

Chapter 6

Infections of the Central Nervous System

MENINGITIS: in children with bacteremia, 15% of all children and 5% of children < 1 y not receiving antibiotic at time develop meningitis after lumbar puncture; poor prognosis if coma, delay in starting therapy, CSF glucose < 10 mg/dL, protein > 300 mg/dL, bacteremia (found in nearly all fatal cases), coexisting illness; overall fatality rate 4-20%; total rate of sequelae in survivors 4%; complications: 32% headache, 31% difficulty in concentrating, 24% loss of memory, 23% hearing impairment, 21% dizziness, 18% visual disturbances, 5% convulsions, 20% no complaint

Agents (Bacterial): 45-46% *Haemophilus influenzae* type b (case-fatality rate 3-7%), 14-27% *Neisseria meningitidis* (47% of meningococcal infections; case-fatality rate 0.4-14%), 13-19% *Streptococcus pneumoniae* (case rates 1-2/100,000; case-fatality rate 19-30%; 3% in < 5 y, 31-60% in > 60 y; neurologic sequelae widespread in survivors), 3-6% *Streptococcus agalactiae* (case-fatality rate 12-24%), 2-3% *Listeria monocytogenes* (case-fatality rate 22-30%), anthrax

Diagnosis: sudden onset of fever, headache, nausea, vomiting, signs of meningeal irritation, delirium, coma; blood cultures within 30 minutes of initial assessment; lumbar puncture if patient has none of anticoagulant therapy, bleeding diathesis, signs of localised spinal sepsis, history of CNS disease, focal neurological signs, papilledema, new onset seizure, abnormal level of consciousness (adults) or rapidly deteriorating consciousness or obtundation (children) or immunosuppression, or if CT scan shows lumbar puncture not contraindicated; microscopy, Gram stain (positive in 25% of bacterial with $\leq 10^3$ cfu/mL and 97% with $\geq 10^5$, 70% positive in *Haemophilus influenzae*), chemistry and culture of CSF; acridine orange stain detects bacteria causing meningitis at $\geq 10^4$ cfu/mL in 10 minutes; CSF lactate (elevated in bacterial meningitis; enzymatic method or gas liquid chromatography < 1 h; distinguishes bacterial from viral meningitis; false positive and negative reactions occur); C-reactive protein determination on CSF (97% positive in bacterial meningitis, 50% in intracranial hemorrhage, 44% in Kawasaki syndrome, 30% in malignancies, 20% in neurological symptoms without infection, 6% in fever without bacterial meningitis and in increased intracranial pressure secondary to pseudotumour cerebri or hydrocephalus, negative in viral meningitis); coagulation (common organisms causing meningitis detected in CSF in < 5 min; may require treating specimen to eliminate nonspecific agglutination; *Haemophilus influenzae* type b sensitivity 77-100%, specificity 97-100%; *Streptococcus pneumoniae* sensitivity 71%, specificity 96%; *Neisseria meningitidis*, *Streptococcus agalactiae*); latex agglutination (false positives and negatives); counterimmunoelectrophoresis (difficult, less sensitive, more time-consuming) of CSF (results in < 1 h; *Haemophilus influenzae* type b sensitivity 67%, specificity 67%; *Neisseria meningitidis* A, B, C and W135 sensitivity 50%, specificity 50%; *Streptococcus pneumoniae*, *Streptococcus agalactiae*), serum (*Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*) and urine (*Haemophilus influenzae*, *Streptococcus pneumoniae*); gas liquid chromatography (detects anaerobes and selected aerobes in CSF in < 1 h; difficult sample preparation; research tool); limulus lysate (research tool; endotoxin determination detects Gram negative bacteria in CSF in < 2 h; 97% sensitivity and 99% specificity for *Haemophilus/Neisseria*); ELISA (higher sensitivity than counterimmunoelectrophoresis but more time-consuming and results not available same day); if tests normal, look for other explanation of signs and symptoms; if clearly suggestive of viral etiology, no specific therapy; if unclear, observe patient and repeat lumbar puncture if condition worsens or in 8-24 h; if clearly suggestive of 'chronic meningitis', perform appropriate smears and cultures and start immediate therapy or await results and further testing depending on clinical situation; if clearly suggestive of suppurative bacterial etiology, start appropriate antimicrobial therapy as indicated by Gram stain and/or other tests immediately or treat empirically as below

Bacterial Meningitis: CSF white cell count > 1000/ μ L (if > 50,000/ μ L, consider ruptured brain abscess), > 60% polymorphs, red blood cells absent, glucose < 45 mg/dL (≤ 1 mmol/L; < 40-66% of blood glucose; normal in 40-50%), protein > 80 mg/dL, Gram stain positive in 80% (60% in partially treated), culture positive in 90% (66% in partially treated); peripheral blood leucocyte count > 16×10^9 /L; broad range bacterial PCR (sensitivity 100%, specificity 98%, positive predictive value 94%, negative predictive value 100%)

Viral Meningitis: CSF white cell count < 1000/ μ L in 83% (rarely > 2800/ μ L), polymorphs increased in 10%, lymphocytes increased, red blood cells variable, glucose normal, protein normal or slightly increased, Gram stain and bacterial culture negative

Fungal Meningitis: CSF white cell count < 5000/ μ L, lymphocytes increased, red blood cells absent, glucose normal or slightly decreased, protein > 60 mg/dL, Gram stain and bacterial culture negative

Tuberculous Meningitis: CSF white cell count < 1000/ μ L, polymorphs increased, red blood cells absent, glucose < 45 mg/dL, acid-fast stain positive in 80% if 10 mL of CSF centrifuged and sediment examined for 30-90 minutes, acid-fast bacilli culture positive in 85%

Carcinomatous Meningitis: CSF white cell count 0-500/ μ L, 0-95% polymorphs, red blood cells variable, glucose decreased or normal, protein usually increased, Gram stain and bacterial culture negative

Brain Abscess: CSF white cell count 10-500/ μ L, red blood cells variable, glucose decreased in 25%, protein increased in 75%, Gram stain positive in < 10%, culture positive in 16%

Endocarditis: CSF white cell count < 50/ μ L, polymorphs increased in 28%, lymphocytes increased in 25%, red blood cells occasionally raised, glucose normal or decreased, protein normal or increased, bacterial culture positive in 16%

Traumatic Tap: leucocytes:erythrocytes \approx 1:500

Note that contaminating bacteria may be obtained from slides on which smears are made, tubes in which CSF is collected, needles and syringes in which CSF taken, stains used for staining smear

Treatment: see categories below; if bacterial meningitis is suspected, immediately administer benzylpenicillin (< 1 y: 300 mg; 1-9 y: 600 mg; \geq 10 y: 1200 mg) or ceftriaxone 50 mg/kg to 2 g i.v. if penicillin hypersensitive or likely delay of > 6 h in further therapy and transfer to hospital; in hospital, dexamethasone 0.15 mg/kg to 10 mg i.v. +

Community Acquired: ceftriaxone 100 mg/kg to 4 g i.v. daily or 50 mg/kg to 2 g i.v. 12 hourly for 7-10 d or cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 7-10 d (+ benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly for 7-10 d or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly for 7-10 d if *Listeria monocytogenes* suspected or immunosuppressed)

Gram Positive Cocci Seen, Pneumococcal Antigen Assay Positive, Neutrophils But No Organisms Seen: add vancomycin 12.5 mg/kg to 500 mg (child < 12 y: 15 mg/kg to 500 mg) i.v. 6 hourly by slow infusion (monitor blood levels and adjust dose accordingly)

Immediate Penicillin or Cephalosporin Hypersensitivity: vancomycin 12.5 mg/kg to 500 mg (child < 12 y: 15 mg/kg to 500 mg) i.v. 6 hourly by slow infusion (monitor blood levels and adjust dose accordingly) + ciprofloxacin 10 mg/kg to 400 mg i.v. 12 hourly or moxifloxacin 10 mg/kg to 400 mg i.v. daily

Neisseria meningitidis: benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly for 3-5 d, then ceftriaxone 250 mg (child 125 mg) i.m. as single dose or ciprofloxacin 500 mg orally as single dose (\geq 12 y) or rifampicin 10 mg/kg to 600 mg (< 1 mo: 5 mg/kg) orally 12 hourly for 2 d and/or immunisation; activated protein C; steroids

Penicillin Hypersensitive (Not Immediate): ceftriaxone 100 mg/kg to 4 g i.v. daily for 3-5 d or 50 mg/kg to 2 g i.v. 12 hourly for 3-5 d or cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 3-5 d

Immediate Penicillin or Cephalosporin Hypersensitive: ciprofloxacin 10 mg/kg to 400 mg i.v. 12 hourly for 3-5 d

Streptococcus pneumoniae:

Penicillin MIC < 0.125 mg/L: benzylpenicillin 45 mg/kg to 1.8 g i.v. 4 hourly for 10-14 d

Penicillin MIC \geq 0.125 mg/L: vancomycin 15 mg/kg to 500 mg i.v. 6 hourly + cefotaxime 50 mg/kg to 2 g i.v. 6 hourly or ceftriaxone 50 mg/kg to 2 g i.v. 12 hourly

Haemophilus influenzae type b:

Penicillin Susceptible: benzylpenicillin 60 mg/kg to 2.4 g i.v. 4 hourly for 7 d or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly for 7 d

Penicillin Resistant: ceftriaxone 100 mg/kg to 4 g i.v. daily for 7 d or 50 mg/kg to 2 g i.v. 12 hourly for 7 d or cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 7 d

Immediate Penicillin or Cephalosporin Hypersensitive: chloramphenicol 20-25 mg/kg to a g i.v. 6 hourly for 7 d or ciprofloxacin 10 mg/kg to 400 mg i.v. 12 hourly for 7 d

Listeria monocytogenes: benzylpenicillin 60 mg/kg to 2.4 g i.v. 4 hourly or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly

Penicillin Hypersensitive: cotrimoxazole 4/20 mg/kg to 160/800 mg i.v. 6 hourly

Anthrax: ciprofloxacin 10 mg/kg to 400 mg i.v. 12 hourly + benzylpenicillin or amoxy/ampicillin or chloramphenicol

Health Care-Associated: vancomycin 12.5 mg/kg to 500 mg (child < 12 y: 15 mg/kg to 500 mg) i.v. 6 hourly + ceftazidime 50 mg/kg to 2 g i.v. 8 hourly or meropenem 40 mg/kg to 2 g i.v. 8 hourly

Prophylaxis

Neisseria meningitidis: ceftriaxone 250 mg (< 15 y: 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin

10 mg/kg (< 1 mo: 5 mg/kg) to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children); vaccines (quadrivalent polysaccharide, quadrivalent conjugate, and serogroup conjugate) available

***Haemophilus influenzae* type b:** given to index case before discharge, to all household contacts of another child who is incompletely immunised against *Haemophilus influenzae* type b and to all household contacts of index case < 2 y; rifampicin 20 mg/kg to maximum 600 mg (child < 1 mo: 10 mg/kg) orally daily for 4 d (not pregnant; give ceftriaxone 1g in lignocaine hydrochloride 1% i.m. as single dose); vaccine to index case under 2 y even if previous immunisation and to unvaccinated contacts < 5 y

Streptococcus pneumoniae: pneumococcal polysaccharide vaccine recommended to adults \geq 65 y, individuals > 2 y with chronic illness, anatomic or functional asplenia, immunocompromise (disease, chemotherapy, steroids), HIV infection, environment or settings with increased risk, or cochlear implants; pain, swelling and redness at injection site in 30-50%, fever and muscle aches in < 1%, rare severe reactions; revaccination after 5 y for \geq 2 y with functional or anatomic asplenia, immunosuppression, malignancy, transplant, chronic renal failure, nephritic syndrome, HIV infection, chronic systemic steroids, or < 65 y at time of first vaccination; pneumococcal conjugate vaccine recommended for routine vaccination of children < 24 mo and 24-59 mo with high risk medical conditions; pain, swelling and redness at injection site in 10-20%; reduces invasive disease due to serotypes in the vaccine by 97% and to those not in the vaccine by 89%

NEONATAL MENINGITIS: incidence 28/100 000 live births; case-fatality rate 26-27%; high morbidity; ventriculitis
Agents: 50-60% Gram negative bacilli (11-47% *Escherichia coli* (early and late; increased risk in galactosemia), 5% *Pseudomonas aeruginosa*, 0-16% *Klebsiella pneumoniae* (mainly late), 0-7% *Serratia*, 0-3% *Haemophilus influenzae* (50% of cases associated with maternal complication; 83% in premature infants; 33% mortality); *Proteus*, *Salmonella*, *Citrobacter diversus* (brain abscess common), *Enterobacter sakazaki*, other coliforms, *Flavobacterium meningosepticum* (virulent; always nosocomial), *Campylobacter fetus* subsp *fetus*), 24-34% *Streptococcus agalactiae* (mainly early; case-fatality rate 24%), 2-10% *Listeria monocytogenes* (early and late; case-fatality rate 30%), 0-7% *Streptococcus pneumoniae* (early), 0-5% *Staphylococcus aureus* (late), 0-5% *Enterococcus* (early), group C *Streptococcus*, *Streptococcus mitis*, *Bacillus* (very rare), *Neisseria gonorrhoeae*, *Sphingobacterium mizutaii* (prematures), *Alcaligenes xylosoxidans*, *Aeromonas*

Diagnosis: Gram stain and acridine orange stain of cytocentrifuged specimen of CSF; micro and culture of CSF; latex agglutination of concentrated urine, CSF and serum; counterimmunoelectrophoresis of CSF; ELISA

Haemophilus influenzae: CSF protein 486 mg/dL, glucose 39 mg/dL, leucocytes 11,500/ μ L, 90% polymorphonuclears; latex agglutination on CSF (sensitivity 77-100%, specificity 97-100%); radioimmunoassay (sensitivity 95%)

Listeria monocytogenes: opening pressure > 200 mm H₂O, protein 100-200 mg/dL, glucose 30-100 mg/dL (\geq 50% serum glucose), leucocytes 100-4000/ μ L, 75-100% polymorphs, Gram stain positive in 50%

Streptococcus agalactiae: latex agglutination on concentrated urine (sensitivity 93%), CSF (sensitivity 80%), serum (sensitivity 27%); radioimmunoassay

Treatment: dexamethasone or oxindanac +:

Enteric Gram Negative Bacilli or Organism Not Known: cefotaxime 200 mg/kg daily in 4 equal divided doses or ceftriaxone 100 mg/kg daily in 2 equal divided doses + aminoglycoside for 21 d

Flavobacterium meningosepticum: rifampicin

Streptococcus pneumoniae:

Penicillin MIC \leq 0.125 mg/L: benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly for 10 d

Penicillin MIC > 0.125 mg/L: ceftriaxone or cefotaxime + vancomycin or rifampicin

Streptococcus agalactiae: benzylpenicillin 60 mg/kg to 2.4 g i.v. 4 hourly for 14-21 d

Listeria monocytogenes: cotrimoxazole 5/25 mg/kg to 160/800 mg i.v. 6 hourly + benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly

Pseudomonas aeruginosa: azlocillin 225 mg/kg i.v. daily in 3 divided doses or ceftazidime 100-200 mg/kg i.v. daily in divided doses + amikacin 5 mg/kg i.v. 8 hourly during first week; ticarcillin 200-300 mg/kg i.v. daily in divided doses every 4-6 h + tobramycin 1.5-2.5 mg/kg 8 hourly

Neisseria gonorrhoeae: benzylpenicillin 100 000 U/kg i.v. daily in 4 divided doses for at least 10 d

POST-NEONATAL PURULENT MENINGITIS: commonly related to upper respiratory infection with invasion of subarachnoid space by organisms arising from nasopharynx or by septicemic spread from lungs; also to urinary tract infection in the aged; \approx 9 cases/100,000 person-years; case-fatality rate 14%

Agents: 40-46% (40-60% in aged 1 mo - 15 y, 1-3% in > 15 y) *Haemophilus influenzae* (usually type b; cosmopolitan; 1.2/100,000 total, 59/100,000 age 6-8 mo; case-fatality rate 4-7%; exclude CSF leak in adult; 29% associated with acute otitis media; more common isolate in antibody-mediated deficiency and asplenicism, less frequent isolate in granulocyte disorders; also associated with spinal cord trauma; 8% of bacteremic and 8% of nonbacteremic invasive *Haemophilus influenzae* infections in older children and adults; ≈ 40 notified cases/y in Australia; neurologic sequelae (hearing impairment, mental retardation, seizure disorder, developmental delay, paralysis) in 15-30%), 27-29% (25-40% in aged 1 mo - 15 y, 10-35% in > 15 y) *Neisseria meningitidis* (epidemic cerebrospinal meningitis, epidemic meningitis, diplococcal meningitis, meningitis *Neisseria*, meningococcal meningitis; usually types A, B, C; particularly prevalent in Sub-Saharan Africa, Middle East and upland parts of Indian subcontinent; 0.7/100,000 total, 13/100,000 age 3-8 mo; case-fatality rate 0.4-14%; ≈ 600 notified cases/y in Australia (≈ 40% in New South Wales); usually arising as a result of hematogenous spread from asymptomatic colonisation of nasopharynx or from meningococcal nasopharyngitis, with an intervening phase of meningococcal septicemia or of asymptomatic meningococcal bacteremia; 14% associated with acute otitis media; epidemics and may be acute (sometimes fulminant) or chronic; spread may affect optic and other nerves; less frequent isolate in granulocyte disorders and antibody-mediated deficiency, infrequent isolate in asplenicism; transmission respiratory; incubation period 2-10 d), 11-13% (10-20% in aged 1 mo - 15 y, 30-50% in > 15 y) *Streptococcus pneumoniae* (0.3/100,000 total, 8/100,000 age 3-5 mo; case-fatality rate 19-28%; sequelae common in survivors: 54% neurological, 42% neuropsychological, 25% otological, 16% various degrees of cerebral and cerebellar atrophy; 33% associated with acute otitis media; also from pulmonary focus, sinusitis; common isolate in granulocyte disorders, antibody-mediated deficiency and asplenicism; also associated with cranial defect from previous head and spinal cord trauma; more common in infants, elderly, alcoholics), 3% *Streptococcus agalactiae* (0.1/100,000 total, 42/100,000 age < 1 mo; case-fatality rate 12-24%), 1% other streptococci (case-fatality rate 44%; 22% associated with brain abscess; also associated with ventriculoatrial and other shunts; *Streptococcus pyogenes* and *Enterococcus faecalis* infrequent isolates in granulocyte disorders and AIDS; *Streptococcus pyogenes* less common isolate in antibody-mediated deficiency, infrequent isolate in asplenicism; community acquired; otitis media, pharyngitis or sinusitis usually present; *Streptococcus suis* in pig workers; *Streptococcus canis*), 1-9% *Staphylococcus aureus* (case-fatality rate 27% overall, 56% in hematogenous, 18% in postoperative; 18% associated with acute otitis media, 18% associated with pneumonia; common isolate in granulocyte disorders, less common isolate in antibody-mediated deficiency; also associated with surgery, ventriculoatrial and other shunts, nosocomial infections, foreign body, parameningeal or brain abscess), 1% mixed bacteria (children, adults with contiguous infection or tumour or fistulous communication with CNS); *Listeria monocytogenes* (1-2% in age 1 mo - 15 y, 5% in > 15 y; in lymphoproliferative malignancy, lung carcinoma, neonates, immunosuppressed, elderly, others; case-fatality rate 22-30%), enteric Gram negative bacilli (1-2% in age 1 mo - 15 y, 1-10% in > 15 y; *Escherichia coli* (usually K1; sepsis—respiratory tract infection or pneumonia; immunocompromised and immunosuppressed; common isolate in granulocyte disorders, infrequent isolate in asplenicism; also associated with head trauma, neurological procedure and nosocomial infections), *Klebsiella* (less frequent isolate in granulocyte disorders), *Enterobacter* (less frequent isolate in granulocyte disorders), *Proteus* (infrequent isolate in granulocyte disorders), *Serratia* (nosocomial; mainly neonates and infants), *Salmonella*, *Pseudomonas aeruginosa* (10% of cases in cancer patients; common isolate in granulocyte disorders, less common isolate in antibody-mediated deficiency; also associated with surgery and nosocomial infections), *Burkholderia cepacia*, *Stenotrophomonas maltophilia*, *Neisseria gonorrhoeae*, *Neisseria lactamica* (following skull trauma), *Neisseria mucosa* (female infants and children with predisposing conditions), *Neisseria subflava*, *Neisseria flavescens*, *Moraxella catarrhalis*, *Moraxella lacunata*, *Moraxella osloensis*, *Bacteroides* (associated with surgery), *Dialister pneumosintes* (chronic), *Francisella tularensis* (rare), *Campylobacter fetus* subsp *fetus* (rare), *Campylobacter jejuni* (rare), *Aeromonas hydrophila* (infrequent isolate in granulocyte disorders, others), *Aeromonas sobria* (rare isolates in chronic alcoholic liver disease), *Flavobacterium meningosepticum* (in immunocompromised), *Acinetobacter* (nosocomial; mainly associated with indwelling ventriculostomy tubes or CSF fistulae in patients receiving antimicrobials), *Yersinia pestis* (rare complication of bubonic plague), *Pasteurella multocida* (rare; animal contact; case-fatality rate 30%), *Bacillus* (*Bacillus anthracis*: hemorrhagic meningitis (anthrax meningitis, meningeal anthrax) as complication in about 5% of cases of anthrax (39% inhalational, 29% cutaneous, 17% gastrointestinal, 16% unknown); and cases with no primary focus (up to 59% in some outbreaks in India), other species (especially *Bacillus cereus*) in immunocompromised, infrequent isolate in granulocyte disorders), *Clostridium* (infrequent isolate in granulocyte disorders; also associated with head and spinal cord trauma), diphtheroids (associated with ventriculoatrial and other shunts), *Corynebacterium bovis* (rare), *Nocardia asteroides* (common in impaired cell-mediated immunity; case-fatality rate 57%), *Kingella kingae* (sickle cell anemia), *Bergeyella zoohelcum*, *Capnocytophaga canimorsus*, *Bordetella bronchiseptica* (posttraumatic), *Vibrio cincinnatii*, *Plesiomonas shigelloides*, *Haemophilus parainfluenzae*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Aerococcus viridans* (rare),

Fusobacterium necrophorum (uncommon), *Candida* (infrequent isolate in granulocyte disorders and asplenic; also nosocomial and in AIDS), *Coccidioides immitis* (25% of AIDS patients in endemic areas), *Histoplasma capsulatum* (in AIDS; ≈ 60% fatality rate), *Ajellomyces dermatitidis* (AIDS), *Aspergillus* (rare in AIDS), *Plasmodium malariae* (infrequent isolate in asplenic), *Plasmodium falciparum* (in therapy for nutritional deficiency), *Trichomonas* (associated with surgery), almost any other pathogen

Diagnosis: micro (≥ 1000 polymorphs/ μL), protein (100-1000 mg/dL), glucose ($< 1/3$ of blood), culture, latex agglutination and C-reactive protein on CSF; Gram stain and acridine orange stain on cytocentrifuged CSF; counterimmunoelectrophoresis on serum and urine; ELISA on urine; latex agglutination on serum; increased lactic acid in CSF

Neisseria meningitidis: hemorrhagic skin lesions; protein 770 mg/dL, glucose 6 mg/dL, leucocytes 20,700-212,000/ μL , 98% neutrophils, multiple extracellular and intracellular Gram negative diplococci; direct immunofluorescence and ELISA of CSF; latex agglutination of CSF (sensitivity 33%, specificity 100%)

Streptococcus pneumoniae: slight enlargement of lateral ventricles on air encephalogram; mild communicating hydrocephalus on computerised axial tomography; CSF 9000 neutrophils/ μL , 100 lymphocytes/ μL ; direct immunofluorescence of CSF; latex agglutination of CSF (sensitivity 71-100%, specificity 96%); radioimmunoassay; white cell count 17,400/ μL , 87% neutrophils, 2% bands

Haemophilus influenzae: septic arthritis, cellulitis of face or upper extremity; can be fulminant but commonly mild illness followed by significant deterioration; protein 486 mg/dL, glucose 39 mg/dL, leucocytes 11,500/ μL , 90% polymorphonuclears; ELISA on CSF; latex agglutination on CSF (sensitivity 77-100%, specificity 97-100%), radioimmunoassay (sensitivity 75%)

Listeria monocytogenes: opening pressure > 200 mm H₂O, protein 100-200 mg/dL, glucose 30-100 mg/dL ($\geq 50\%$ serum glucose; depressed in 60%), leucocytes 100-4000/ μL , 75-100% polymorphs changing to 98% mononuclears; Gram stain positive in 50%

Staphylococcus aureus: fever in 75-90%, altered mental status in 38-55%; CSF protein > 80 mg/dL in 83-86%, CSF glucose $< 50\%$ of serum level in 57-67%, CSF white cell count $> 5/\mu\text{L}$ in 83-88%, $> 1000/\mu\text{L}$ in 34%, $> 66\%$ neutrophils in 80-100%; Gram stain positive in 40-62%; blood culture positive in 60-86%

Nocardia asteroides: subacute to chronic presentation; 68% fever, 66% stiff neck, 55% headache; neutrophil pleocytosis; 83% > 500 leucocytes/ μL , 66% < 40 mg glucose/dL, 61% > 100 mg/dL protein; 43% associated brain abscess; histology and culture of tissue

Anthrax: fever, malaise, meningeal signs, hyperreflexia, delirium, stupor, coma; hemorrhagic meningitis, multifocal subarachnoid and intraparenchymal hemorrhages, vasculitis, cerebral edema; 94% case-fatality rate (75% within 24 h of presentation); Gram stain, India ink stain and culture of CSF sediment; ELISA, Western blot, toxin detection, chromatographic assay, fluorescent antibody test

Bacillus cereus: diarrhoea, fever, altered mental status; Gram stain and culture of CSF

Candida: glucose decreased and protein increased in 60% of cases; leucocytes 6000/ μL (lymphocytes and neutrophils); organisms in Gram stain in 40%; culture of biopsy

Coccidioides immitis: EIA of CSF using combination of antigens (sensitivity 100%, specificity 96%), RIA of CSF (sensitivity 100%), overnight binding complement fixation test on CSF (sensitivity 95%)

Histoplasma capsulatum: RIA or EIA for histoplasma polysaccharide antigen in body fluids (sensitivity 90-97%), culture of bone marrow, lymph nodes, ulcers (positive in 90%), CSF (often negative)

Ajellomyces dermatitidis: EIA using purified antigen A (false positives in some cases of histoplasmosis and sporotrichosis)

Aspergillus: stroke or intracranial hemorrhage in immunosuppressed HIV-positive patient with single or multiple contrast-enhancing lesions; CSF nonspecifically abnormal, culture usually negative; serology insensitive

Treatment: dexamethasone 3 mg/kg i.v. initially followed by 1 mg/kg 6 hourly over period of 48 h or oxindanac +:

Neisseria meningitidis: benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly for 5-7 d; i.v. heparin + i.v. hydrocortisone if any evidence of Waterhouse-Friderichsen syndrome

Neisseria gonorrhoeae: ceftriaxone 1-2 g i.v. every 12 h

Penicillin Susceptible Streptococci (MIC < 0.125 mg/L): benzylpenicillin + aminoglycoside if warranted

Penicillin Hypersensitive Patient with *Neisseria*, Any Patient With Relatively Resistant (MIC 0.125- ≤ 1 mg/L) *Streptococcus pneumoniae:* cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 5-7 d or ceftriaxone 200 mg/kg to 4 g i.v. daily or 50 mg/kg to 2 g i.v. 12 hourly for 5-7 d

Penicillin Resistant (MIC > 1 mg/L) or Cefotaxime Resistant *Streptococcus pneumoniae*: ceftriaxone + vancomycin 2 g every 12 h or rifampicin; seek specialist advice

***Haemophilus influenzae*:** cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 7-10 d, ceftriaxone 100 mg/kg to 4 g i.v. daily or 50 mg/kg to 2 g i.v. 12 hourly for 7-10 d, (amoxy)ampicillin 50 mg/kg to 2 g i.v. 4 hourly for 7-10 d (if susceptible)

***Staphylococci*:** oxacillin 200 mg/kg/d to 12-16 g/d 4-6 hourly, vancomycin 60 mg/kg/d up to 2 g/d 6-12 hourly

***Francisella tularensis, Yersinia pestis*:** streptomycin

***Campylobacter*:** chloramphenicol

***Flavobacterium meningosepticum*:** sulphadiazine + rifampicin

***Pseudomonas aeruginosa*:** azlocillin 3 g i.v. 4 hourly (child: 225 mg/kg i.v. daily in 3 divided doses) or ceftazidime 6-12 g (child: 100-200 mg/kg) i.v. daily in divided doses for 9-50 d + amikacin 5mg/kg i.v. 8 hourly during first week; ticarcillin 3 g i.v. 4 hourly (< 40 kg: 200-300 mg/kg i.v. daily in divided doses every 4-6 h) + tobramycin 1.3 mg/kg (child: 1.5-2.5 mg/kg) i.v. 8 hourly, meropenem

***Burkholderia cepacia*:** imipenem

***Stenotrophomonas maltophilia*:** cotrimoxazole ± rifampicin

***Moraxella catarrhalis*:** amoxicillin-clavulanate

***Salmonella typhi*:** chloramphenicol 100mg/kg daily i.v. in 4 equally divided doses, substituting oral treatment as soon as possible

Enteric Gram Negative Bacilli: cefotaxime 2g i.v. 4 hourly (child: 200 mg/kg daily in 4 equally divided doses) or ceftriaxone 2-4 g i.v. daily (child: 100 mg/kg daily in 2 equally divided doses) + aminoglycoside for 21 d

***Bacteroides*:** metronidazole

***Acinetobacter*:** imipenem, minocycline, ciprofloxacin, polymyxin, ampicillin-sulbactam, ceperazone-sulbactam

***Pasteurella multocida, Kingella kingae*:** penicillin, ampicillin, third generation cephalosporin, chloramphenicol

***Listeria monocytogenes*:** cotrimoxazole 5/25 mg/kg to 160/800 mg i.v. 6 hourly + benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly or (amoxy)ampicillin 50 mg/kg to 2 g i.v. 4 hourly
***Nocardia asteroides*:** sulphonamides, cotrimoxazole, minocycline 200 mg bid, amikacin for at least 6 mo; cefotaxime 2g i.v. 8 hourly + imipenem 500 mg i.v. 6 hourly in severely ill

Anthrax: ciprofloxacin 10 mg/kg to 400 mg i.v. 12 hourly + penicillin or amoxy/ampicillin or chloramphenicol for 14-21 d then ciprofloxacin 15 mg/kg to 500 mg orally 12 hourly or doxycycline 2 mg/kg to 100 mg orally 12 hourly (child: amoxicillin 15 mg/kg to 500 mg orally 8 hourly) for total 60 d

***Bacillus cereus*:** vancomycin + carbapenem

Fungal: amphotericin B ± flucytosine

***Plasmodium*:** chloroquine

Others or Unknown: chloramphenicol 1 g i.v. 6 hourly ± benzylpenicillin 1.2-2.4 g i.v. 4 hourly

Hospital Acquired: vancomycin 15 mg/kg to 500 mg i.v. 6 hourly + cefotaxime 50 mg/kg to 2 g i.v. 6 hourly or ceftriaxone 50 mg/kg to 2 g i.v. 12 hourly or meropenem 40 mg/kg to 2 g i.v. 8 hourly

Prophylaxis:

Meningococcal (Index Case After Treatment and Close Contacts): ceftriaxone 250 mg (child 125 mg) i.m. as single dose (preferred if pregnant), ciprofloxacin 500 mg orally as single dose (not < 12 y; preferred for women taking oral contraceptive), rifampicin 10 mg/kg to 600 mg orally 12 hourly for 2 d (not pregnant, alcoholic, severe liver disease; preferred for children); single 0.5 mL s.c. dose (adults and children

> 2 y) of vaccine for *Neisseria meningitidis* types A, C, Y and W135 recommended for patients with deficiency of terminal complement component, travellers and long-term residents who will be living in or travelling through such endemic and hyperendemic areas as rural communities in Brazil, Burkina Faso, Chad, Egypt, Ghana, Mali, Mongolia, Nepal, Nigeria, Sudan, Vietnam, health care workers going to Saudi Arabia and Gulf States, in conjunction with antimicrobial prophylaxis for intimate contacts; mass immunisation may be indicated if several cases appear over a period of several weeks or if attack rates exceed 0.66-1.25/100,000 of population

***Haemophilus influenzae* type b:** given to index case before discharge, and within 7 d to all household contacts of index case, including incompletely immunised children < 4y and any immunocompromised child; also adults and children at day care centres with 2 or more cases of invasive disease in 60 d period and with incompletely immunised children; rifampicin 20 mg/kg to maximum 600 mg (child < 1 mo: 10 mg/kg) orally daily for 4 d (not pregnant; give

ceftriaxone 1 g in lignocaine hydrochloride 1% i.m. as single dose); vaccine to index case under 2 y even if previous immunisation and to unvaccinated contacts < 5 y; all children should be routinely vaccinated beginning at 2 mo (95-100% efficacy; swelling, redness and pain at injection site in 5-30%, fever and irritability uncommon, serious reactions rare; contraindicated if anaphylaxis to vaccine components or previous dose and serious illnesses)

Streptococcus pneumoniae: 1 dose of a 23 valent pneumococcal vaccine is recommended for adults with cardiovascular disease and chronic pulmonary disease entailing increased morbidity from respiratory infection, alcoholism, cirrhosis of liver, CSF leaks, diabetes mellitus, Hodgkin's disease, immunosuppression (preferably administered 6 w before initiation of immunosuppressive therapy), multiple myeloma, post-renal transplant, postsplenectomy, skull fracture with recurrent pneumococcal meningitis, splenic dysfunction and otherwise healthy adults aged 66 or older, and in children aged 2 y or older with anatomic splenectomy or persistent asplenia associated with sickle cells, CSF leaks, immunosuppression, nephrotic syndrome or splenectomy (administer 2 w before operation if possible)

Asplenic and Postsplenectomy: pneumococcal, meningococcal, Hib and standard schedule immunisation (including annual influenza); antibiotic prophylaxis in asplenic children < 5 y, children < 5 y with sickle cell anemia, for at least 2 y following splenectomy and patients with severe underlying immunosuppression: amoxycillin 125 mg orally 12 hourly (< 2 y: 20 mg/kg orally daily) or phenoxymethylpenicillin 250 mg (< 2 y: 125 mg) orally 12 hourly or if penicillin hypersensitive roxithromycin 4 mg/kg to 150 mg orally daily or erythromycin 250 mg orally daily or erythromycin ethyl succinate 400 mg orally daily

CSF FISTULA: may result in recurrent meningitis

Agent: especially *Streptococcus pneumoniae*

Diagnosis: recurrent meningitis, history of trauma, congenital anomalies; unilateral, clear, watery rhinorrhoea; hearing loss, especially unilateral; protein electrophoresis or ring test on fluid (rhinorrhoeal or otic) suspected of being CSF; high resolution CT in axial and coronal plane; MRI; contrast cisternography with iopamidole or iohexal, intrathecal injections of fluorescein diluted in CSF and observation of pledgets placed in sphenothmoid region, cribriform area, roof of nasal cavity and eustachian tube orifice

Treatment: head elevation at angle of 45°; spinal drain if necessary; surgical correction (extracranial approach preferred) if persistent rhinorrhoea (> 5-7 d), recurrent meningitis or spontaneous rhinorrhoea from anterior, middle or posterior fossa

NON-PUYOCENIC (LYMPHOCYTTIC, ASEPTIC) MENINGITIS

Agents: 70% of cases unclassified; 70-79% of documented cases enterovirus (transmission fecal and respiratory; incubation period 1 to several weeks; infrequent infections in impaired cell-mediated immunity and in antibody-mediated deficiency); 54% *human echovirus* (23% of *human echovirus* infections; attack rate 107/100,000; 38% *human echovirus 11*, 26% *human echovirus 30*, 21% *human echovirus 7*, 6% *human echovirus 4*, 3% *human echovirus 1*, 3% *human echovirus 17*, 3% *human echovirus 25*), 22% *human coxsackievirus B3*, 22% *human coxsackievirus B4*, 1% *human coxsackievirus B5*, remainder *human coxsackievirus A1, A2, A4-A7, A9, A10, A12, A14, A16, A22, echo 9 virus, human coxsackievirus B1, B2, B6, human echovirus 2-7, 11, 13-21, 24, 25, 30, 31, 33, human parechovirus 1, human parechovirus 2, other enteroviruses*), 6% influenza A, 4-10% *simplexvirus* (common in impaired cell-mediated immunity), 4% *measles virus*, 4% arboviruses, 2-15% *human adenovirus*, 1-4% *mumps virus* (0.7/1000 mumps cases symptomatic but CSF pleocytosis in ≥ 50%), *poliovirus* (in 28% of poliovirus cases; infrequent infections in antibody-mediated deficiency and cell-mediated immunity deficiency), *lymphocytic choriomeningitis virus* (probably worldwide but not in Australia; often spread from mice and probably pet hamsters; frequently in children), *mengo encephalomyocarditis virus, simplexvirus 3* (common in impaired cell-mediated immunity), hepatitis viruses, *Epstein-Barr virus* (Duncan's syndrome), Kawasaki syndrome, reoviruses, *vaccinia virus* (postvaccination; infrequent infections in impaired cell-mediated immunity), *rubella virus, parainfluenza 3*, many other viruses, *Nocardia asteroides* (common in impaired cell-mediated immunity), *Mycobacterium tuberculosis* (1% of tuberculosis cases; fatality rate 15-40%; less common infection in impaired cell-mediated immunity; also in therapy for nutritional deficiency), *Brucella* (< 5% of cases of systemic brucellosis; infrequent infections in impaired cell-mediated immunity; also in therapy for nutritional deficiency), *Listeria monocytogenes* (common in impaired cell-mediated immunity), *Leptospira, Treponema pallidum* subsp *pallidum* (uncommon), *Mycoplasma hominis* (rare), *Mycoplasma pneumoniae, Cryptococcus neoformans* (see **CRYPTOCOCCAL MENINGITIS**), *Coccidioides immitis* (see **COCCIDIOIDOSIS**; travel to San Joaquin Valley), *Histoplasma capsulatum* (see **HISTOPLASMOSIS**), *Aspergillus* (infrequent infections in neutropenics and impaired cell-mediated immunity), *Mucor* (infrequent infections in neutropenics and impaired cell-mediated immunity), *Absidia* (infrequent infections in neutropenics and impaired cell-mediated immunity), *Rhizopus* (infrequent infections in neutropenics and impaired cell-mediated immunity), *Drechslera* (associated with lymphoma), *Candida* (uncommon), *Pseudallescheria boydii* (uncommon), *Toxoplasma gondii* (in immunosuppressed, particularly Hodgkin's disease; infrequent infections in impaired cell-mediated immunity), *Strongyloides stercoralis* (associated with corticosteroid treatment; extremely infrequent infections in impaired cell-mediated immunity),

Taenia solium (infrequent infections in impaired cell-mediated immunity), *Trichinella spiralis*, myiasis (extremely infrequent infections in impaired cell-mediated immunity), *Naegleria* (see **AMOEBIIC MENINGOENCEPHALITIS**); also cancer, sarcoidosis, Behcet's disease, Mollaret's meningitis, systemic lupus erythematosus, Sjögren's syndrome, reaction to ibuprofen and other NSAIDS, azathioprine, tolmetin, zimeldin, trimethoprim and other antibiotics, carbamazepine, allopurinol, i.v. immunoglobulins, OKT3 monoclonal antibodies

Diagnosis: fever, signs of meningeal irritation (eg., stiff neck), variable degree of drowsiness, confusion, stupor, rarely coma, ≥ 10 lymphocytes/ μL in CSF, no neurologic abnormality of recent onset; human coxsackievirus A2, A7, A9, B1, B2, B4, B5, human echovirus 3, 4, 6, 9, 11, 14, 17, 18, 25, 30, 33, human parechovirus 1 and 2 and human enterovirus 71 produce exanthem; Gram stain, acridine orange stain and acid-fast stain, culture and serology of CSF; blood culture using DuPont Isolator or Bactec fungal medium; viral culture of serum in RD and BGM cells; viral culture of feces and throat swab; complement fixation test, hemagglutination inhibition, neutralisation

Viral: protein normal or increased, glucose normal, chloride normal, cell counts normal to 25-100 lymphocytes/ μL , polymorphs early in illness

Arboviruses: paired sera

Enteroviral: protein 15-100 mg/dL, glucose 44-86 mg/dL, 17-912 leucocytes/ μL ; positive serology in 17%; virus isolation

Simplexvirus: PCR on CSF

Lymphocytic choriomeningitis virus: paired sera

Mumps virus: age 5-14 y, males > females, with parotitis in spring, without parotitis in summer; up to 2000 leucocytes/ μL , usually lymphocytes predominant, but may be polymorphs; protein normal or very mildly increased, glucose normal or mildly decreased; sequelae extremely rare; encephalitis \approx 1:5000 cases; virus isolation

Epstein-Barr virus: perseveration, impulsivity, complex-partial seizures, emotional lability, obsessive-compulsive behaviour; CSF PCR

Mycobacterium tuberculosis: most commonly, complication of primary lung lesions in very young children, but also in adults; ophthalmoplegia or facial paralysis; headache in 86%, abnormal mental state in 57%, fever in 55%, night sweats or rigours in 52%; CSF: protein ≥ 200 mg/dL in 70-80% of cases (36% 1000-1500 mg/dL), glucose ≤ 45 mg/dL in 70-85% (26% 2.3-2.6 mmol/L), ≥ 100 leucocytes/ μL in 60-80% (26% 200-400/ μL), increased lymphocytes \pm increased neutrophils (29% 0-10%); serial AFB smears positive in 87%; latex agglutination (sensitivity 100%, specificity 99%); ELISA; adenosine deaminase activity; PCR

Brucella: acute or insidious onset with continued, intermittent or irregular fever of variable duration, profuse sweating particularly at night, fatigue, anorexia, weight loss, headache, arthralgia, generalised aching; isolation; *Brucella* tube agglutination titre on serum > 160; ELISA (IgA, IgG, IgM), 2-mercaptoethanol test, complement fixation test, Coombs, fluorescent antibody test, antipolysaccharide antibody radioimmunoassay, counterimmunoelectrophoresis

Leptospira: protein increased, cell count 300-2000/ μL ; neutrophilia becoming lymphocytosis

Treponema pallidum subsp pallidum: VDRL positive in 90% of cases; protein 50-150 mg/dL (IgG increased), glucose normal, lymphocytes 10-500/ μL

Listeria monocytogenes: protein generally increased, glucose decreased in 60%, leucocytes few to several thousand, polymorphs 0-100%

Aspergillus: protein increased, glucose decreased, cells variable

Zygomycetes: CSF normal

Metastatic Carcinoma, Lymphoma, Meningeal Sarcoma: glucose reduced

Differential Diagnosis: partially treated pyogenic meningitis, brain abscess, parameningeal focus of infection, subdural hematoma, subarachnoid hemorrhage, brain tumour, multiple sclerosis, malignant hypertension, thrombotic thrombocytopenic purpura, systemic lupus erythematosus, temporal arteritis, carcinomatous meningitis

Treatment:

Simplexvirus: aciclovir 5 mg/kg i.v. 8 hourly as a 1 h infusion for 14 d or vidarabine 15 mg/kg daily as a 12-24 h infusion for 10 d + dexamethasone

Other Viral: non-specific (disoxaril in persistent enteroviral infections in agammaglobulinemic individuals; corticosteroids in *Epstein-Barr*)

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 12 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 12 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (12 mo if not

known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 µM/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isoniazid and rifampicin (to 12 mo) + prednisolone 60 mg (child: 1-3 mg/kg) daily for 1-2 w, gradually reducing over next 4-6 w

Nocardia: cotrimoxazole, sulphonamides, minocycline, amikacin, imipenem for at least 6 mo

Brucella: doxycycline 100 mg orally twice a day + rifampicin 600 mg orally 4 times a day or streptomycin 1 g i.m. 4 times a day for 45 d, ciprofloxacin 500 mg orally twice a day + rifampicin 600 mg orally twice a day for 30 d

Treponema pallidum subsp pallidum: penicillin

Leptospira: oxytetracycline

Listeria monocytogenes: cotrimoxazole 5/25 mg/kg to 160/800 mg i.v. 6 hourly + benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly

Fungal: amphotericin B 0.75 mg/kg i.v. daily ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 14 d; diagnostic and therapeutic resection possibly helpful

Toxoplasma gondii: pyrimethamine 100-200 mg loading dose, then 50-100 mg/d orally + folic acid 10 mg/d orally + sulphadiazine 4-8 g/d in divided doses; pyrimethamine 100-200 mg loading dose, then 50-100 mg/d orally + folic acid 10 mg/d orally + clindamycin 900-1200 mg i.v. every 6 h or 300-450 mg orally every 6 h; spiramycin

Taenia solium: mebendazole

Strongyloides stercoralis: thiabendazole, albendazole

Prophylaxis: immunisation against *Poliovirus*; experimental antiviral drugs

CRYPTOCOCCAL MENINGITIS: ≈ 0.2 cases/100,000 person-years; occurs in impaired cell-mediated immunity (particularly associated with lymphomas) but also in others

Agent: *Cryptococcus neoformans*, *Cryptococcus gatii*

Diagnosis: intermittent headache of increasing frequency and severity, usually frontal, temporal or postorbital, may be accompanied by vomiting and vertigo, confusion, personality change, decreased memory, meningeal signs (nuchal rigidity, positive Kernig's and Brudzinski's signs) in 50% of cases, cranial nerve involvement (hearing loss, diplopia, ophthalmoplegia, facial nerve palsy) in 20%, increased cranial pressure hyperreflexia, pathologic reflexes, ataxia, convulsions, fever, progressive delirium and psychosis in 10%; CSF protein increased (50-200 mg/dL), glucose normal to slightly low, 25-500 leucocytes/µL, lymphocytes usually predominate; India ink preparation (budding yeasts with wide capsules; positive in 30-60%) and culture (positive in 40-70%) of CSF; latex agglutination of CSF and serum for antigen (positive in 80-90%); serology (tube agglutination test for antibody positive in ≈ 40%); evaluate inner and middle ear for temporal bone involvement; poor prognosis if markedly positive India ink test, spinal fluid pressure > 300 mm, CSF glucose < 20 g/dL, CSF leucocytes < 20/µL, cryptococci isolated from other sources (eg., blood, urine), no detectable cryptococcal antibody, CSF antigen

> 1:32, patient with malignancy or receiving corticosteroids

Treatment: measure opening pressure and consider means to reduce pressure if > 25 cm H₂O; amphotericin B desoxycholate 0.7 mg/kg i.v. daily for 6-10 w (adjust dose according to tolerance) ± flucytosine 25 mg/kg i.v. or orally 6 hourly for 6-10 w (monitor plasma levels); fluconazole 20 mg/kg to 800 mg/kg orally or i.v. initially, then 10 mg/kg to 400 mg daily for at least 10 w (in immunocompromised, follow with fluconazole 5 mg/kg to 200 mg orally daily indefinitely as prophylaxis); itraconazole + flucytosine; intrathecal amphotericin B for patients who relapse or fail to respond or if nephrotoxicity precludes i.v. (many complications of therapy); increased chance of relapse following therapy if no detectable antibody, persistent malignancy and/or corticosteroid therapy; surgical excision of focal brain lesions associated with high mortality; transfer factor (investigational)

VIRAL MENINGOENCEPHALITIS

Agents: *Crimean-Congo hemorrhagic fever virus*, *mumps virus* (1:6000 mumps cases), enteroviruses (especially chronic *human echovirus 11* infections in agammaglobulinemic patients), *rubella virus* (rare), *simplexvirus 1*, *Russian spring-summer encephalitis virus*, *human parainfluenza virus 4*, *human adenovirus*

Diagnosis: clinical; CSF examination; serology; isolation of virus from blood, CSF or autopsy specimens

Mumps virus: decreased consciousness, focal neurologic deficits; death rate 0.5-2.3%; protein 146-320 mg/dL, glucose 24-43 mg/dL, 208-774 leucocytes/µL, 2-26% polymorphs, 74-98% lymphocytes, 66-6000 erythrocytes/µL

Treatment: oral prednisone; intraventricular immunoglobulin; supportive

BACTERIAL MENINGOENCEPHALITIS

Agents: *Listeria monocytogenes* (≥ 6 d postnatal; may be preceded by septicemia in adult; may mimic tuberculous meningitis), *Brucella*, *Coxiella burnetii*, *Mycoplasma* (rare); also in 2% of cases of Lyme disease

Diagnosis: micro and culture of CSF

Treatment:

Listeria monocytogenes: ampicillin + gentamicin

Brucella: rifampicin 900 mg/d orally for 90 d + cotrimoxazole 5/25 mg/kg/d orally or i.v. for 90 d (add corticosteroid briefly)

Coxiella burnetii, *Mycoplasma:* doxycycline for 2-3 w

RABIES (HYDROPHOBIA): meningoencephalitis prevalent in Africa, India, Indonesia, Philippines, Mexico; > 50,000 deaths/y worldwide; ≈ 3 cases/y (74% from bats) in USA; few bat-associated cases in Australia; in Europe, 70% of cases are in foxes; in Thailand, 95% are in dogs; transmission by saliva of infected animal; human to human transmission by corneal transplantation recorded; incubation period 10 d to 6 mo; $\approx 100\%$ mortality

Agent: *Lyssavirus*

Diagnosis: no signs or symptoms during incubation period; fever, malaise, anorexia, headache, paresthesias or pain at site of bite during prodrome lasting 2-10 d; agitation, hyperventilation, aphasia, paralysis, hydrophobia (17-50% of cases), pharyngeal spasms, delirium during acute neurological stage lasting 2-7 d; hypotension, cardiac arrhythmia, hypoventilation, pituitary dysfunction, coma, infection, thromboembolism in coma stage which lasts days to weeks; death or recovery (only 2 case reports) after months; CAT scan normal or temporal lobe edema; diffuse, slow, non-focal dysrhythmia in electroencephalogram; fluorescent antibody staining or PCR on corneal impressions (positive in 50% of cases), skin, temporal lobe biopsy, neck biopsy, brain tissue postmortem or after inoculation of saliva, tissue (Ammon horn of brain) postmortem or CSF into cell culture, mice or suckling mice; light microscopy (hematoxylin-eosin stained sections of tissue postmortem show Negri bodies) and electron microscopy (*Lyssavirus*) of fixed biopsy material; high antibody titres (rapid fluorescent focus-inhibition titres) in serum or CSF; neutralisation antibody titre of CSF (unvaccinated); virus isolation from clinical specimens followed by direct fluorescent antibody testing; CSF protein 85-133 mg/dL, glucose 105-158 mg/dL, 4-6 neutrophils/ μ L, 6-43 lymphocytes/ μ L, 8-16 red cells/ μ L; white cell count increased; possible complications include hydrophobia (spasms of pharynx), seizures, cerebral edema, inappropriate ADH secretion, diabetes insipidus, hypothermia and hyperthermia, arrhythmia, congestive heart failure, hypotension, aspiration, atelectasis, hypoxemia, pneumonia, gastrointestinal haemorrhage

Treatment (All Persons Exposed to a Bite, Scratch or Abrasion Inflicted by a Brain-positive Animal, in an Unprovoked Attack by a Domestic Dog or Cat in a Rabies Area or in a Provoked or Unprovoked Attack by an Escaped Carnivorous Wild Animal in Such an Area): thorough immediate cleansing of wounds with soap solution or detergent and thorough rinsing under running water, followed by 0.1% benzalkonium chloride or other quaternary ammonium detergent or, if unavailable, 70% alcohol or tincture of iodine +:

Unimmunised: rabies immune globulin 20 U/kg, half applied by instillation deep into the wound and half i.m., followed by human diploid cell vaccine 6 doses i.m. on days 0, 3, 7, 14, 28, 90

Previously Immunised: human diploid cell vaccine 2 doses i.m. on days 0 and 3
leave wound unsutured for a few days; give tetanus antiserum and systemic antibiotics

Prophylaxis: highly effective killed vaccine (human diploid cell); 5 doses lead to $\geq 1:16$ titre in 100%; no rabies cases have resulted in > 120 persons who have received HDCV and been bitten by rabid animals; pain and swelling at injection site in $\approx 25\%$, mild systemic (eg., headache, dizziness) in $\approx 20\%$, 1 reported case of Guillain-Barré syndrome; local or mild systemic reactions should be treated with aspirin; not contraindicated in pregnancy

Prevention and Control: animal immunisation and other control procedures aimed at stray and wild animals

FUNGAL MENINGOENCEPHALITIS

Agent: *Bipolaris* (2 cases in patients with cancer)

Diagnosis: histology and culture of biopsy

Treatment: resection of localised lesions; itraconazole

EOSINOPHILIC MENINGOENCEPHALITIS

Agents: *Angiostrongylus cantonesis* (China, Far East, Hong Kong, Papua New Guinea), *Angiostrongylus malaysiensis* (Malaysia), *Baylisascaris procyonis* (cases in USA from raccoons), *Toxocara*, *Gnathostoma spinigerum*; also

NEUROCYSTICERCOSIS, ventriculoperitoneal shunt

Diagnosis: history of exposure to snails, slugs, molluscs; severe headache, nausea, vomiting, paresthesias, low grade or absent fever, cranial nerve abnormalities, moderate to high eosinophilia in CSF and blood; parasite may be recovered from CSF or anterior chamber of eye; serology (*Angiostrongylus* cross-reacts with *Toxocara canis* in ELISA test)

Differential Diagnosis: cerebral cysticercosis (computed tomography), gnathostomiasis (involvement of nerve roots, bloody or xanthochromic CSF, sudden impairment of sensorium due to cerebral hemorrhage), paragonimiasis (chronic hemoptysis, cavities on chest X rays, punctate nodular calcifications on skull X-rays; skin testing, serology of blood and CSF), schistosomiasis (clinical, recovery of *Schistosoma japonicum* eggs from stool), fungal infections (fungal cultures), allergic conditions, multiple sclerosis (characteristic CSF immunoglobulin pattern and chronic clinical course without symptoms of increased intracranial pressure), neurosyphilis (syphilis serology), tuberculous meningitis (mycobacterial culture), Hodgkin's disease (lymphadenopathy, bone marrow involvement, weight loss, night sweats, pruritus, deteriorating course of illness), reaction to foreign bodies (eg., neurological shunts), lymphocytic choriomeningitis (viral culture)

Treatment: dexamethasone + analgesics; death common and neurological deficits usual with *Bayliascaris procyonis*; with other agents, recovery in mild disease is usually spontaneous, but occasionally disease has been fatal

AMOEBIC MENINGOENCEPHALITIS

Agents: *Naegleria fowleri* (primary amoebic meningoencephalitis; rare; acute; probably worldwide in heated water such as swimming pools, warm springs and in brackish water; invasion of CNS via nasal mucosa and olfactory nerve after bathing in amoeba-infested water or inhaling dust contaminated with viable cysts), *Acanthamoeba* (granulomatous amoebic meningoencephalitis; rare; more insidious onset and more prolonged course; in chronically ill, diabetic, alcoholic, immunocompromised, immunosuppressed; no history of swimming; route of infection probably hematogenous, with portal of entry primary focus in skin, lung, kidney, eye, grafts), *Balamuthia mandrillaris* (granulomatous amoebic meningoencephalitis; 5 cases in Australia; not yet detected in environment)

Diagnosis: mental status abnormalities, headache, fever, nausea and vomiting, stiff neck, seizures, anorexia, diplopia and blurred vision, photophobia, visual hallucinations, papilledema, cranial nerve palsies, nystagmus, gait ataxia, Babinski's sign, Kernig's sign

Naegleriasis: sudden onset, sore throat, rhinitis, ageusia, parosmia, anisocoria, disconjugate gaze, coma on admission or shortly thereafter; death by cardiorespiratory arrest, pulmonary edema, brain edema

Acanthamoebiasis: sleep disturbances, hearing difficulties, hemiparesis, aphasia, coma at end of clinical course; death from bronchopneumonia and liver or kidney failure

multifocal areas of decreased density in subcortical gray matter, gyriform pattern of enhancement in computerised axial tomography; cerebral angiography normal; wet mount (motile trophozoites 8-15 μm), Giemsa-Wright and modified trichome stains and culture of CSF and pus; amoebic trophozoites on electron microscopy, indirect fluorescent antibody test of brain biopsy (positive in 67% of cases); serology (positive in 50%); white cell count 8000/ μL ; CSF protein increased, glucose normal or decreased, 20-7300 leucocytes/ μL , all mononuclears to predominance of polymorphs

Differential Diagnosis:

Naegleria: bacterial meningitis (including partially treated), early viral meningitis

Acanthamoeba: partially treated bacterial meningitis, viral meningonecephalitis, tuberculous meningitis, fungal meningitis, parameningeal infectious focus, carcinomatous meningitis, CNS vasculitis

Treatment: recovery very rare; amphotericin B 1.5 mg/kg/d i.v. in 2 divided doses then 1 mg/kg/d for 6 d + amphotericin B 1.5 mg intrathecally for 2 d then 1 mg intrathecally on alternate days for 8 d + miconazole 350 mg/m² daily i.v. in 3 divided doses for 9 d + miconazole 10 mg intrathecally daily for 2 d then 10 mg intrathecally on alternate days for 8 d + rifampicin 10 mg/kg daily in 3 divided doses for 9 d

ENCEPHALITIS: \approx 7 cases/100,000 person-years; arboviral, enteroviral, associated with childhood infections (*measles virus*, *mumps virus*, *simplexvirus 3*, *rubella virus*), associated with respiratory infections, other infectious agents (< 1% of total cases, no deaths)

Agents: 70-74% indeterminate (69% of total encephalitis deaths, case-fatality rate 11%); 21-27% of documented cases childhood viral (5% of total encephalitis deaths, case-fatality rate 6%; transmitted by aerosolised droplets; 10% *simplexvirus 3* (also common in impaired cell-mediated immunity), 6-10% *mumps virus* (1:6000 mumps cases; 0.5-2.3% case-fatality rate), 6-7% *measles virus* (33% of measles deaths, 67% of measles deaths in patients > 18 y; 0.6/1000 cases; case-fatality rate 14%), *rubella virus* (< 1% of total cases; 1/5000-1/6000 cases; in 4% of adults with rubella; 20-50% case-fatality rate)), 12-21% *simplexvirus* (15% of total encephalitis deaths, case-fatality rate 40-70% untreated, 10-20% treated with acyclovir; most common cause of sporadic fatal encephalitis in USA; all age groups but usually newborn, children and young adults; whites > blacks; no seasonal predominance; usually reactivation; common in impaired cell-mediated immunity; may result in late persistent or recurrent disease of CNS; 67% of affected neonates with significant neurologic sequelae), 10-53% several arboviruses (6% of total encephalitis deaths; case-fatality rate 4%; transmission by mosquito bite and other arthropods; incubation period 4-21 d; mainly in summer, autumn, early winter; St Louis encephalitis (9% of total cases in USA; 5% of total encephalitis deaths; case-fatality rate 7%; USA, Central America, Caribbean Islands, Colombia, Brazil, Argentina;

reservoir birds and bats; vector *Culex* mosquito), California encephalitis (4% of total cases in USA; rare deaths; North-Central USA; reservoir rabbits, squirrels, mice; vector *Aedes* and *Culex* mosquitoes), Western equine encephalitis (3% of total cases in USA; case-fatality rate 10%; all of USA, Canada, Central America, Guyana, Brazil, Argentina; reservoir birds and horses; vector *Culex tarsalis* mosquito), Eastern equine encephalitis (\approx 8 cases/y in USA; case-fatality rate 30-75%; $<$ 1% of total encephalitis deaths; Eastern USA, Central America, Caribbean Islands, Brazil, Guyana, Argentina; reservoir horses (attack rate 18/1000) and birds; vector *Aedes* mosquito; also highly infectious as aerosol, possible biowarfare agent), Japanese B encephalitis ($>$ 50,000 cases/y worldwide; mosquito vector and reservoir; other reservoirs pigs, water birds; attack rate 4/100 000; case-fatality rate $>$ 20%), Venezuelan equine encephalitis (Florida, Texas, Central America, Northern S America; reservoir horse, rodents, dogs, bats, birds; vector *Culex*, *Aedes* and *Deinocerites* mosquitoes; also highly infectious as aerosol (10-100 organisms required for infection), possible biowarfare agent; case-fatality rate 1% but morbidity and mortality may be much higher in biological attack; no person-to-person spread), Powassan encephalitis (NE and Central Europe, Canada, Northern USA; reservoir rodents; vector tick; case-fatality rate 10-20%), *Russian spring-summer encephalitis virus*, *Rio Bravo virus*, *Murray Valley encephalitis virus*, *Ilheus virus*, *Colorado tick fever virus*, *West Nile virus*, *Bunyavirus La Crosse* (20-30/100,000 children/y in many parts of US Midwest; mainly children $<$ 15 y), 6% *influenza A virus* (postinfectious encephalomyelitis), 6% *human adenovirus* (especially serotype 7), 3-40% enteroviral ($<$ 1% of total encephalitis deaths, case-fatality rate 6%; 15% *human echovirus 11*, 9% *human echovirus 7*; *human echovirus 2-4, 6, 16, 18, 19, 30*, *Coxsackievirus*, *Poliovirus*, *human enterovirus 71*; infrequent infections in impaired cell-mediated immunity; may cause chronic disease in primary hypogammaglobulinemia), 3% *simplexvirus 3* (4% of total encephalitis deaths, case-fatality rate 50%); infectious mononucleosis ($<$ 1% of total cases; $<$ 1% of total encephalitis deaths), *vaccinia virus* (postvaccination; infrequent infections in impaired cell-mediated immunity), Rift Valley fever (in $<$ 1% of infections), rabies, *JC polyomavirus* (progressive multifocal leucoencephalopathy; infrequent infections in impaired cell-mediated immunity; also in AIDS), *Human cytomegalovirus* (extremely infrequent infections in impaired cell-mediated immunity and in AIDS), *cercopithecine herpesvirus 1* (herpesvirus of monkeys; occasional fatal encephalitis and ascending paralysis in man), *lassa virus*, bunyaviruses, *lymphocytic choriomeningitis virus*, *Nipah virus*, slow infections, rickettsias, *Coxiella burnetii*, *Mycoplasma* (rare), *Chlamydia*, bacteria associated with brain abscess and meningitis, *Listeria monocytogenes* (rhombencephalitis; nonimmunosuppressed adults; case-fatality rate 51%; sequelae in 61% of survivors), spirochetes, mycobacteria, *Drechslera* (granulomatous), *Cryptococcus neoformans*, *Coccidioides immitis*, *Candida*, *Histoplasma capsulatum*, *Aspergillus*, phycomycetes, *Toxoplasma gondii* (3-40% of AIDS patients), *Trichinella spiralis*, *Baylisascaris procyonis* (from raccoons)

Diagnosis: fever, neurologic abnormality of recent onset; MRI; culture of blood, CSF, throat washings, rectal swab, urine, fluid from skin lesions, brain biopsy in embryonated eggs, laboratory animals, tissue culture; serology (complement fixation test, microagglutination, indirect fluorescent antibody titre, hemagglutination inhibition, neutralisation); immunofluorescent antibody tests on CSF, brain biopsy; PCR on CSF (HSV, CMV, VZV, EBV, JE, rabies, HIV, enteroviruses, certain arboviruses)

Viral: CSF protein increased in 75% of cases, glucose normal, cells 200-2000/ μ L, 60-90% neutrophils in early stages, lymphoid pleocytosis in 80% of later cases, erythrocytes or xanthochromia frequently present

Measles:

Acute: recrudescence of fever during convalescence from measles, headache, seizures, changes in mental status; generalised swelling of brain on computerised axial tomography; diminished activity on electroencephalogram; protein increased in 75% of cases, glucose normal, lymphoid pleocytosis in 80% of cases

Atypical: CSF protein 104 mg/dL, glucose 50 mg/dL, 9 leucocytes/ μ L, 2 erythrocytes/ μ L

Subacute: 1-7 mo after measles attack; immunocompromised patients (70% acute lymphoblastic leukemia); 100% altered levels of consciousness, 97% seizures (78% focal); histologic and PCR studies of brain tissue

Subacute Sclerosing Panencephalitis (Subacute Inclusion

Panencephalitis, Von Brogaert's Disease): rare and fatal; stage 1: \approx 6 y after attack of measles; subtle changes in intellectual skills, mood swings, inappropriate affect, drooling and changes in speech (less common); stage 2: myoclonic jerks, clumsiness, ataxia, choreoathetosis, ocular changes (cortical blindness, optic atrophy, etc) in \approx 50%; stage 3: marked mental deterioration, coma, opisthotonus, decerebrate or decorticate posturing, autonomic nervous dysfunction, often death due to infection; stage 4: patient calmer, nearly total loss of cortical function, purposeless responses (eye movements, episodic laughing or crying), severe autonomic nervous dysfunction, death from vasomotor collapse or infection; electroencephalogram (60% 'pseudoperiodic' patterns, 40% atypical alterations); ELISA titres on 1:5 CSF and 1:2000 serum; microscopy, electron microscopy and immunofluorescence of brain tissue

Arboviral: culture of acute phase blood and CSF; serology (paired sera; complement fixation test, hemagglutination, ELISA (IgM), hemadsorption); inoculation of suckling mouse with blood, brain post mortem

St Louis Encephalitis: temporal lobe lesions on computerised axial tomography; protein > 50 mg/dL in 91% of cases, glucose > 45 mg/dL in 81%, leucocytes \approx 10/ μ L in 75% of cases, lymphocytes \approx 50% in 71%

Venezuelean Equine Encephalitis:

Influenzal: only constitutional symptoms, febrile course 1-4 d

Fulminant: short febrile course with rapid progression to shock, coma and convulsions, disseminated intravascular coagulation; survivors often have sequelae

Encephalitic: fever for 2 w or more, sometimes diphasic; CNS symptoms and signs develop during latter phase; usually no sequelae

Eastern Equine Encephalitis: may have influenzalike prodrome with fever, headache, vomiting, malaise and, rarely, relatively mild encephalitic phase with somnolence but, more commonly, abrupt illness with high fever, convulsions and rapidly progressive coma; may exhibit diffuse or focal signs mimicking herpes encephalitis; magnetic resonance imaging

West Nile Virus: oculomotor abnormalities, movement disorders, myoclonus, features of Parkinson's disease; isolation from tissue, blood, CSF, other body fluid; PCR on tissue, blood, CSF, other body fluid; IgM capture EIA on CSF or serum; plaque reduction neutralising antibody titre on serum or CSF (> 4X change in paired, appropriately timed specimens); EIA for IgM + EIA or HI (confirmed by plaque reduction neutralising antibody titre) in single serum specimen

Bunyavirus La Crosse: fever in 86%, headache in 83%, vomiting in 70%, seizures in 46%, disorientation in 42%; indirect immunofluorescence of serial IgM and IgG titres

Simplexvirus: focal neurologic signs in 85-90%, fever in 80-95%, headache in 55-70%, stiff neck in 45-55%, herpes labialis in 15-20%; CSF abnormal in 85-100%, 10-100 leucocytes/ μ L in 80-100%, > 10 erythrocytes/ μ L in 66-75%, elevated protein in 55-90%, hypoglycorrhachia in 0-25%; localised findings on EEG, brain scan or arteriogram, usually localised to temporoparietal lobe, in 60-95%; MRI—T2 prolongation or gyriform enhancement of medial temporal lobe, insular cortex or cingulate gyrus, petechial hemorrhage of temporal or orbitotemporal lobes, effacement of adjacent CSF spaces; PCR on CSF; brain biopsy positive in \approx 90% and may discover another treatable cause—cryptococcal meningoencephalitis, tuberculosis, brain abscess, brain tumour

Enteroviral: virus isolation; PCR

Mumps virus: virus isolation

Nipah virus: associated with pigs in Malaysia and Singapore; headache, drowsiness, fever; low lymphocyte counts in 82%, high levels of CSF protein in 73%, elevated white blood cell counts in 64%, low platelet counts, low serum sodium levels and elevated aspartate aminotransferase in 46%; MRI (small lesions primarily within white matter, with transient punctate cortical hyperintensities on T1-weighted images); immunohistochemistry + serology

Listeria monocytogenes: prodrome of headache, nausea or vomiting and fever, lasting several days, followed by progressive asymmetrical cranial nerve palsies, cerebellar signs, hemiparesis or hypesthesia and impairment of consciousness; culture of blood (61% positive), CSF (41% positive); magnetic resonance imaging

Mycoplasma pneumoniae: 78% meningeal signs/symptoms, 53% temperature \geq 39°C

Trichinosis: enlarging areas of hemorrhage in parietal regions on computerised axial tomography

Toxoplasma: focal or generalised neurologic abnormalities; contrast-enhanced computerised axial tomography (ring or nodular enhancement in > 90%); magnetic resonance imaging; serology (IgG and IgM); Giemsa-Wright stained smears of centrifuged sediment of CSF or brain aspirate, or impression smears of brain biopsy

Treatment:

Measles: ribavirin 20 mg/kg/d i.v.

Simplexvirus, Nipah virus:

Neonates: aciclovir 20 mg/kg i.v. 8 hourly for 21 d (adjust dose for renal function)

Others: aciclovir 10 mg/kg i.v. 8 hourly for at least 14 d (adjust dose for renal function)

Chlamydia, Mycoplasma, Rickettsia: i.v. doxycycline

Toxoplasma: pyrimethamine 2 mg/kg to 50-100 mg orally as loading dose then 1 mg/kg to 50 mg orally daily + sulphadiazine 50 mg/kg to 1-1.5 g orally or i.v. 6 hourly or clindamycin 15 mg/kg to 600 mg orally or i.v. 6 hourly if allergic to sulphonamides + calcium folinate acid 15 mg orally daily (to reduce incidence of bone marrow suppression) for 3-6 w; 5-fluorouracil; spiramycin

Maintenance Therapy in HIV/AIDS: pyrimethamine 25-50 mg orally daily + sulphadiazine 500 mg orally 6 hourly or 1 g orally 12 hourly or clindamycin 600 mg orally 8 hourly if hypersensitive to sulphonamides

St Louis Encephalitis: interferon α -2b

Others: see under MENINGITIS and BRAIN ABSCESS

Prophylaxis:

Varicella-zoster in Patients with Leukemia, Congenital or Acquired Immunodeficiency, < 24 mo after Haemopoietic Stem Cell Transplant, on Immunosuppressive Medication or with Chronic Graft-versus-host Disease, or Newborn of Mother with Varicella: varicella-zoster immune globulin 625 U i.m. within 96 h of exposure to varicella or zoster from household contact, playmate contact (> 1 h play indoors), hospital contact (in same 2-4 room bedroom or adjacent beds in a large ward), or newborn whose mother contracted varicella 5 d before delivery or within

48 h of delivery), if negative or unknown prior disease history and age < 15 y; live attenuated vaccine (all susceptible health care workers, household contacts and family members \geq 12 mo and not pregnant or immunocompromised; 85% effective)

Japanese B Encephalitis: effective vaccine

Toxoplasma gondii in HIV/AIDS CD4 Count < 200/ μ g: cotrimoxazole 80/400 or 160/800 mg daily or 160/800 mg orally 3 times weekly

ENCEPHALITIS LETHARGICA: epidemics in 1920s, sporadic cases reported in recent years

Agent: *influenzavirus*

Diagnosis: Parkinsonian signs in a young person after influenza

Treatment: ? steroids

NONINFECTIOUS NONTYPHOIDAL SALMONELLA ENCEPHALOPATHY

Agent: non-typhoidal *Salmonella*

Diagnosis: diffuse and rapidly progressive brain dysfunction and circulatory failure following enteritis; elevated CSF opening pressure, minimal ischemic damage and mild edema on brain CT, slow waves on EEG, microvesicular fatty change in liver, severe enterocolitis

Treatment: supportive

ENCEPHALOMYOCARDITIS

Agent: *encephalomyocarditis virus*

Diagnosis: on symptoms; exposure to rodents

Treatment: non-specific

NEUROSYPHILIS: generalised or focal seizures; stroke; changes in personality, affect, sensorium, intellect, insight, judgment; hyperactive reflexes; Argyll-Robertson pupil; optic atrophy; ataxia; impotence; bladder disturbances; peripheral neuropathy; Romberg's sign; cranial nerves II-VII involvement

Agent: *Treponema pallidum subsp pallidum*

Diagnosis: see SYPHILIS

Treatment: benzylpenicillin 3-4 MU i.v. 4 hourly or 18-24 MU/d as continuous infusion for 10-14 d, procaine penicillin 2.4 MU i.m. once daily + probenecid 500 mg orally 4 times a day for 10-14

NEUROCYSTICERCOSIS: 12% of admissions to neurological wards and leading cause of acquired epilepsy in adults in Central and South America, sub-Saharan Africa, east and south Asia; > 50,000 deaths/y; 58% parenchymal calcifications, 48% arachnoiditis, 26% hydrocephalus secondary to meningeal inflammation, 13% parenchymal cysts, 4% hydrocephalus secondary to meningeal fibrosis, 2% brain infarction secondary to vasculitis, 1% mass defect due to large cyst or clump of cysts, 0.7% intraventricular cysts, 0.7% spinal cysts, rare optic nerve

Agent: *Taenia solium*

Diagnosis: epilepsy in 70%; CSF monocytes 300-5000/ μ L, protein 50-1600 mg/dL, glucose low in 18%; computed tomography, magnetic resonance; IgG and IgM ELISA (sensitivity 87%, specificity 95%) and complement fixation test (sensitivity 22-83%) on CSF; histology of biopsy from brain or spinal cord

Treatment:

Intraventricular Cyst, Spinal Cysts: surgical extirpation (+ ventricular shunt with intraventricular cyst)

Parenchymal Cysts, Vasculitis and Encephalitis, Arachnoiditis, Intraocular Cysts: albendazole 15 mg/kg/d for 1 mo, praziquantel 50 mg/kg/d for 2 w; + antiepileptic drugs if epilepsy; + dexamethasone 24-32 mg/d in vasculitis and encephalitis; + ventricular shunt in arachnoiditis with hydrocephalus; + periocular methylprednisolone acetate 80 mg every 30-60 d and aspiration of intravitreal cysts in intraocular cysts

Granulomas or Calcifications: symptomatic treatment (eg, antiepileptic drugs)

Hydrocephalus Due to Basal Fibrosis: ventricular shunt

Cranial Nerve Dysfunction Due to Basal Fibrosis: specific treatments (eg, surgery for diplopia)

Optic Nerve: dexamethasone sodium phosphate 100 mg i.v. daily for 3 d then oral steroids

CEREBRAL COENUROSIS

Agent: *Multiceps* species

Diagnosis: paraplegia and hemiplegia or leptomeningitis

Treatment: usually fatal

CEREBRAL SPIROMETROSIS

Agent: *Spirometra*

Diagnosis: computed tomography and MRI, followed by stereotactic biopsy

Treatment: surgical resection

CEREBRAL MALARIA

Agent: *Plasmodium falciparum*

Diagnosis: clinical manifestations of acute falciparum malaria; coma, convulsions, other neurological signs and symptoms (particularly inability to localise a painful stimulus) compatible with an acute diffuse meningitis or with an encephalitic process; peripheral asexual *Plasmodium falciparum* parasitemia

Treatment: see **MALARIA**; often fatal

BRAIN ABSCESS AND SUBDURAL EMPYEMA: \approx 1 case/100,000 person-years; case-fatality rate 10-22% (90% if comatose, 80-90% if rupture into ventricles, 70-100% if multiple, 100% if distant source of infection, 51-53% in pituitary infection); may spread from nearby tissue such as paranasal sinuses, ear and mastoid process, or by metastatic spread from distant organs following, eg, trauma

Agents: 61% *Staphylococcus aureus* (common after trauma or surgery), 18% aerobic Gram negative bacilli (including *Haemophilus arophilus* and enterics (common with site of origin in ear or paranasal sinuses; *Citrobacter diversus* in neonates; *Klebsiella pneumoniae* hematogenous spread, frequent in diabetics); uncommonly, *Salmonella*, *Actinobacillus actinomycetemcomitans*, rarely, *Brucella melitensis*, *Haemophilus parainfluenzae*, *Enterobacter agglomerans*, *Pasteurella multocida* (infants and adults), *Haemophilus paraprofilus*, *Streptobacillus moniliformis*, anaerobic *Campylobacter*), 8% streptococci (including *Streptococcus milleri*, *Streptococcus sanguis* in intermittently treated jaw infections; occasionally, *Streptococcus pneumoniae*; hematogenous spread, paranasal sinusitis), 2% anaerobes (nontraumatic; especially *Peptostreptococcus* and *Propionibacterium*, also *Actinomyces*, *Prevotella bivia*), 2% *Staphylococcus epidermidis*; *Nocardia asteroides* (in impaired cell-mediated immunity), *Listeria monocytogenes* (especially in leukemia and renal transplant recipients; case-fatality rate 57%), *Mycobacterium tuberculosis*, *Actinomyces pyogenes*, *Corynebacterium equii* (heart transplant recipient), any vascular pathogen secondary to bacteremia (especially in neutropenics), *Aspergillus* (in neutropenics), *Mucor* (in neutropenics), *Absidia* (in neutropenics), *Rhizopus* (in neutropenics), *Pseudallescheria boydii* (in malignant lymphoma and immunosuppression), *Exophiala dermatitidis*, *Fonsecaea pedrosoi*, *Dactylaria constricta*, *Bipolaris hawaiiensis*, *Bipolaris spicifera*, *Curvularia pallescens*, *Cladophialophora bantiana*, *Rhinoctadiella atrovirens* (1 case in HIV-infected i.v. drug abuser), *Curvularia lunata* (rare), *Scedosporium apiospermum* (in immunosuppressed), *Entamoeba histolytica* (amoebic brain abscess usually arises from hematogenous spread of causative organism from lungs or liver; fatal), *Toxoplasma gondii* (in impaired cell-mediated immunity)

Diagnosis: headache in 70%, fever in 50%, retarded consciousness in 50%, papilledema in 50%, focal neurologic deficits in 40%, seizures in 25%, nuchal rigidity rare; culture and histology (Gomori's methenamine silver or PAS shows broad, septate hyphae in mycetoma; Brown and Breen modification of Gram stain shows Gram positive filamentous or branching rods in actinomycetoma, and cocci, coccobacilli or bacilli in botryomycosis) of biopsy; blood cultures; computerised axial tomography (\approx 100% accurate); radionuclide scan (\approx 100% accurate); do not do lumbar puncture (risk of cerebral herniation; CSF, if obtained, will show protein 20-600 mg/dL, glucose

16-93 mg/dL, 0-2300 leucocytes/ μ L, 30-100% polymorphs); agglutinations; analysis of pus from primary organ and obtained by aspiration or biopsy of abscess

Fungal: Fontura-Masson stained histology and culture of biopsy

Pituitary Gland Infection: headache in all cases, fever in 75% of tuberculous and 100% of other bacterial infections, visual disturbances in all tuberculous and 88% of other bacterial infections, associated tumour or cyst in 94%, sellar erosion or enlargement in 63% of tuberculous and 90% of other bacterial infections, associated sphenoid sinusitis in 89%, abnormal carotid angiogram in 50% of tuberculous and 86% of other bacterial infections, hypopituitarism in 80% of

tuberculous and 73% of other bacterial infections, abnormal pneumoencephalogram in 50% of tuberculous and 75% of other bacterial infections; smear and culture usually negative in tuberculous, positive in 55% of other bacterial infections; > 10,000 leucocytes/ μ L in all tuberculous and 21% of other bacterial infections

Treatment: surgical drainage or excision; benzylpenicillin 60 mg/kg to 2.4 g i.v. 4 hourly + metronidazole 12.5 mg/kg to 500 mg i.v. 8 hourly + ceftriaxone 100 mg/kg to 4 g i.v. daily or 50 mg/kg to 2 g i.v. 12 hourly or cefotaxime 50 mg/kg to 2 g every 6 h

Post Neurosurgery: vancomycin 12.5 mg/kg to 500 mg (child < 12 y: 15 mg/kg to 500 mg) i.v. 6 hourly + ceftazidime 50 mg/kg to 2 g i.v. 8 hourly or meropenem 40 mg/kg to 2 g i.v. 8 hourly

From Frontal Sinuses, Teeth: metronidazole + cefotaxime

From Ear and Mastoid: amoxicillin + metronidazole

Secondary to Penetrating Trauma: penicillin + cefotaxime

Metastatic: penicillin + cefotaxime + metronidazole

Staphylococci: fusidic acid 20 mg/kg i.v. 12 hourly as 2 h infusion + clindamycin 600 mg i.v. 8 hourly (child: 15-40 mg/kg i.v. daily in divided doses)

Nocardia asteroides: cotrimoxazole 4/20 mg/kg to 160/800 mg i.v. or orally 6 hourly for 3-4 w, then orally 12 hourly for 3-6 mo

Streptococcus pneumoniae:

Penicillin MIC \leq 0.125 mg/L: benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly for 10 d

Penicillin MIC $>$ 0.125 mg/L: ceftriaxone or cefotaxime + vancomycin or rifampicin

Other Streptococci, Actinomyces: high dose benzylpenicillin

Listeria monocytogenes: cotrimoxazole 5/25 mg/kg to 160/800 mg i.v. 6 hourly + benzylpenicillin 60 mg/kg to 1.8-2.4 g i.v. 4 hourly or amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly

Haemophilus: cefotaxime 50 mg/kg to 2 g i.v. 6 hourly for 7-10 d, ceftriaxone 100 mg/kg to 4 g i.v. daily or 50 mg/kg to 2 g i.v. 12 hourly for 7-10 d, amoxy/ampicillin 50 mg/kg to 2 g i.v. 4 hourly for 7-10 d (if susceptible)

Brucella: cotrimoxazole

Other Aerobic Gram Negative Bacilli: chloramphenicol

Mycobacterium tuberculosis: isoniazid 10 mg/kg to 300 mg orally once daily or 15 mg/kg to 600 mg orally 3 times weekly for 12 mo [+ pyridoxine 25 mg (breastfed baby 5 mg) orally with each dose] + rifampicin 10 mg/kg to 600 mg orally once daily 1 h before breakfast or 15 mg/kg to 600 mg orally 3 times a week for 12 mo + pyrazinamide 25-35 mg/kg to 2 g orally once daily or 50 mg/kg to 3 g orally 3 times weekly for 2 mo (12 mo if not known to be susceptible to isoniazid and rifampicin) + ethambutol 15 mg/kg orally daily (not < 6 y or plasma creatinine > 160 μ M/L; regular ocular monitoring) or 30 mg/kg orally 3 times weekly for 2 mo or until known to be susceptible to isoniazid and rifampicin (to 12 mo) + corticosteroids for first few weeks

Anaerobes: benzylpenicillin 2.4 g i.v. 4-6 hourly + metronidazole 500 mg i.v. infused over 20 minutes 8 hourly, chloramphenicol 1 g i.v. 6 hourly

Fungi:

Bipolaris, Rhinocladiella atrovirens: resection; itraconazole

Others: amphotericin B + flucytosine; decompression of spinal cord essential in management of epidural abscess

Entamoeba histolytica: metronidazole

Toxoplasma gondii: sulphadiazine 50 mg/kg to 1-1.5 g orally or i.v. 6 hourly + pyrimethamine 2 mg/kg to 50-100 mg orally initially then 1 mg/kg to 25-50 mg orally daily + calcium folinate 15 mg orally daily for 3-6 w

Sulphonamide Hypersensitive: clindamycin 600 mg orally or i.v. 6 hourly + pyrimethamine as above

Maintenance Therapy in HIV/AIDS: pyrimethamine 25-50 mg orally daily + sulphadiazine 500 mg orally 6 hourly or 1 g orally 12 hourly or if hypersensitive to sulphonamides clindamycin 600 mg orally 8 hourly

Prophylaxis (Toxoplasma gondii in HIV/AIDS CD4 Count < 200/ μ L): cotrimoxazole 80/400 or 160/800 mg orally daily or 160/800 mg orally 3 times weekly

EPIDURAL ABSCESS: 0.2-2 episodes/10,000 hospital admissions; frequently associated with adjacent osteomyelitis or disc infection

Agents: 63-79% *Staphylococcus aureus*, 4% *Streptococcus pneumoniae*, 4% *Streptococcus viridans*, single report of *Streptococcus pyogenes*; also other organisms causing osteomyelitis

Diagnosis: spinal ache, root pain, weakness (including bowel and bladder dysfunction), paralysis, focal neurologic deficits rare; MRI or CT with contrast medium; blood cultures positive in 62%; Gram stain and culture of operative material or aspiration; lumbar puncture contraindicated

Treatment: urgent surgery essential; di(fl)cloxacillin 50 mg/kg to 2 g i.v. 6 hourly + gentamicin 4-6 mg/kg (child < 10 y: 7.5 mg/kg; ≥ 10 y: 6 mg/kg) i.v. daily (adjust dose for renal function)

RAISED INTRACRANIAL PRESSURE

Agent: *Echinococcus granulosus* (hydatid cyst)

Diagnosis: X-ray; serology; exposure to dogs

Treatment: surgery ± albendazole 7.5 mg/kg to 400 mg orally 12 hourly (not < 6 y)

CEREBROSPINAL FLUID SHUNT INFECTIONS

Agents: *Staphylococcus epidermidis*, *Staphylococcus aureus*, streptococci, *Enterococcus*, aerobic Gram negative bacilli, diphtheroids, *Propionibacterium*, *Haemophilus influenzae*, *Pseudomonas*

Diagnosis: fever, evidence of increased intracranial pressure, abdominal pseudocyst; culture of CSF and peritoneal fluid

Treatment: externalisation of peritoneal catheter + intraventricular and systemic antibiotics and later replacement of catheter

Staphylococci: vancomycin 10-20 mg intrashunt daily + rifampicin 10 mg/kg orally 12 hourly + cotrimoxazole 5 mg/kg orally 8 hourly or vancomycin 15 mg/kg i.v. 8 hourly

Enterococcus faecalis and Streptococci with Penicillin MIC ≥ 0.2 mg/L: vancomycin 10-20 mg intrathecal daily + 15 mg/kg i.v. 8-12 hourly + gentamicin 8 mg intrathecal daily

Streptococci with Penicillin MIC ≤ 0.1 mg/L: gentamicin 8 mg intrathecal daily + i.v. benzylpenicillin

Aerobic Gram Negative Bacilli: gentamicin 8 mg intrathecal daily + cefotaxime 50 mg/kg i.v. 12 hourly to 30 mg/kg 4 hourly

Diphtheroids and Propionibacterium: intrathecal vancomycin 10-20 mg daily + i.v. vancomycin 15 mg/kg 8-12 hourly or cotrimoxazole 15 mg/kg orally 8 hourly

GUILLAIN-BARRÉ SYNDROME (ACUTE POLYRADICULONEURITIS): symmetrical ascending paralysis, usually self-limited and reversible but 5-10% fatal; 1-2 cases/100,000; 0.7 deaths/million doses of influenza vaccine

Agent: influenza A virus, hepatitis B virus, human cytomegalovirus, Epstein-Barr virus, simplexvirus 3, rubella virus, human immunodeficiency virus, mumps virus (rare), HIV, *Campylobacter jejuni*, *Mycoplasma pneumoniae*, *Plasmodium falciparum*

Diagnosis: acute or subacute onset of distal paraesthesia, weakness and muscle pain, with tendency for proximal spread over 2 w and with albuminocytologic dissociation in CSF; fever absent at onset of paralysis, meningeal irritation usually absent, residual paralysis usually absent, sensation may be diminished (cramps, tingling, hypesthesia of palms and soles), deep tendon reflexes diminished but may return in several days

Differential Diagnosis: poliomyelitis (high fever always present at onset of flaccid paralysis, severe myalgia and backache, dysautonomia, inflammatory CSF, abnormal electromyogram at 3 w, severe asymmetrical atrophy at 3 mo), traumatic neuritis (pain in gluteus, hypothermia, frequent blood pressure alterations, sweating, blushing and body temperature fluctuations, CSF normal, symmetrical atrophy of peroneal muscles at 3 mo), transverse myelitis (anesthesia of lower limbs with sensory perception, hypothermia in affected limb, CSF normal to mild increase in cells, moderate atrophy of affected lower limb at 3 mo)

Treatment: none specific

ACUTE PARALYTIC POLIOMYELITIS: 1948 laboratory confirmed cases in 2005; Afghanistan, India and Pakistan major reservoirs; eradicated in Western Hemisphere in 1994; last notification of wild poliovirus infection in USA in 1979 and in Australia in 1986; transmission fecal and respiratory; incubation period 1-3 w, latent period 1-3 d, infectious period 14-20 d, interepidemic period 2-5 y

Agents: human poliovirus 1-3, also some coxsackieviruses (sustained paralysis with human coxsackievirus A4, A1, A9, echo 9 virus, transient paralysis with human coxsackievirus A2, B2-B5), human echovirus 1, 2, 4, 6, 7, 11, 16, 18, 30, human cytomegalovirus in AIDS, West Nile virus

Diagnosis: 95% asymptomatic; 4-5% mild febrile illness (upper respiratory tract infection, gastrointestinal illness, flulike illness); 1-2% mild prodromal illness followed by aseptic meningitis; <1% acute flaccid paralysis; fever at onset of paralysis, meningeal irritation (stiff neck, headache, vomiting) usually present, severe pain in muscles, backache, paralysis usually asymmetrical, progression of paralysis 3-4 d, residual paralysis usually present, paresthesia rare, sensation normal, deep tendon reflexes diminished or absent, electromyogram at 3 w abnormal, severe asymmetrical atrophy at 3 mo, skeletal

deformation developing later; spinal disease 79% of cases, bulbar 2%, combination 19%; case-fatality rate for paralytic illness 2-5% in children, 15-30% in adults and 25-75% in bulbar disease; viral culture of feces or rectal swab (2 specimens at least 24 h apart) or spinal cord, grey matter, medulla, pons, cerebrum, Peyer's patches, intestinal contents post mortem (within 24 h of death) in monkey or human cell culture; CSF protein 38-154 mg/dL, glucose 81 mg/dL, 10-335 leucocytes/ μ L, 5% polymorphs, 80% lymphocytes, 15% monocytes, 9 erythrocytes/ μ L; neutralisation antibody titre or complement fixation test on serum ($\geq 4X$ increase or $\geq 1:512$)

Differential Diagnosis: Guillain-Barré syndrome (fever not common, cramps, tingling, hypesthesia of palms and soles, CSF albumin-cytological dissociation, normal EMG at 3 w, mild sequelae at 3 mo), traumatic neuritis (pain in gluteus, hypothermia, frequent blood pressure alterations, sweating, blushing and body temperature fluctuations, CSF normal, EMG normal at 3 w, symmetrical atrophy of peroneal muscle at 3 mo), transverse myelitis (fever rarely present, anesthesia of lower limbs with sensory perception, hypothermia in affected limb, CSF normal or mild increase in cells, EMG normal at 3 w, moderate atrophy in affected limb at 3 mo)

Treatment: non-specific

Prophylaxis (*human poliovirus*): oral vaccine phased out in USA by 2000 because of continued vaccine-associated paralytic poliomyelitis, but is still recommended for mass vaccination during polio outbreaks; all infants and children, incompletely vaccinated children, travellers to areas or countries where polio is epidemic or endemic, immunocompromised individuals, communities or population groups with disease caused by wild poliovirus, laboratory workers who handle poliovirus specimens, healthcare workers who have contact with patients excreting wild poliovirus, and unvaccinated adults whose children will receive oral poliovirus vaccine should receive 4 doses inactivated vaccine (contraindicated if severe febrile illness, allergy to streptomycin or neomycin, vomiting or diarrhoea, some malignant conditions, *HIV* infection in individual or household contacts, pregnant woman in first 4 months of gestation); vaccine 90-100% efficacy, lifetime immunity, marginally cost effective

POST-POLIO SYNDROME: development of new muscle weakness and fatigue in skeletal or in bulbar-controlled muscles, unrelated to any known cause, that begins between 25 and 40 y after an acute attack of paralytic poliomyelitis; occurs in 25-40% of survivors infected in childhood

Agent: *human poliovirus*

Diagnosis: history of acute paralytic poliomyelitis in childhood or adolescence; history of partial recovery of motor function and maintenance of function for at least 15 y; residual muscle atrophy in at least one limb, accompanied by weak or missing reflexes but normal sensation; normal functioning of sphincter muscle

Treatment: supportive

BOTULISM: paralytic illness caused by neurotoxin; associated with home-canned foods with low acid content, improperly canned commercial foods, home-canned or fermented fish or other marine or freshwater animals, herb-infused oils, baked potatoes in aluminium foil, cheese sauce, bottled garlic, foods held warm for extended periods; 0.5% of foodborne disease outbreaks in USA, 0.1% of cases, 3% of deaths; 226 cases from 114 outbreaks in Alaska in 1950-2000 (all from fermented foods); last case in Australia in 1998; also inhalational

Agent: *Clostridium botulinum*

Diagnosis: incubation period 2 h - 10 d (usually 12-36 h); vomiting, diarrhoea; developing cranial nerve paralysis causing blurred vision, ptosis, mydriasis, diplopia, dilated and fixed pupils, dysphonia, dysphagia and dry throat; dysarthria, symmetrical, descending, progressive skeletal muscle weakness, respiratory impairment, motor palsy, diffuse flaccid paralysis follow; sometimes postural hypotension; patient alert and afebrile; duration of illness days to months; electromyogram with rapid repetitive stimulation of affected area at 20-50 Hertz, tensilon test, CSF protein normal, computerised tomography scan of head, magnetic resonance imaging; ELISA test for botulinum toxin in serum, stool and food or from swab of nares; mouse bioassay

Differential Diagnosis: Guillain-Barré syndrome, myasthenia gravis, poliomyelitis, tick paralysis, cerebral vascular accident, heavy metal (thallium, arsenic, lead) or organophosphate toxicity

Treatment: supportive + antitoxin (no deaths if early diagnosis)

Prophylaxis: passive with antitoxin or active with toxoid

AIDS DEMENTIA COMPLEX (HIV ENCEPHALOPATHY)

Agent: *human immunodeficiency virus*

Diagnosis: 'subcortical dementia' with slowing of mental and motor functions, diffuse cognitive impairment, behavioural torpor, in *human immunodeficiency virus* positive individual; computed tomography and magnetic resonance imaging; CSF examination

Treatment: zidovudine

TICK PARALYSIS: case-fatality rate 10%

Agents: various hard tick species (*Ixodes holocyclus* in Australia, *Dermacentor andersoni* in southern and western USA, *Dermacentor variabilis* and *Amblyomma americanum* in southern and eastern USA)

Diagnosis: weakness, pulmonary complication (respiratory failure; bilateral raised hemidiaphragms on chest X-ray); presence of tick; history; CSF protein and cell count normal; compound action potentials of nerves and associated muscles decreased, nerve conduction velocity decreased

Treatment: tick removal; usually supportive only, but antitoxin may be given

KURU: age > 4 y, insidious onset, dementia ±, sensory defects ±; mainly women and children of an isolated tribe (Fore) in Papua-New Guinea; transmitted by eating infected brain tissue in ritual ceremony for dead tribal member

Agent: prion

Diagnosis: clinical (ambulant stage: subjective unsteadiness, ataxic gait, convergent strabismus, shivering-like truncal tremor, dysarthria; sedentary stage: needs support for walking, rigidity of limbs, clonus, emotional lability with outbursts of pathologic laughter, no mental deterioration or sensory changes; terminal: unable to sit without support, urinary and fecal incontinence, bulbar signs, inanition, decubitus ulcers, pneumonia)

Treatment: none

CREUTZFELDT-JAKOB DISEASE: age > 18 y (average 63 y), insidious onset, dementia and sensory defects present; disease duration 1 mo - 10 y; inherited form with worldwide incidence ≈ 1:1,000,000 and apparently infectious form

Agent: prion

Diagnosis: muscular spasms, reduced mental function, loss of higher brain function, abnormal behaviour; periodic sharp waves in EEG in 65-70%; CSF 14-3-3 protein in ≈ 90%; histology

Treatment: none

VARIANT OF CREUTZFELDT-JAKOB DISEASE: form associated with bovine spongiform encephalopathy, occurring in younger patients

Agent: prion

Diagnosis: psychiatric signs, depression or schizophrenia, stickiness of the skin, instability, walking difficulties, involuntary movements, prostration and death; median age at death 29 y; pulvinar sign (high T2 signal in posterior thalamus on magnetic resonance imaging; ≈ 75% of cases); no periodic sharp waves on EEG; CSF 14-3-3 protein in 50%; histology of tonsils (presence of disease-associated glycoforms of protease-resistant prion protein)

Treatment: none; possible benefit from quinacrine, chlorpromazine

GERSTMAN-STRAÜSSLER-SCHEINKERS DISEASE: discoordination followed by increasing dementia; ≈ 50 families affected; inheritance of PrP gene mutation involved

Agent: prion

Treatment: none

FATAL FAMILIAL INSOMNIA: sleep problems and autonomic nervous system manifestations, followed by full-blown insomnia and dementia; described in 9 families; inheritance of PrP gene mutation involved; disease lasts about 1 y

Agent: prion