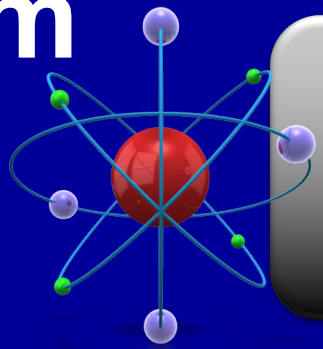
INFECTIONS OF THE NERVOUS SYSTEM

Prof. M. Gavriliuc

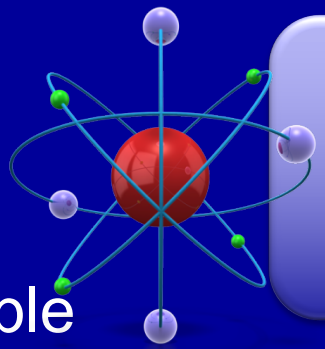
Infections of the nervous system



EARLY RECOGNITION!!!

Are among the most important problems in medicine.

May present with a nonspecific prodrome of fever and headache until altered consciousness, focal neurologic signs, or seizures appear.

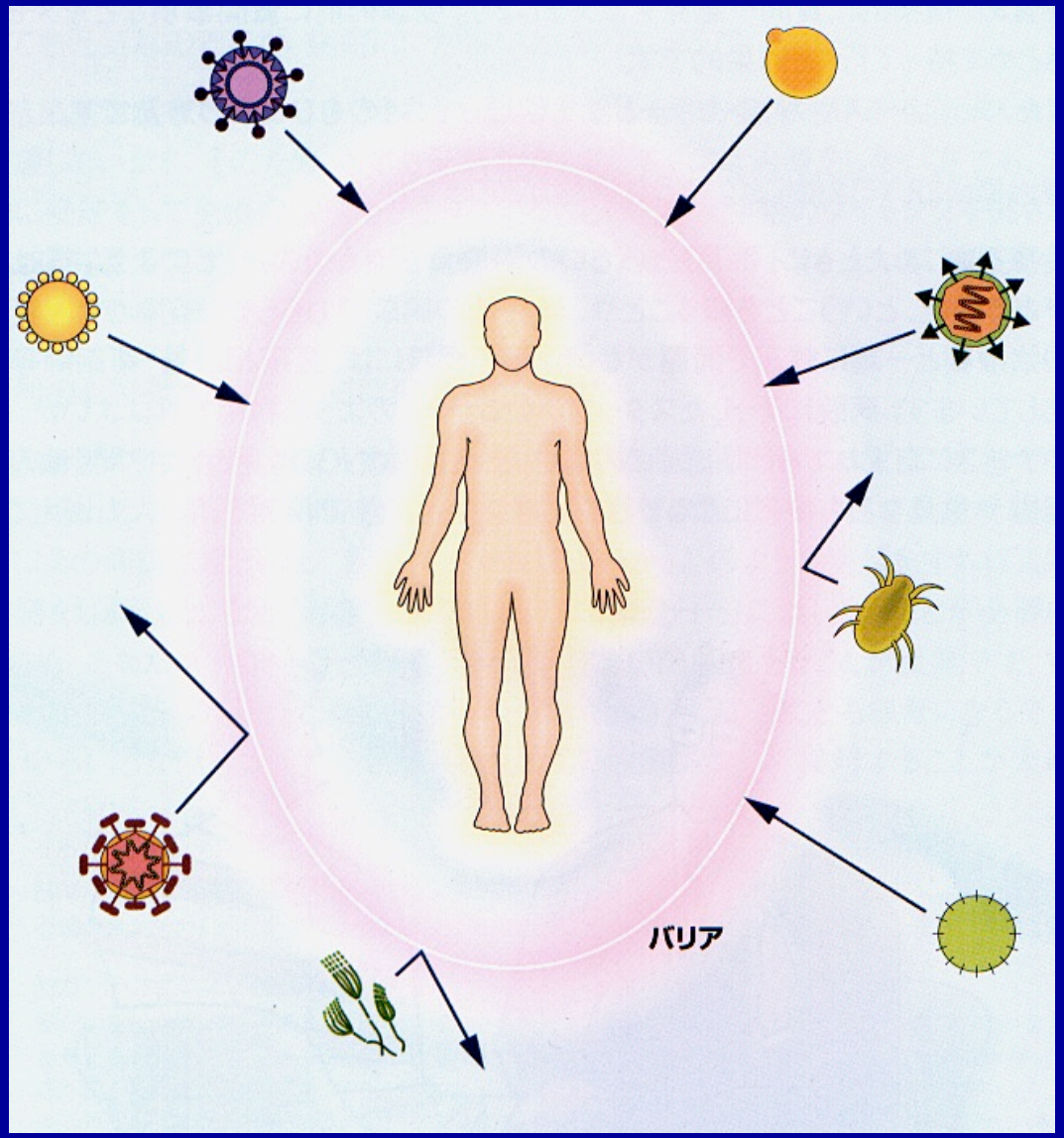


RAPID THERAPY!!!

Key goals of early management are to emergently distinguish the disease, identify the responsible pathogen, and initiate appropriate therapy.

INFECTIONS OF THE NERVOUS SYSTEM

The immediate effect of bacteria or other microorganisms in the subarachnoid space is to cause an inflammatory reaction in the pia and arachnoid, in the cerebrospinal fluid (CSF), and in the ventricles, involving all the structures that lie within or adjacent to these spaces.



We are protected from pathogenic microorganisms by immunological barriers.

Risk factor of infection

1.skin injury

surgical operation、 dermatitis、 traum、 burn or scald

2.mocosal impairment

drug（chemicals、 anticancer、 H2inhibitors...）、

stomatitis、 viral infection、 bacterial translocation→sepsis

3.malnutrition

hypoprotein、 vitamin deficiency、 alcholic damage

4.artificials

artificial substance、 catheters、 endotracheal tube, urethral tube

5.retardation of blood flow

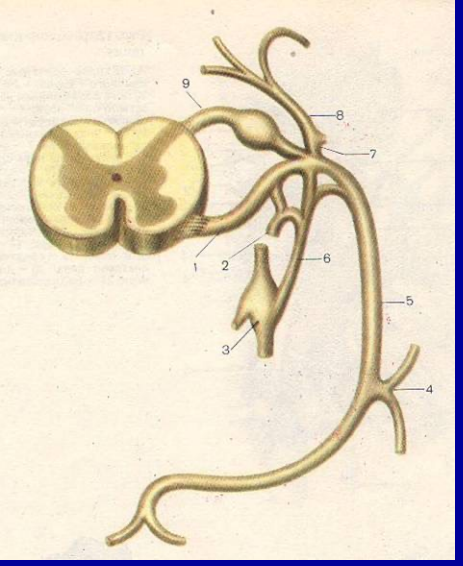
decubitus、 skin ulceration

6.dysfunction of reticuloendothelial system

liver cirrhosis、 post splenectomy

7.decreasing of immunity

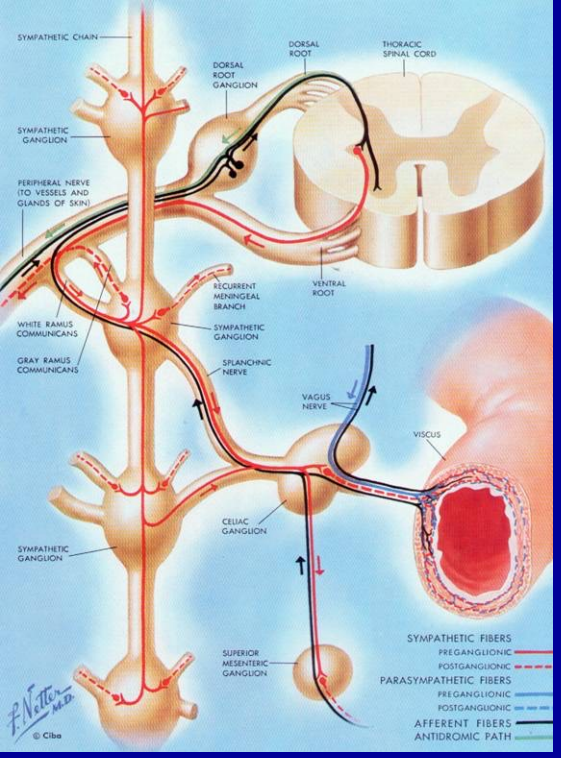
anti cancer、 cancer patients、 HIV、 DM、 steroid hormone



INFECTIONS OF THE NERVOUS SYSTEM

CLASSIFICATION

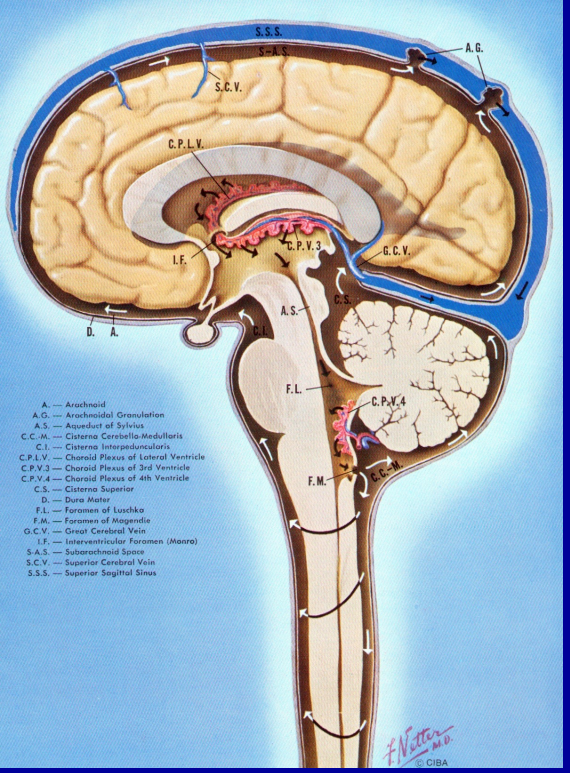
ANATOMICAL CONSIDERATIONS	CATEGORIES
Peripheral nervous system	Mononeuritis Multineuritis Polineuritis Plexitis Funiculitis Ganglionitis Radiculitis Poliradiculoneuritis



INFECTIONS OF THE NERVOUS SYSTEM

CLASSIFICATION

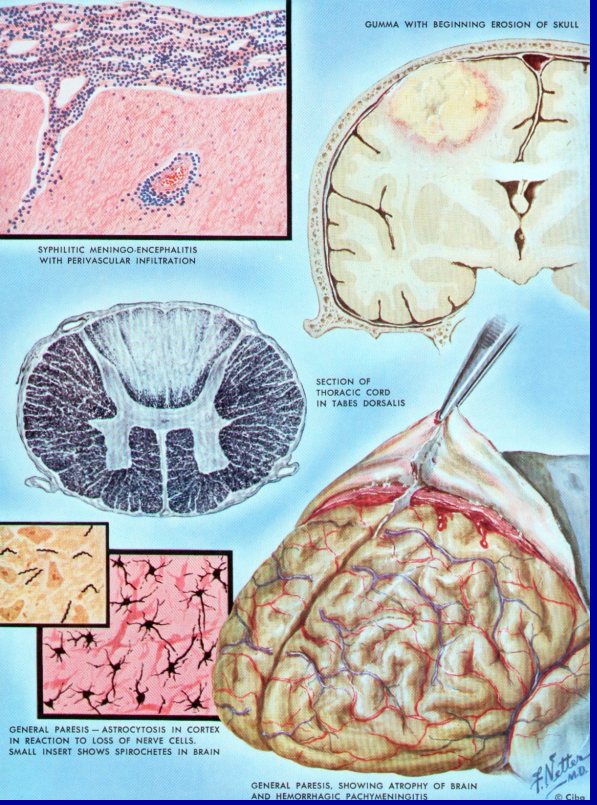
ANATOMICAL SUBSTRATUM	CATEGORIES
Autonomic nervous system	Neuritis Ganglionitis Truncitis



INFECTIONS OF THE NERVOUS SYSTEM

CLASSIFICATION

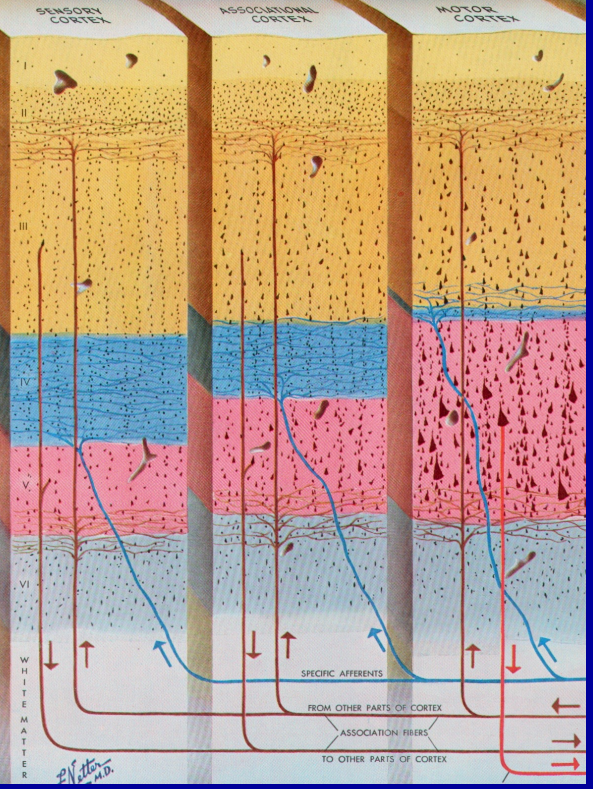
ANATOMICAL CONSIDERATIONS	CATEGORIES CATEGORIES	
Spinal and cerebral meninx	Meningitis	Leptomeningitis Arahnoiditis Pahimeningitis Leptopahimeningitis



INFECTIONS OF THE NERVOUS SYSTEM

CLASSIFICATION

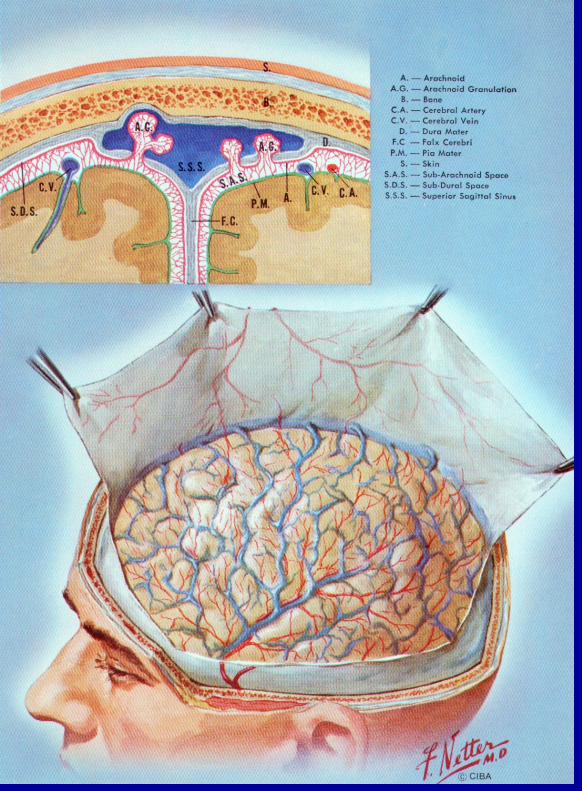
ANATOMICAL CONSIDERATIONS	CATEGORIES	
Cerebral parenchyma	Encephalitis	Polioencephalitis Leucoencephalitis Panencefalită
Medullar parenchyma	Myelities	Transversal Poliomielită



INFECTIONS OF THE NERVOUS SYSTEM

CLASSIFICATION

ANATOMICAL CONSIDERATIONS	CATEGORIES
Cerebral and medullar parenchyma	Encephalomyelitis
Meninx and cerebral and/or medullar parenchima	Meningoencephalitis Meningomyelitis Meningoencephalomyelitis



INFECTIONS OF THE NERVOUS SYSTEM

CLASSIFICATION

ANATOMICAL CONSIDERATIONS	CATEGORIES	ANATOMICAL CONSIDERATIONS
Cerebral and/or medullar vessels	Vasculitis	Arteriitis Phlebitis Pahimeningitis Sinusitis (cerebral)

INFECTIONS OF THE NERVOUS SYSTEM

CLASSIFICATION

Evolutional criterion:

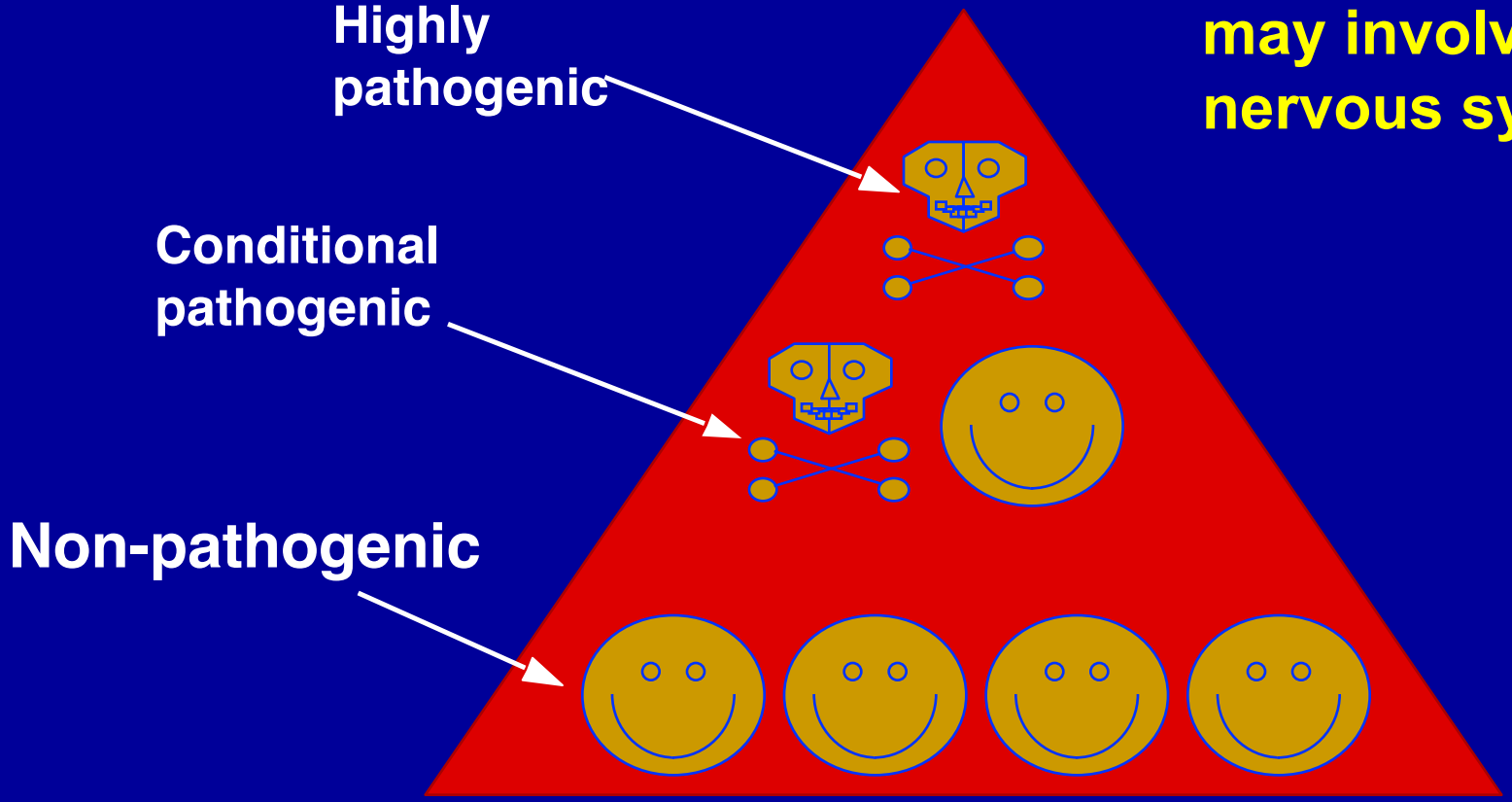
acute

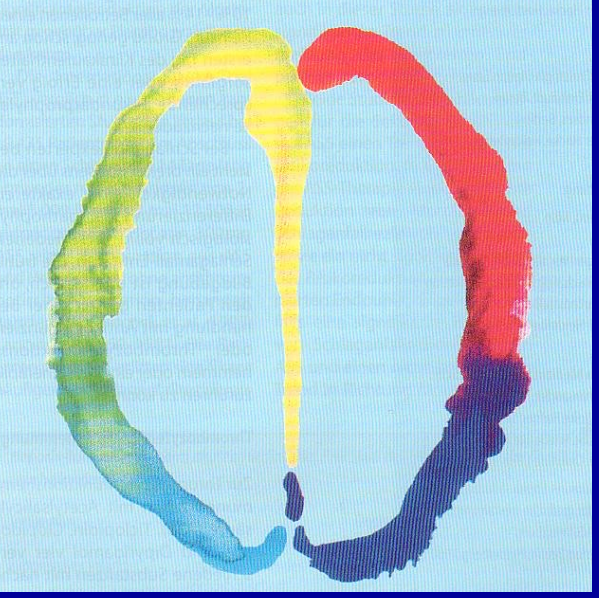
subacute

chronic

Infectious agents

Nearly all known infectious agents may involve the nervous system

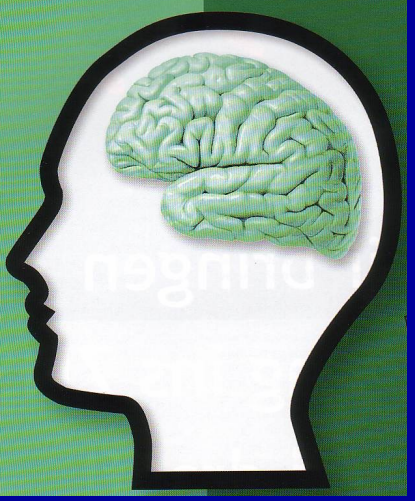




Management

ENTEROVIRAL (Echoviruses and Coxsackieviruses) ASEPTIC MENINGITIS

Because the majority of enteroviral infections are spread by the fecal-oral route, enteroviral infections are best prevented by proper hand washing techniques



INFECTIONS OF THE NERVOUS SYSTEM

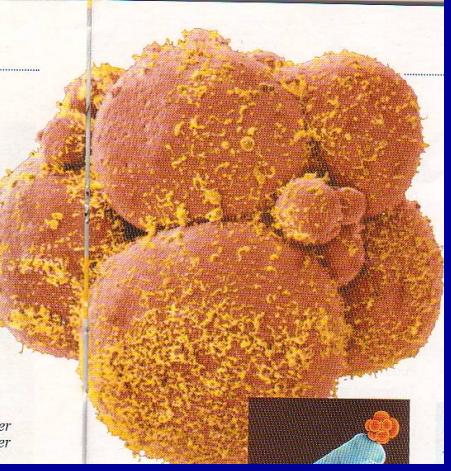
CLASSIFICATION

INFECTION	NAME
VIRUSES	***ADN*** *(parvoviridae, papovaviridae, adenoviridae, herpetoviridae, poxviridae, hepanaviridae)* ***ARN*** *(retroviridae, picornaviridae, togaviridae, bunzaviridae, coronaviridae, ortomyxoviridae, paramyxoviridae, rabdoviridae, arenaviridae, retroviridae)* ***Other***
CHLAMYDIES	***Chlamydia psittaci*** ***Chlamydia trachomatis***

INFECTIONS OF THE NERVOUS SYSTEM

CLASSIFICATION

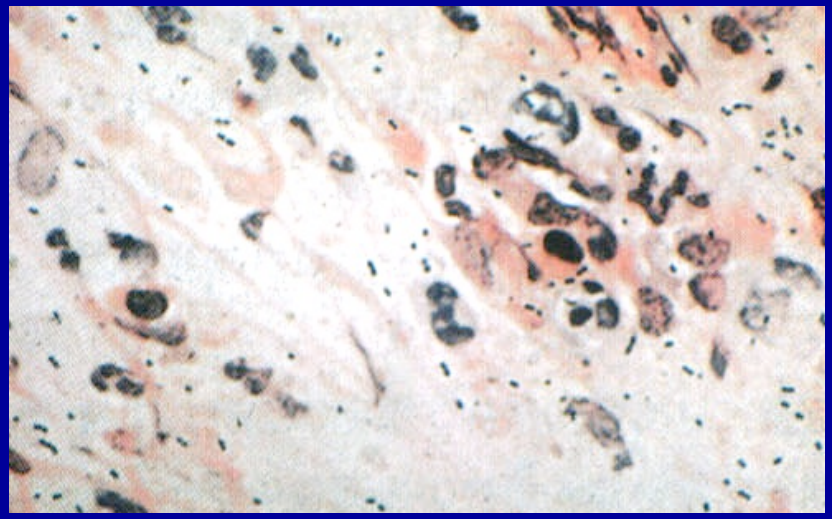
INFECTION	NAME
MYCOPLASMS	*Mycoplasmataceae* Family *Acholeplasmae* Family
RICKETSIES	*Ricketsia Coxiella Rochalimea*
BACTERIES	*Group B Streptococci, Gram-negative enteric bacilli (Escherichi Colli), Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae*



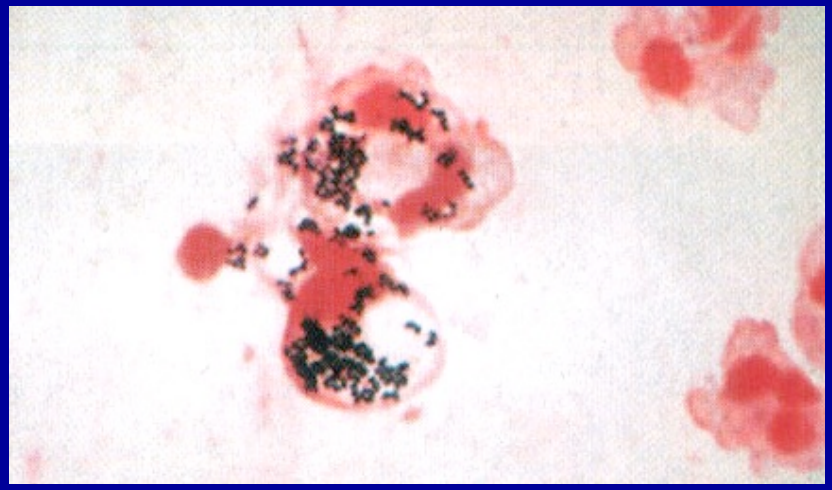
INFECTIONS OF THE NERVOUS SYSTEM

CLASSIFICATION

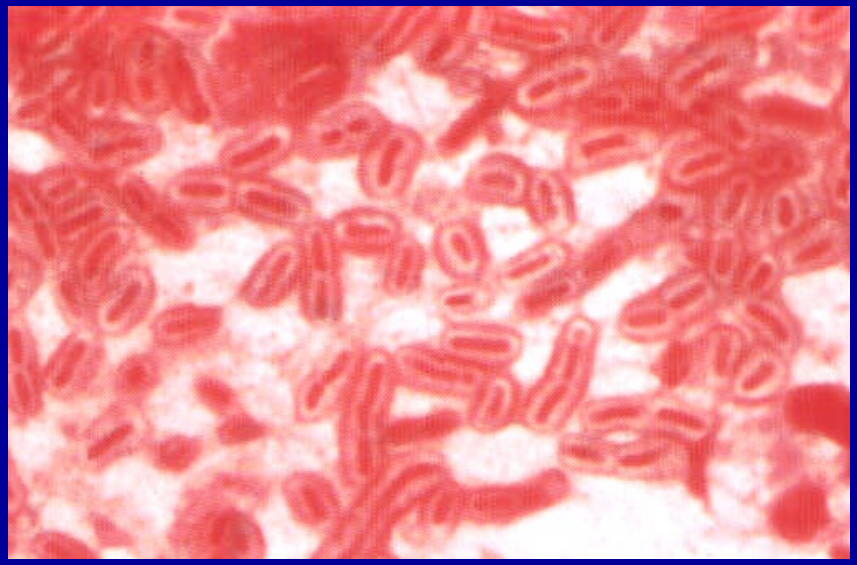
INFECTION	NAME
FUNGAL	*Candida, Histoplsma capsulatum, Cryptococcus neoformans, Coccidioides immitis, Actinomyces israelii, Nocardia, Aspergillus* etc.
PROTOZORAE	*Entamoeba histolytica, Balantidium coli, Giardia lamblia, Plasmodium, Babesia, Leishmania, Toxoplasma, Pneumocystis carinii).*
PARASITIC	*Trichinella spiralis, Schistosoma, Ancylostoma duodenalis* şi *Necator americanus, Strongyloide* etc.

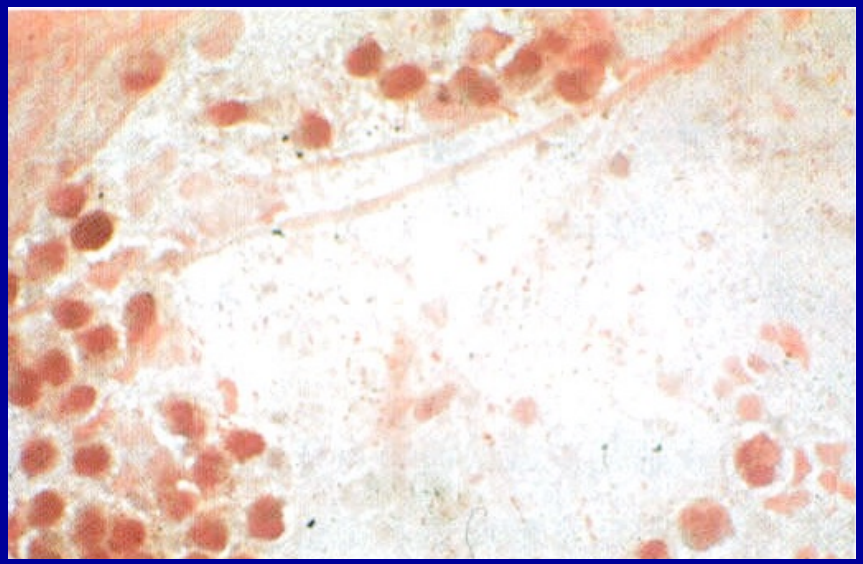


Streptococcus pneumoniae

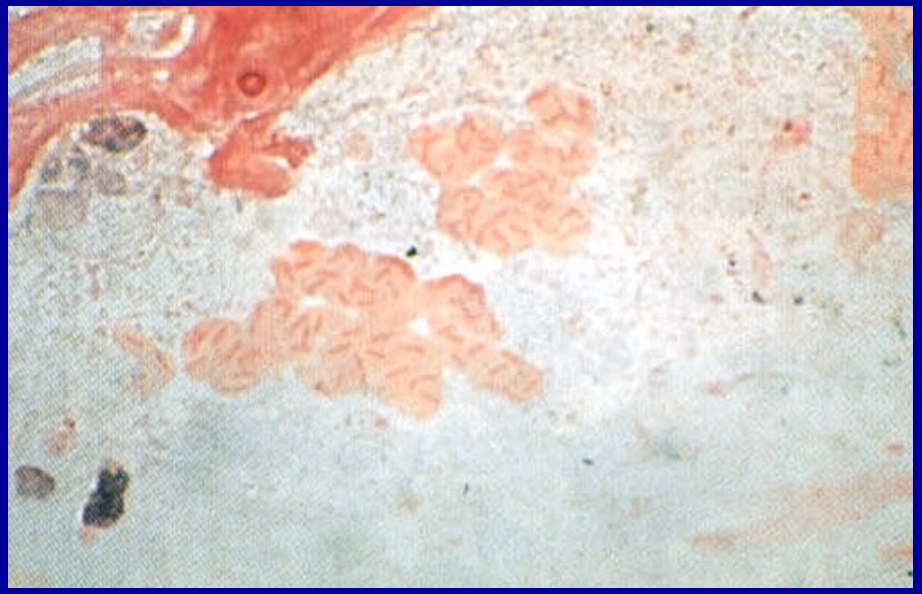


Staphylococcus aureus

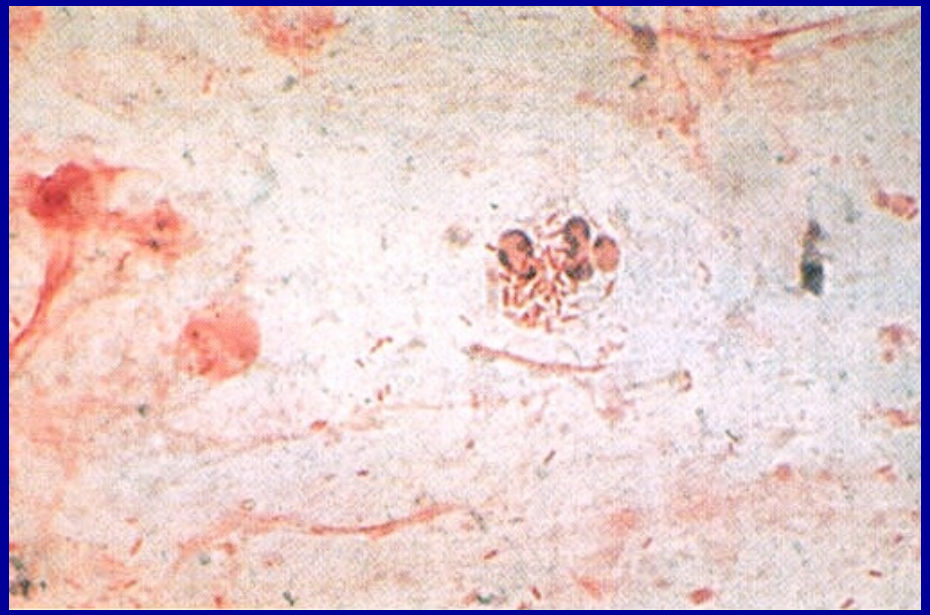




Klebsiella pneumoniae



Pseudomonas aerginosa
Mucoid type form biofilm



Pseudomonas aerginosa
Unmucoid type
Phagocyted by neutrophil

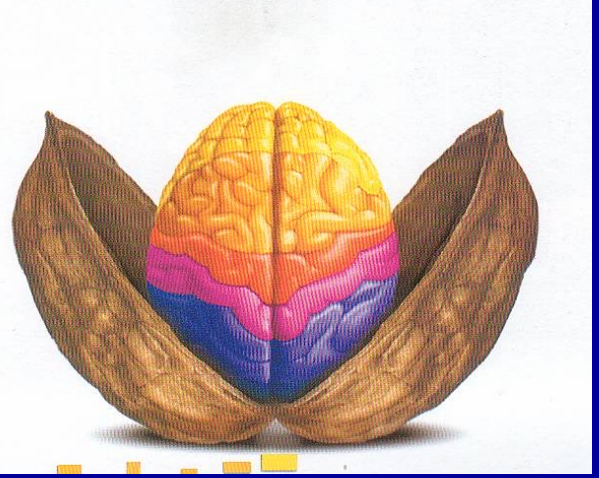
ETIOLOGY

BACTERIAL	***Streptococcus pneumoniae (47-51%)*** ***Neisseria meningitidis (25-37%)*** ***Listeria monocytogenes (4-8%)***	Schuchat et al 1997; van de Beek et al. 2004.
VIRAL	***Enteroviruses (eg, Coxsakie A and B, echovirus)*** ***Herpes simplex virus (types 1 and 2)*** ***Cytomegalovirus (CMV)*** ***Epstein-Barr virus (EBV)*** ***Varicella zoster virus (VZV)*** ***Mumps virus*** ***Human immunodeficiency virus (HIV)***	Logan and MacMahon 2008
OTHER	***Mycobacterium tuberculosis*** ***Cryptococcus*** ***Nocardia*** ***Coccidomycosis***	

INFECTIONS OF THE NERVOUS SYSTEM

ETIOLOGIC AGENTS OF VIRAL MENINGITIS

Herpes simplex virus types 1 and 2
Enteroviruses
Mumps
HIV
Lymphocytic choriomeningitis virus
Epstein-Barr virus
Influenza virus types A and B



PATHWAYS OF INFECTION

Infectious organisms reach the nervous system by hematogenous spread, local extension, or, rarely, by direct (mechanical) inoculation, as in open head injures.

Respiratory passages (Mumps, measles, and varicella)

Oral-intestinal route (Polioviruses and other enteroviruses)

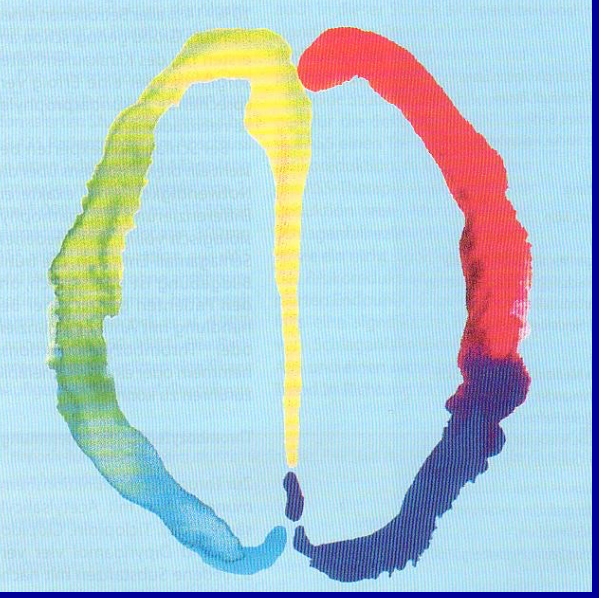
Inoculation, as a result of the bites of animals (e.g., rabies) mosquitoes (arthropod-borne or arbovirus infections).

Oral or genital mucosal route (HSV).

Transplacentally (rubella virus, CMV, and human immunodeficiency virus (HIV).

Approach to the Patient:
CNS INFECTION

The first task is to identify whether an infection predominantly involves the subarachnoid space (meningitis) or whether there is evidence of either generalized or focal involvement of brain tissue in the cerebral hemispheres, cerebellum, or brainstem.



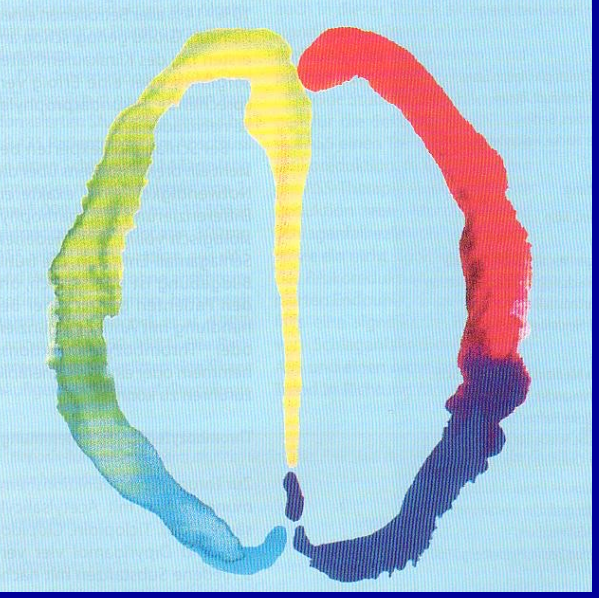
MENINGITIS

Clinical Presentation

Meningitis **is an infection of thr pia-archnoid an of the cerbrospinal fluid in the subarchnoid space.**

The ”Classic” clinical TRIAD of MENINGITIS:

1. **Fever**
2. **Headache**
3. **Nuchal rigidity ”stiff neck”.**



ACUTE MENINGITIS (LEPTOMENINGITIS)

Clinical Features

THE ”MODERN” MENINGITICAL TRIAD:

1. General inflammatory signs
2. Positive signs of meningeal irritation
3. CSF meninigitical syndrome.

1) general inflammatory signs

- Headache
- Fever
- Altered mental status
- Nausea
- Vomiting
- Photophobia
- Lethargy
- Rash
- Stupor
- Seizure activity
- Phonophobia
- Somnolence
- Backache
- Myalgias
- Arthralgia
- Gastrointestinal symptoms

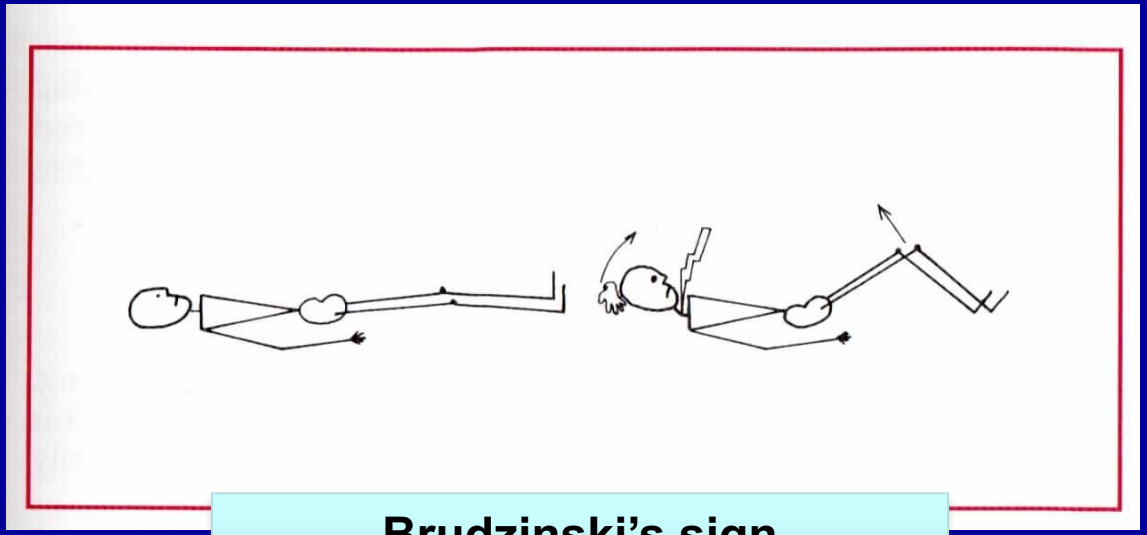
2) signs of meningeal irritation

- Nuchal rigidity (neck stiffness)
- Brudzinski's signs
- Kernig's sign
- Lessaje's sign
- Mendel's sign
- Bechterew's sign
- Weiss-Edelman's sign
- etc.

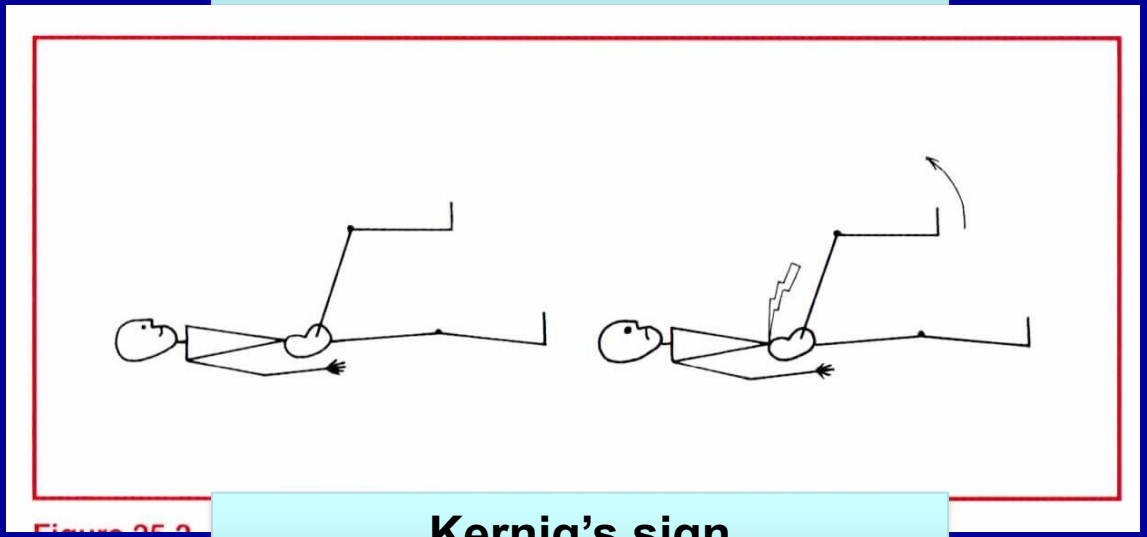
signs of meningeal irritation

nuchal rigidity
Kernig's and Brudzinski's signs
etc

Why?



Brudzinski's sign



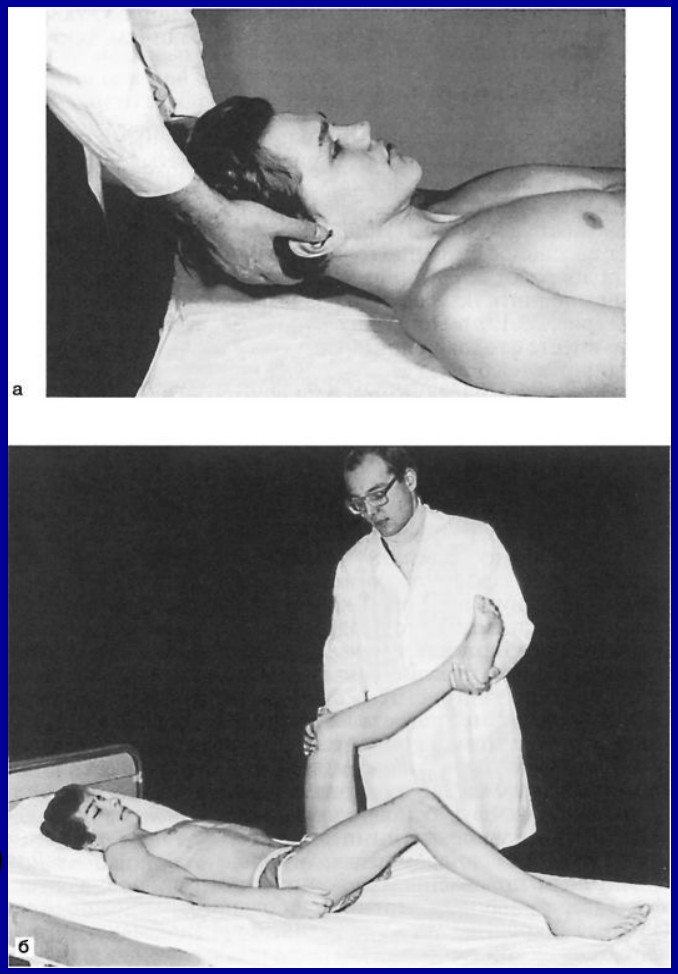
Kernig's sign

DE CE?

Porquoi?

Quam Veni?

למה?



لماذا؟

Why?

Warum?

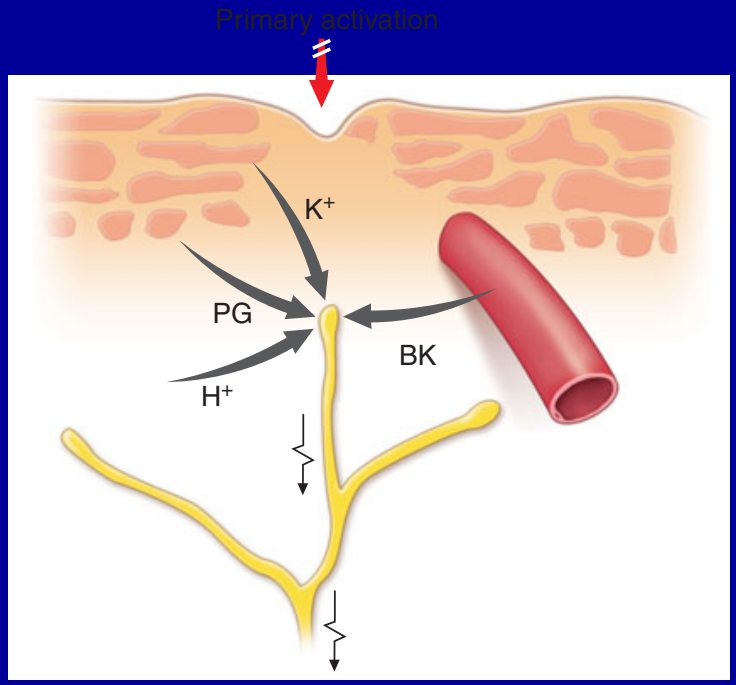
Почему?

Sensitization !!!

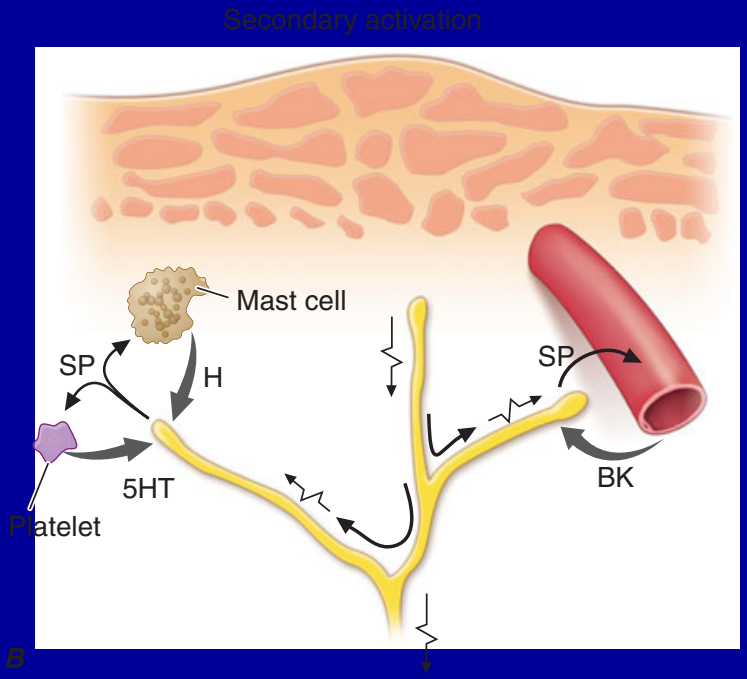
- A large proportion of Aδ and C afferents innervating meninx are completely insensitive in normal noninjured, noninflamed tissue.
- However, in the presence of inflammatory mediators, these afferents become sensitive to mechanical stimuli. Such afferents have been termed ***silent nociceptors.***
- Low pH, prostaglandins, leukotrienes, and other inflammatory mediators such as bradykinin play a significant role in sensitization.

PERIPHERAL MECHANISMS

A. Primary activation.



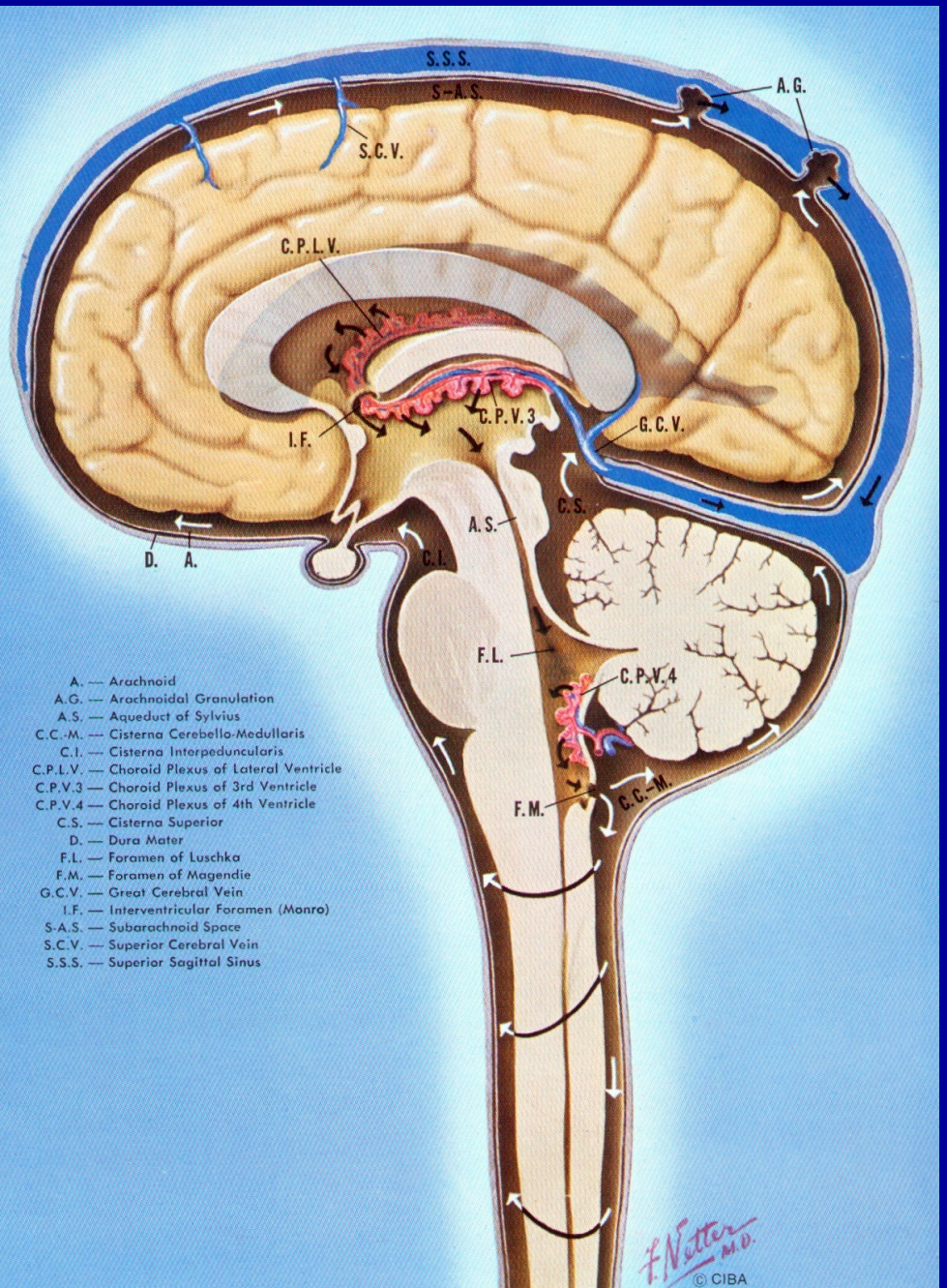
B. Secondary activation.



3) CSF meninigitical syndrome:

PROTEIN ↑ + CELLS↑

Cerebrospinal Fluid Circulation

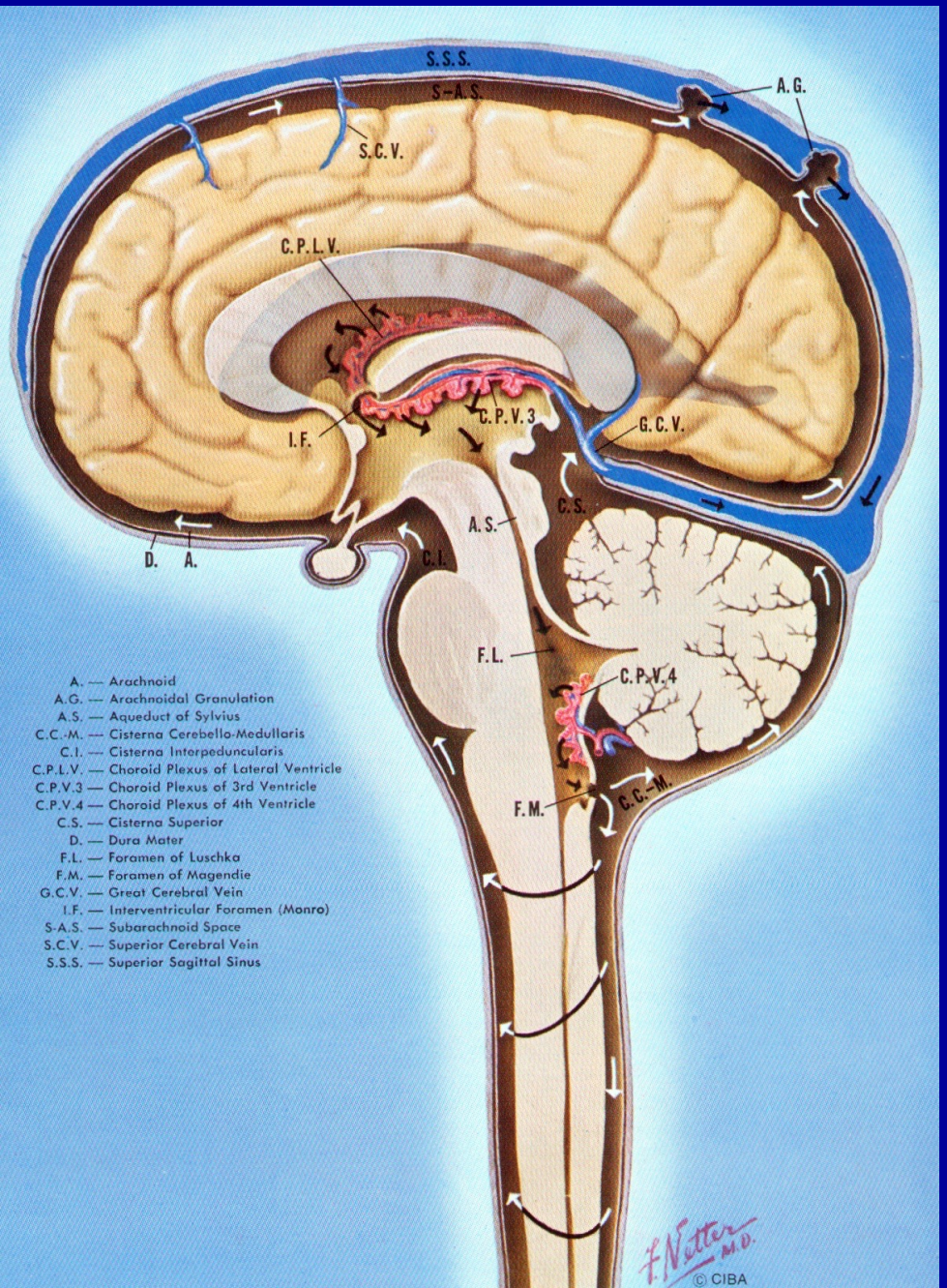


1. The greater part of the cerebrospinal fluid is elaborated by the choroid plexus.

2. The CSF passes into the lateral ventricles.

3. The CSF flows through the interventricular foramen (Monro) into the third ventricle and way of the aqueduct of Sylvius into the fourth ventricle.

Cerebrospinal Fluid Circulation



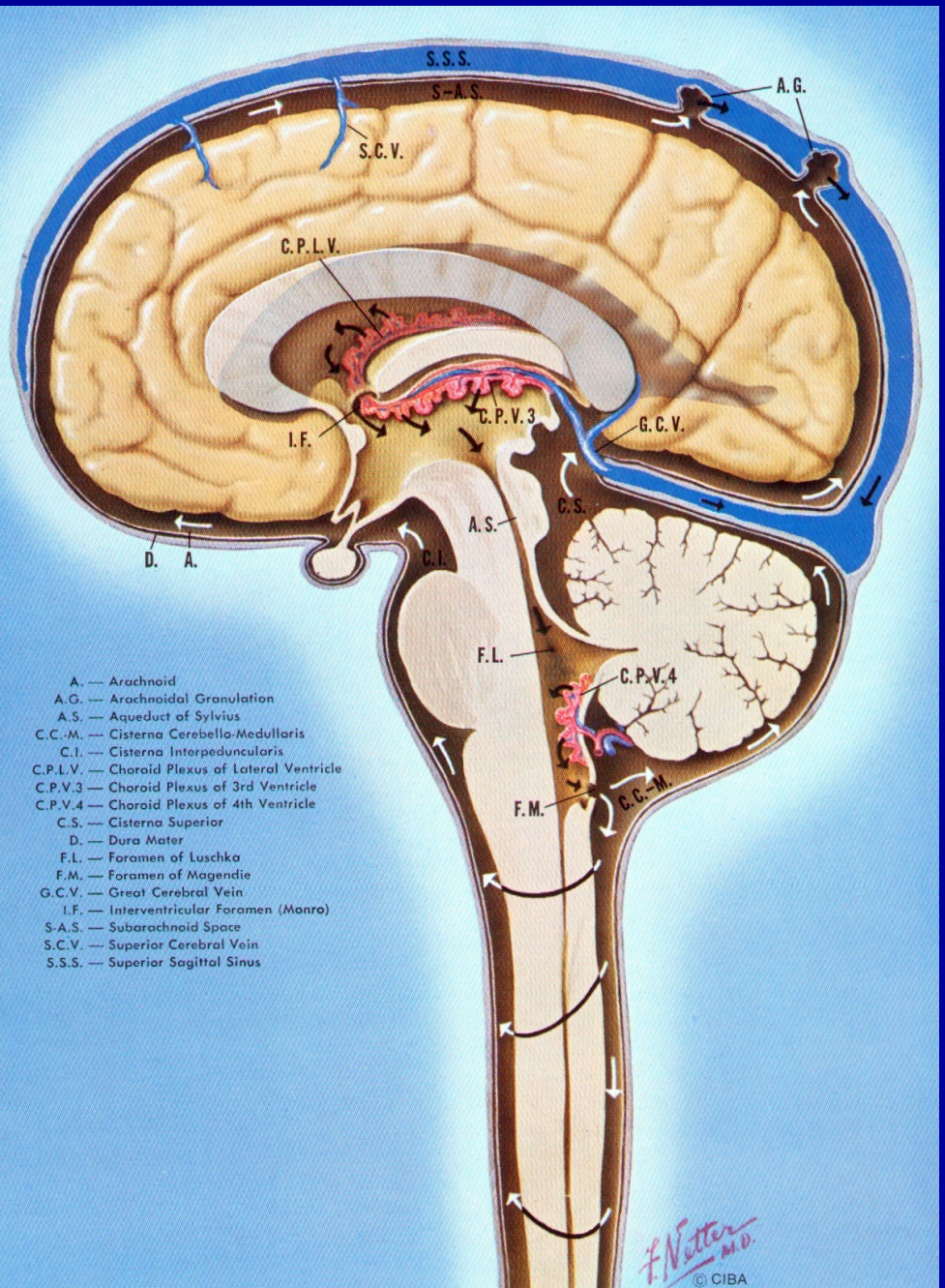
4. Exits of CSF into the sub-arachnoid space:

(1) through the foramen of Magendie in the roof of the fourth ventricle, thereby entering the cisterna magna or the cisterna cerebello-medullaris,

(2) through either foramina of Luschka (situated at the extreme lateral portions of the fourth ventricle), thereby emptying into the cisterna pontis,

(3) from the cisterna magna the cerebrospinal fluid may be directed over the cerebellar hemispheres to the cisterna superior.

Cerebrospinal Fluid Circulation



5. From the cisterna pontis the flow of the cerebrospinal fluid is forward to the cisterna interpeduncularis and cisterna chiamatis. From these cisternae the fluid sweeps upward over the surface of both lateral hemispheres, anteriorly, upward between the two hemispheres along the longitudinal fissure, over the corpus callosum, along the Sylvian fissure and over the temporal lobes.

The fluid finally reaches the arachnoidal villi where, by a process of osmosis, it is emptied into the great venous dural sinuses, particularly the superior sagittal sinus.

LUMBAR PUNCTURE

INDICATIONS:

- Acute meningitis
- SAH

(if CT – negative)

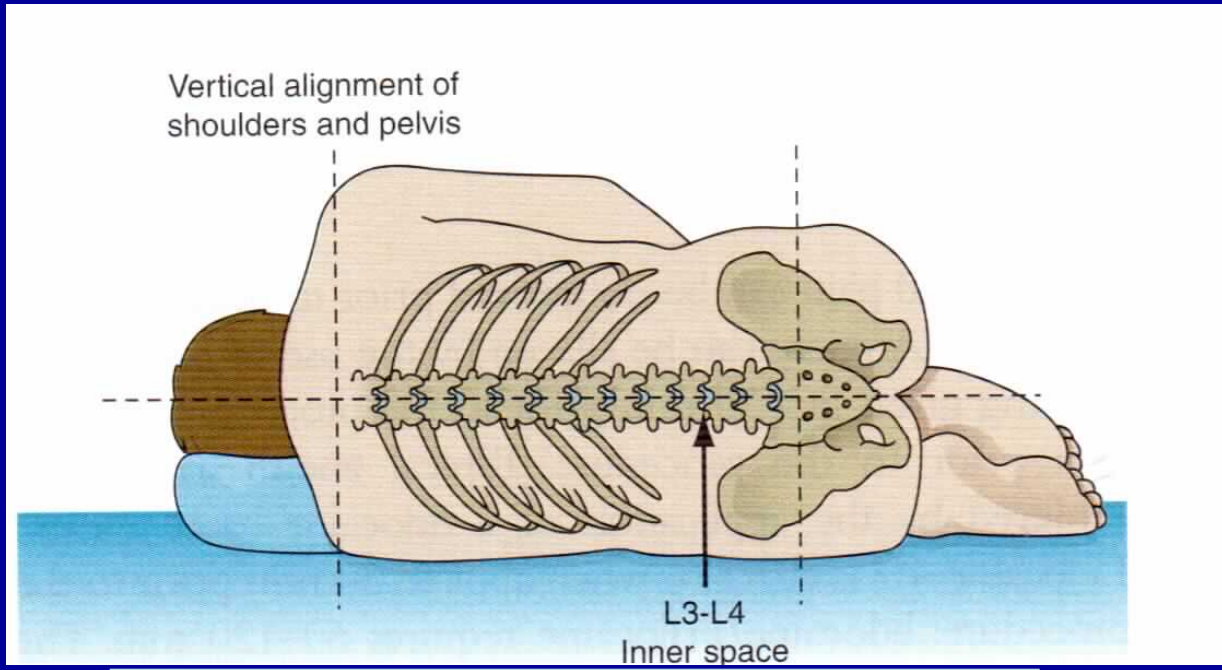
CONTRANDICATIONS:

Absolute

- Intracranial hypertension
- Platelet count under 5.000

Relative

- Anticoagulation
- Platelet count under 5.000-20.00
- Lumbar paraspinal abscess or other infection



Proper positioning of a patient in the lateral decubitus position

The RISKS:

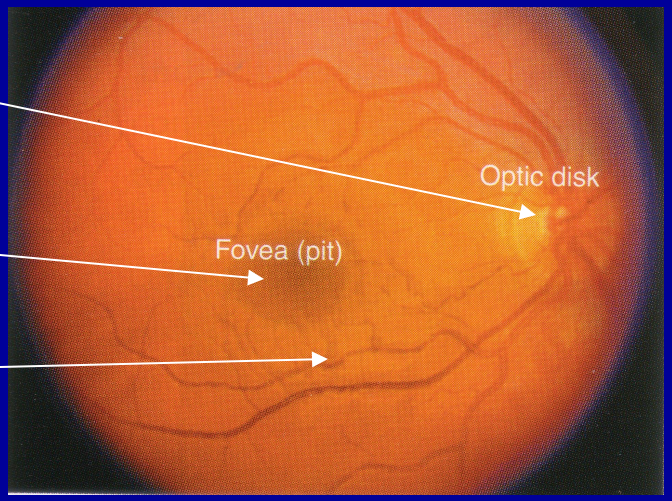
- Transtentorial or transforaminal herniation
- Worsening of paraparesis (if there is a partial block to the flow of SCF)
- Epidural, subdural, and subarachnoid hemorrhage (less than 1%)

OPTIC NERV CLINICAL EXAM: ophtalmoscopy

Optic disk

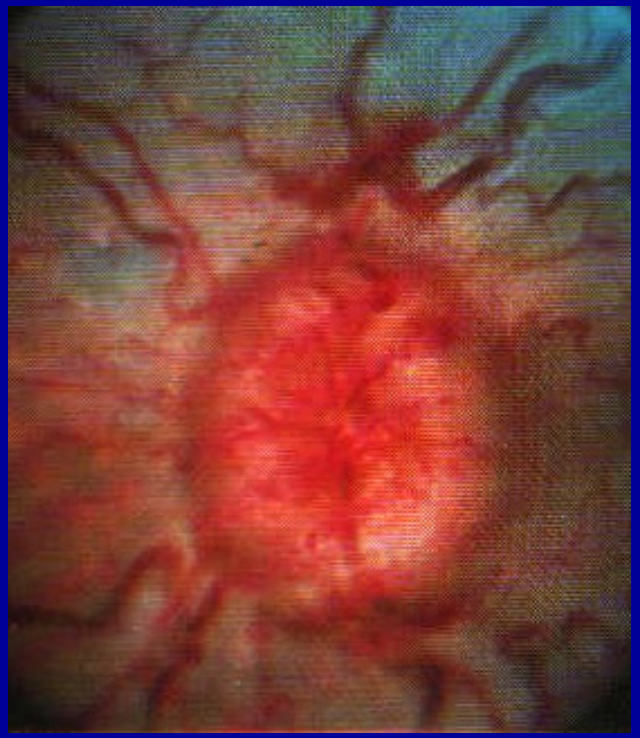
Fovea

Vessels

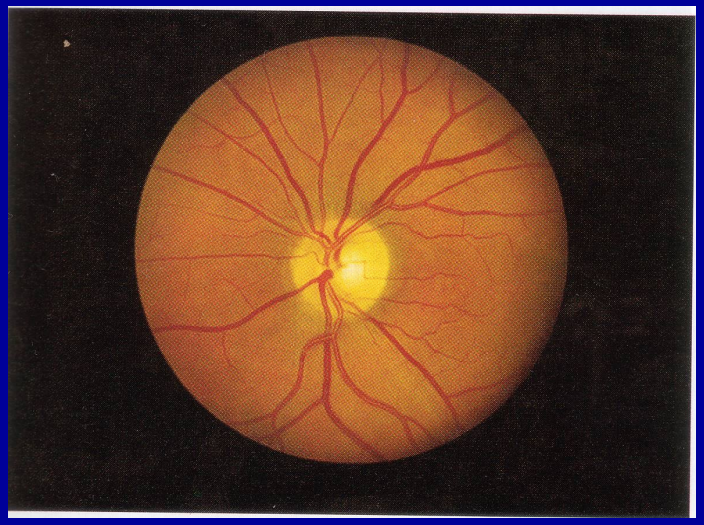


PAPILLOEDEMA associated with raised intracranial pressure

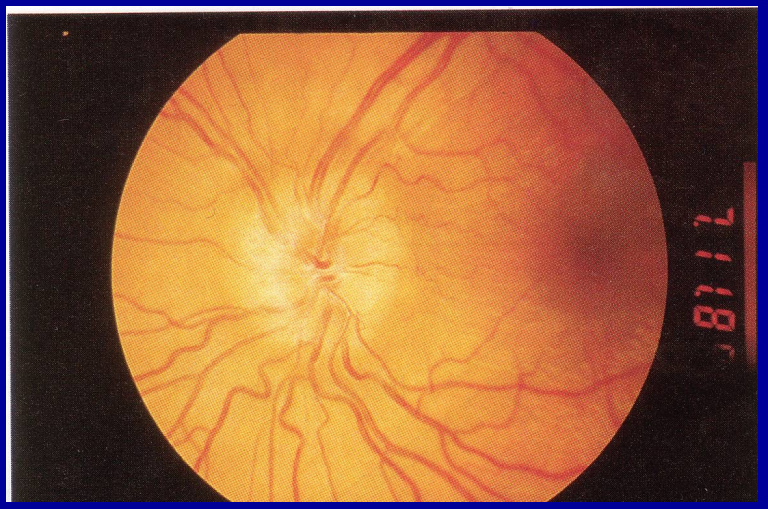
- The definitive sign of raised intracranial pressure.
- Is due to transmission of the raised pressure along the subarachnoid sheath of the optic nerve.



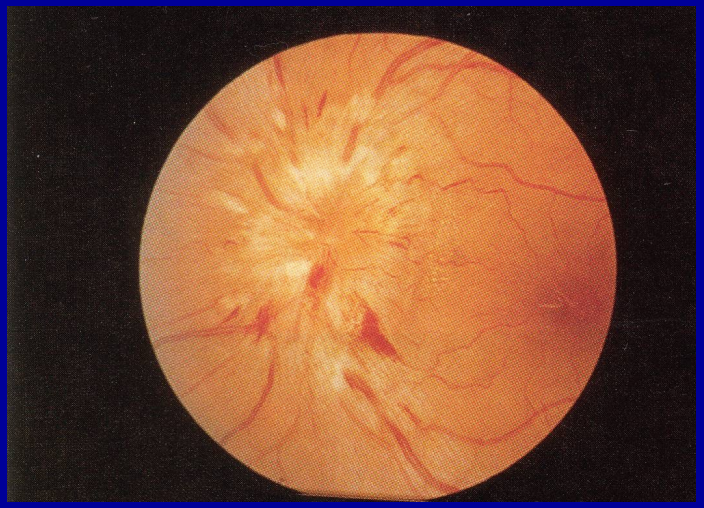
OPTIC DISK



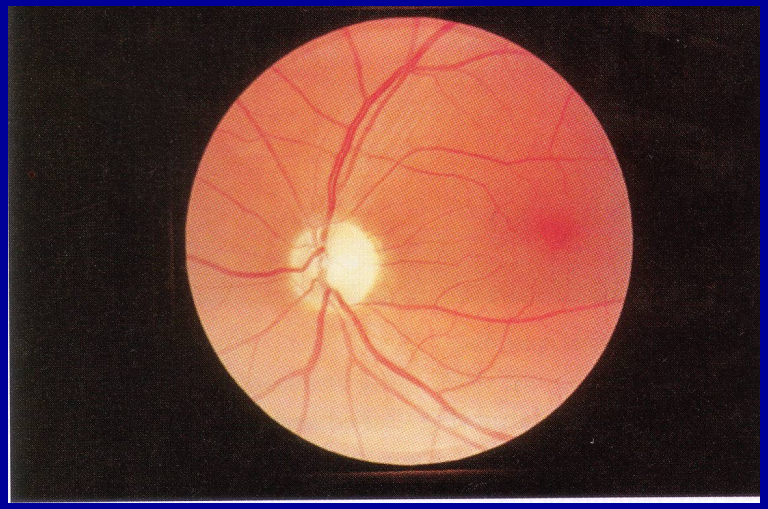
NORMAL



OEDEMA

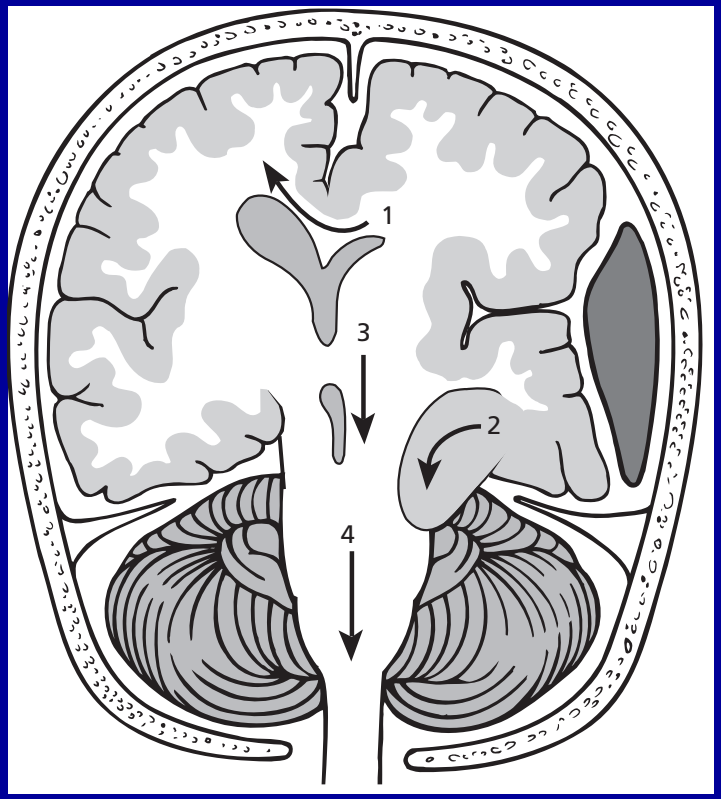


STAZIS



ATROPHY

raised intracranial pressure



- may result from brain herniation, and
- from the mass lesion that has caused the rise in pressure.

Brain herniations. A lateral supratentorial mass will cause displacement of the lateral ventricles with: (1) subfalcine herniation of the cingulate gyrus below the falx cerebri; (2) herniation of the uncus into the tentorial hiatus; (3) caudal displacement of the brainstem. Raised pressure within the posterior fossa may cause herniation of the cerebellar tonsils into the foramen magnum (4).

LUMBAR PUNCTURE

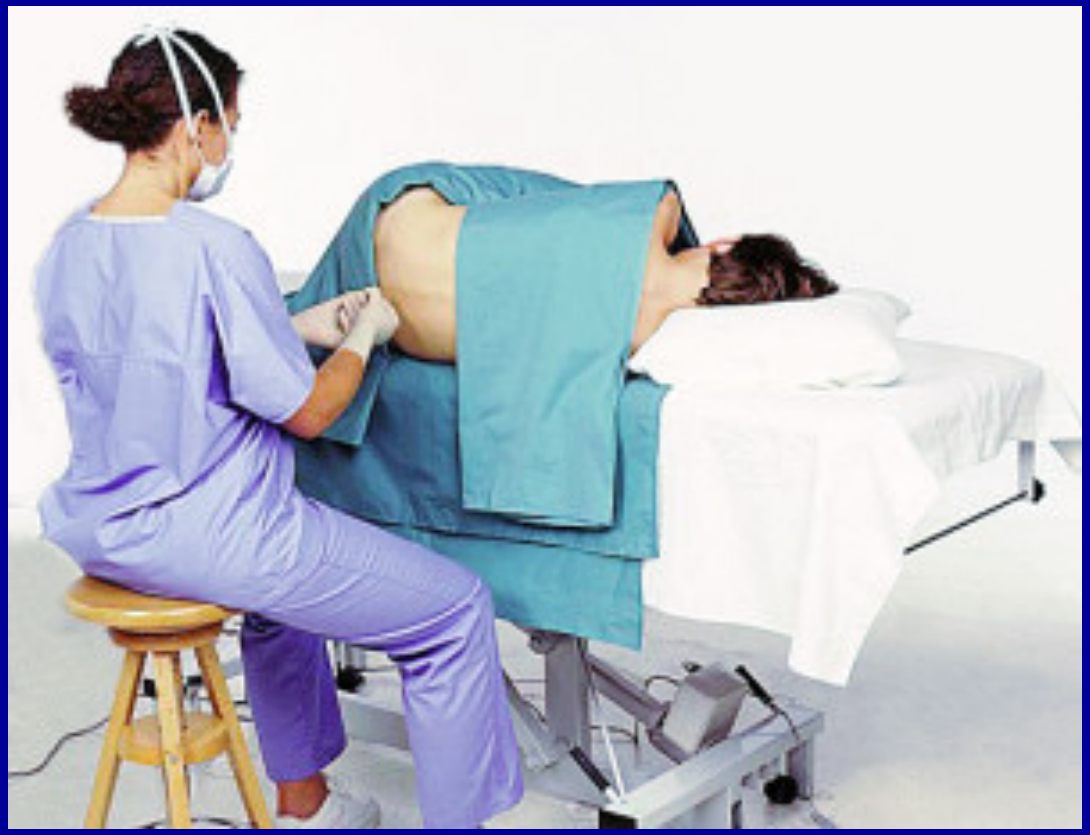
LUMBAR PUNCTURE

MAJOR COMPLICATIONS:

- cerebral herniation
- injury to the spinal cord or nerve roots
- hemorrhage
- infection

MINOR COMPLICATIONS:

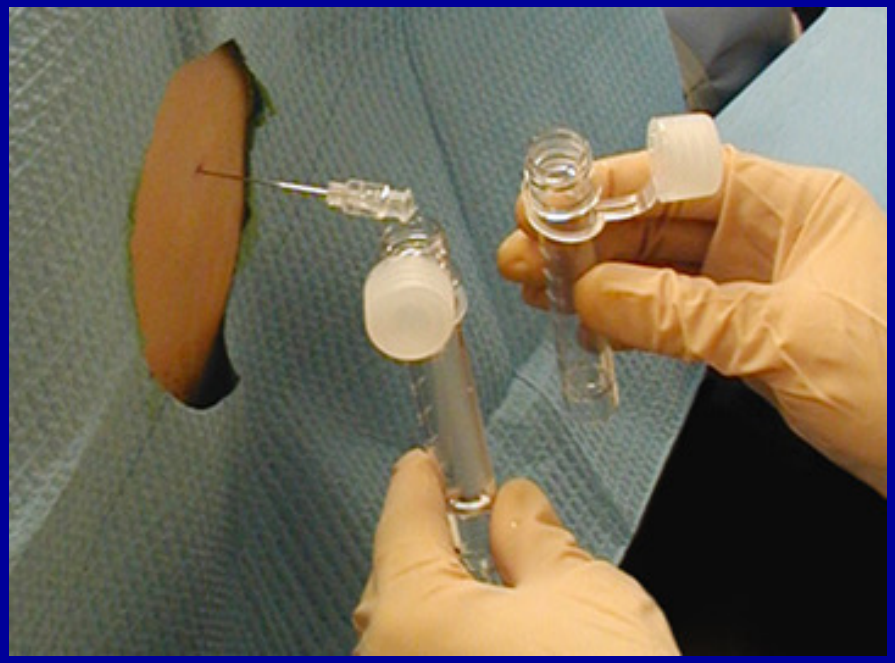
- backache
- post-LP headache
- radicular pain
- numbness



LUMBAR PUNCTURE

CSF routine investigations:

- Pressure, Queckenstedt test
- Color (turbidity? xanthocromia? bloody tinge?)
- Absolute and differential cell count
- Protein
- Glucose



Normal values in CSF and serum in adults

Values	CSF	Serum
Pressure	5-18 cm H_20	
Volume	100 -160 mL	
Osmolarity	292-297 moslm/L	285-295 mosm/L
Electrolytes		
• Na • K • Ca • Cl	137-145 mmol/L 2.7-3.9 mmol/L 1-1.5 mmol/L 116-122 mmol/L	136-145 mmol/L 3.5-5.0 mmol/L 2.2-2.6 mmol/L 98-106 mmol/L
pH	7.31 – 7.34	7.38 – 7.44
Glucose	2.2 – 3.9 mmol/L	4.2-6.4 mmol/L
• CSF/Serum glucose quotient >0.5-0.6		
Lactate	1.0-2.0 mmol/L	0.6-1.7 mmol/L
Total protein	0.2-0.5 g/l	55-80 g/l
Leukocytes	<4/µL	
Lymphocytes	60-70%	

Clinical Correlate

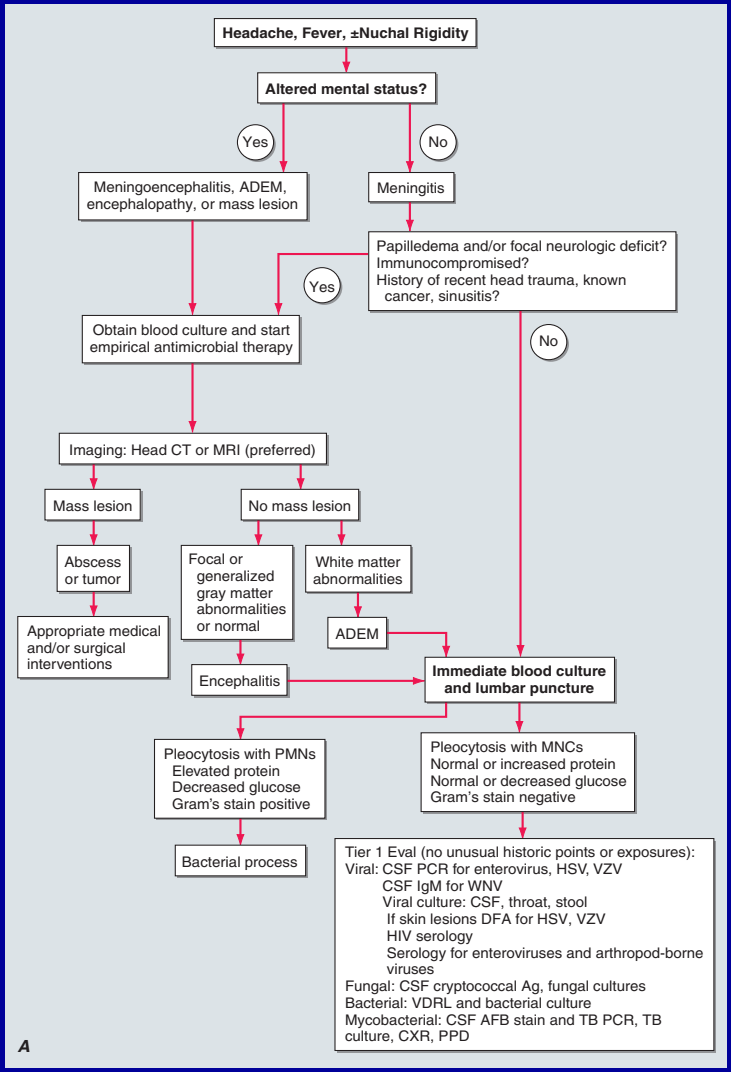
- Concentration of protein (including all immunoglobulins) is much lower in the CSF as compared with serum.
- Normal CSF has 0-4 lymphocytes or mononuclear cells per cubic millimeter. Though the presence of a few monocytes or lymphocytes is normal, the presence of polymorphonuclear leukocytes is always abnormal.
- RBS not normally found in CSF but may be present posttraumatic spinal tap or subarachnoid hemorrhage.
- Increased protein levels may indicate a CNS tumor.
- Tumor cells may be present in the CSF in cases with meningeal involvement.

Approach to the Patient:
CNS INFECTION

ADEM, acute disseminated enchephalomyelitis;

PMNs, polymorpho-nuclear leukocytes;

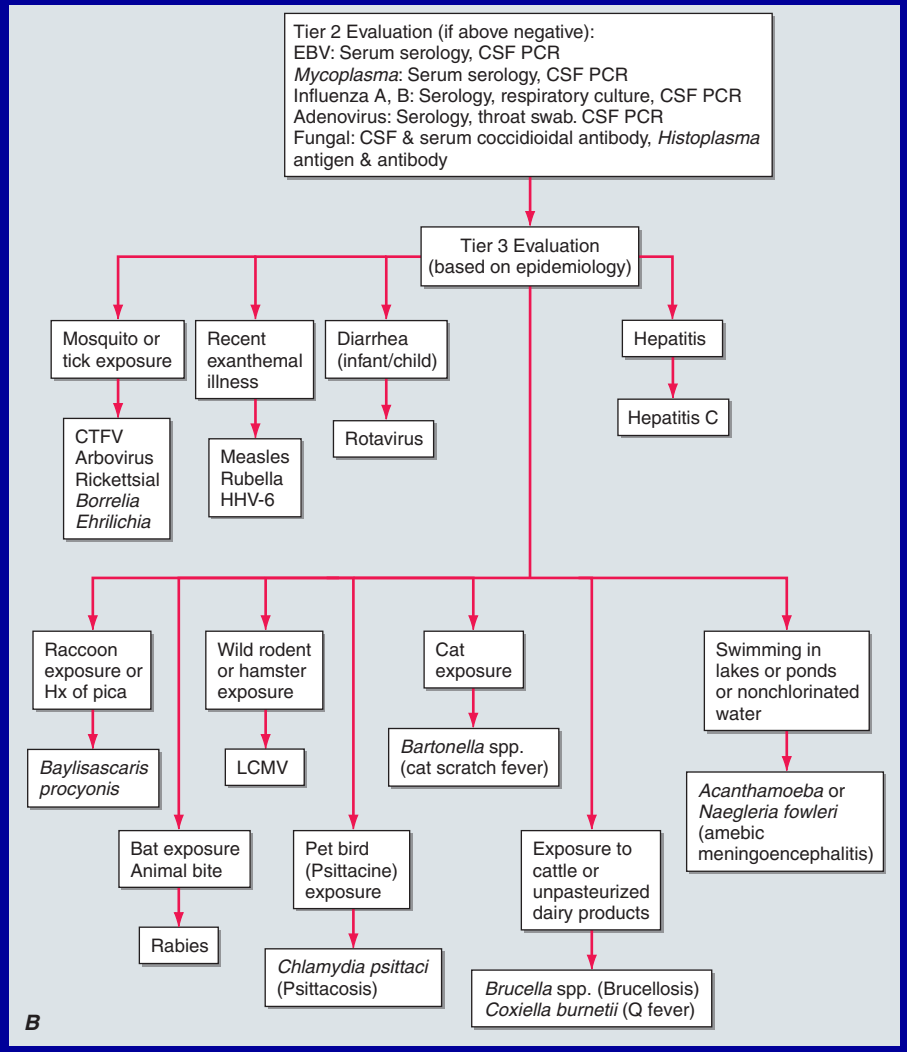
MINCs, mononuclear cells.



CSF, cerebrospinal fluid;
PCR, polymerase chain reaction;
HSV, herpes simplex virus;
VZV, varicella-zoster virus;
WNV, West Nile virus;
DFA, direct fluorescent antibody;
VDRL, Veneral Disease Research Laboratory;
AFB, acid-fast bacillus; Research Laboratory;
TB, tuberculosis;
CXR, chest x-ray;
PPD, purified protein derivative

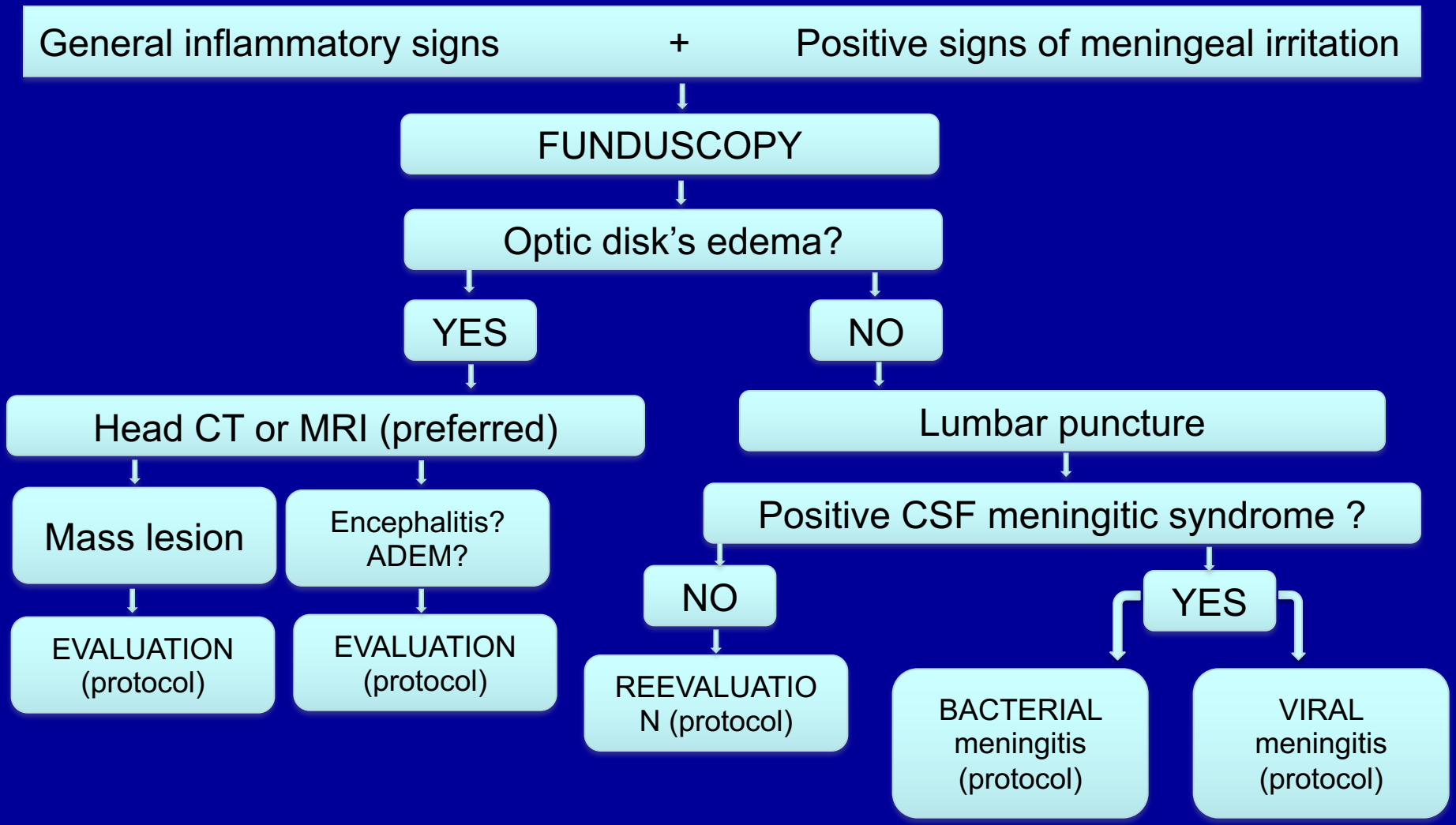
Approach to the Patient:
CNS INFECTION

EBV, Epstein-Barr virus.

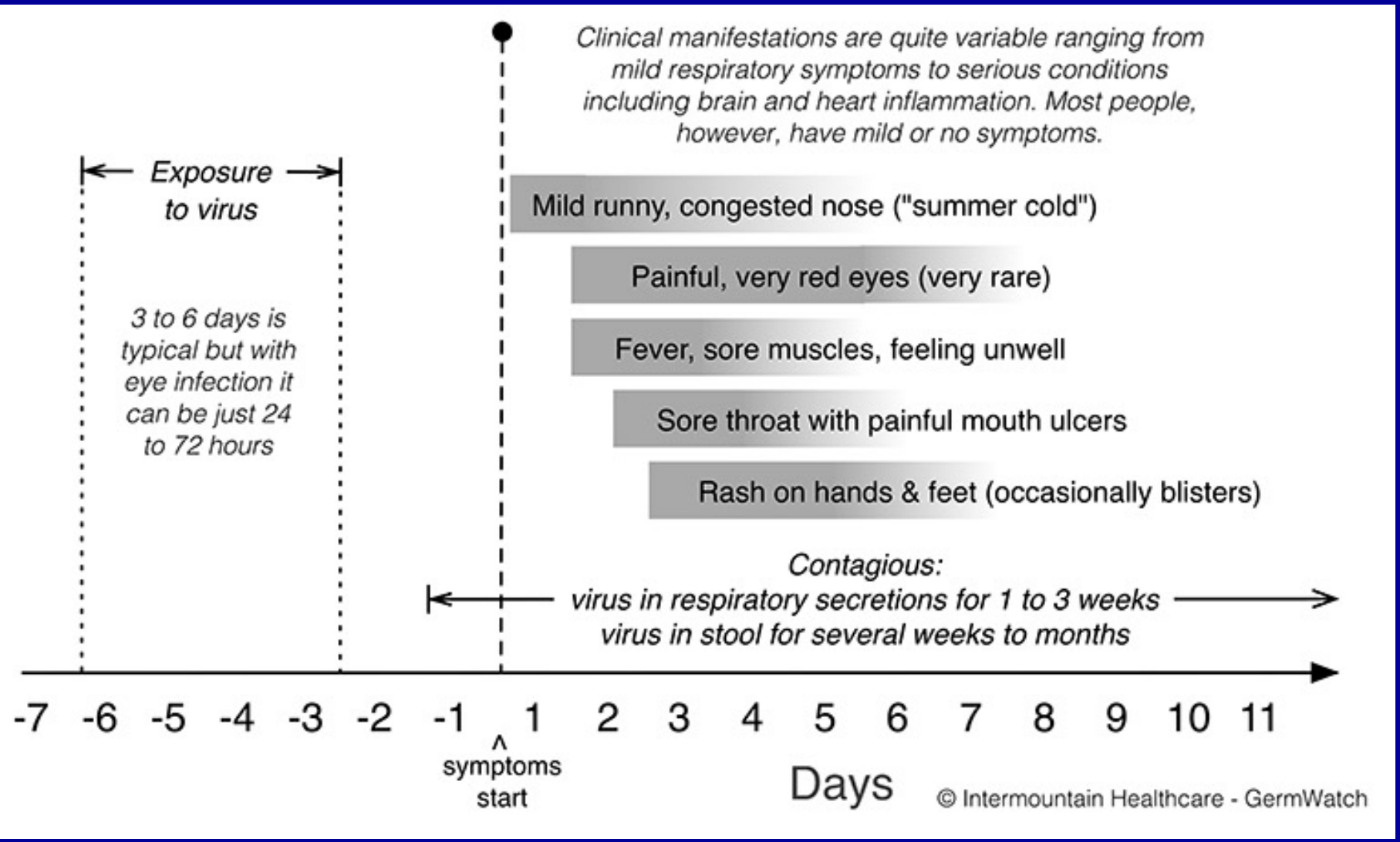


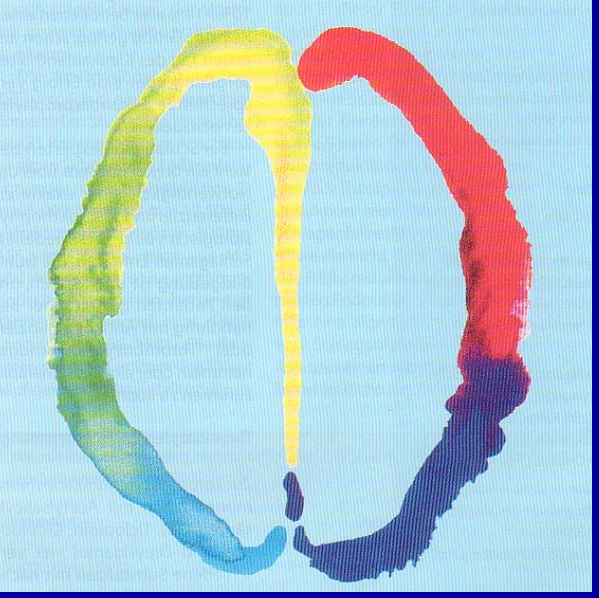
CSF, cerebrospinal fluid;
PCR, polymerase chain reaction;
HHV, human herpes virus;
LCMV, lymphocytic choriomeningitis virus.

ALGORITHM TO DIAGNOSE MENINGITIS



Enterovirus Infection Timeline



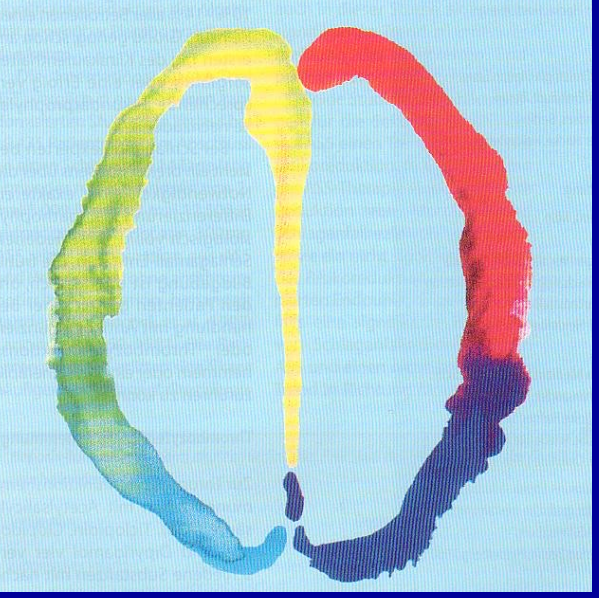


ENTEROVIRAL (Echoviruses and Coxsackieviruses) ASEPTIC MENINGITIS

Epidemiology and Risk Factors

Enteroviral infections occur primarily in the summer and autumn months in temperate climates; infants, young children, and immunocompromised patients are at greatest risk of infection.

The enteroviruses comprise a total of 68 distinct serotypes of human pathogens, but the most common enteroviruses that cause aseptic meningitis are the coxsackieviruses B5, B3, B4, and A9; the echoviruses 30, 11, 7, 9, 6, 4, and 18; and enteroviruses 70 and 71.

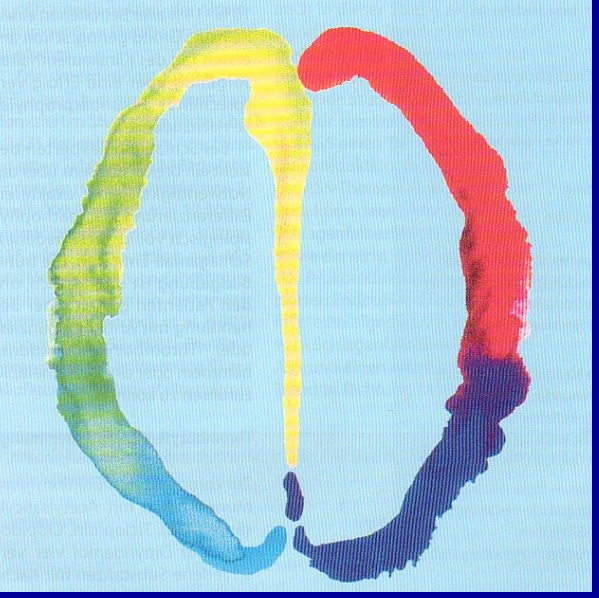


ENTEROVIRAL (Echoviruses and Coxsackieviruses) ASEPTIC MENINGITIS

Pathogenesis and Pathophysiology

Enteroviruses may enter the host through the mucosal surfaces of the gastrointestinal or respiratory tract. Enteroviruses are acquired most commonly by fecal-oral contamination and, less commonly, via aerosolized respiratory droplets.

Most enteroviruses spread to the CNS via the bloodstream, but a small percentage may reach the CNS by direct neural spread from nerves terminating in the intestinal tissue. Virus traverses the blood-brain barrier either at the choroid plexus, where it may infect endothelial cells and spread into the cerebrospinal fluid causing a meningitis, or at the endothelium of the cerebral capillary cells in the brain parenchyma causing an encephalitis.

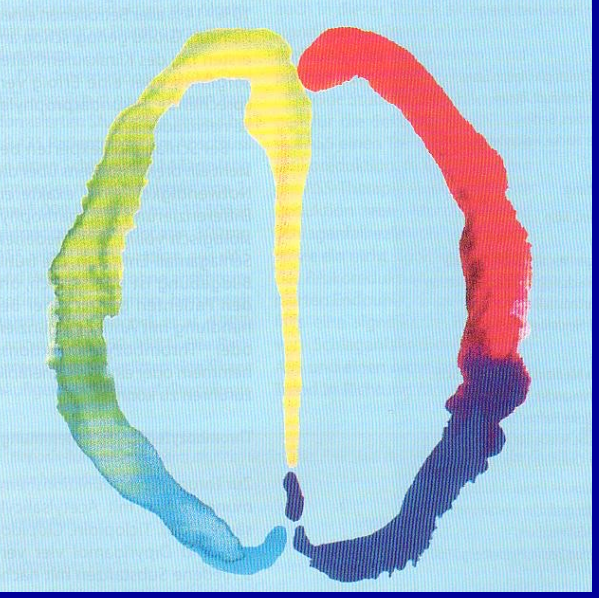


ENTEROVIRAL (Echoviruses and Coxsackieviruses) ASEPTIC MENINGITIS

The clinical Presentation

The clinical presentation of aseptic meningitis includes fever (38˚ to 40˚ C), severe headache, nausea and vomiting, photophobia, and nuchal rigidity.

Neurological abnormalities are rare, and enteroviral meningitis in otherwise healthy children and adults is rarely associated with severe disease or poor outcome.

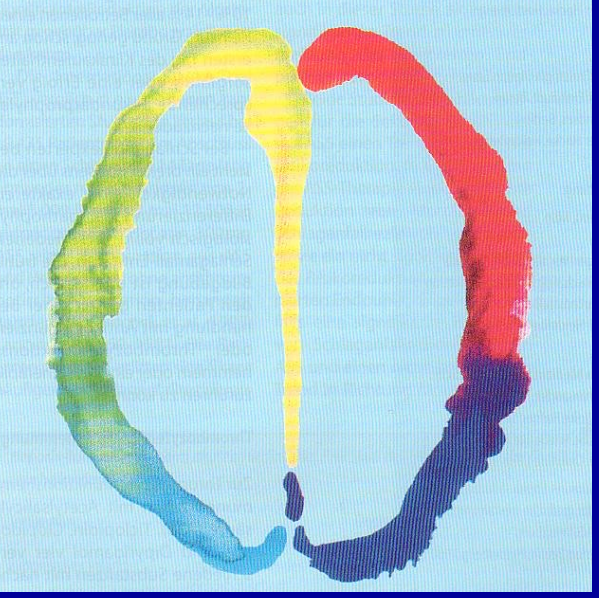


ENTEROVIRAL (Echoviruses and Coxsackieviruses) ASEPTIC MENINGITIS

Differential Diagnosis

The diagnosis of enteroviral aseptic meningitis is based on examination of the cerebrospinal fluid (CSF).

The opening pressure should be normal or slightly increased, and there is a mild lymphocytic pleocytosis, a normal or slightly increased protein concentration, and a normal glucose concentration. The white blood cell count typically is less than 1000 cells/mm3 .

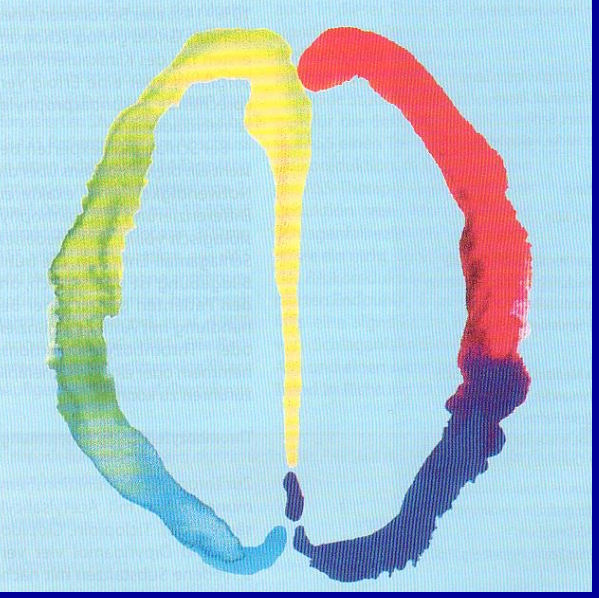


ENTEROVIRAL (Echoviruses and Coxsackieviruses) ASEPTIC MENINGITIS

Differential Diagnosis

At the present time, isolation of an enterovirus by CSF viral culture is the gold standard for diagnosis of an enteroviral CNS infection.

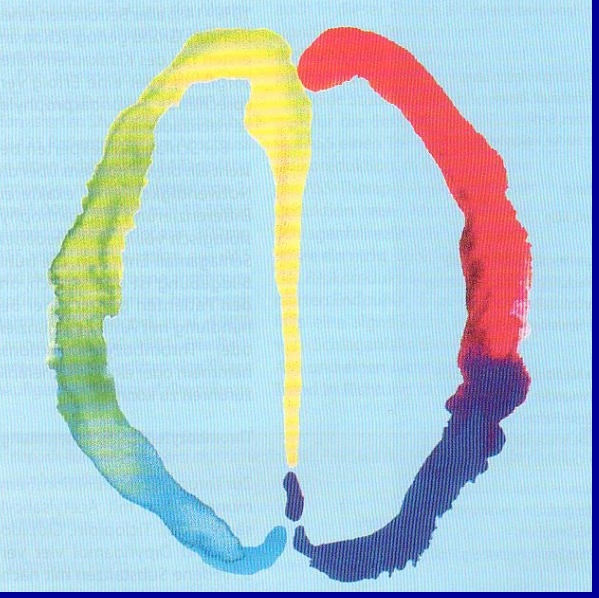
When an enterovirus is isolated from a non-CSF site (throat, stool, serum, urine) in conjunction with a CSF pleocytosis and an absence of bacteria by Gram's stain or the latex agglutination technique, enteroviral meningitis is the presumptive diagnosis. An enterovirus isolated from a non-CSF site may, however, be unrelated to the CNS infection.



ENTEROVIRAL (Echoviruses and Coxsackieviruses) ASEPTIC MENINGITIS

Management

There is no specific antiviral therapy for enteroviral CNS infection. Intravenous immune globulin has been used to treat enterovirus infections in newborns and in patients with agammaglobulinemia and other immunodeficiency states with good success, but it is not recommended in children and adults with uncomplicated enteroviral aseptic meningitis.



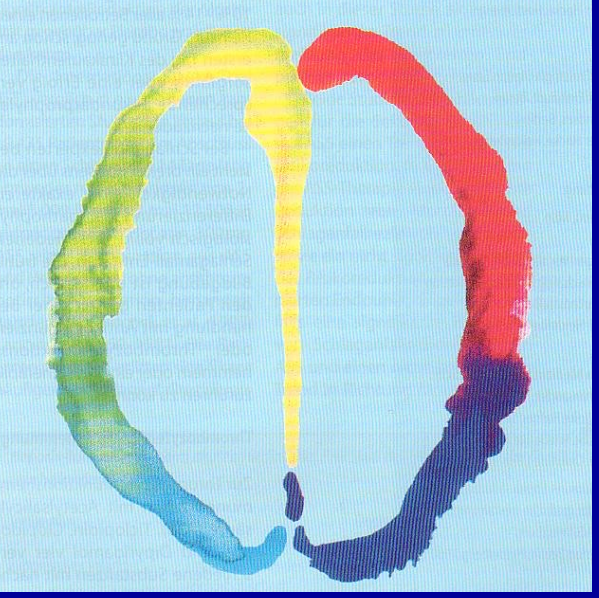
ARENAVIRUS (Lymphocytic Choriomeningitis Virus) ASEPTIC MENINGITIS

Epidemiology and Risk Factors

The natural reservoir for the lymphocytic choriomeningitis virus (LCMV) is the common house mouse.

Hamsters and laboratory animals can also be infected with this virus.

Most human infections result from contact with house mice.

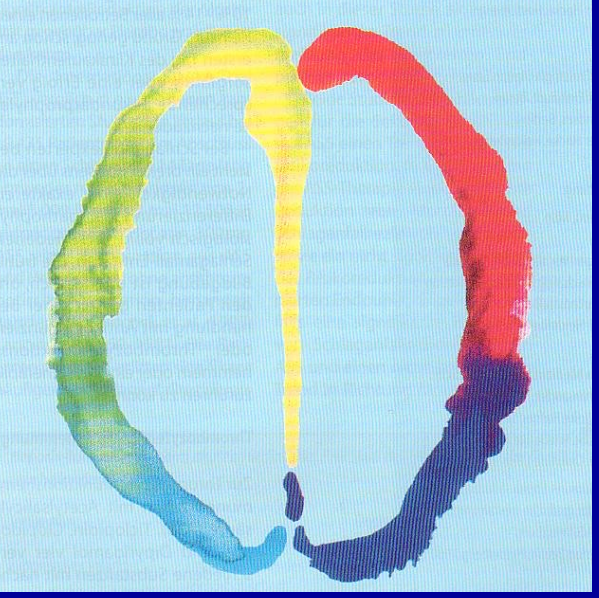


ARENAVIRUS (Lymphocytic Choriomeningitis Virus) ASEPTIC MENINGITIS

Pathogenesis and Pathophysiology

The LCMV is a member of the arenavirus family and is maintained in nature primarily by vertical intrauterine infection in mice, hamsters, and rodents, producing a chronic asymptomatic infection in the offspring.

These animals shed the virus in saliva, nasal secretions, semen, milk, urine, and feces.



ARENAVIRUS (Lymphocytic Choriomeningitis Virus) ASEPTIC MENINGITIS

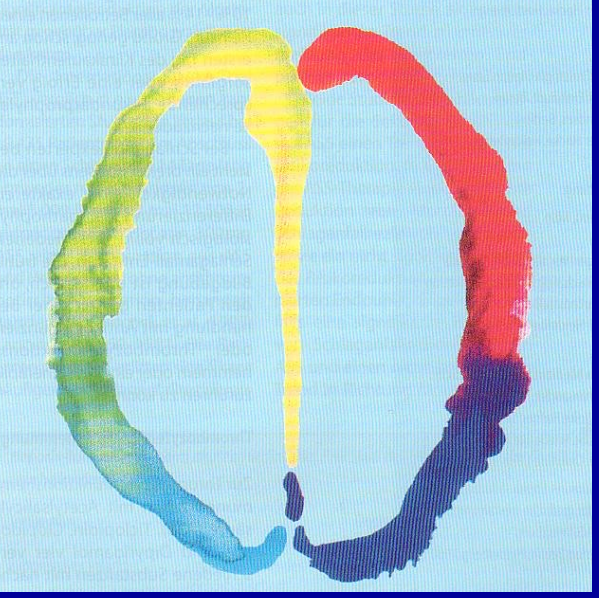
Pathogenesis and Pathophysiology

The route of transmission to humans remains unknown but is presumed to occur through contamination of open cuts or aerosolized spread of virus.

There is no evidence of person- to-person transmission of LCMV infection.

Local replication of LCMV is followed by dissemination to the reticuloendothelial system with a subsequent viremia.

The CNS is infected during the course of the viremia.



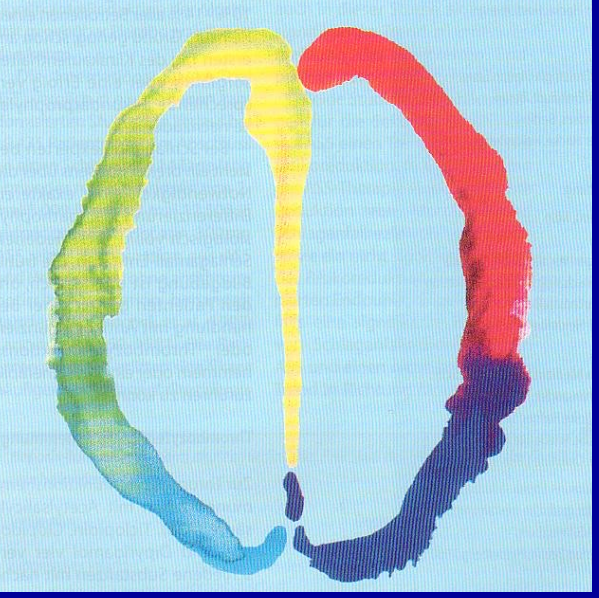
ARENAVIRUS (Lymphocytic Choriomeningitis Virus) ASEPTIC MENINGITIS

Clinical Manifestations

In patients with aseptic meningitis there is often a history of a biphasic illness.

The first stage resembles an influenza-like illness.

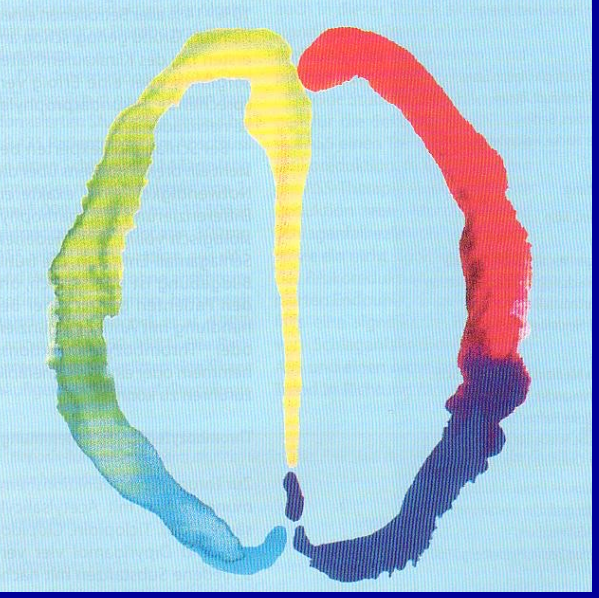
This is then followed by a symptom-free period of time varying from a few days to 3 weeks, which is followed in turn by the acute onset of high fever, headache, vomiting, and signs of meningeal irritation.



ARENAVIRUS (Lymphocytic Choriomeningitis Virus) ASEPTIC MENINGITIS

Differential Diagnosis

The diagnosis of LCMV infection can be made by the appearance of IgM antibodies in a serum sample or by a fourfold or greater rise in antibody titer between the acute and convalescent serum samples.



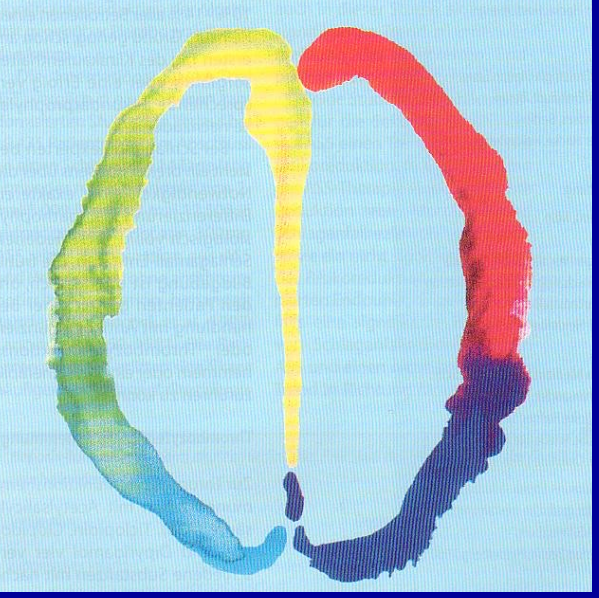
ARENAVIRUS (Lymphocytic Choriomeningitis Virus) ASEPTIC MENINGITIS

Differential Diagnosis

The classic cerebrospinal fluid abnormalities include the following: (1) a lymphocytic pleocytosis of 300 to 3000 cells/mm3 , and (2) hypoglycorrhachia.

LCMV is one of the few etiological agents of an aseptic meningitis with hypoglycorrhachia.

LCMV can be isolated from the CSF. The diagnosis of congenital LCMV infection is based on the clinical presentation and laboratory evidence of persistently high IgG immunofluorescent antibody (IFA) titers.



ARENAVIRUS (Lymphocytic Choriomeningitis Virus) ASEPTIC MENINGITIS

Management

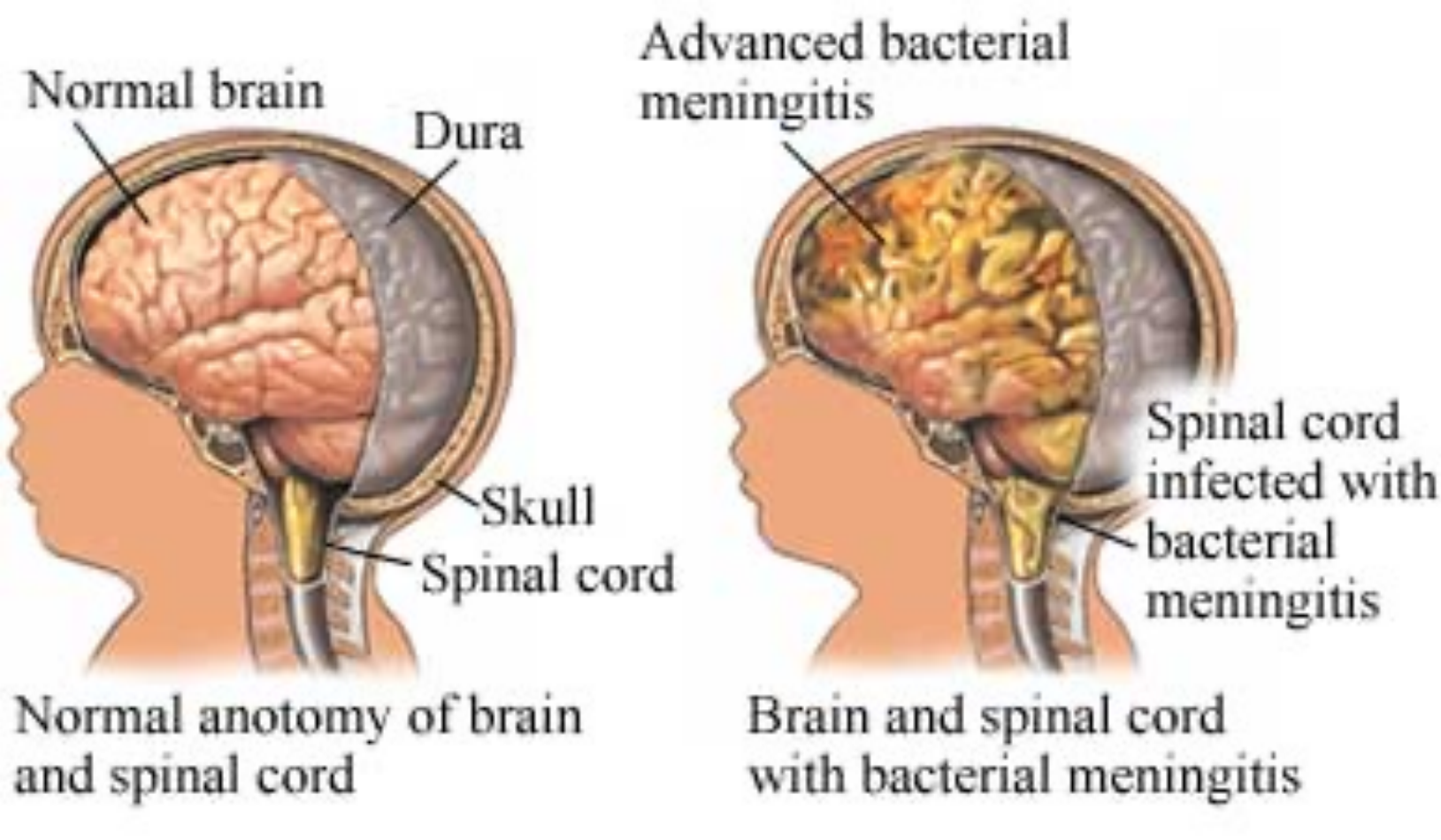
Prevention of LCMV infection is the priority.

Laboratory animals acquired from areas where arenaviruses are indigenous should be tested for LCMV infection.

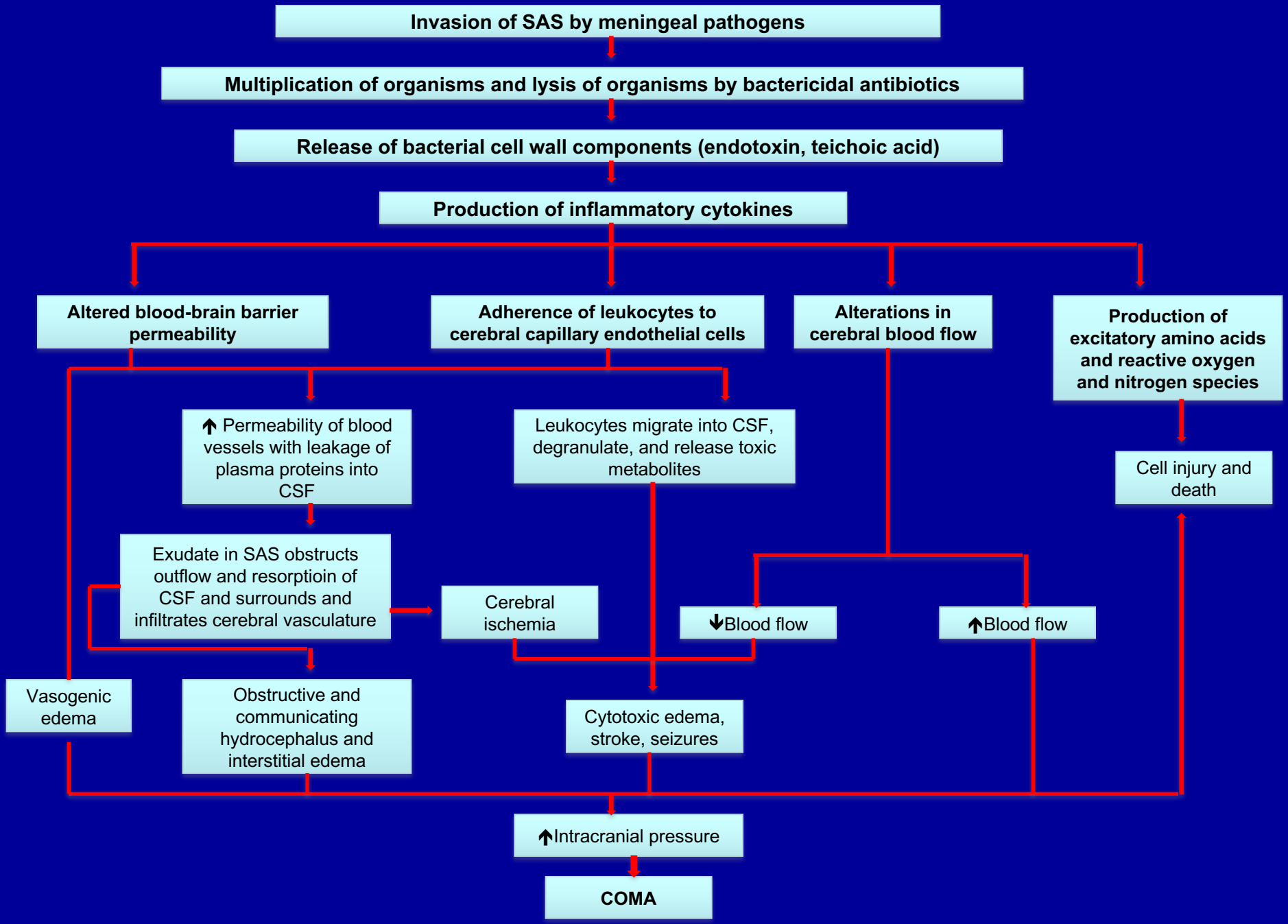
Pregnant women should avoid contact with laboratory and household mice and hamsters.

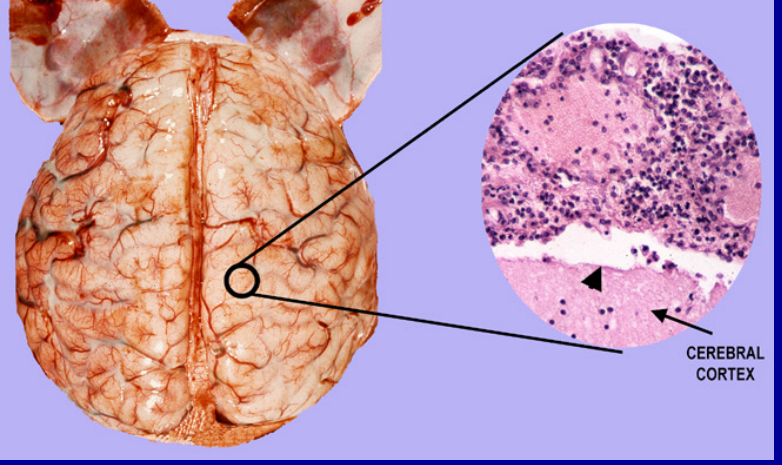
LCMV aseptic meningitis in children and adults is self-limited and complete recovery is the rule.

Bacterial Meningitis



PATHOPHYSIOLOGY OF ACUTE BACTERIAL MENINGITIS





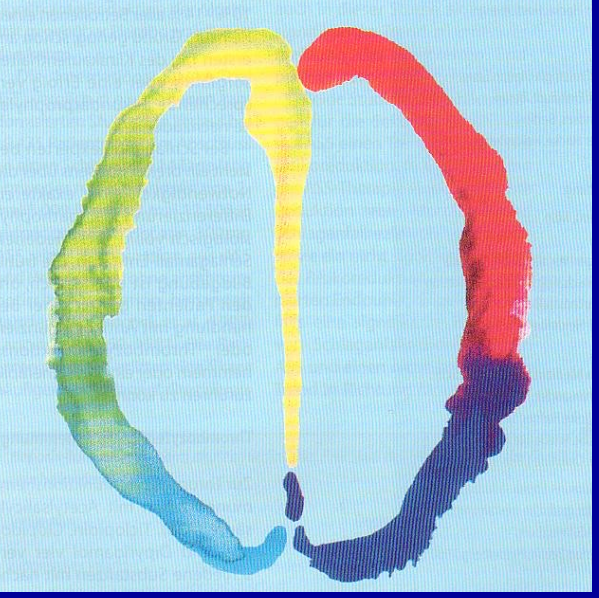
ACUTE BACTERIAL MENINGITIS

Epidemiology and Risk Factors

There are approximately 25,000 cases of bacterial meningitis in the United States each year, but this disease is much more prevalent in developing countries.

Group B streptococci and gram- negative enteric bacilli are the etiological organisms of the majority of cases of bacterial meningitis during the neonatal period in developed countries.

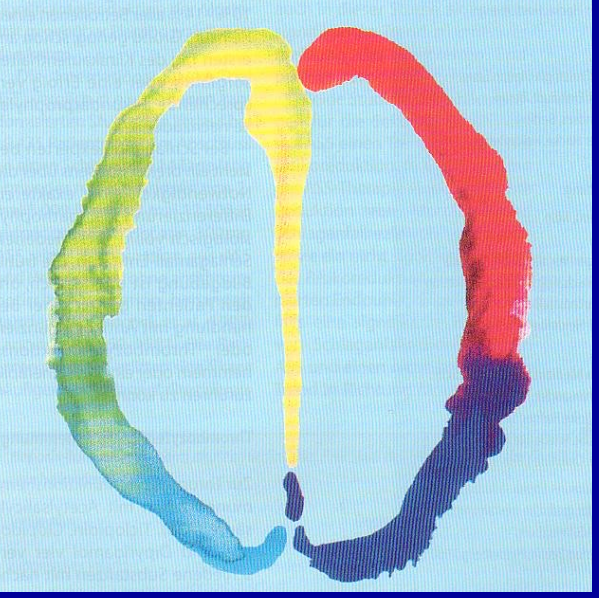
In underdeveloped countries, gram-negative bacilli, predominantly *Escherichia coli*, are the most common pathogens.



ACUTE BACTERIAL MENINGITIS

Epidemiology and Risk Factors

Risk factors that predispose the newborn to bacterial meningitis include maternal infections, particularly of the urinary tract and uterus, obstetrical risk factors, including prolonged rupture of membranes and birth trauma, prematurity, low birth weight (less than 2500 g), congenital anomalies, perinatal hypoxia/ asphyxia, cardiopulmonary resuscitation and monitoring, prolonged ventilatory support, and intravenous lines.

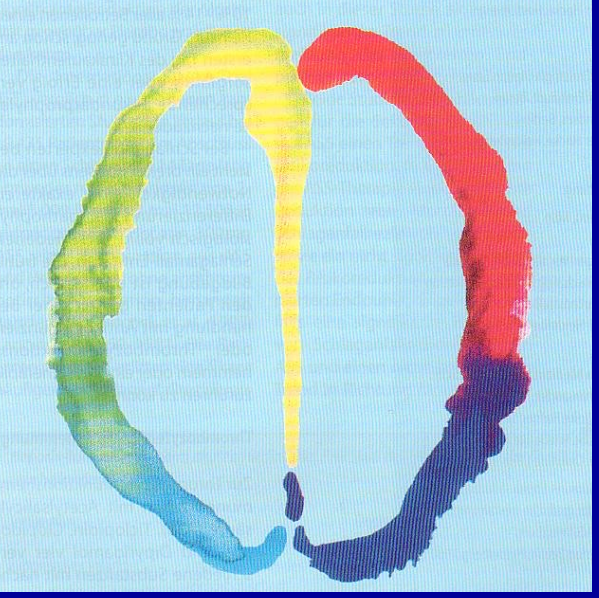


ACUTE BACTERIAL MENINGITIS

Epidemiology and Risk Factors

After the neonatal period, *Streptococcus pneumoniae* and *Neisseria meningitidis* are the most common etiological agents of bacterial meningitis.

Haemophilus influenzae type b (Hib) was the leading cause of bacterial meningitis in young children before the widespread use of the Hib conjugate vaccine. The latter has resulted in a marked reduction in the incidence of invasive infections caused by Hib in the United States.

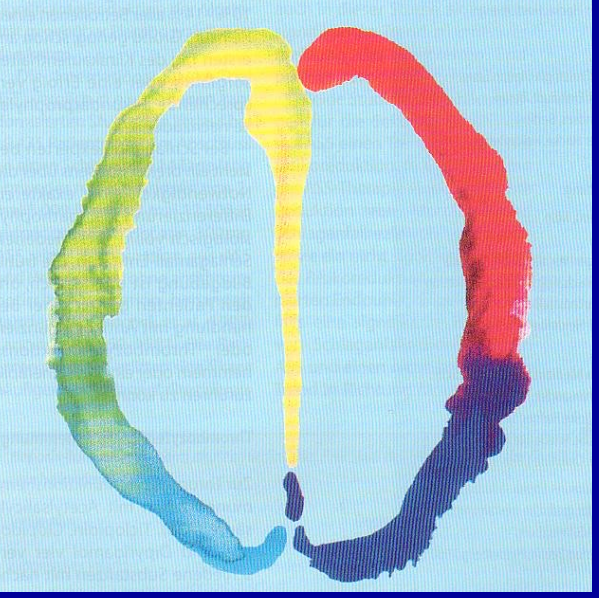


ACUTE BACTERIAL MENINGITIS

Epidemiology and Risk Factors

N. meningitidis causes meningitis primarily in children and young adults, with the majority of cases occurring in individuals under age 30. Major epidemics are heralded by disease occurring in older age groups.

The "meningitis belt" of sub-Saharan Africa refers to areas of Africa in which there are repeated epidemics of serogroup A meningococcal meningitis.

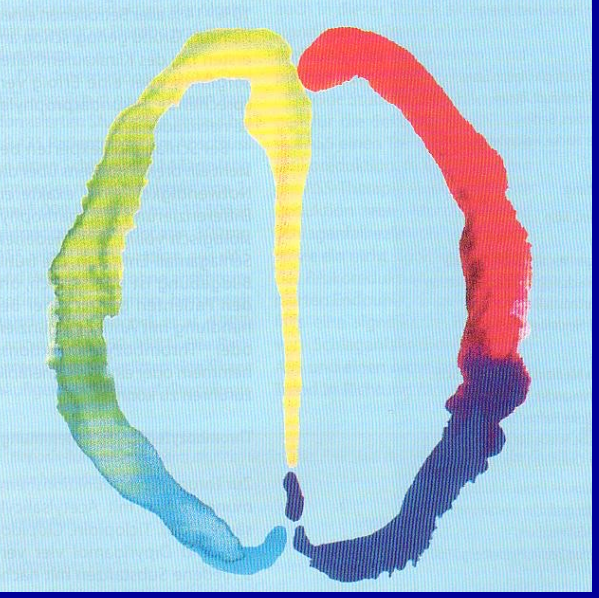


ACUTE BACTERIAL MENINGITIS

Epidemiology and Risk Factors

S. pneumoniae is the most common causative organism of community-acquired bacterial meningitis in the adult.

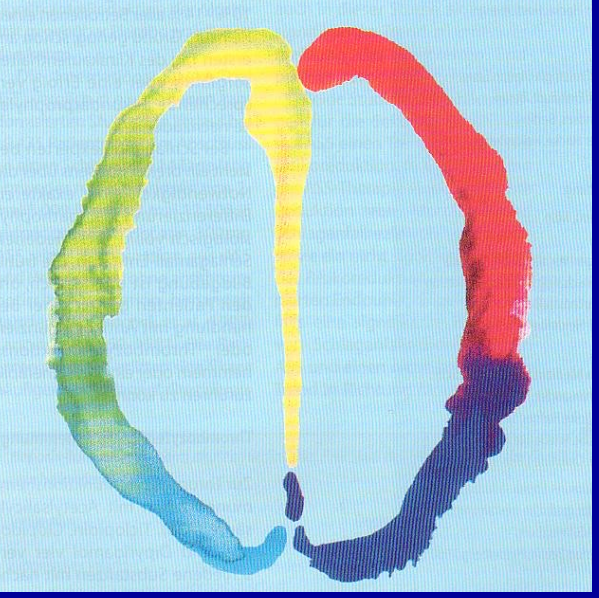
Pneumonia and acute and chronic otitis media are important antecedent events. Chronic disease, specifically alcoholism, sickle cell anemia, diabetes, renal failure, cirrhosis, splenectomy, hypogammaglobulinemia, and organ transplantation are predisposing conditions for pneumococcal bacteremia and meningitis.



ACUTE BACTERIAL MENINGITIS

Pathogenesis and Pathophysiology

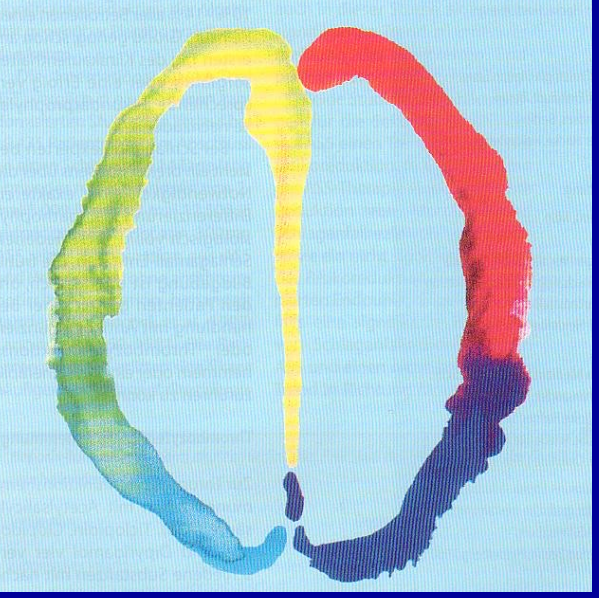
The most common bacteria that cause meningitis, *N. meningitidis* and *S. pneumoniae,* initially colonize the nasopharynx by attaching to the nasopharyngeal epithelial cells.



ACUTE BACTERIAL MENINGITIS

Pathogenesis and Pathophysiology

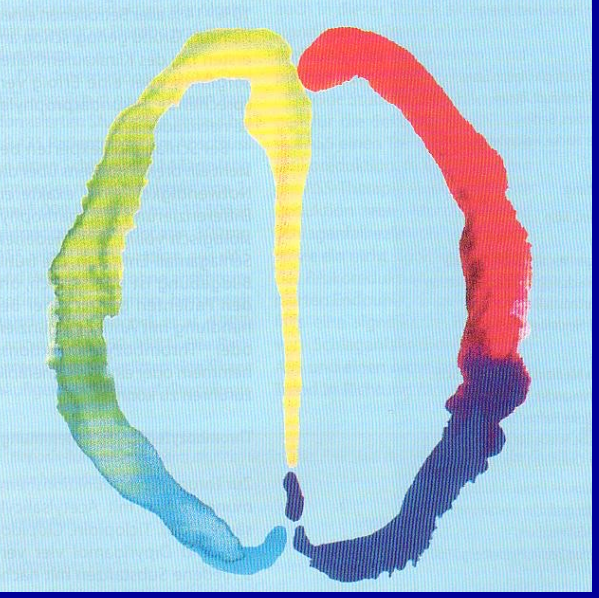
The organisms are able to attach to the nasopharyngeal epithelial cells via an interaction between bacterial surface structures, such as the fimbriae of *N. meningitidis* and host cell surface receptors.



ACUTE BACTERIAL MENINGITIS

Pathogenesis and Pathophysiology

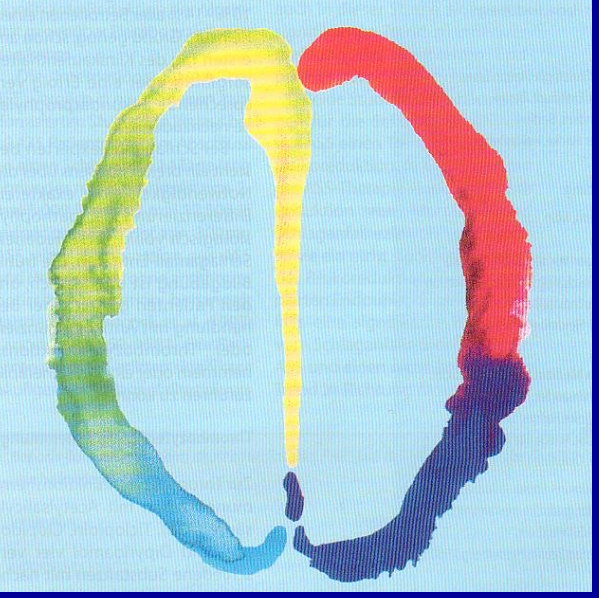
The bacteria are then either carried across the cell in membrane-bound vacuoles to the intravascular space or invade the intravascular space by creating separations in the apical tight junctions of columnar epithelial cells.



ACUTE BACTERIAL MENINGITIS

Pathogenesis and Pathophysiology

S. pneumoniae and *N. meningitidis* are both encapsulated bacteria, and once they gain access to the bloodstream, they are successful in avoiding phagocytosis by neutrophils and classic complement-mediated bactericidal activity because of the presence of the polysaccharide capsule.

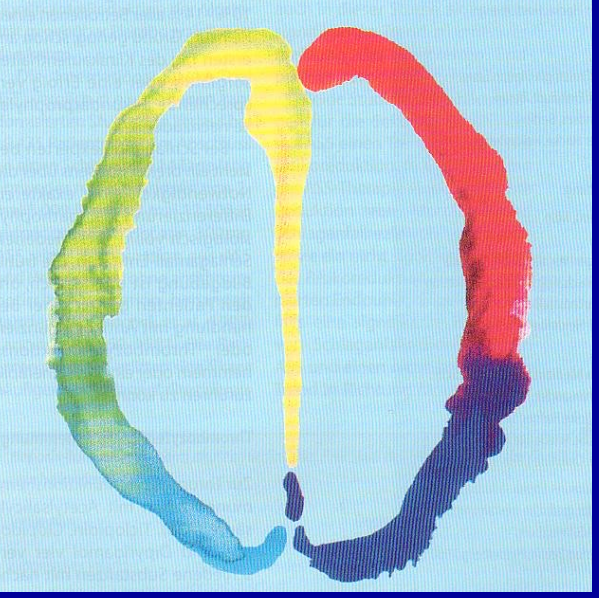


ACUTE BACTERIAL MENINGITIS

Pathogenesis and Pathophysiology

Bacteria that are able to survive in the circulation enter the CSF from the bloodstream through the choroid plexus of the lateral ventricles and other areas of altered blood-brain barrier permeability.

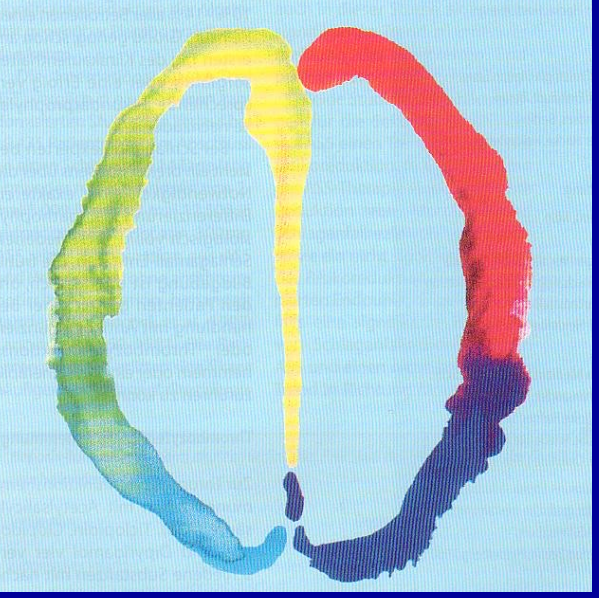
The CSF is an area of impaired host defense because of a lack of sufficient numbers of complement components and immunoglobulins for the opsonization of bacteria.



ACUTE BACTERIAL MENINGITIS

Pathogenesis and Pathophysiology

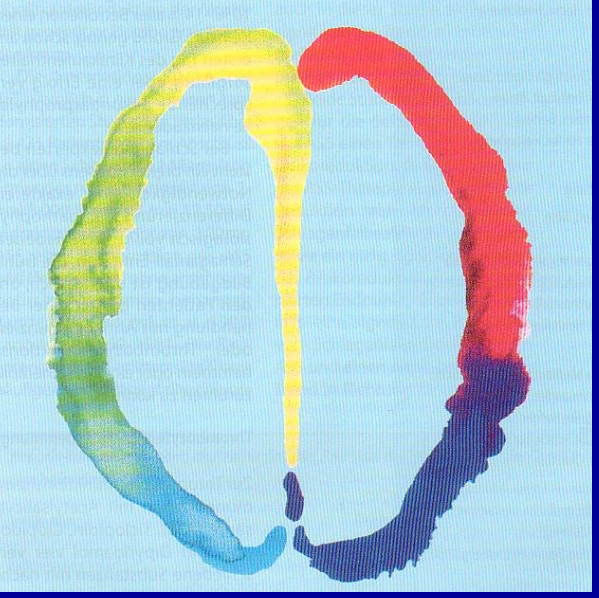
Bacteria multiply rapidly in the subarachnoid space. Both the multiplication of bacteria and the lysis of bacteria by bactericidal antibiotics result in the release of bacterial cell wall components.



ACUTE BACTERIAL MENINGITIS

Pathogenesis and Pathophysiology

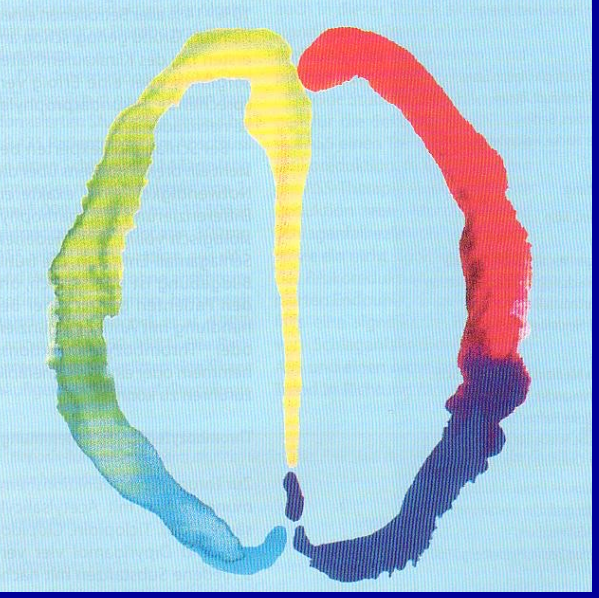
These induce the formation of the inflammatory cytokines, interleukin-1 (IL-1) and tumor necrosis factor (TNF), by monocytes, macrophages, brain astrocytes, and microglial cells, which leads to altered blood-brain barrier permeability and the recruitment of polymorphonuclear leukocytes.



ACUTE BACTERIAL MENINGITIS

Pathogenesis and Pathophysiology

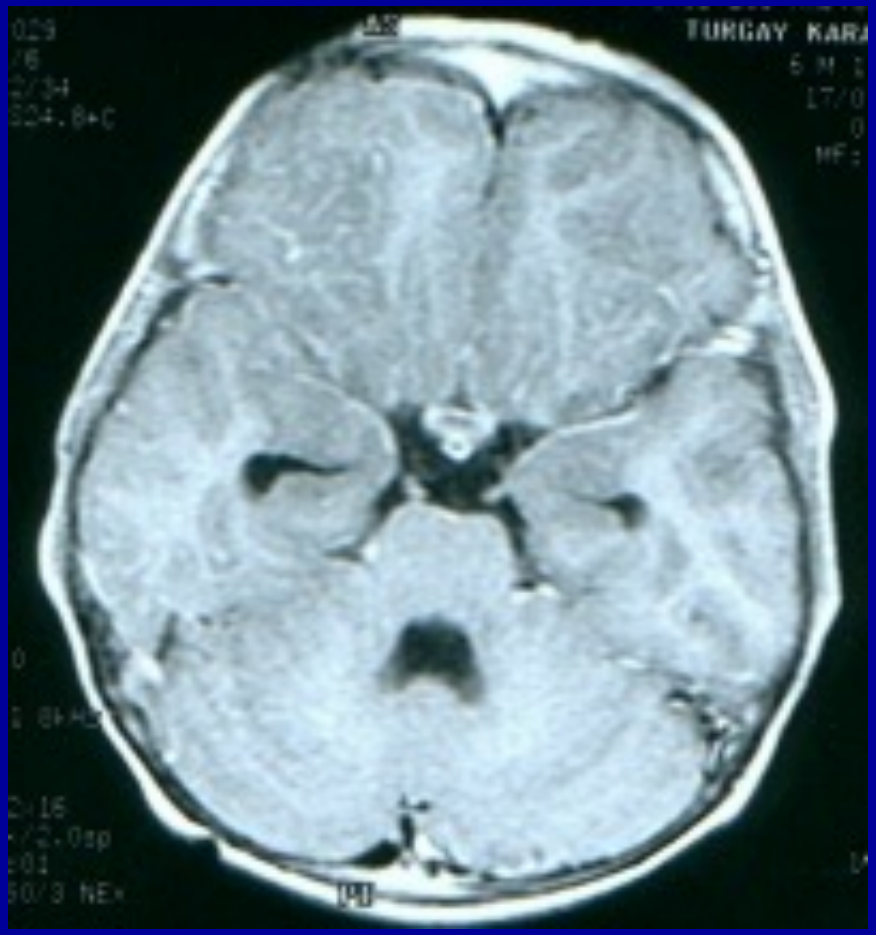
This process results in the formation of a purulent exudate in the subarachnoid space, which is the basis for the neurological complications of bacterial meningitis.



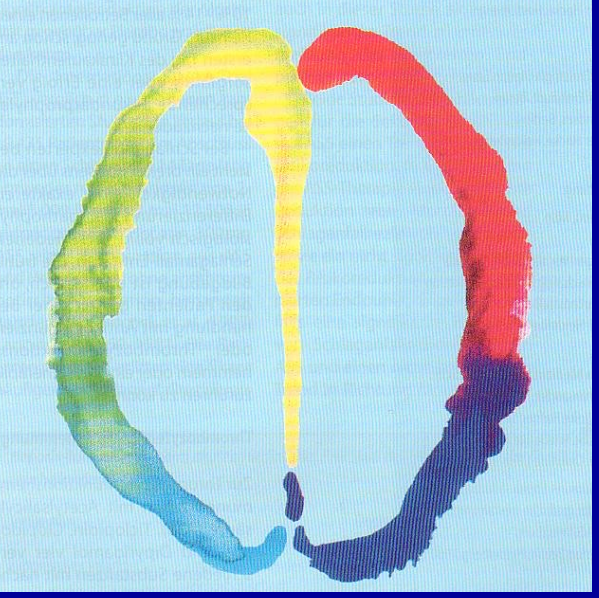
ACUTE BACTERIAL MENINGITIS

Pathogenesis and Pathophysiology

The alteration in blood-brain barrier permeability during bacterial meningitis results in vasogenic cerebral edema, which contributes to increased intracranial pressure. It also allows for the leakage of plasma proteins into the CSF that contribute to the inflammatory exudate in the subarachnoid space.



Contrast enhanced T1-weighted MR image of patient with meningitis. Diffuse pial meningeal enhancement.

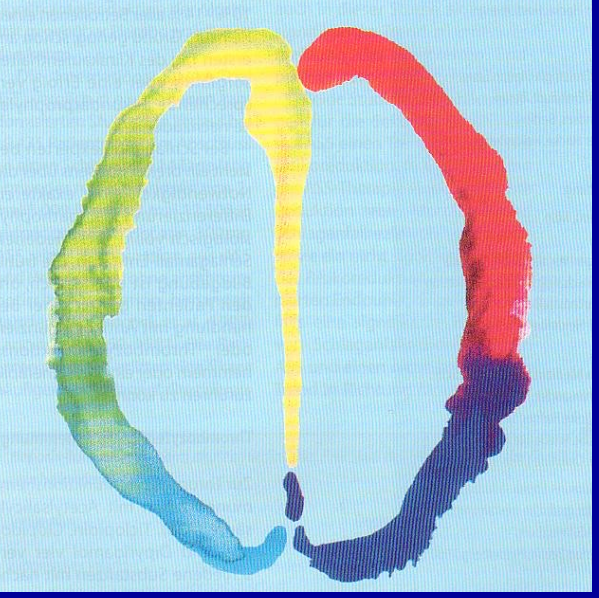


ACUTE BACTERIAL MENINGITIS

Pathogenesis and Pathophysiology

The purulent exudate in the subarachnoid space interferes with the resorptive function of the arachnoid granulations.

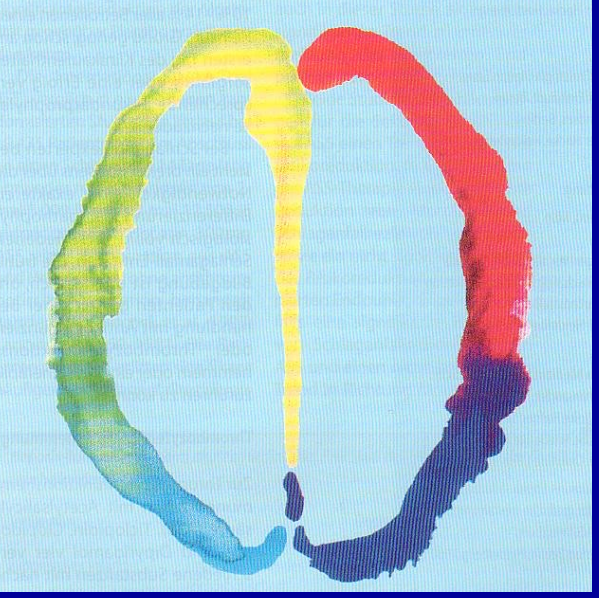
As resorption is obstructed, CSF dynamics are altered, and there is transependymal movement of fluid from the ventricular system into the brain parenchyma, which contributes to interstitial edema.



ACUTE BACTERIAL MENINGITIS

Clinical Features and Differential Diagnosis

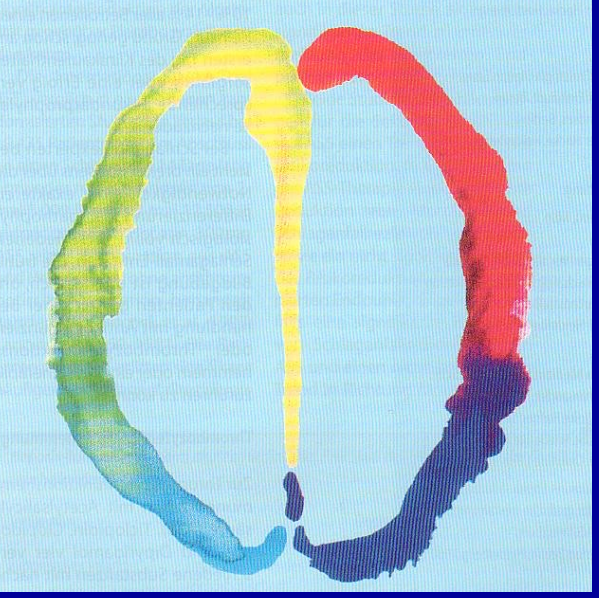
The classic presentation of bacterial meningitis is headache, fever, stiff neck, and an altered level of consciousness, but the clinical symptoms and signs may vary depending on the age of the patient and the duration of illness before presentation.



ACUTE BACTERIAL MENINGITIS

Clinical Features and Differential Diagnosis

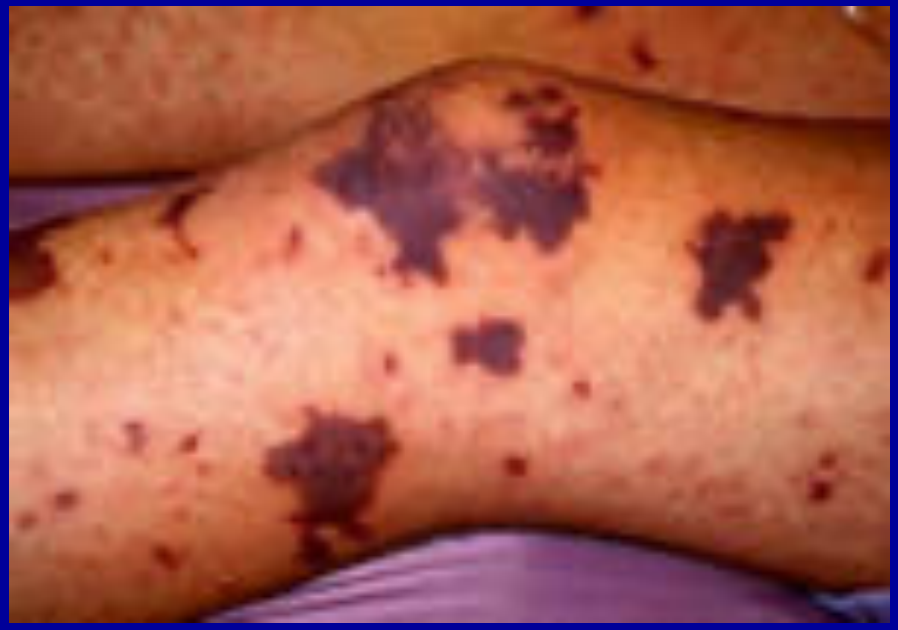
In children and adults, the symptoms and signs of bacterial meningitis are fever, headache, vomiting, photophobia, nuchal rigidity, lethargy, confusion, or coma.

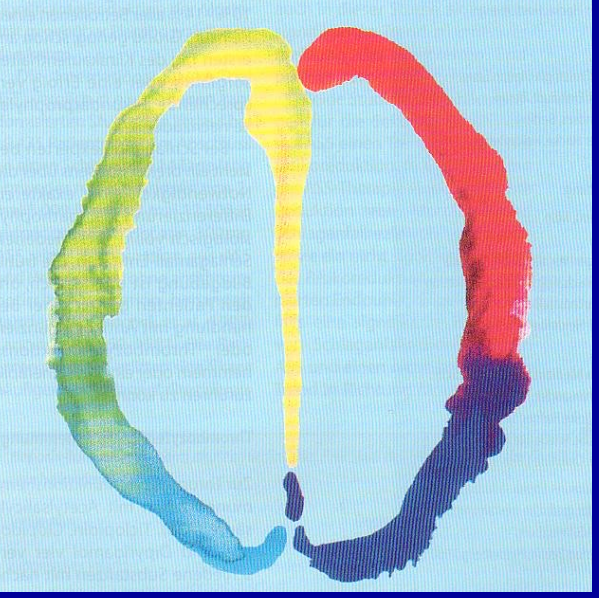


ACUTE BACTERIAL MENINGITIS

Clinical Features and Differential Diagnosis

The typical rash of meningococcemia is a petechial-purpuric rash that develops on the trunk, lower extremities, mucous membranes, conjunctiva, and occasionally on the palms and soles.

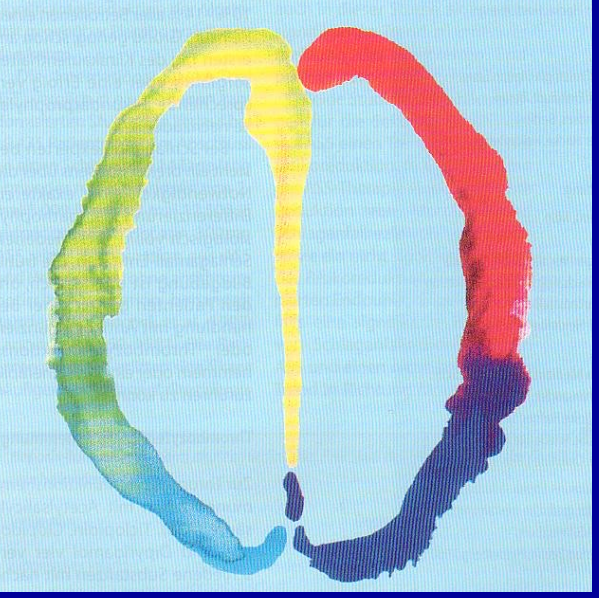




ACUTE BACTERIAL MENINGITIS

Clinical Features and Differential Diagnosis

Cranial nerve palsies, and most notably sensorineural hearing loss, are a common complication of bacterial meningitis and may be present early in the course of the illness. A stiff neck is the pathognomonic sign of meningeal irritation, resulting from a purulent exudate or hemorrhage in the subarachnoid space.

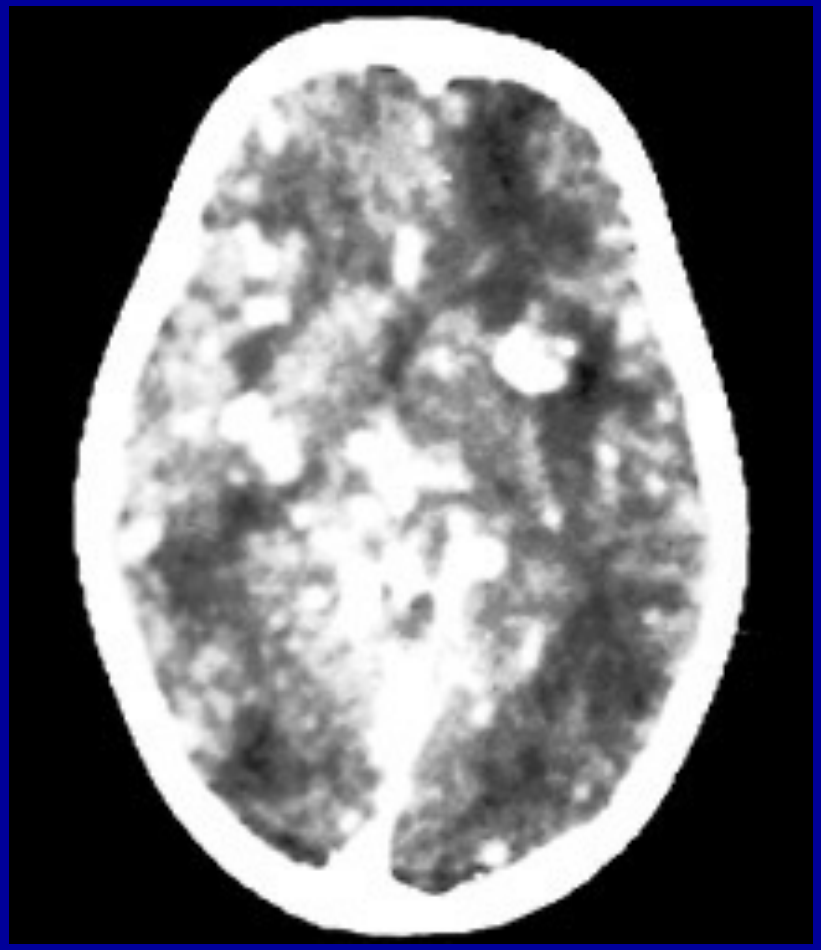


ACUTE BACTERIAL MENINGITIS

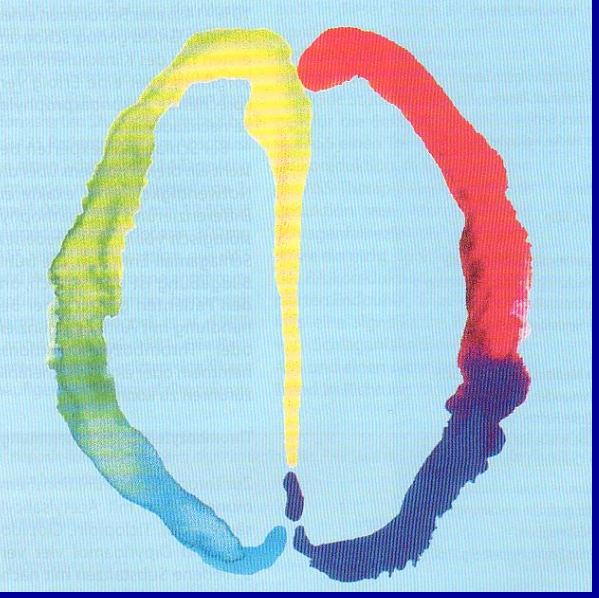
Clinical Features and Differential Diagnosis

Nuchal rigidity or meningismus is present when the neck resists passive flexion. Kernig's sign is also a classic sign of meningeal irritation.

Jozef Brudzinski described at least five different meningeal signs. His best known sign, the nape of the neck sign, is elicited with the patient in the supine position and is positive when passive flexion of the neck results in spontaneous flexion of the hips and knees.



CT scan of thickening meninges
CT demonstrates contrast enhancement of thickening meninges and multiple intraparenchymal enhancing lesions.



ACUTE BACTERIAL MENINGITIS

Clinical Features and Differential Diagnosis

Seizures occur in 40 percent of patients with bacterial meningitis typically during the first week of illness.

The etiology of seizure activity can be attributed to either one or a combination of the following:

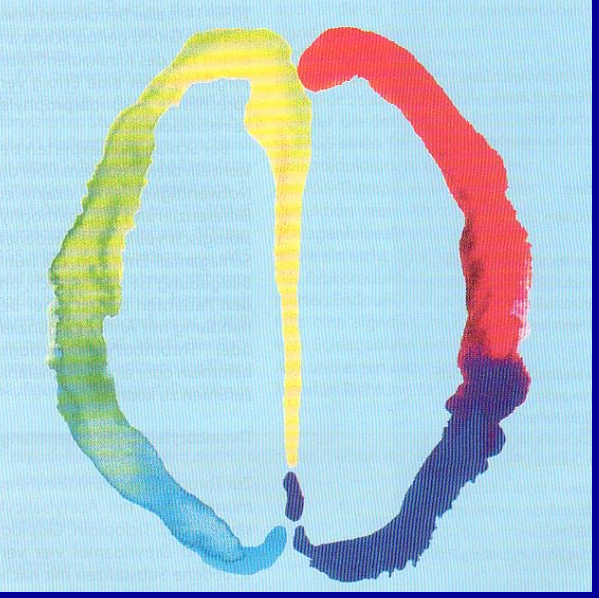
(1) fever;

(2) cerebrovascular disease consisting of either focal arterial ischemia, infarction or cortical venous thrombosis with hemorrhage;

(3) hyponatremia;

(4) subdural effusion or empyema producing a mass effect; and

(5) antimicrobial agents (e.g., imipenem, penicillin).

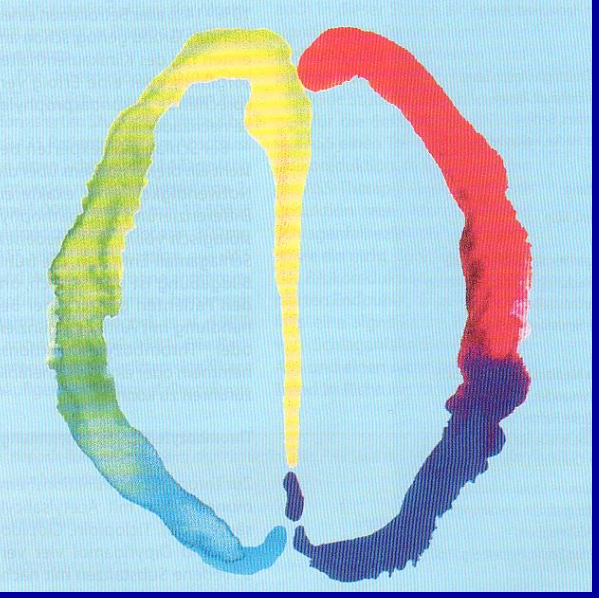


ACUTE BACTERIAL MENINGITIS

Clinical Features and Differential Diagnosis

Raised ICP is an expected complication of bacterial meningitis and presents as one or a combination of the following clinical signs:

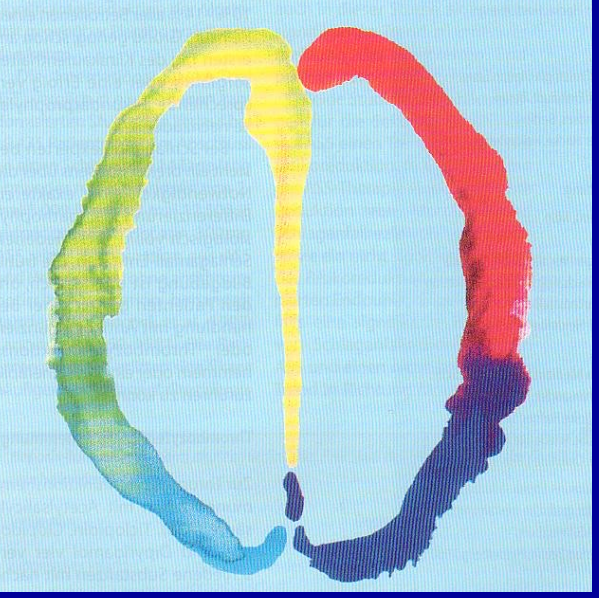
(1) an altered level of consciousness;
(2) the Cushing reflex--bradycardia, hypertension, and irregular respirations;
(3) dilated, nonreactive pupil or pupils;
(4) unilateral or bilateral cranial nerve six palsies;
(5) papilledema;
(6) neck stiffness;
(7) hiccups;
(8) projectile vomiting; and,
(9) decerebrate posturing.



ACUTE BACTERIAL MENINGITIS

Clinical Features and Differential Diagnosis

The differential diagnosis includes viral meningoencephalitis, fungal meningitis, tuberculous meningitis, focal intracranial mass lesions, subarachnoid hemorrhage, Rocky Mountain spotted fever, and neuroleptic malignant syndrome.



ACUTE BACTERIAL MENINGITIS

Evaluation

The gold standard for the diagnosis of bacterial meningitis is the examination of the CSF.

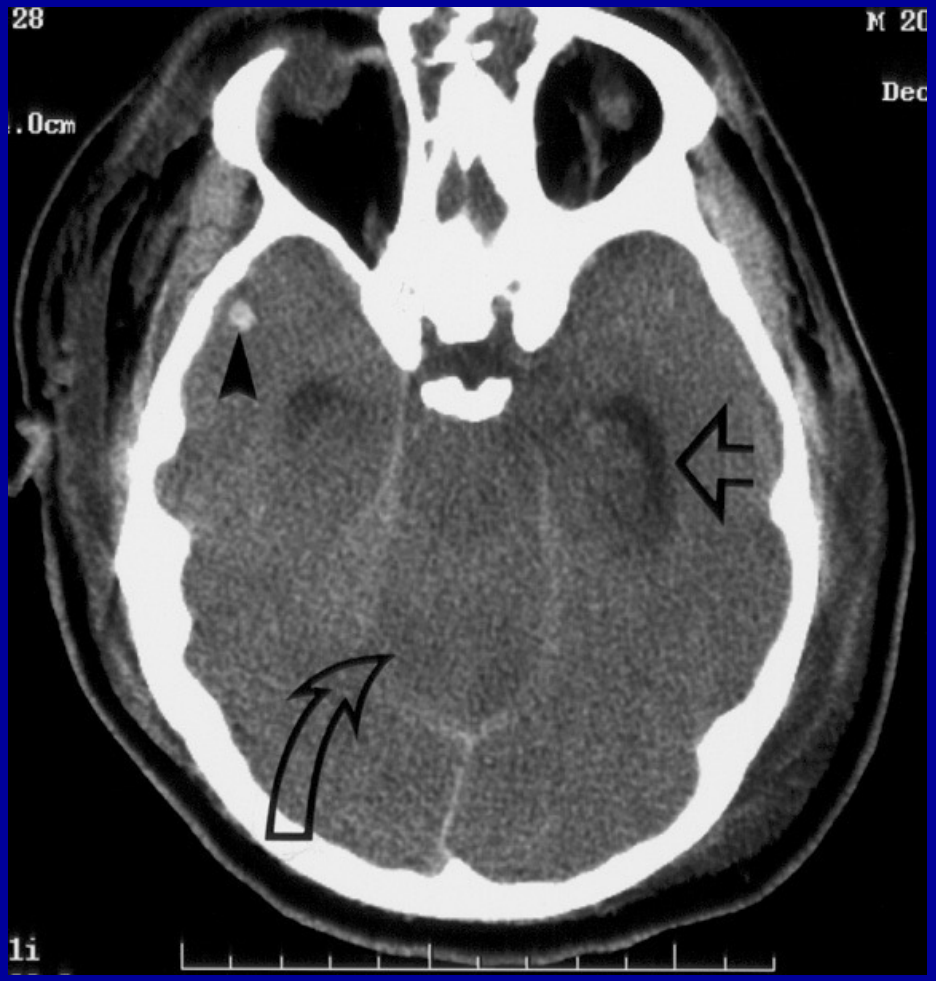
The classic CSF abnormalities in bacterial meningitis are

(1)an increased opening pressure;

(2) a polymorphonuclear leukocytic pleocytosis;

(3) a decreased glucose concentration; and

(4) an increased protein concentration.



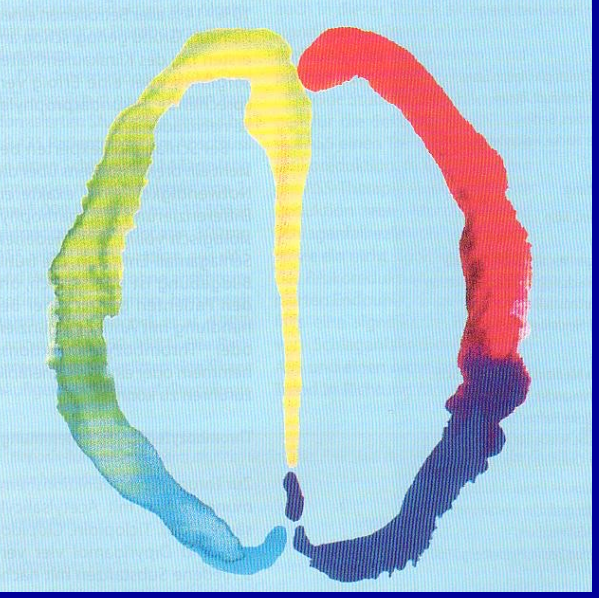
Meningococcal Meningitis: Head CT demonstrates enlargement of the temporal horns.

Meningococcal meningitis: Grossly purulent exudate is seen in the leptomeninges.

ANTIBIOTICS USED IN EMPIRICAL THERAPY OF BACTERIAL MENINGITIS AND FOCAL CNS INFECTIONS[a]

INDICATION	ANTIBIOTIC
Preterm infants to infants < 1 month Infants 1-3 months	Ampicillin + cefotaxime Ampicillin + cefotaxime or ceftriaxone
Immunocompetent children >3 months and adults <55 years	Cefotaxime or ceftriaxone + vancomycin
Adults >55 years and adults of any age with alcoholism or other debilitating illnesses	Ampicillin + cefotaxime or ceftriaxone + vancomycin
Hospital-acquired meningitis, posttraumatic or postneurosurgery meningitis, neutropenic patients, or patients with impaired cell-mediated immunity	Ampicillin + ceftazidime + vancomycin

[a] All antibiotics are administered intravenously; doses indicated assume normal renal and hepatic function.

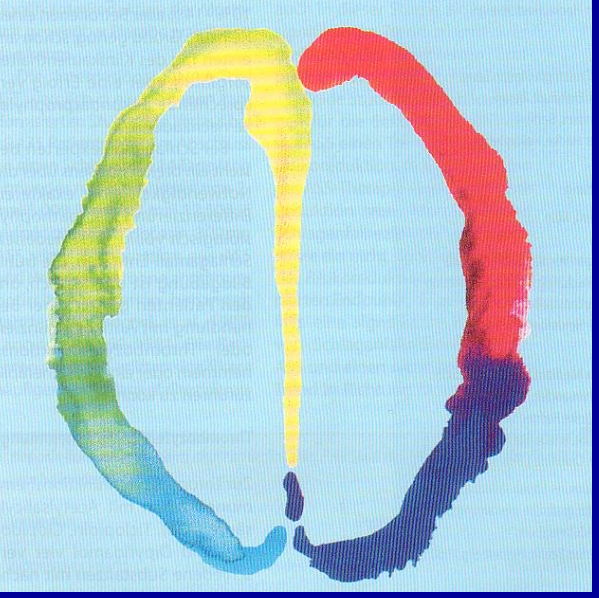


ACUTE BACTERIAL MENINGITIS

Management

Empirical therapy of bacterial meningitis in adults should include a combination of ceftriaxone (2 g intravenously twice daily) or cefotaxime (8 to 12 g/d intravenously in divided doses q 4 hr) plus vancomycin (500 mg intravenously q 6 hr).

In the older adult and in the immunocompromised adult in whom *L. monocytogenes* may be the etiological organism, ampicillin (12 g/d in divided doses q 4 hr) should be added to this regimen.



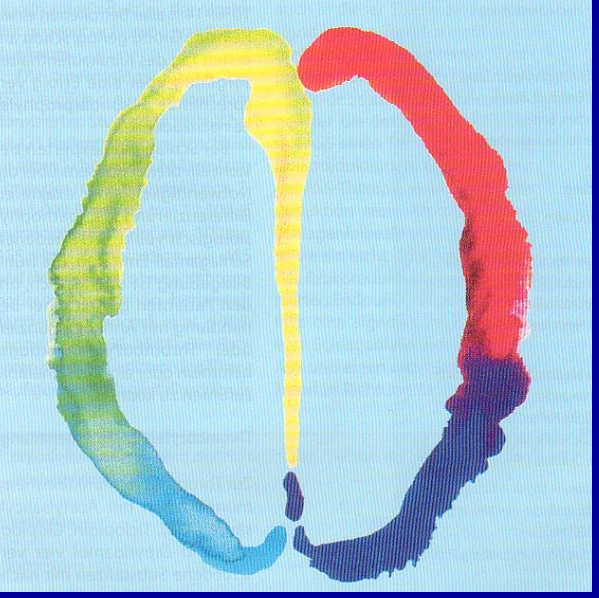
ACUTE BACTERIAL MENINGITIS

Management

It is also entirely reasonable to use dexamethasone for bacterial meningitis.

The recommended dose is 0.6 mg/kg/d in four divided doses (0.15 mg/kg/dose) given intravenously for the first 4 days of antimicrobial therapy.
The first dose of dexamethasone should be administered 20 minutes before the first dose of antimicrobial therapy.

Dexamethasone is beneficial in preventing the neurological complications of bacterial meningitis by decreasing meningeal inflammation.



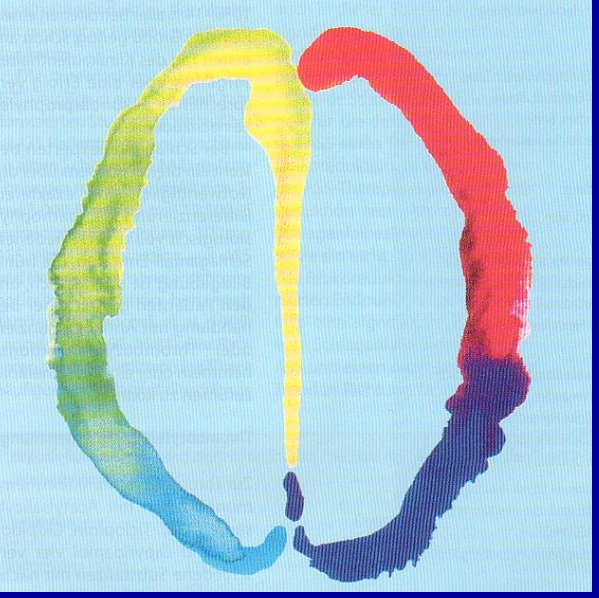
ACUTE BACTERIAL MENINGITIS

Management

The present recommendations are to limit the initial rate of intravenous fluid administration to approximately three quarters of the normal maintenance requirements (or 1000 to 1200 ml/m2 / 24 hr).

The intravenous fluid should be a multielectrolyte solution containing between one quarter and one half normal saline and potassium at 20 to 40 mEq/L in 5 percent dextrose.

Once the serum sodium concentration increases above 135 mEq/L, the volume of the fluids administered can be gradually increased.



ACUTE BACTERIAL MENINGITIS

Management

The treatment of raised ICP in bacterial meningitis includes one or more of the following:

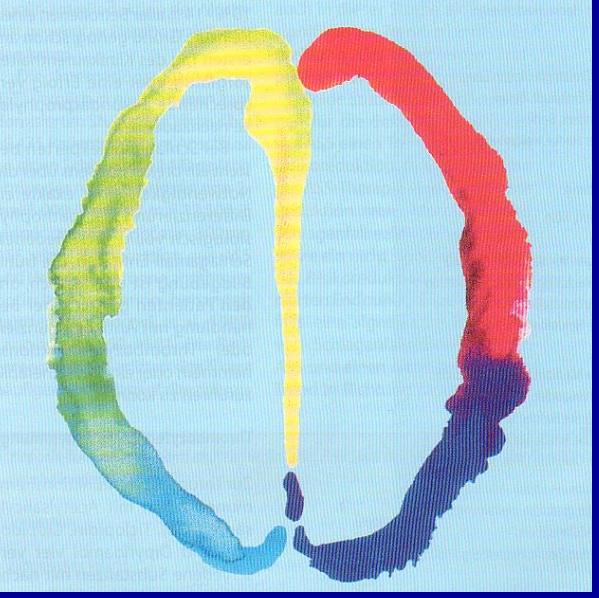
(1) elevation of the head of the bed 30 degrees;

(2) hyperventilation to maintain the $PaCO_2$ between 25 to 33 mm Hg;

(3) mannitol 1.0 g/kg bolus intravenous injection, then 0.25 to 0.5 g/kg intravenous every 3 to 5 hours to achieve a serum osmolarity of 295 to 320 mOsm/L;

(4) dexamethasone 0.15 mg/kg q 6 hr; and

(5) pentobarbital coma with a loading dose 5 to 10 mg/kg administered intravenously at a rate of 1 mg/kg/min and a maintenance dose of 1 to 3 mg/kg/hr.



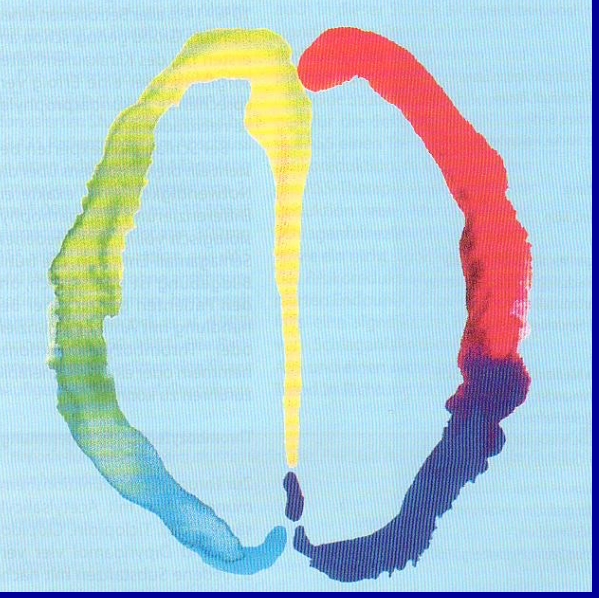
ACUTE BACTERIAL MENINGITIS

Management

The development of seizure activity should be anticipated in the patient with bacterial meningitis.

Seizure activity occurs in approximately 30 to 40 percent of children with acute bacterial meningitis and in more than 30 percent of adults with pneumococcal meningitis, typically occurring in the first few days of the illness.

There is an increased risk of epilepsy following bacterial meningitis especially in those individuals who have seizures in the first few days of infection.



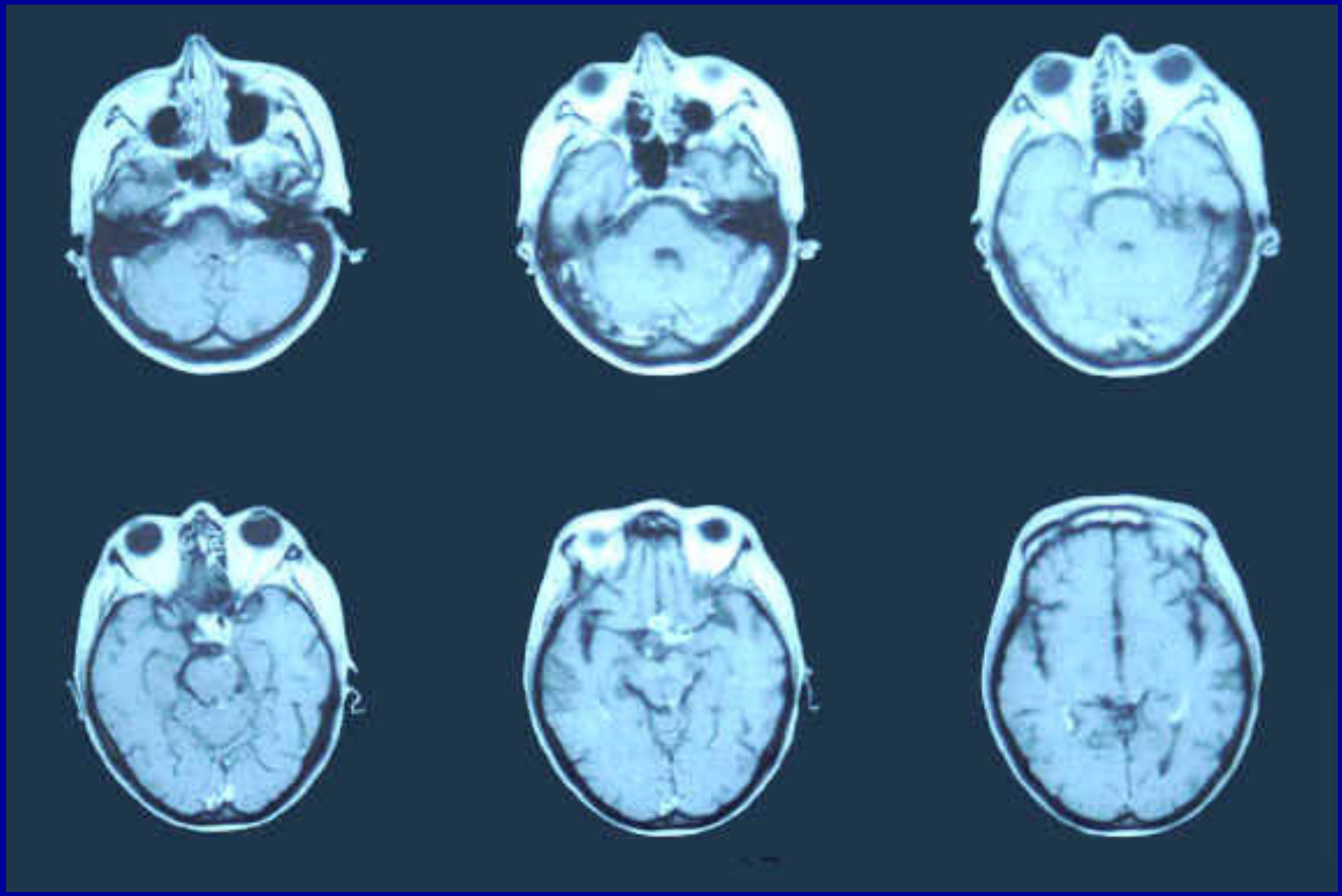
TUBERCULOUS MENINGITIS

Epidemiology and Risk Factors

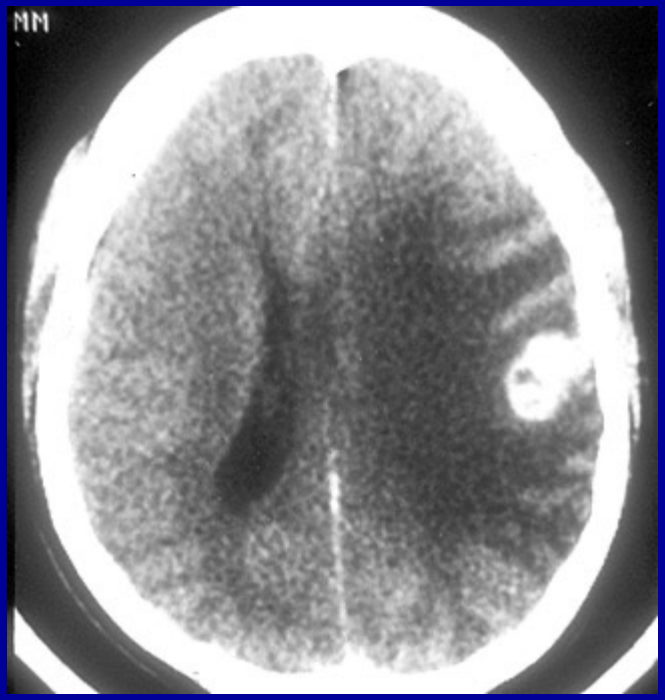
Tuberculosis and CNS tuberculosis continued to be prevalent in developing countries.

CNS tuberculosis is considerably more frequent in individuals with AIDS and tuberculosis involving other organ systems than in immunocompetent persons with tuberculosis.

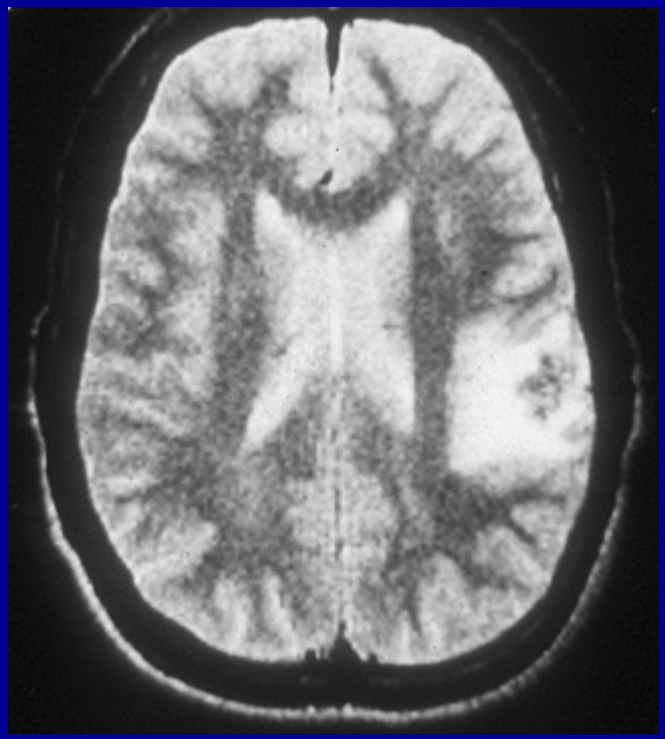
In some parts of the world, the most common AIDS-associated CNS infection is tuberculous meningitis.



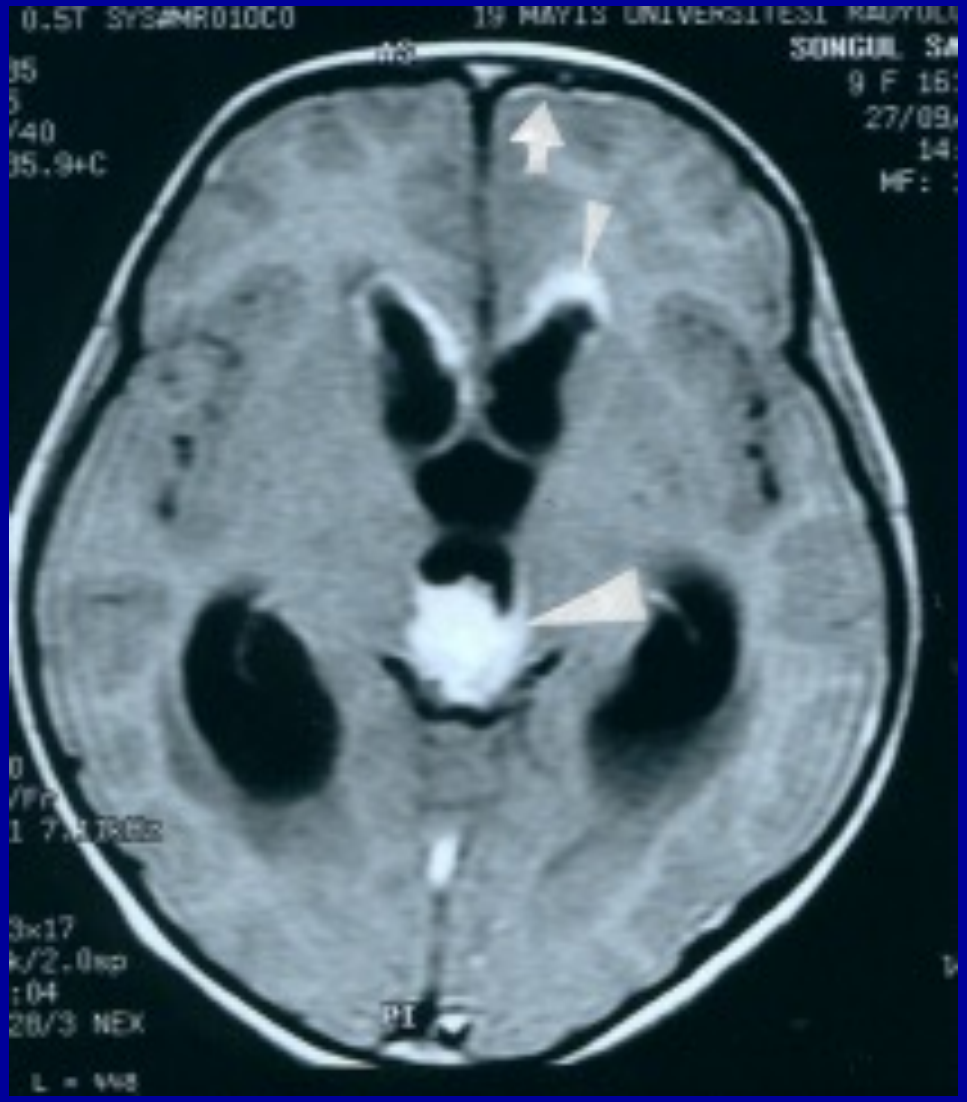
Tuberculous meningitis. MRI of the brain.



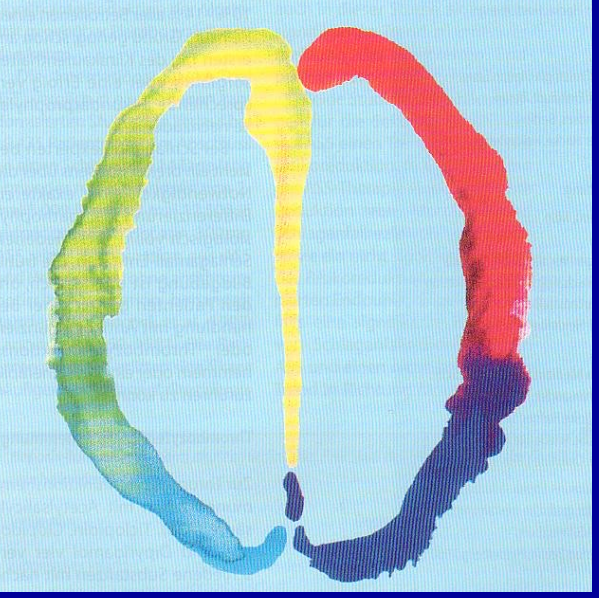
Intracranial tuberculoma: Caseating granuloma (1)
Contrast-enhanced axial CT shows numerous conglomerate areas of dense ring-enhancements at grey-white matter junction of left fronto-parietal lobe. Extensive low-attenuating white matter edema is seen at left cerebral hemisphere.



Intracranial tuberculoma: Caseating granuloma (3)
T2-weighted axial image shows lobulated low T2 signal lesion with specks of central high signal corresponding to central caseation. Surrounding high T2-signal edema is appreciated.



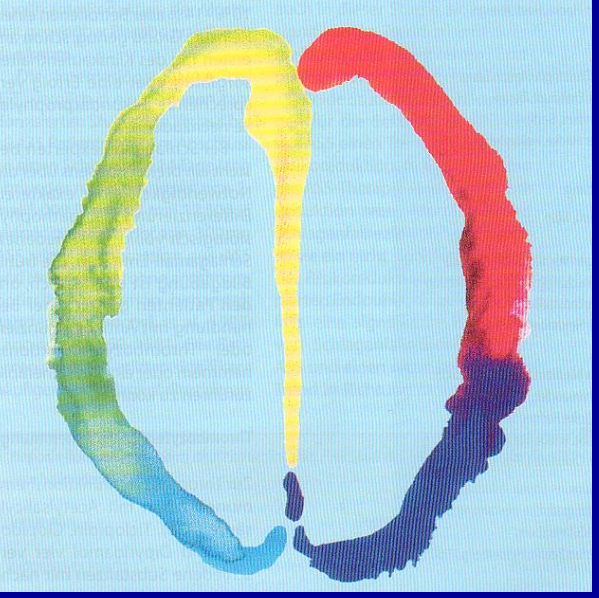
Contrast enhanced T1-weighted Mr image of Tuberculous meningitis.



TUBERCULOUS MENINGITIS Pathogenesis and Pathophysiology

Tuberculous meningitis develops from the hematogenous spread of tubercle bacilli to the meninges from a pulmonary source of acute infection.

Isolated miliary tubercles form in the parenchyma of the brain or the meninges during the hematogenous dissemination of tubercle bacilli during the course of the primary infection or episodically from the endogenous reactivation of latent tuberculosis elsewhere in the body.

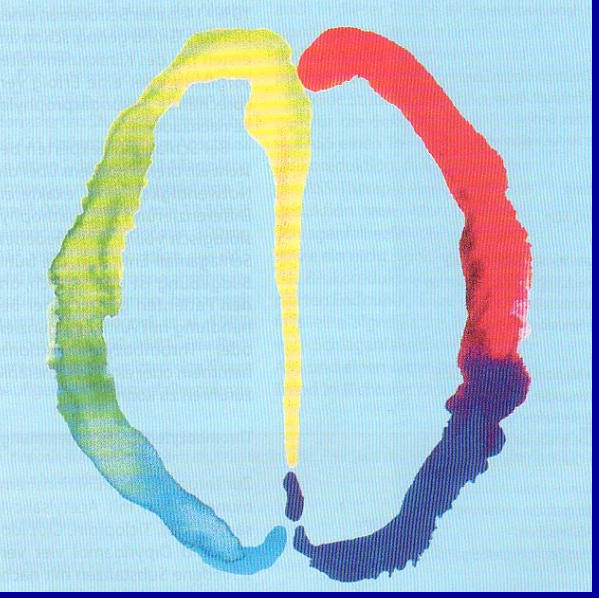


TUBERCULOUS MENINGITIS

Clinical Features

Acute meningoencephalitis characterized by coma, raised intracranial pressure, seizures, and focal neurological deficits or a slowly progressive illness with persistent and intractable headache followed by confusion, lethargy, and cranial nerve deficits.

Fever may or may not be present in the course of this infection.



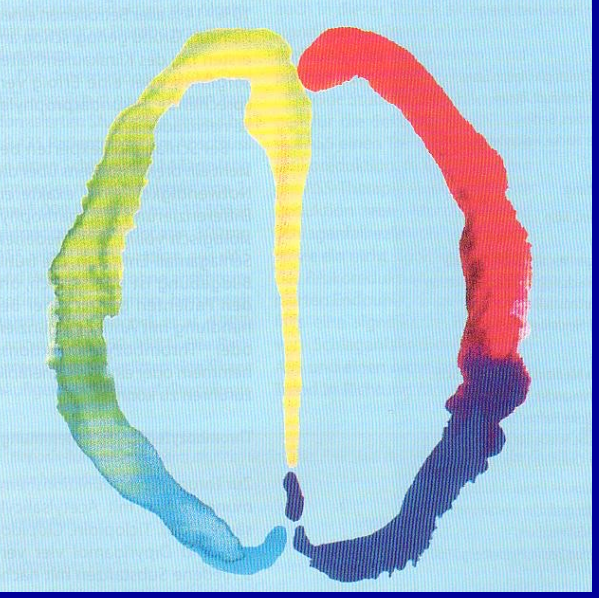
TUBERCULOUS MENINGITIS

Clinical Features

The sixth cranial nerve is the most frequently affected by tuberculous meningitis followed by the third, fourth, seventh, and less commonly, the second, eighth, tenth, eleventh, and twelfth cranial nerves.

Hemiparesis may develop as a result of ischemic infarction in the medial striate and thalamoperforating arteries.

Seizures are an infrequent presenting sign, although more than 50 percent develop seizures during the initial hospitalization.

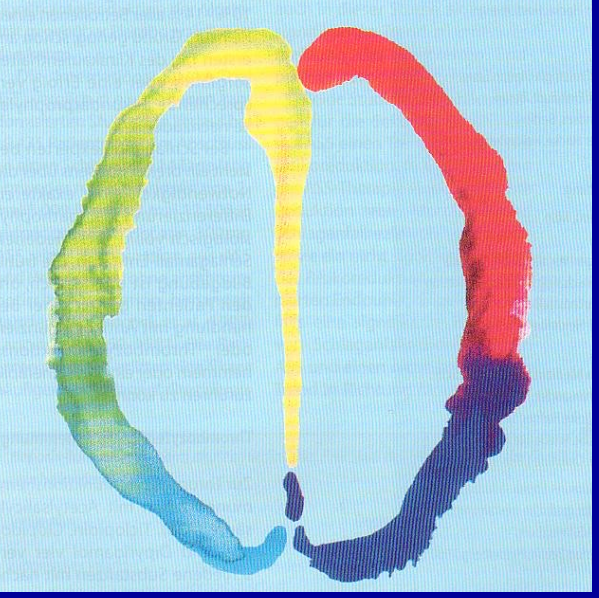


TUBERCULOUS MENINGITIS

Clinical Features

In patients with an acute meningoencephalitis syndrome, coma may evolve rapidly and is because of increased ICP from both cerebral edema and communicating and obstructive hydrocephalus.

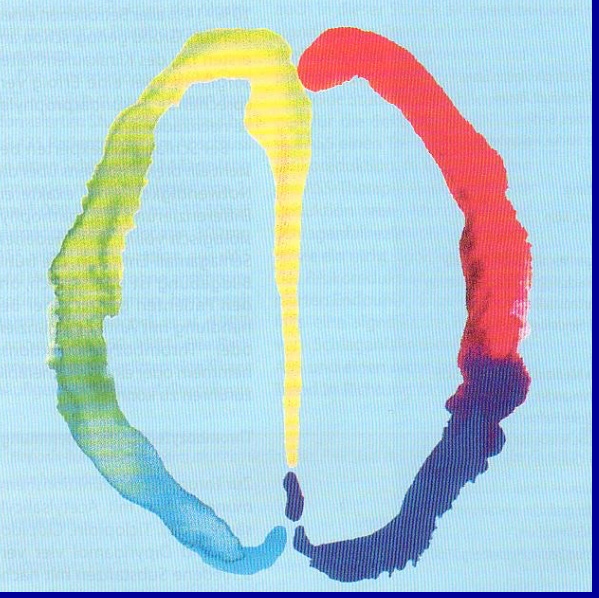
The clinical syndrome of tuberculous encephalopathy is characterized by convulsions, stupor, coma, involuntary movements, paralysis, and decerebrate spasms or rigidity with or without clinical signs of meningitis or CSF abnormalities of tuberculous meningitis.



TUBERCULOUS MENINGITIS

Clinical Features

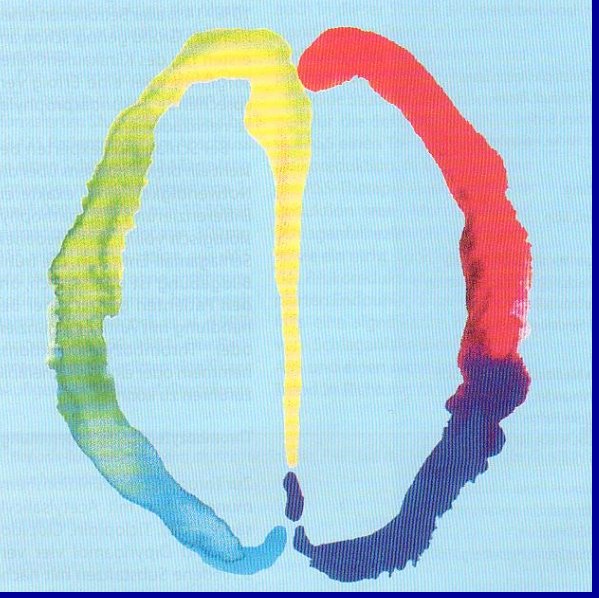
The combination of an unrelenting headache (+/- low grade fever) with malaise and anorexia and a CSF lymphocytic pleocytosis with a mild decrease in the glucose concentration is suggestive of tuberculous meningitis.



TUBERCULOUS MENINGITIS

Clinical Features

The combination of an unrelenting headache (+/- low grade fever) with malaise and anorexia and a CSF lymphocytic pleocytosis with a mild decrease in the glucose concentration is suggestive of tuberculous meningitis.



TUBERCULOUS MENINGITIS

Clinical Features

The classic CSF abnormalities in tuberculous meningitis are as follows:

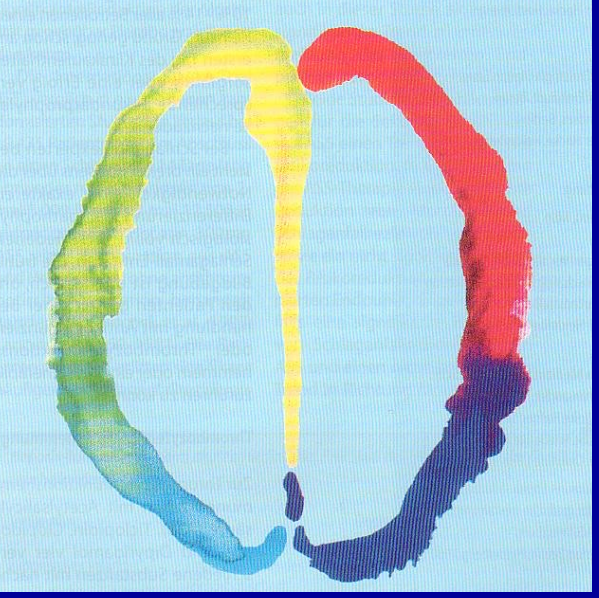
(1) an elevated opening lumbar pressure;

(2) increased WBC count between 10 to 500 cells/mm3 with a predominance of lymphocytes;

(3) an elevated protein concentration in the range of 100 to 500 mg/dL;

(4) a decreased glucose concentration (the median glucose concentration is approximately 40 mg percent); and,

(5) a positive culture in 75 percent of patients requiring 3 to 6 weeks for growth.



TUBERCULOUS MENINGITIS

Clinical Features

The PCR technique and other molecular diagnostic techniques for the detection of *M. tuberculosis* DNA in the CSF hold the greatest promise.

The sensitivity of the PCR technique for the detection of *M. tuberculosis* DNA in CSF is approximately 54 percent; however, false-positive results occur with rates of 3 to 20 percent.

EMPIRICAL THERAPY FOR TUBERCULOUS MENINGITIS

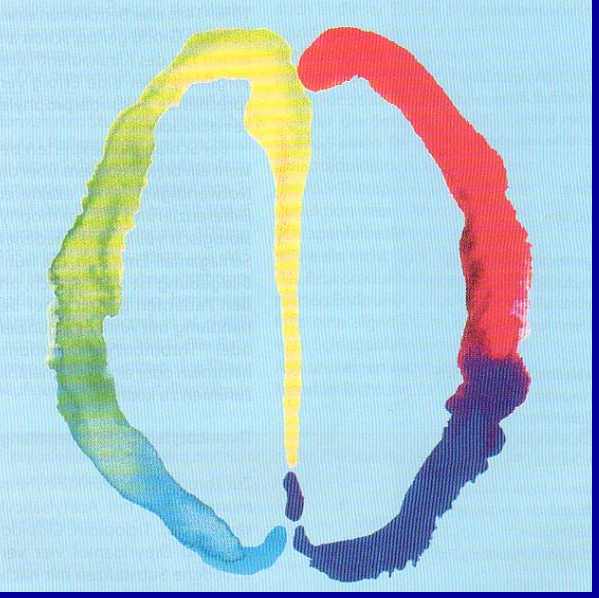
Drug	Dosage	
	Children	***Adults***
Isoniazid (INH)	10 mg/kg/d once daily	300 mg/d
Pyridoxine		50 mg/d
Rifampin	10 mg/kg/d	600 mg/d
Pyrazinamide	30 mg/kg/d	30 mg/kg/d
Ethambutol*	15 to 25 mg/kg/d	15 to 25 mg/kg/d
Streptomycin†	20 to 40 mg/kg/d	
Dexamethasone†	0.15 mg/kg every 6 hr	0.15 mg/kg every 6 hr
Prednisone §	1 mg/kg/d	1 mg/kg/d

***When antimicrobial resistance is suspected.**

†The American Academy of Pediatrics recommends a combination of INH, rifampin, pyrazinamide, and streptomycin for tuberculous meningitis in children.

† For altered consciousness, papilledema, focal neurological signs, impending herniation, spinal block, hydrocephalus.

§ For intractable headache, papilledema with otherwise normal neurological examination

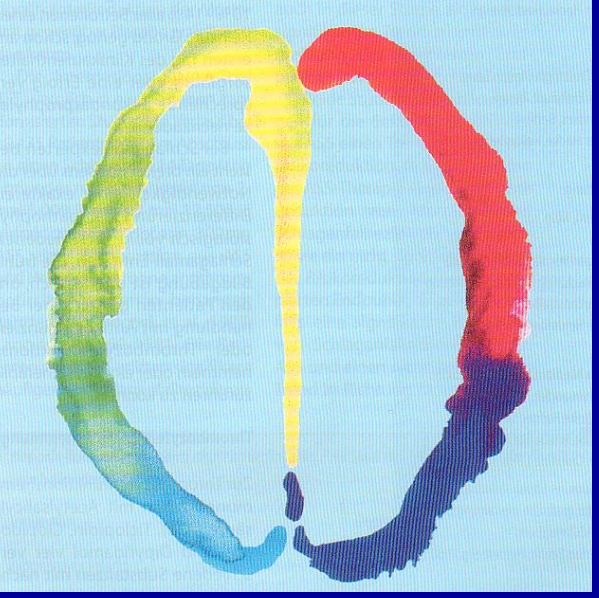


BRAIN ABSCESS

DEFINITION

A brain abscess is a focal, suppurative infection within the brain parenchyma, typically surrounded by a vascularized capsule.

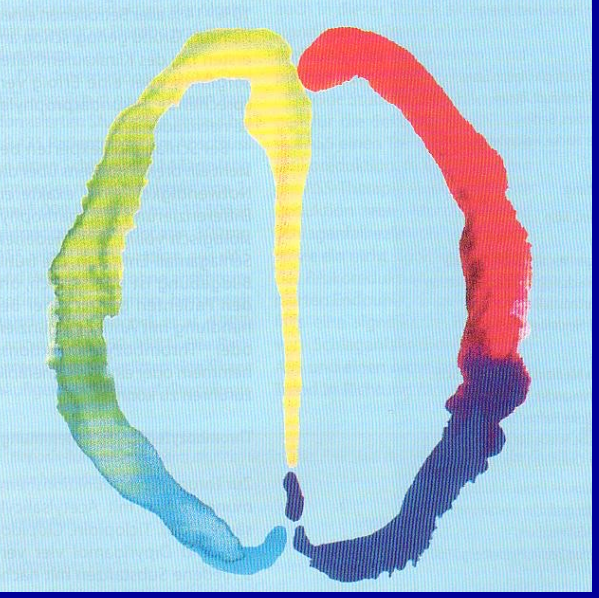
The term *cerebritis* is often employed to describe a nonencapsulated brain abscess.



BRAIN ABSCESS

PATHOPHYSIOLOGY

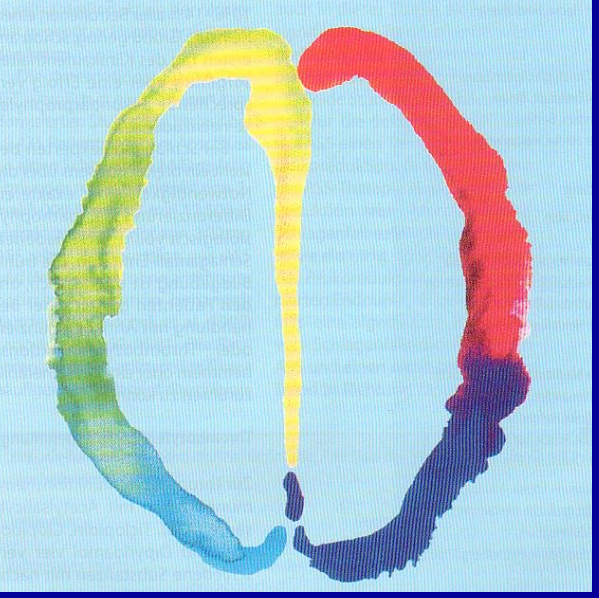
A brain abscess may develop (1) by direct spread from a contiguous cranial site of infection, such as paranasal sinusitis, otitis media, mastoiditis, or dental infection; (2) following head trauma or a neurosurgical procedure; or (3) as a result of hematogenous spread from a remote site of infection. In up to 25% of cases, no obvious pri- mary source of infection is apparent (cryptogenic brain abscess).



BRAIN ABSCESS

CLINICAL PRESENTATION

A brain abscess typically presents as an expanding intracranial mass lesion rather than as an infectious process. Although the evolution of signs and symptoms is extremely variable, ranging from hours to weeks or even months, most patients present to the hospital 11–12 days following onset of symptoms. The classic clinical triad of headache, fever, and a focal neurologic deficit is present in <50% of cases.



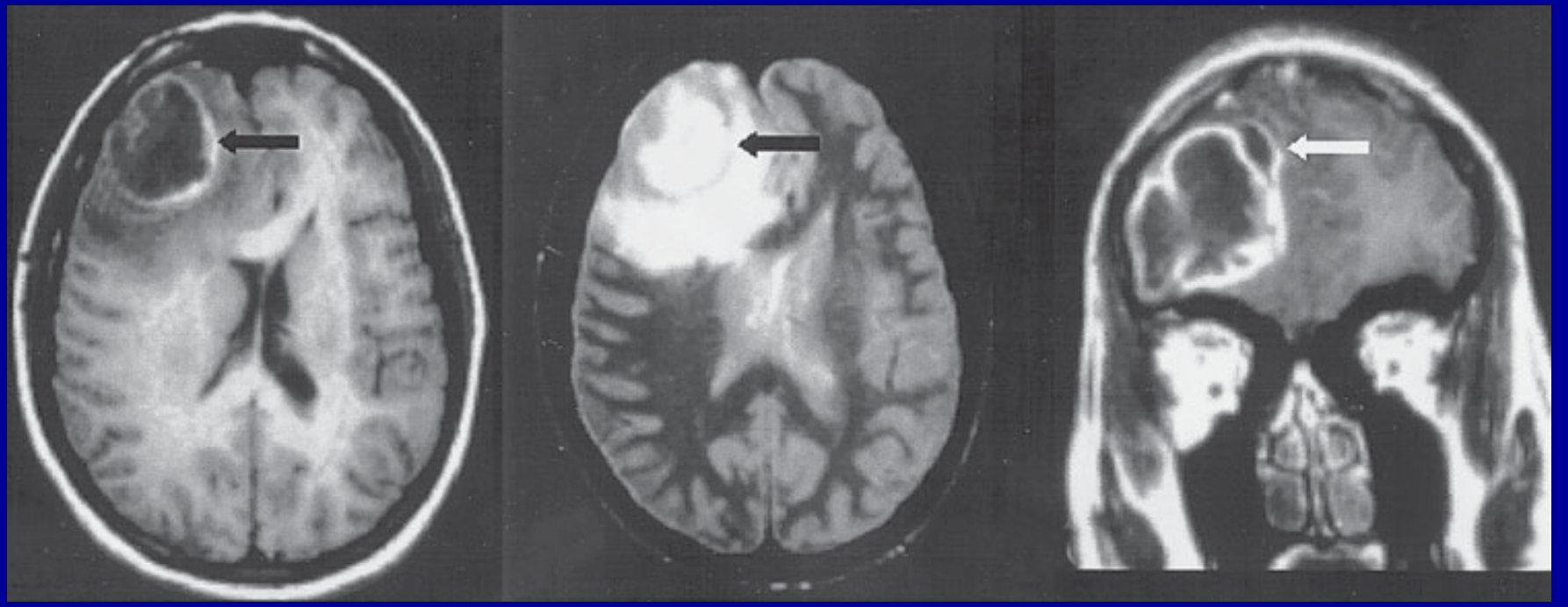
BRAIN ABSCESS

TREATMENT

Optimal therapy of brain abscesses involves a combination of high-dose parenteral antibiotics and neurosurgical drainage.

Empirical therapy of community-acquired brain abscess in an immunocompetent patient typically includes a third-generation cephalosporin (e.g., cefotaxime or ceftriaxone) and metronidazole.

Pneumococcal brain abscess



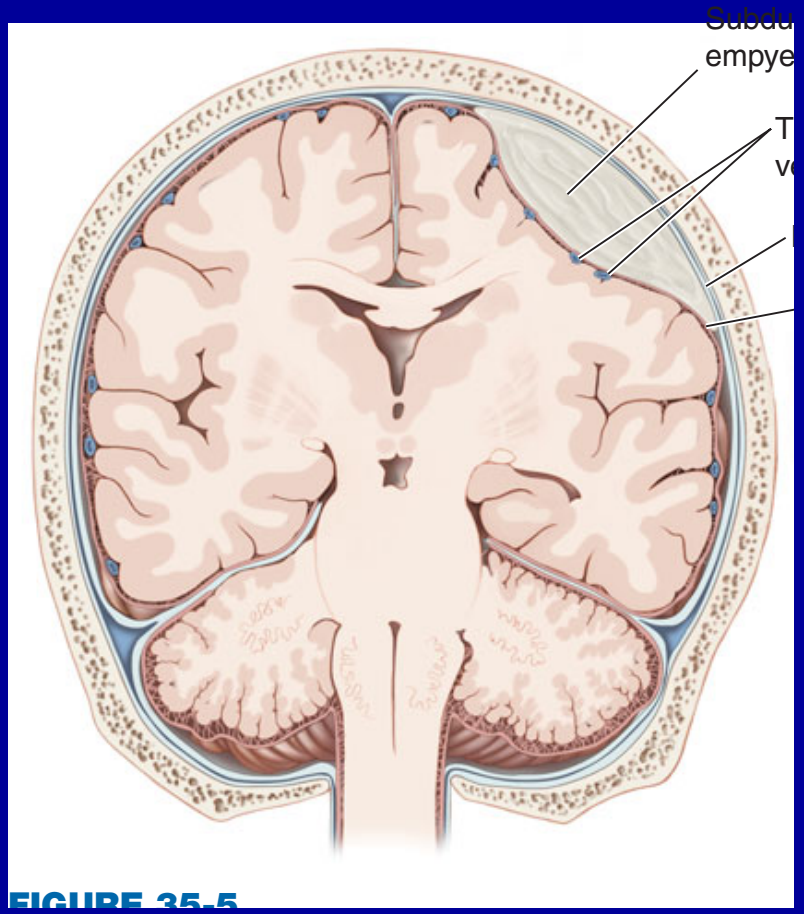
A B C

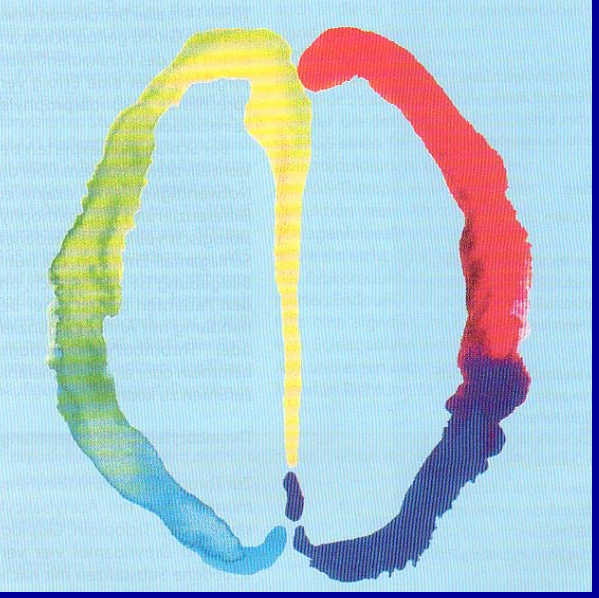
Note that the abscess wall has hyperintense signal on the axial T1-weighted MRI (***A****, black arrow*), hypointense signal on the axial proton density images (***B****, black arrow*), and enhances prominently after

gadolinium administration on the coronal T1-weighted image (C). The abscess is surrounded by a large amount of vasogenic edema and has a small "daughter" abscess (C, *white arrow).* (Courtesy *of Joseph Lurito, MD; with permission.)*

SUBDURAL EMPYEMA

A subdural empyema (SDE) is a collection of pus between the dura and arachnoid membranes.



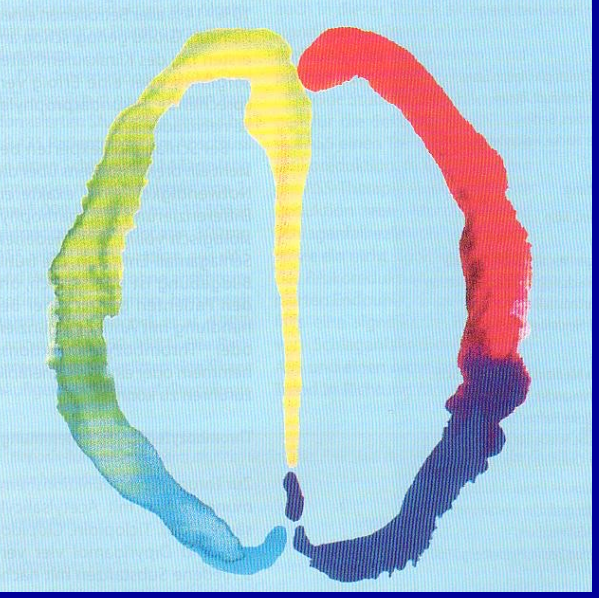


SUBDURAL EMPYEMA

PATHOPHYSIOLOGY

Sinusitis-associated SDE develops as a result of either retro- grade spread of infection from septic thrombophlebitis of the mucosal veins draining the sinuses or contiguous spread of infection to the brain from osteomyelitis in the posterior wall of the frontal or other sinuses.

SDE may also develop from direct introduction of bacteria into the subdural space as a complication of a neurosurgical procedure.

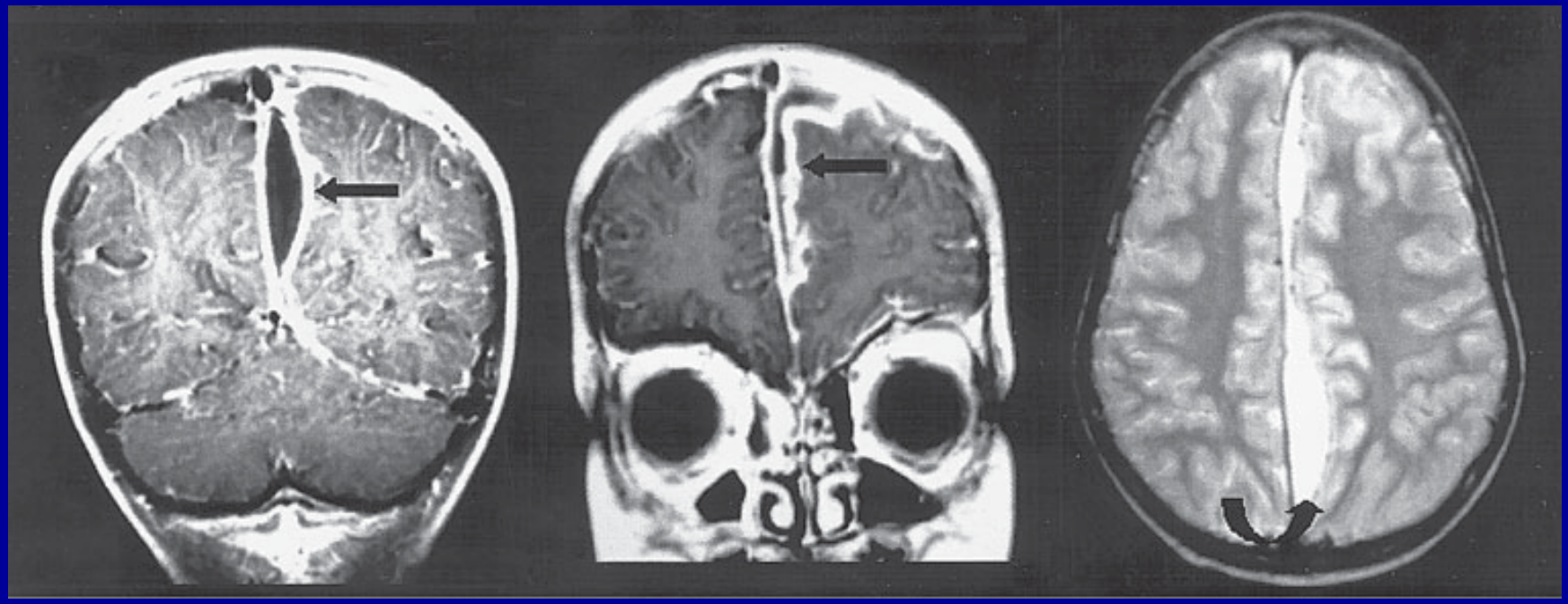


SUBDURAL EMPYEMA

CLINICAL PRESENTATION

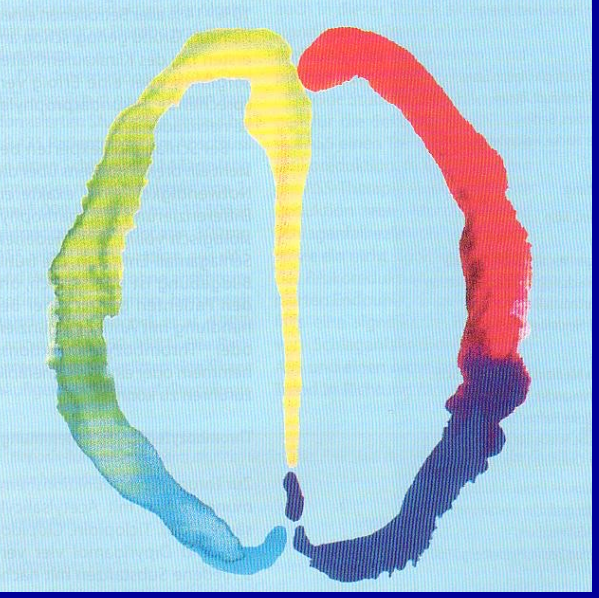
Headache is the most common complaint at the time of presentation; initially it is localized to the side of the subdural infection, but then it becomes more severe and generalized. Contralateral hemiparesis or hemiplegia is the most common focal neurologic deficit and can occur from the direct effects of the SDE on the cortex or as a consequence of venous infarction. Seizures begin as partial motor seizures that then become secondarily generalized.

SUBDURAL EMPYEMA



A B C

There is marked enhancement of the dura and leptomeninges (A, ***B,*** *straight arrows)* along the left medial hemisphere. The pus is hypointense on T1-weighted images (A, B) but markedly hyperintense on the proton density–weighted (C, *curved arrow)* image. (Courtesy *of Joseph Lurito, MD; with permission.)*

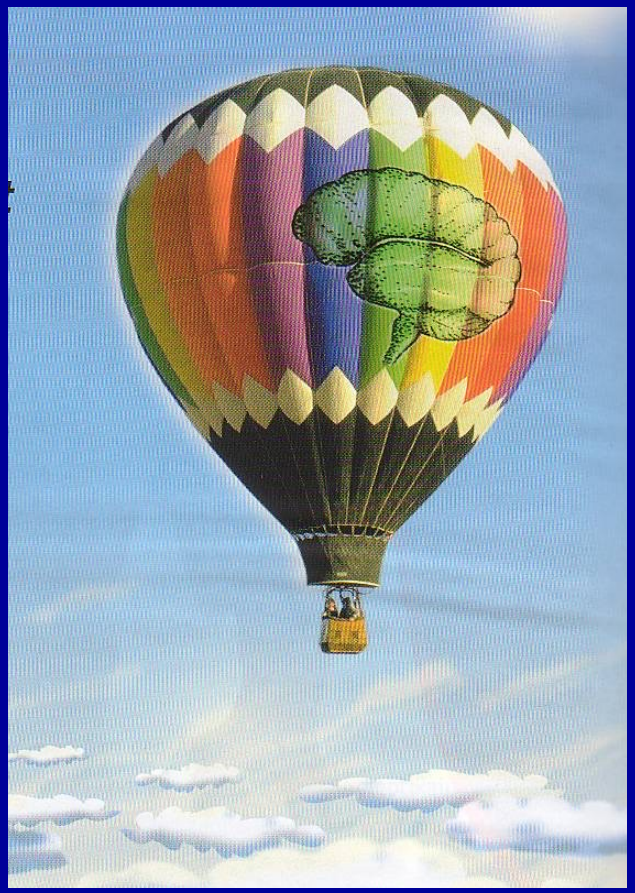


SUBDURAL EMPYEMA

TREATMENT

Emergent neurosurgical evacuation of the empyema, either through burr-hole drainage or craniotomy, is the definitive step in the management of this infection. Empirical antimicrobial therapy should include a combination of a third-generation cephalosporin (e.g., cefotaxime or ceftriaxone), vancomycin, and metronidazole.

NEUROLOGY



"Knowledge is of two kinds. We know a subject ourselves, or we know where we can find information on it."
-- Samuel Johnson

THE END

QUESTIONS ? ? ?