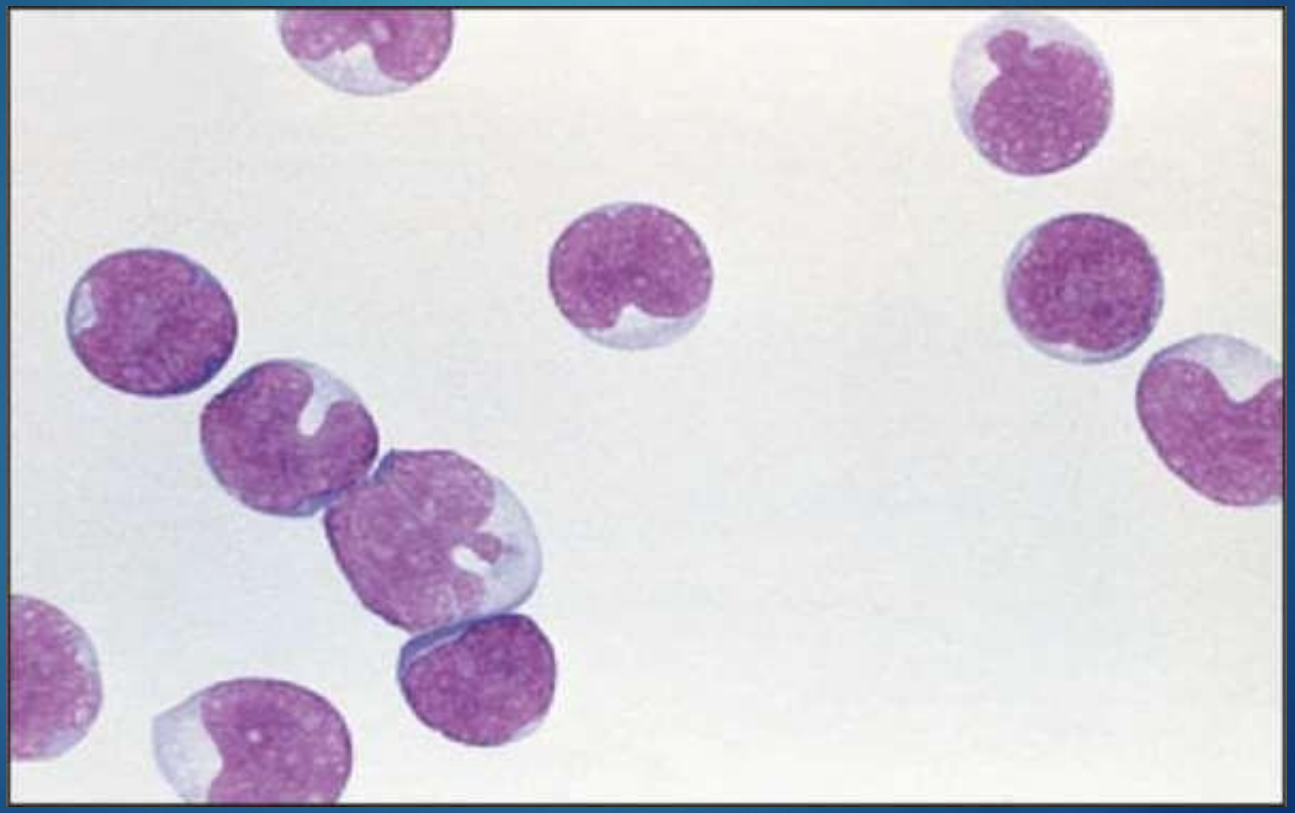
- Leukemic involvement of the tumors is more frequent in ALL than in AML.
- A leukocyte count over 5cells/uL with unequivocal lymphoblasts in centrifuged preparations is commonly accepted as evidence of CSF involvement.
- Lymphomatous involvement produces a very cellular smear which is composed of monomorphic appearing atypical lymphoid cells and calls for immunocytochemical studies and flow cytometry.

- Acute lymphoblastic leukaemia is the most common lymphoproliferative disorder involving the subarachnoid space in children. Diagnostic difficulties arise when there are only a few abnormal cells admixed with reactive lymphocytes in the CSF. IHC, including positivity for CD10, cALLA, CD22, kappa lambda and flow cytometric analysis are helpful.

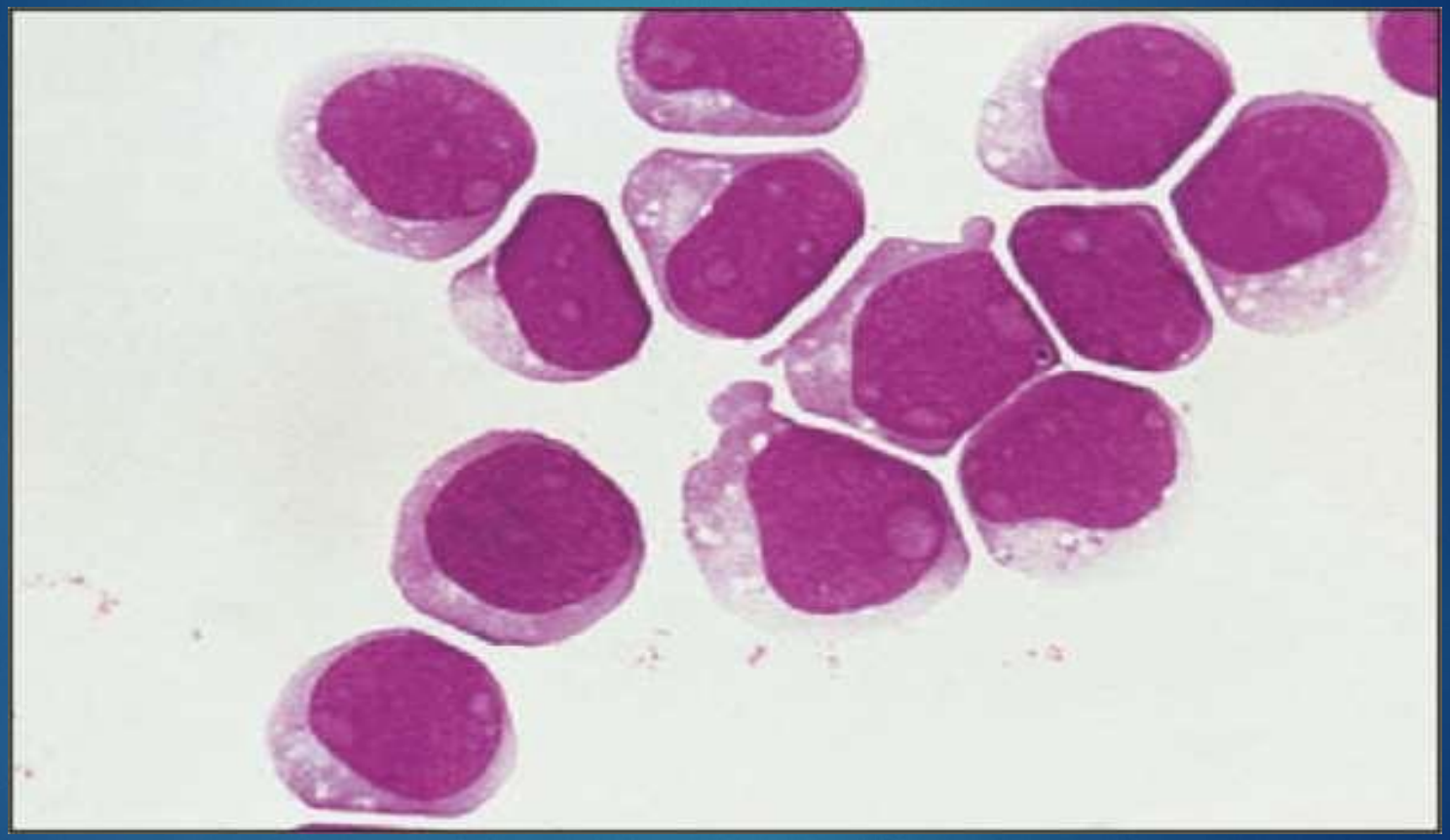
- Immature myloid cells or blasts can be identified in CSF. Blasts have generally large nuclei, irregular nuclear membranes, powdery chromatin, bizzarely shaped nucleoli and abnormal mitoses.

Acute lymphoblastic leukemia in CSF

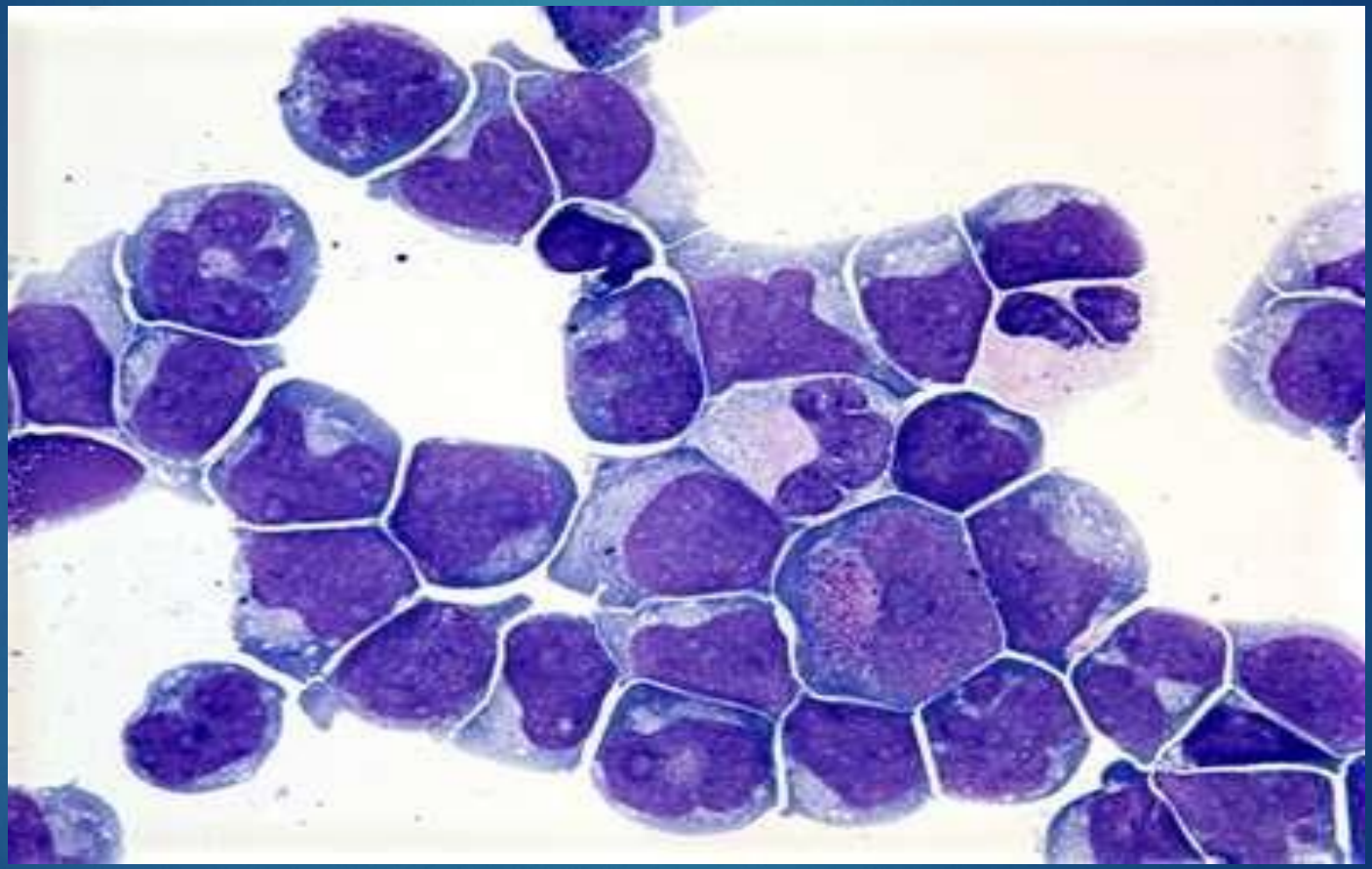
Note uniformity of the blast cells that have scant blue cytoplasm, fine chromatin and one or two nucleoli



Acute myeloblastic leukemia in CSF



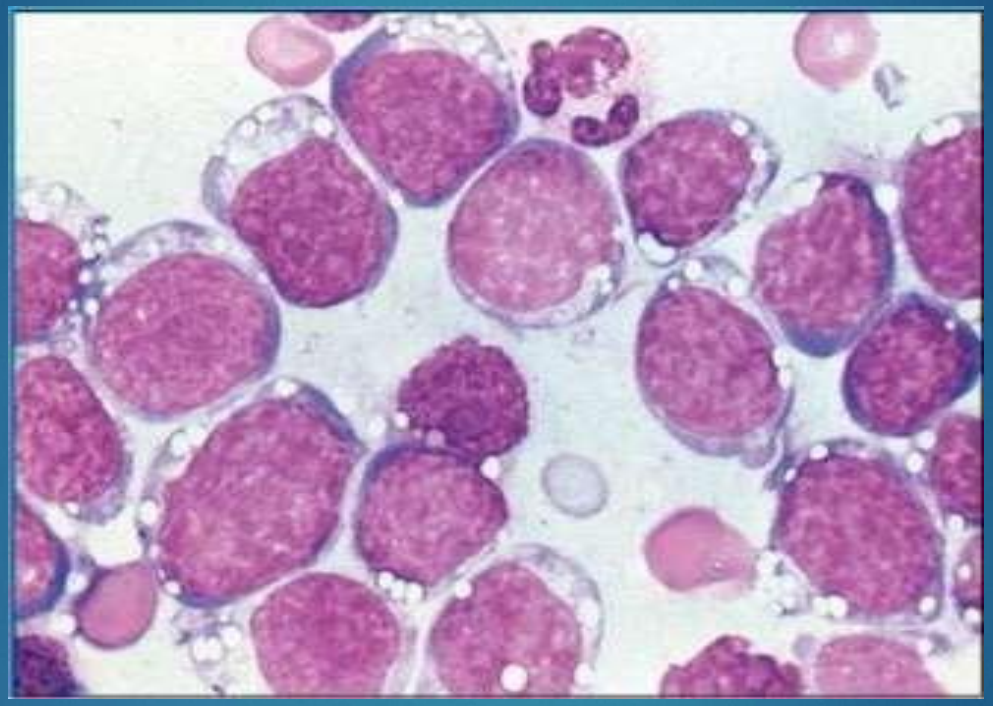
Leukemic cells in CSF



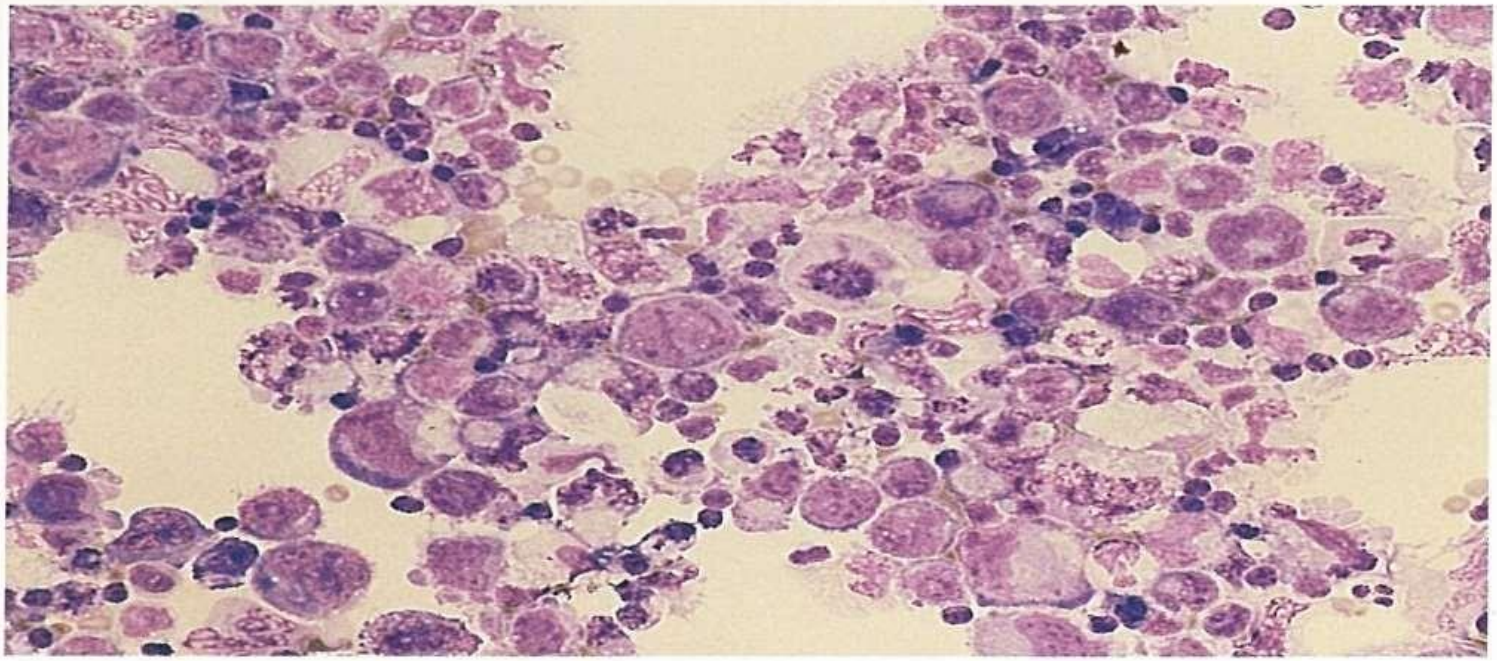
Lymphoma in CSF

- Non Hodjkin's lymphoma involving the leptomeninges are usually high grade tumors with prominent nucleoli and expresses a B- cell phenotype (CD20 and CD 79a positive)
  - Lymphoblastic
  - Large cell immunoblastic
  - Burkitt's lymphoma
- CSF cytology is of diagnostic value in only upto 30% of primary CNS lymphomas and 80% of systemic lymphomas involving the CNS. Therefore, differential diagnosis should always include lymphocytic pleocytosis, which can be due to radiation, chemotherapy and infections in immunosuppressed patients

Burkitt's lymphoma in CSF



The cells are characterized by blue cytoplasm with vacuoles and slightly clumped chromatin pattern.

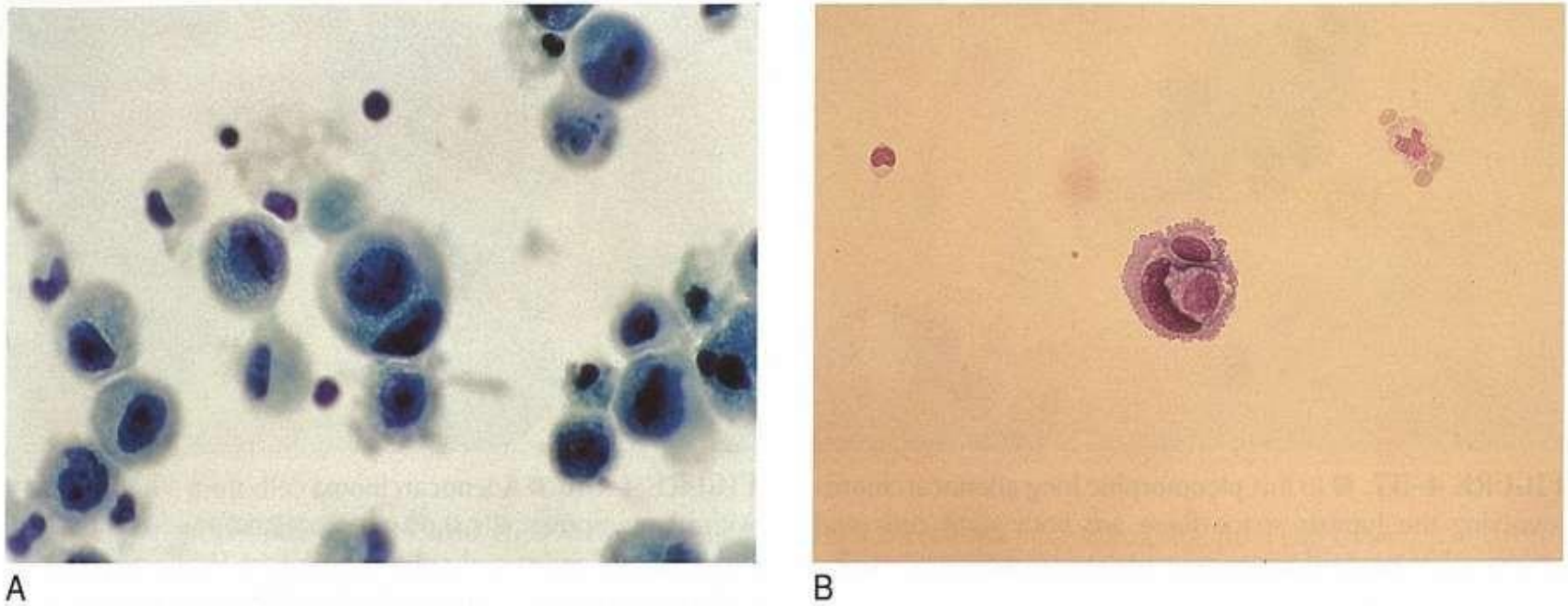


Primary brain lymphoma, large cell type, is seen here in CSF of a 54 year old man. B cell lymphomas are far more common than T cell type. The cells are large, pleomorphic, with brisk mitotic activity. Diagnosis was established by flow cytometry and immunophenotyping.

Metastatic tumors in CSF

- Metastasis represent half of the tumors found in CSF specimens.
- In adults, the most common malignancies to spread to CSF are in order of frequency: carcinoma of breast, lung and melanoma etc.
- Mostly the primary tumor is already known.
- Cells shed from these tumors have malignant cytologic appearance. They all have in common cells with a high nuclear to cytoplasmic ratio, irregular nuclei, coarse chromatin and nucleoli, with dense sharply defined cytoplasm.
- Immunocytochemical studies are warranted if the primary is unknown as they do not retain their morphological characteristics.

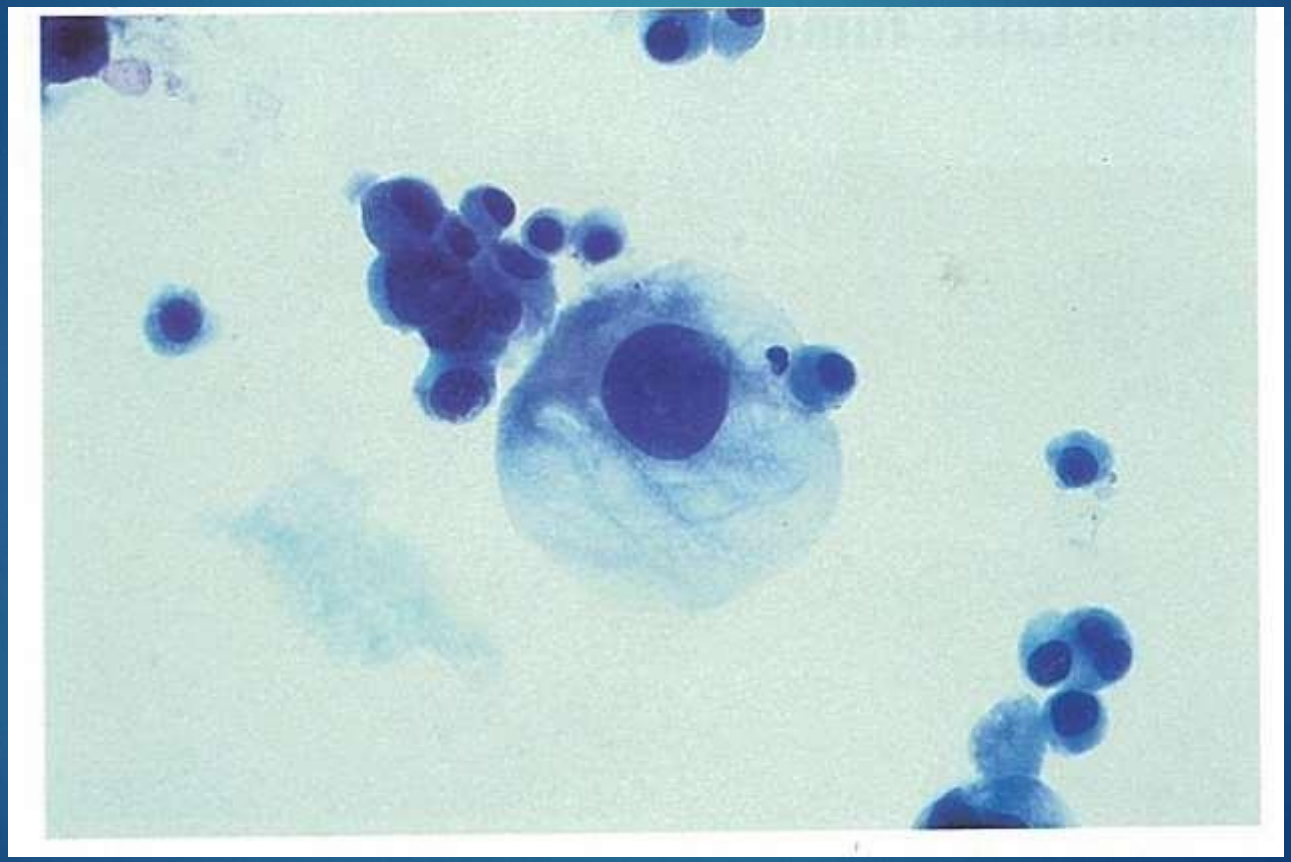
CSF, Breast carcinoma cells



A B

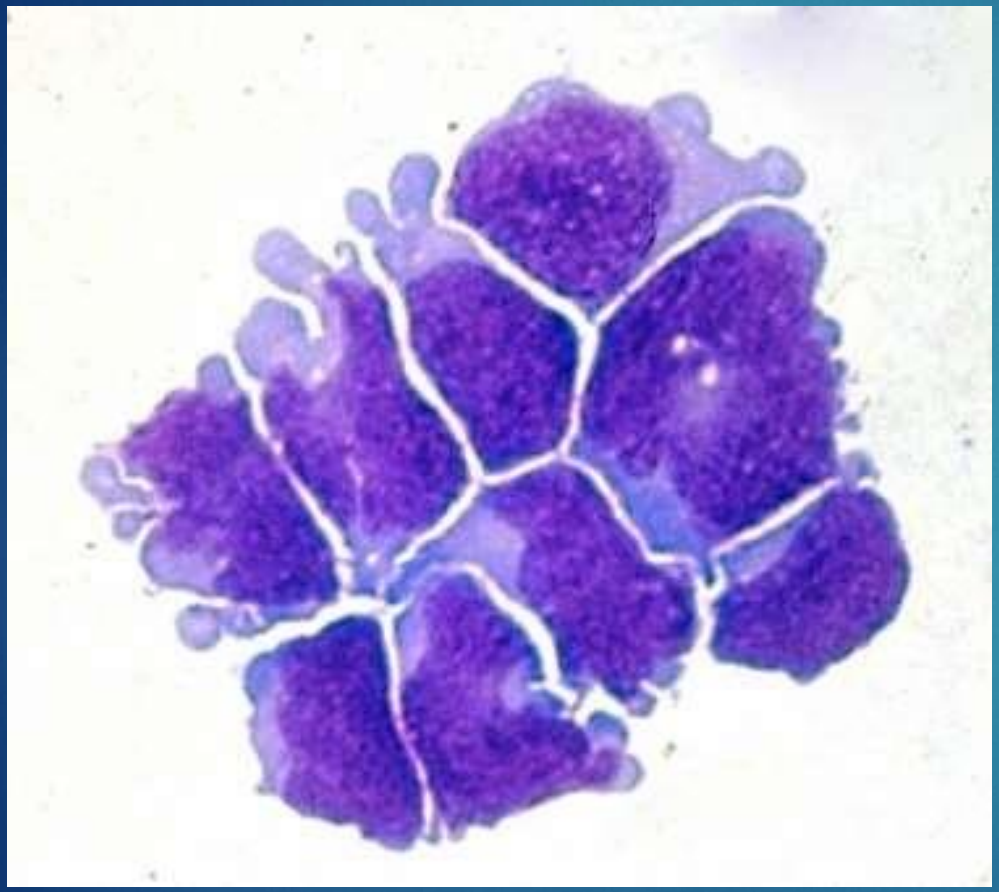
FIGURE 4–55 A and B. ■ This **breast carcinoma** metastatic to the subarachnoid space shows a classic cell-in-cell arrangement, betraying its epithelial nature **(A)**. The Diff-Quik stain underlines prominent cytoplasmic blebs, probably a degenerative change **(B)**. Compare the large size of the malignant cells to the adjacent red blood cells and monocytes (A: Papanicolaou stain, ×1000; B: Diff-Quik stain, ×400).

In this pleomorphic lung adenocarcinoma involving the lumbar space there are both giant cells and smaller plasmacytoid tumor cells.



Primary CNS tumors

- Primary CNS tumors form only10-20% of positive CSF specimens.
- High grade glioma in adults and medulloblastoma / PNET in children are the main tumors that lead to a positive CSF in patients who have a primary CNS neoplasm.
- In high grade glioma, tmor cells have meager, wispy cytoplasm and pleomorphic irregular nuclei with vesicular chromatin.
- Medulloblastoma are composed of small round blue cells arranged in clusters. These cells have scant basophillic cytoplasm, molded dark nuclei and inconspicuous nucleoli.
- However., clinical history and immunostains are required to avoid a diagnostic error.



Medulloblastoma. Cluster of tumor cells with characteristically lobulated nuclei and a thin rim of cytoplasm in the CSF.

Primary Brain Tumors

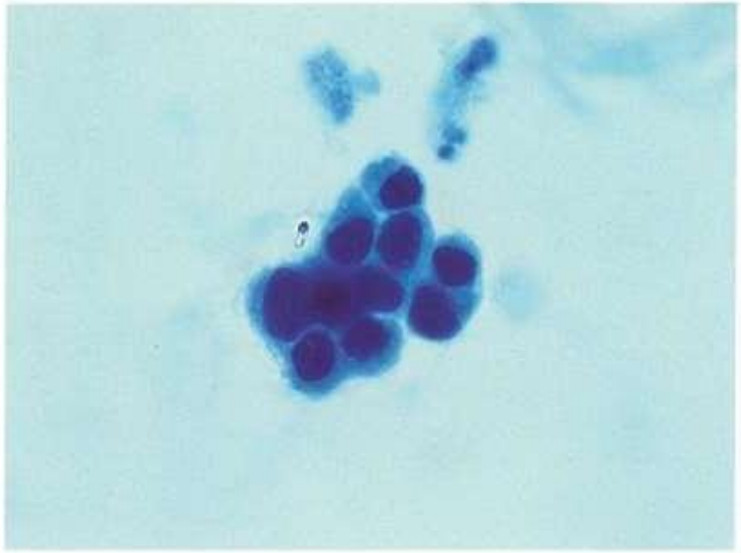


FIGURE 4–66. ■ This **medulloblastoma/primitive neuroectodermal tumor** was found in the cerebrospinal fluid of a 5-year-old child who had a posterior fossa brain tumor. The clinical presentation and the cohesiveness of the cells speak against a diagnosis of lymphoma/leukemia, another relatively common neoplasm in that age range (Papanicolaou stain, ×400).

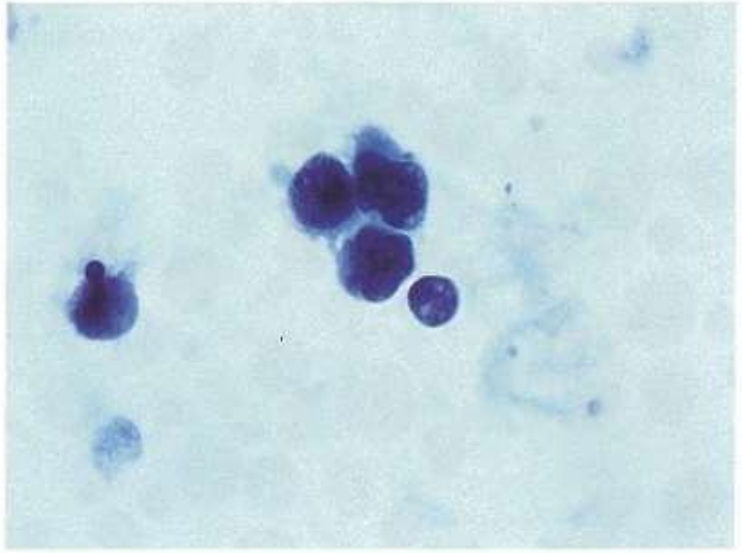
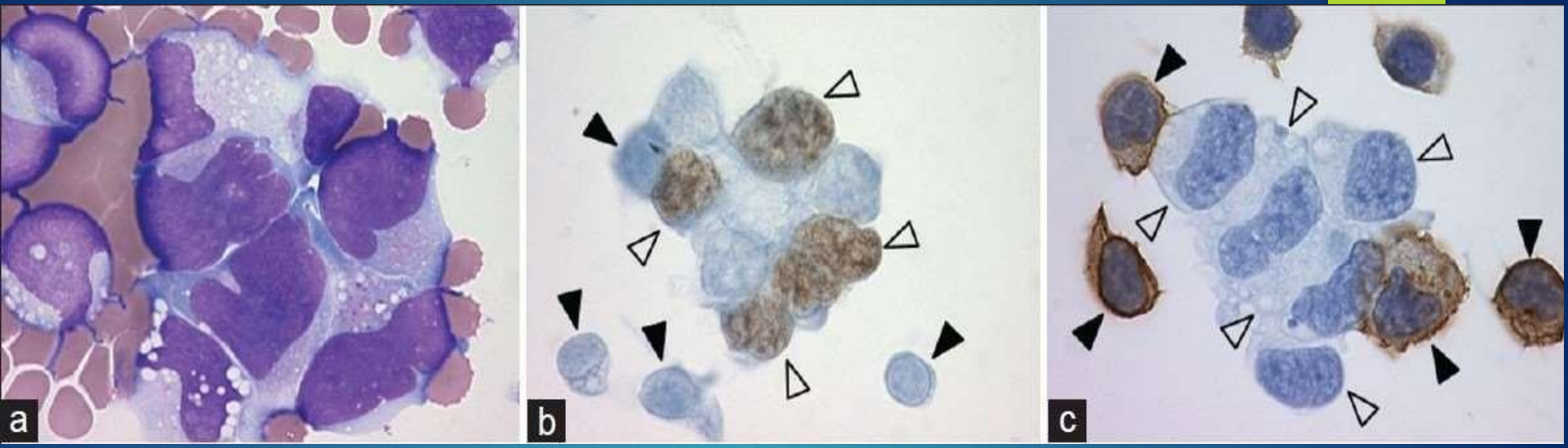


FIGURE 4–67. ■ **Pineoblastoma** (pineal PNET) was found in the cerebrospinal fluid from an 18-year-old young woman. No rosettes were identified (Papanicolaou stain, ×1000).

CSF tumor markers

- Carcinoembryonic antigen(CEA)
  Metastatic carcinoma of leptomeninges
- Human chorionic gonadotropin(HCG)
  Choriocarcinoma and malignant germ cell tumors with a trophoblastic component.
- Alpha fetoprotein
  Increased in germ cell tumors with yolk sac elements
- Elevation of CSF Ferittin is a sensitive indicator for CNS malignancy but has very low specificity.

Immunocytochemistry for cytokeartin shows strong cytoplasmic positivity in CSF sample from a case of ovarian carcinoma

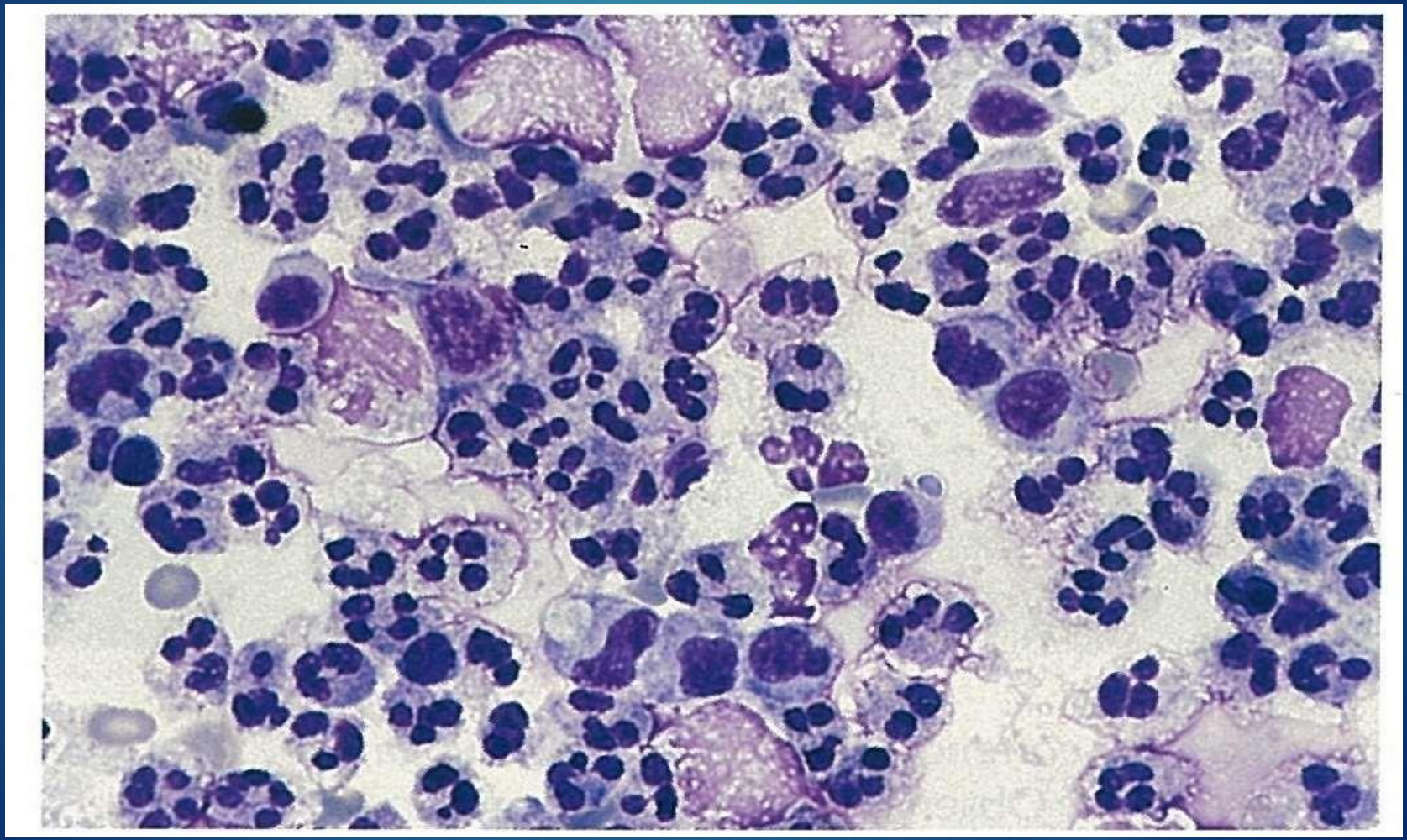


(a) May-Giemsa staining of the CSF sediment showing atypical cells, (b, c) Immunocytochemistry of the CSF sediment showing atypical cells (white arrowheads) with enlarged hyperchromatic delicate irregular nuclei that are positive for Olig2, (b) and negative for LCA (c), The surrounding lymphocytes (black arrowheads) are positive for LCA, (c) and negative for Olig2 (b) (100 × objective)

Bacterial Meningitis

- Usually diagnosed clinically.
- The fluid contains many acute inflammatory cells (>1,000 per mm^3), majority being neutrophil polymorphs.
- Cloudy and turbid CSF (if severe).
- Raised protein >1.5 g/L.
- Glucose level is <50% of the plasma level.
- May see organisms, eg Gram-negative diplococci in Neisseria meningitidis.

Numerous neutrophils are seen here in CSF sample of a 23 year old woman with bacterial meningitis.



Tuberculous meningitis

- Clear or slightly cloudy appearance
- Raised protein >1.5 g/L (much higher than bacterial meningitis).
- Glucose level is <50% of the plasma level.
- Cell count is high with a mixed pleocytosis and mainly lymphocytes (small and reactive).
- Rarely clumps of epithelioid cells and giant cells may be
  - seen.
- Sensitivity of CSF for acid fast stains is highly variable.

Tubercular meningitis

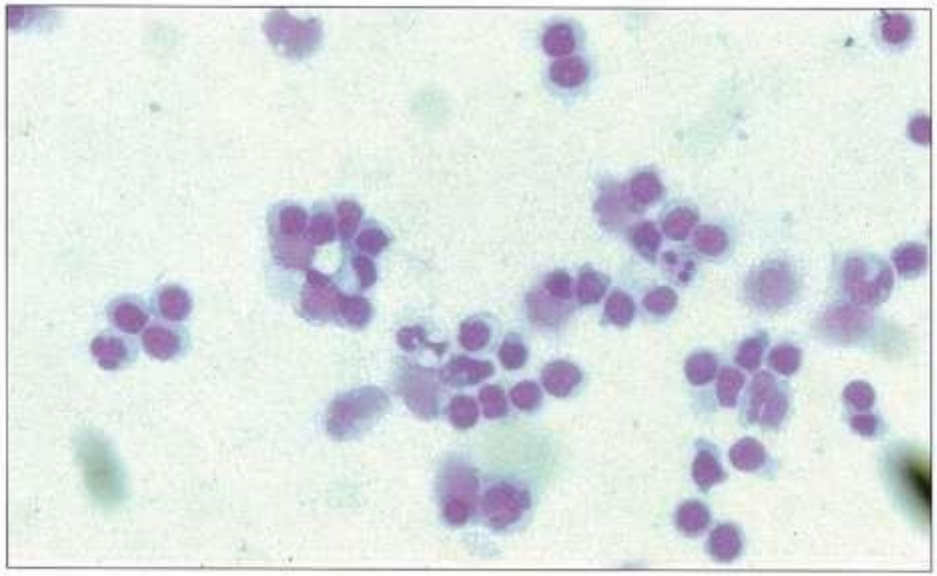


Fig. 18.12 Tuberculous meningitis – MGG x40. This CSF is another sample from the same patient as shown in **Figure 18.11** and illustrates a few neutrophils with abundant lymphocytes and a few monocytes.

Mixed cell reaction as seen in tubercular meningitis.

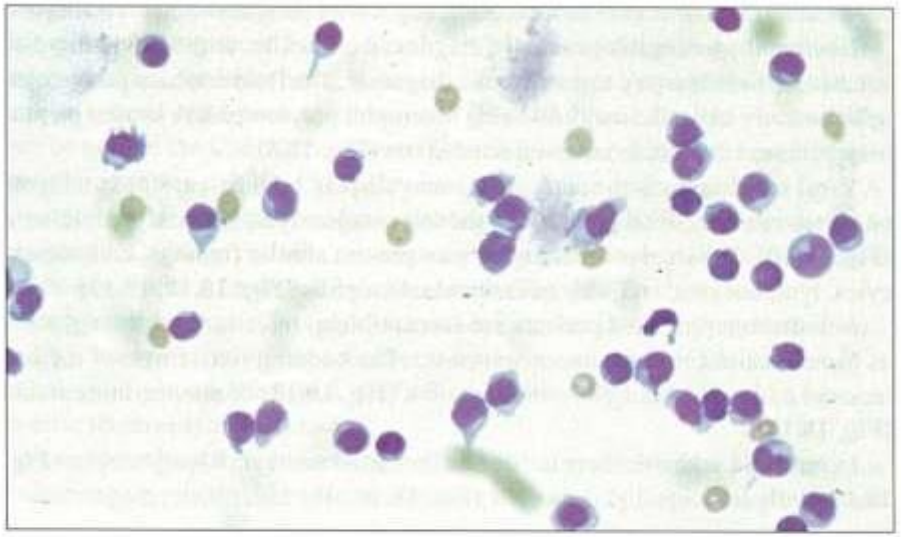


Fig. 18.11 Tuberculous meningitis – MGG x40. This CSF contains numerous lymphocytes and an occasional monocyte. A few neutrophils may also be seen in some cases. The appearances are not specific and should be interpreted in conjunction with the clinical details, and biochemical and bacteriological tests.

Viral meningitis

- Clear CSF.
- Protein is raised or at the high end of normal.
- Glucose level is usually within normal limits.
- Predominance of polymorphs can occur in the first 6 hours.
- Lymphocytosis with reactive lymphocytes and occasional plasma cell.
- IHC helpful in differentiation from lymphoma in atypical cells.
- No organisms usually and PCR or special stains may be needed to identify cause.

Reactive lymphocytes in CSF in viral meningitis

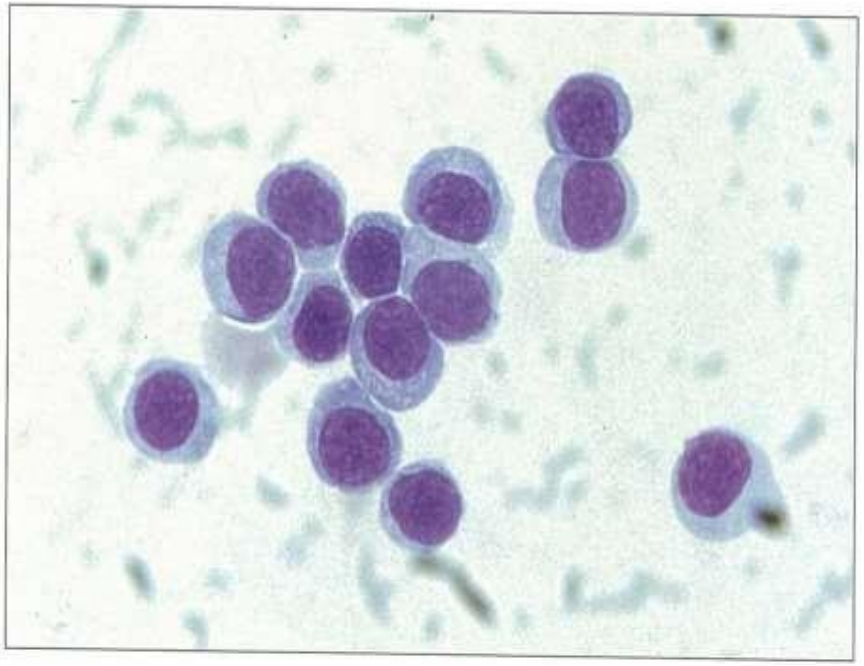


Fig. 18.6 Reactive lymphocytosis – MGG x100. These beautifully preserved lymphocytes have uniform hyperchromatic nuclei and a thin rim of cytoplasm. No specific features are visible.

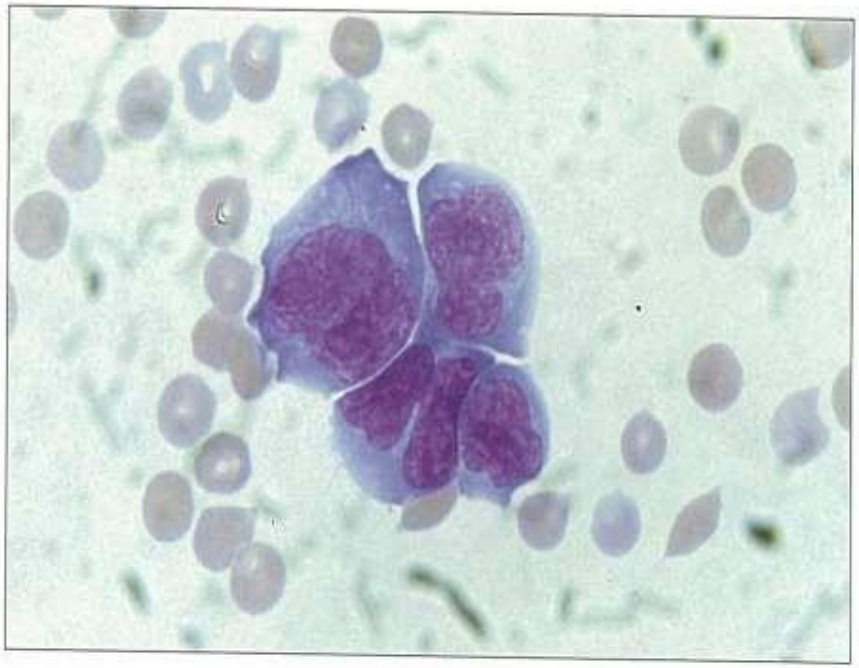
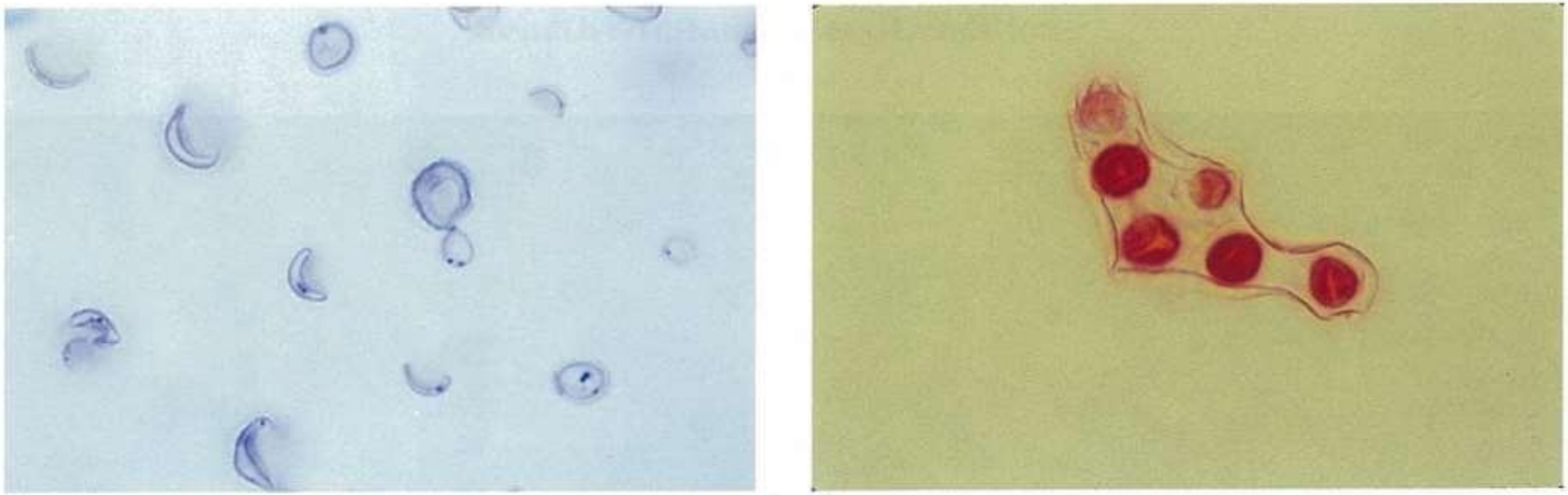


Fig. 18.7 Reactive lymphocytosis – MGG x100. The lymphocytes seen in this field show marked variability in nuclear size and shape. However, the next few samples examined showed a normal scanty population of lymphocytes and the patient became asymptomatic, suggesting that this was a reactive lymphocytosis.

Fungal meningitis

- Cryptococcus neoformans is the most common cause of chronic infectious meningitis in immunosupressed patients, but can also occur in immunocompetent patients.
- India ink or nigrosin stains show cryptococcus capsular halos.
- Lymphocytosis seen in CSF.
- Cryptococcal organisms demonstrated with MGG or PAP stains and confirmed with alcian blue or india blue stains.
- The organism may be intracellular in macrophages.

Meningeal cryptococcosis

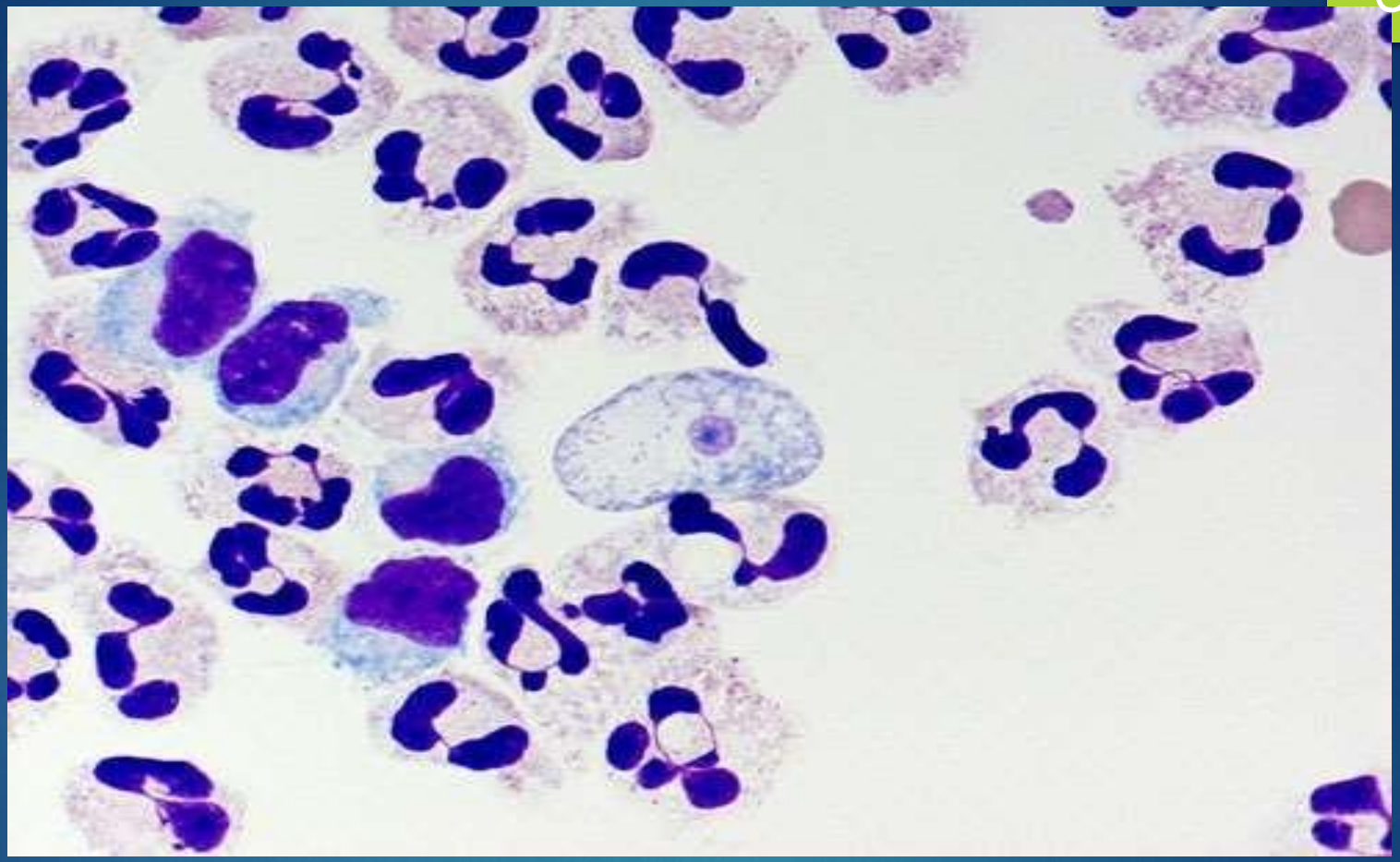


A B

FIGURE 4–54 A and B. ***Cryptococcus neoformans*** is the most common etiologic agent of fungal meningitis. It was found here in a 28-year-old HIV-positive patient. Observe the teardrop shape and narrow budding of the yeast forms in a clean background **(A)**. A mucicarmine stain highlights the thick capsule **(B)** (A: Papanicolaou stain, ×1000; B: mucin stain, ×1000).

Primary Amebic Meningoencephalitis

- Caused by Naegleria fowleri or Acanthamoeba species.
- Neutrophillic pleocytosis, decreased glucose levels, elevated protein concentration and presence of erythrocytes seen.
- Can be visualized by light, phase contrast microscopy in direct wet mounts.
- Also identified on Wright's or Giemsa- stained slides.
- Acridine orange stain is useful to differentiate ameba(brick red) from leukocytes(bright green)



A cytospin of CSF showing Naegleria fowleri trophozoite amidst polymorphonuclear leukocytes and a few lymphocytes.

HIV meningitis

A wide variety of CSF abnormalities are seen:

- Lymphocytic pleocytosis
- Elevated IgG indexes
- Oligoclonal bands
- Identifying opportunistic infections is the most important indication for examining CSF.
- Serious fungal infections may exist in the presence of little or no CSF parameter abnormalities.

CSF findings in meningitis

TEST	BACTERIAL	VIRAL	FUNGAL	TUBERCULOUS
PRESSURE	INCREASE	NORMAL	VARIABLE	VARIABLE
COUNT	>1000	<100	VARIABLE	VARIABLE
DIFFERENTIAL COUNT	NEUTROHIL	LYMPHOCYTE	LYMPHOCYTE	LYMPHOCYTE
PROTEIN	Mild↑	NORMAL	↑	↑
GLUCOSE	<40mg%	NORMAL	↓	↓
LACTATE	Mild↑	N-Mild↑	Mild-Mod ↑	Mild-Mod ↑


Thank You!