Bacterial meningitis: bacterial infection of the Leptomeninges.

- The most common cause of bacterial meningitis in neonates is B group streptococcus and Gram negative bacteria (E.coli and Citrobacter)-ampicillin and gentamycin or third generation cephalosporines. Citrobacter is associated with high incidence of multiple brain abscesses. The most common cause of bacterial meningitis in age group 3 months-5 years are H.influenzae and streptococcus pneumoniae-penecillinnes and third generation cephalosporines. The most common cause in older children and adults are strept. Pneumoniae and Neisseria meningitides-penecillinnes and cephalosporines. The most common cause of viral meningitis is enteroviruses (echo and Cocksakie viruses).
- The clinical picture depends on the age: neonates and children present with sepsis. Adults and old children (fever, headaches, vomiting, neck stiffness and decreased level of consciousness. Hemorrhagic rash in case of Neisseria meningitides). Patients should be started on high dose Abs and in the absence of increased ICP , LP should be performed (high protein, decreased glucose, pleocytosis. Neutrophils in thousands. In the presence of raised ICP start Abs and get CT head. Duration of treatment 10-14 days iv Abs.
- Individuals exposed to N.meningidites infection should be given Rifampicin for 3-5 days. Vaccines are available.
- Talk about TB meningitis (basal meningitis with multiple cranial nerve palsies and sometimes hydrocephalus) and
- Discuss the indications and contraindications of LP in CNS infections: LP is an important test in the diagnosis of meningitis and encephalitis. It is contraindicated in the presence signs of increased ICP due to space occupying lesion such as abscess, subdural and epidural empyema (papilloedema, decreased level of consciousness). If there is suspicion of SOL start Abs empirically and get CT head. The yield in brain abscess and subdural empyema is low < 20% while there is potential risk of herniation.

Brain abscess: 5% of intracranial masses. 44% occur in children younger than 15.

- **Bacteria** can reach the brain by the following routes;

1. From infected paranasal sinuses and mastoiditis (Osteomyelitis and bone destruction or retrograde thrombophlebitis). The most common organisms are streptococcus Melleri (microaerophylic or obligatory anaerobic Beta haemolytic streptococcus, normal inhabitant of mouth and upper respiratory tract), streptococcus pneumoniae and less commonly staph, bacteroids fragiles and gram negative bacteria. The abscess is localized to the temporal lobe or cerebellum in otogenic infection and to frontal lobe in frontal and ethmoid sinusitis. Sinuses develop between 5-15 years of age.
2. Haematogenous spread: multiple abscesses in MCA territory particularly in children with cyanotic heart disease (tetraogy of Fallot). Septic emboli containing streptococcus viridians, anaerobic strept, staph.
3. Direct inoculation (surgery or trauma): the most common pathogen is staph.
4. Postmeningitic abscesses: in neonates secondary to cortical vasculitis and venous infarction, usually multiple and periventricular.Bacteriology depends on the age as above. Citrobacter meningitis is associated with high incidence of brain abscesses (2/3 in one review)

The most common cause of brain abscess in patients with **AIDS is toxoplasma gondii**.

In old series no organism was found in25% (now a days this is rare because of the advanced techniques in culturing anaerobic and microaerophylic organisms)

- **Pathology** : 4 stages and 5 zones:

1. Early cerebritis: In the first 3 days after inoculation characterized by **infiltration** with WBCs, plasma cells and **early formation of necrotic center**. Hypodense on CT scan. Hyperintense on MRI (T2).**Minimal or no enhancement**.
2. Late cerebritis 3-9 days: rapid **expansion of the necrotic center** towards the ventricle, the necrotic center is surrounded by **a zone of fibroblast and foamy macrophages and neovascularity develops on the cortical side**. CT and MRI with contrast will show necrotic center and faint ring enhancement.
3. Early capsule formation (10-14): **4 zones** (**necrotic center**, **compact zone of inflammatory** cells, **reticulin net of mature collagen** and **zone of perivascular inflammatory infiltrate in the area of neovascularity**. MRI and CT scan show the classical appearance of necrotic center and ring enhancement
4. Late capsule stage > 2 weeks: mature fibrous capsule and **fifth zone of gliotic brain.** Antibiotics and steroids can affect this sequence (steroid may delay or stop capsule formation and Abs may result in resolution of the abscess at the stage of cerebritis).

- **Presentation**:

1. The classical triad of fever, headaches and focal deficit (depends on the location of the abscess is present in< 50% of patients. 45% has no fever. 25% develop seizures.
2. The clinical picture of the underlying disease: sinusitis, mastoiditis, OM etc…

- **Diagnosis**: CT with contrast or MRI with Gadolinium is diagnostic (ring enhancing mass with necrotic center and extensive surrounding oedema). Other tests –FBC, CRP, ESR, blood cultures. Differential diagnosis includes GBM, metastasis, fungal and parasitic, TB infections). LP carries the risk of herniation and has a low yield and should not be done. Look for a source of infection (ENT , dental opinion, blood cultures, cardiac echo)
- **Treatment options**:

1. *Surgical excision* + 6weeks of antibiotics: for single abscess in not eloquent brain, particularly in the presence of thick mature capsule. Theoretically removing the abscess capsule can speed recovery and potentially decrease the incidence of seizures and decrease the mass effect. On the other hand excising deep lesions and lesions ineloquent brain is associated with high neurological morbidity. Also there potential risk of bone flap infection.
2. *Stereotactic aspiration* repeated as needed + Abs for 6 weeks and frequent follow up scans is the treatment option of choice for most abscesses particularly deep ones and ones in eloquent brain. This is associated with similar cure rate as excision of abscess, less surgical morbidity , no bone flap infection, however often it has to be repeated and close clinical and radiological follow up are necessary
3. *Abs alone*: for patients diagnosed at the cerebritis stage and for multiple small **abscesses < 2.5 cm in diameter**. 74% success rate in 67 reported cases.

In addition elimination of the underlying cause (paranasal infection, mastoiditis, OM, dental infection and SBE) is of paramount importance. **The use of steroids is controversia**l. It may be indicated in patients with extensive oedema and increased ICP. If the abscess continues to enlarge despite appropriate treatment one has to exclude infected tumour cavity and biopsy of the wall should be done

Describe the long term sequelae after meningitis and brain abscess:

- Mortality from brain abscess has decreased from 85% in preantibiotic era to 5-15% in recent series. The most important 2 factors that influence the outcome are the neurological status at presentation and the age of the patient. The third factor is the location of the abscess (outcome is better for frontal and temporal polar abscesses than for deep abscesses)
    1. The mortality of those presenting in coma> 50% and all survivors will have permanent neurological deficit.
    2. 2/3 of children with brain abscess suffer learning disabilities and behavioral problems, 40% suffer epilepsy and 30% hemiparesis (Carey et al 1971).

- Long term sequelae of meningitis: learning disabilities, deafness, hydrocephalus.

Subdural empyema:

- SDE is a collection of pus in the subdural space (potential space between the dura and arachnoid which is continuous over the brain surface across the tentorium and with the spinal subdural space across foramen magnum).The source of infection and bacteriology is similar to brain abscesses:

1. Paranasal sinusitis, OM, mastoiditis: strept. Melleri, strept pneumoniae, staph.
2. Haematogenous infection from lungs, SBE, skin, dental infections. Strept. Melleri, strept pneumoniae, staph., gram negative bacteria (E.coli, pseudomonas)
3. Direct inoculation of the organism (postsurgical and traumatic)-staph .aureus
4. Postmeningitic: H influenzae (rare now a days). Many subdural collections in the context of meningitis are sterile (subdural effusions)

In old series no organism was found in25% (nowadays this is rare because of the advanced techniques in culturing anaerobic and microaerophylic organisms)

- Clinical presentations: clinical picture of the primary infection + headaches, decreased level of consciousness, focal deficit and seizures (**40% of patients develop seizure**s probably due to venous cortical infarctions).
- Diagnosis: CT with contrast (false negative in 12% in one review), MRI is superior (enhancing collection in the SD space, interhemispheric region, falcine region). FBC, ESR, CRP, blood cultures. Look for a source of infection (ENT, dental opinion, blood cultures, and cardiac echo).

- Treatment: Abs for at least 6weeks+ anticonvulsant(3 months in the absence of seizures and for 1-2 years if the patient presented with seizures+ emergency drainage of the pus through burr holes or craniotomy+ treatment of the underlying infection at the same time if possible or soon after the drainage.

- Burr- hole drainage vs. craniotomy: The largest series is from South Africa (no difference in the outcome between the 2 methods. Burr holes have the advantage of avoiding the risk of bone flap infection and can be repeated many times as needed with minimal morbidity. Its disadvantage is the inability to drain multilocular collection and interhemispheric and falcine collections. Craniotomy is indicated in draining multilocular collection, interhemispheric and falcine collections which can not be drained through burr holes. The theoretical risk of bone flap infection probably can be reduced by using osteoplastic flap.

- Mortality and neurological morbidity depends on the level of consciousness at presentation and the age. Mortality > 50% in those who present with coma and < 10% in those who are conscious. Higher mortality in infants and patients > 60 years of age.

Epidural abscess:

- **EA** is a collection of pus in the epidural space. In most reports EA is secondary to infection of paranasal sinuses, mastoiditis, orbit or skull. Congenital dermal sinuses, trauma and surgery are other causes. The spread of infection is either direct or through Thrombophlebitis. Haematogenous spread to epidural space is extremely rare.
- Patients may have swelling of the scalp from underlying osteomyelitis (Potts puffy tumour?). fever , headaches , and the symptoms of primary pathology
- Treatment includes (Abs for at least 6 weeks, drainage of the pus through craniotomy (bone flap can be replaced in primary epidural abscess. In cases of infected craniotomy flap the flap should be removed and delayed cranioplasty should be performed) and treatment of underlying condition. Better prognosis than SDE.
- Epidural abscess in the antibiotic era should carry minimal risk of mortality and neurological morbidity.
- **Gardenigo's** syndrome: apical petrositis and EDA (ipsilateral facial pain and 6th nerve palsy).

Discuss paranasal sinus infections and its relevance to CNS and skull infections:

- Paranasal sinuses develop at the age 5-15 years of age .Infection of paranasal sinuses, mastoid air cells are the most common cause of epidural abscess, subdural empyema and brain abscess in older children and young adults.
- In infection of frontal and ethmoid sinuses the abscess usually is the frontal lobe, SDE-interhemispheric and epidural abscess is frontal with scalp swelling (Potts puffy tumour). If the source of infection is mastoiditis the abscess is usually located in temporal lobe or cerebellum.
- Treatment of CNS infections secondary to sinus infections requires eradication of the source of infection (early ENT consult and intervention). Failure to do so results in persistent or recurrent infection.

Spinal epidural abscess: Infection of spinal epidural space with accumulation of pus or granulation tissue. In the past pyogenic spinal infections were classified as discitis, osteomyelitis and epidural abscess. In adults these three forms occur in combination in most cases. Pyogenic spinal infections are more common in immunocompromised, IVDU, diabetics, patients on steroids etc…

- The infection can reach the spine through the following routes:

1. Arterial embolisation from distant source (lung, heart, GU tract, skin etc…). Embolic occlusion of the metaphysical artery (end artery) results in necrosis of the vertebral end plate and the disc causing discitis and osteomyelitis of the adjacent vertebra. Retrograde thrombosis of basovertebral veins results in spread of the infection into the epidural space and causes epidural abscess -. In children the metaphyseal artery is not an end artery and its occlusion does not cause infarction of end plate and so infection can be localized to the disc space (discitis).
2. Transvenous route from GI and GU tracts through Batson's venous plexus.

3. Direct inoculation of bacteria at the time of epidural injections, LP, discography, surgery and trauma

- **Microbiology**: the most common cause is staph aureus and other gram positive cocci (staph. Epi, streptococcus Melleri, pneumoniae, viridans) gram positive rods (dephtheroids and proprniobacterium acnes). **In IVDU staph and pseudomonas**. Gram negative bacteria are less common cause.
- **Clinical presentations**: high index of suspicion is required. Patients present with low back pain increased at night associated with local tenderness and later fever, night sweats. If untreated **5-50%** develop neurological deficit (secondary **to mechanical compression of the cord by pus, kyphotic deformity or due to cord ischemia)**.
- **Diagnosis:**
    1. FBC, ESR, CRP, blood cultures (30-60% positive)
    2. MRI with gadolinium-enhancing epidural collection
    3. CT and plain films : good in showing bone involvement
    4. Bone scan(technetium-detects increased blood flow to infected area sensitive but not specific, Gallium- binds to iron binding proteins more specific to PSI and WBC scan (WBC tagged with radionuclide) is more specific for infection
    5. CT guided aspiration of infected disc space : positive in 50%
    6. Diagnosis of associated conditions (TOE, ENT, dental, MSU etc…

- Treatment options :

1. **Surgical draining of the epidural pus through anterior or posterior approach+ Abs** for at least 6 weeks. The presence of neurological deficit is an absolute indication for drainage. Other indications include radiological evidence of compression and liquid pus on MRI scan, failure of medical treatment (bone sequestrum) and to identify the causing organism if less invasive tests are negative. Patients should be followed closely clinically and radiologically. Delayed surgery may be indicated for instability.
2. Medical treatment: Abs + close clinical and radiological follow up for small epidural abscess without clinical or radiological evidence of cord compression particularly if the enhancement is diffuse and no evidence of liquid pus

- **Prognosis**: the prognosis depends on the presence or absence of neurological deficit, age of the patient and the presence or absence of sepsis. Patients who present with **incomplete deficit less than 72 hours duration and younger than 75 years of age have better outcome in one large serie**s. Complete deficit, sepsis and failure to improve after drainage may indicate poor prognosis

Spinal osteomyelitis: infection of the vertebrae usually part of pyogenic spinal infection including discitis and epidural abscess

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- **Clinical presentations**: high index of suspicion is required. Patients present with low back pain increased at night associated with local tenderness and later fever, night sweats.
- **Diagnosis:**
    1. FBC, ESR, CRP, blood cultures (30-60% positive)
    2. MRI with gadolinium-enhancing epidural collection
    7. CT and plain films : good in showing bone involvement
    8. Bone scan(technetium-detects increased blood flow to infected area sensitive but not specific, Gallium- binds to iron binding proteins more specific to PSI and WBC scan (WBC tagged with radionuclide) is more specific for infection
    9. CT guided aspiration of infected disc space : positive in 50%
    10. Diagnosis of associated conditions (TOE, ENT, dental, MSU etc…

1. Treatment options:
    1. Medical treatment: Abs and immobilization of the spine (bed rest, braces). In the absence of neurological deficit. Duration of Abs is at least 8 weeks
    2. Surgical: in the presence of neurological deficit due to epidural abscess or kyphotic deformity or instability. Surgery involves debridement of the necrotic bone and stabilisation The approach depends on the level of pathology (cervical-anterior approach corpectomy and cage graft and plates. Upper thoracic –costotransverse approach, lower thoracic-transthoracic intrapleural or extrapleural approach, lumbar-retroperitoneal approach.

TB osteomyelitis (Pott's disease):

1. Involves more than 1 vertebra.
2. Spares intervertebral disc
3. Most commonly involves lower thoracic or upper lumbar lesion and is associated with soft tissue mass (psoas abscess, cold abscess)
4. The onset is insidious and can be asymptomatic for months.
5. Treatment is medical in 90% of cases (antituberculous drugs for 1-2 years and immobilization. Surgery is indicated for cord compression and instability (rarely).

Discitis: discitis in children differs from that in adults

- Discitis in children is almost always **primary** and is due to
    A. **Haematogenous spread** of infection which lodges in the vascular disc or the metaphyseal artery which is not an end artery in children and has anastomosis with periosteal arteries. Occlusion of this artery will not lead to ischemic infarction and osteomyelitis as in adults, but leads to discitis. **The yield of disc aspiration in children is less than in adults**.
    B. It is controversial whether some cases of discitis are due to **trauma or viral infection** and do not require Abs.

The most common organisms are gram positive cocci (staph and strept.). Patients present with back pain, fever. CRP and ESR are elevated. Blood cultures are positive in 30%. MRI is diagnostic (Hyperintense signal on T2 and enhancement with contrast).CT scan is useful in assessing the bone which is usually spared in paediatric discitis. If no organisms are isolated it may be reasonable to treat children with immobilization and close observation. If infection is suspected or proved children should be given Abs for 6 weeks + bed rest and close clinical and radiological follow up.

- Discitis in adults is:
    1. Most commonly secondary to surgery (0.2-4% after discectomy) or less commonly discography (staph aureus or epidermidis). Patients present a few weeks after surgery with back pain and low grade temperature (after a period of improvement). CRP and ESR are elevated. Blood cultures can be positive in 30%.MRI is diagnostic and can exclude epidural collection. CT scan will show bone involvement. Treatment with immobilization and 6 weeks of antibiotics. Prognosis is excellent.
    2. Primary: due to haematogenous or venous spread of infection and is associated with vertebral osteomyelitis and epidural abscess. Usually in immunocompromised. Microbiology, diagnosis and treatment are similar to epidural abscess. Usually is apart of pyogenic spinal infection (discitis, osteomyelitis and epidural abscess).

Immobilization in spinal infections results in early improvement of pain and has no effect on the long term outcome.

Encephalitis: Acute inflammation of the brain.

I. Viral encephalitis is secondary to viral infection: over 100 viruses are reported to cause encephalitis. **The most common cause in western countries is Herpes simplex** virus 10% type 1 and occassionally type 2 (neonatal).**Worldwide arboviruses are the most common cause** of encephalitis. The following viruses are potential causes of viral encephalitis

A. **Viruses transmitted from human to human**: (herpes simplex 1,2, adenoviruses, varicela zoster virus, Epstein-Barr virus, CMV, enteroviruses, influenza A,B, parainfluensa, respiratory syncicial virus, rubella, mumps, hepatitis and human parvovirus, HIV).
B. **Viruses transmitted by mosquitoes and ticks** (Arboviruses such as Japanese encephalitis, California encephalitis etc..
C. Viruses transmitted by **animals** such as rabies

II.Postinfectiuos encephalitis: probably autoimmune mediated demyelination and neuronal injury following viral infections.

- Herpes simplex encephalitis affects 1 /2500 newborn. The inflammation and haemorrhage are localised to the medial temporal and orbital frontal lobes. Untreated the mortality is 70%.
- Presentations: personality changes, psychosis, decreased level of consciousness and seizures commonly difficult to control with medications.
- **Diagnosis**:

1. CSF-pleocytosis initially neutrophiles then monocytes, mildly elevated protein. Isolation of the virus from CSF in 15-50% and takes few weeks. PCR increases the diagnostic accuracy but can be falsely negative in 10-20%.
2. MRI- hyperintensity white matter, basal ganglia (T2 and FLAIR), hypointensity on T1 etc…In HS encephalitis the changes are localised to medial temporal and orbital frontal lobe
3. CT scan is useful in showing intracranial calcifications associated with some congenital viral infections (CMV).
4. SPECT is useful in differentiating toxoplasmosis abscess from lymphoma in patients with HIV infection
5. **Brain biopsy is the most definitive diagnostic test**. Sensitivity is 97% in diagnosing HS encephalitis. Biopsy is indicated if there is no response to treatment.
6. Antibody titres (CSF and blood) for specific infections. May take 14 days for the antibodies to develop.

- **Treatment**:

1. Acyclovir(**30mg/kg X 3** for 14-21 days) should be started immediately if the diagnosis of HS encephalitis is suspected
2. Supportive therapy (anticonvulsants, ventilation if necessary, N/G feeding etc…

- **Outcome:** The overall risk of death is **3-4**% and the risk of permanent neurological disability is **7-10**%. The outcome depends on the age and etiology. Children younger than 1 year has mortality as high as 40-50% in retrospective series. HSV carries the worst prognosis with mortality of 15-30% in children and

neurological morbidity of 50% (seizures, intellectual delay, psychiatric, visual and auditory dysfunction)

Discuss the spectrum of neurological conditions associated with herpes viral infections:

1. HS encephalitis: Greenberg 225
2. Multifocal varicella-zoster leukoencephalitis. Greenberg 227
3. Posherpetic neuralgia

Describe neurological complications of HIV infection: Greenberg 231-235.

I. Direct infection of CNS: AIDS encephalopathy, dementia, aseptic meningitis, cranial neuropathy, and myelitis and peripheral neuropathy.

II. Opportunistic infections:

A. Viral (atypical aseptic meningitis, HS encephalitis, Varicella zoster encephalitis, progressive multifocal leukoencephalopathy (papovavirus CJ)

B. Fungal(aspergillosis, cryptococcus neoformans and coccidiomycosis)

C. Parasitic: toxoplasma gondii; this is the most common cause of mass lesion and accounts for 70-80% of mass lesions.

D. Bacterial (Mycobacterium tuberculosi and avium intracellulare and treponema pallidum.

III. Neoplastic: primary CNS lymphoma (10% of mass lesions), systemic lymphoma with CNS mets and Kaposi sarcoma

IV. Vascular: vasculitis –stroke, ICH

The most common 4 mass lesions are

1. Toxoplasma abscess; multiple bilateral ring enhancing lesions with minimal edema (70-80%)
2. Primary CNS lymphoma; similar radiological appearance
3. Cryptococcal abscess ; single or multiple ring enhancing lesion
4. Progressive multifocal leukodystrophy: multiple hyperintense on T2 lesions with no edema or mass effect.

All HIV patients should have base line toxoplasma titres. If the titre rises start pyrimethamine and sulfadiazine empirically if no response in 2-3 weeks consider biopsy. CSF for cytology (10-25% can diagnose lymphoma-10 ml of CSF), Epstein virus PCR and SPECT can help to differentiate between Toxoplasmosis and lymphoma.

Discuss prion diseases affecting CNS. Clinical manifestation and infection control. Greenberg+:

Humans are susceptible to several prion diseases**:**

1. CJD**:** Creutzfeld-Jacob Disease
2. .GSS**:** Gerstmann-Straussler-Scheinker syndrome
3. FFI**:** Fatal familial Insomnia
4. Kuru
5. Alpers Syndrome

- A prion has been defined as "small proteinaceous infectious particles which resist inactivation by procedures that modify nucleic acids
- Visible end results at post-mortem are non-inflammatory lesions, vacuoles, amyloid protein deposits and astrogliosis**.(spongiform encephalopathy)**
- **GSS** is distinct from CJD, it occurs typically in the 4th-5th decade, characterised by cerebellar ataxia and concomitant motor problems, dementia less common and disease course lasts several years to death. (Originally thought to be familial, but now known to occur sporadically as well).
- **FFI** pathology is characterised by severe selective atrophy of the thalamus. **Alpers syndrome** is the name given to prion diseases in infants.
- **Kuru** is the condition which first brought prion diseases to prominence in the 1950s. Found in geographically isolated tribes in the Fore highlands of New Guinea. Established that ingesting brain tissue of dead relatives for religious reasons was likely to be the route of transmission. They ground up the brain into a pale grey soup, heated it and ate it. Clinically, the disease resembles CJD. Other tribes in the vicinity with same religious habit did not develop the disease. It is speculated that at some point in the past a tribe member developed CJD, and as brain tissue is highly infectious this allowed the disease to spread. Afflicted tribes were encouraged not to ingest brain tissue and the incidence of disease rapidly declined and is now almost unknown

Humans might be infected by prions in 2 ways:

1. Acquired infection (diet and following medical procedures such as surgery, growth hormone injections, and corneal transplants)
2. Apparent hereditary Mendelian transmission where it is an autosomal dominant trait.

- Prophylaxis: Institutional practices vary but disposable instruments should be used on a known/suspected CJD case or

the non-disposable instruments should be quarantined until CJD can be excluded with certainty.

Discuss the role for biopsy in prion disease:

- There is no treatment fro Creutzfeldt- Jakob disease and biopsy carries the risk of iatrogenic transmission (instrument contamination). If the diagnosis of CJD is strongly suspected biopsy is not indicated.
- Biopsy is indicated for dementia of possible vasculitis, encephalitis origin. If CJD is one of the differentials, all instruments should be quarantined and sterilization should follow special protocol.

Discuss the various causes of immunocompromise:

- Congenital:???
- Acquired:

1. AIDS.
2. Organ transplantation and immunosuppressants
3. SLE, RA patients receiving immunosuppressants or steroids.
4. Chemotherapy
5. Leukemia, lymphoma

Fungal infections of CNS

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1. **Aspergillosis**: caused by **aspergilla fumigatus**. Route of entry is **respiratory.** Systemic (haematogenous or through sinuses). Infection develops in immunocompromised. CNS involvement in the form of meningitis, brain abscess and spinal abscess. **Definitive diagnosis** is by **culturing the organism from CSF** or pus (takes few weeks). MRI. CT scan demonstrates abscess w/wo enhancement.This infection is difficult to eradicate. Large abscess should be excised. Primary Ab is **amphotericin B** (Large dose 4gr/d for several months).
2. **Blastomycosis**: entry through respiratory system. CNS involvement in the form of meningitis and multiple abscesses. Diagnosis by **10% KOH wet preparations** of the pus –dimorphic fungi. Treatment with amphotericin B.

3. **Cryptococcosis**; is caused by **Cryptococcus neoformans** found in droppings of birds. The respiratory tract is the usual route of entry. The most common clinical presentations are meningitis, encephalitis and abscess and cryptoccoma (mutinous pseudo cyst). Can affect immunocompromised and immunocompotenet patients. CSF-pleocytosis (mono), increased protein, decreased glucose. Cryptococcus can be identified in CSF USING **India ink stains in 50**% and with **latex agglutination cryptococcal Ag** can be identified **in 95%.** Untreated the infection is fatal within few months. Treatment is with **amphotericin B** and **flucytosine**.

Response rate is 70% in immunocompotenet patients. Poor prognosis in AIDS patients. Meningitis can result in raised ICP with and without hydrocephalus.

4. **Candidiasis** is caused by candida albicans (normal inhabitant of oral GI and vaginal mucosa). Involvement of CNS is by haematogenous spread in immunocompromised. CNS involvement in the form of meningitis and multiple brain abscesses. Definitive diagnosis made by biopsy. The standard treatment is **amphotericin** and **flucytosin**e (recovery rate 88-100%)
5. **Nocardiasis**; (soil born actinomycosis- fungus like bacteria and not fungus) is caused by **nocardia asteroids** found in the soil. Route of entry is through respiratory system. CNS involvement through haematogenous spread (meningitis and multiple brain abscesses). Diagnosis is made by biopsy (**gram positive branching beaded filaments**. Surgical resection of the abscess is necessary because of low response rate to medical treatment (**cotrimoxazole with trimethoprim)**
6. **Others:** histplasmosis, cocidiomycosis, mucormycosis.

Look also Greenberg.

Parasitic infections of CNS:

1. Cysticercosis: infection caused by the larval form of pork tapeworm (Taenia solium). The human is the definite host harboring the adult worm (the pig is the usual intermediate host). Proglattids containing ova are excreted with the feces. Infection occurs when human becomes intermediate host by ingesting food contaminated with ova. Oncospheres (larva) are released and spread to CNS, muscles and eye through haematogenous route. The larva entering the CNS forms cysts. There are 2 forms of parenchymal infection:

A. Cysticercosis cellulare: parenchymal cyst or cysts containing viable larva. Initially the cyst is not enhancing, and not surrounded by oedema (as long as the larva is alive) inflammatory changes around the cyst result in ring enhancement eventually the cyst wall calcifies. The larval life span is 7-10 year. Death of the larva may result in cyst expansion (loss of osmotic regulation)

B. Cysticercosis recemosus: large (4-12 cm) intraventricular and cisternal cysts with grape like multiple daughter cysts that eventually calcify.

- The disease has the following phases:

a. Vesicular: Live larvum with scolex, fluid filled bladder, thin capsule, no inflammation
b. Colloidal Vesicular: Larval death, cyst degenerates, capsule swells, inflammation and oedema
c. Granular nodular: Capsule thickens further, early calcified scolex, oedema diminishing
d. Nodular calcified: Complete calcification of the granuloma. No oedema

Diagnosis is made by radiology and serology (cysticercosis Abs by ELISA). Surgery is rarely indicated to relieve mass effect (spinal), hydrocephalus and for diagnosis. Treatment is with **paraziquantil or albendazole**. (May be followed by exacerbation secondary to inflammatory reaction to dead parasite which can be minimized by giving steroids)

2. **Toxoplasmosis**: is caused by **toxoplasma gondii**, an **obligatory intracellular parasite**. The **cat** is the definite host. Humans are infected by ingestion of contaminated meat and with contact with cats. Oocytes (**eggs)** are excreted with cat's feces. **Sporozoites** released from the eggs cross the bowel wall spread haematiogenously and form **trophozoites** which enter the infected cell causing its death and inflammatory Granulomatous reaction. CNS involvement in the form of meningitis and single or multiple brain abscesses usually in immunocompromised patients.. This is the most common cause of brain abscess in AIDS patients. Diagnosis is made by rising titers of Ig M (95% of adults are positive to Ig M) and positive Ig A. Treatment is by **pyrimethamine** and **sulfadiazine** AND CLINDAMYCIN. If no response consider biopsy to exclude lymphoma.

3. **Amoebic brain abscess**: is caused by **entamoebia histolytica**, the organism causing intestinal amoebiasis. CNS involvement in the form of multiple brain abscesses through haematogenous spread is rare. Diagnosis is made by serological tests and PCR of the aspirate. Treatment is by **metronidazo**le and aspiration of large abscesses.

4. **Echinococcosis** (hydrated cyst): is caused by **Echinococcus granulosus**. Canines are the definite host (harboring the adult worms). Sheep, cattle are the usual intermediate host (larval stage). Human is infected by ingestion of egg contaminated food (from soil). The larval stage spreads to liver, lung and CNS. CNS involvement is in the form of cyst that can be monolocular or multilocular. The cyst contains fluid with CSF density at high pressure and daughter cysts (grape like) and has germinal white cheesy layer, capsule and surrounded by inflammatory reaction. Diagnosis is made by serology. Treatment is surgical excision of the cyst without spilling the contents to prevent dissemination; alternatively the cysts can be injected with **20% saline to kill the scolices**. Albendazole is an alternative for disseminated disease.

Shunt infections: look up paediatric section