

Chapter 5

Prenatal, Perinatal and Puerperal Infections

ABORTION

Agents: rubella, *human cytomegalovirus*, vaccinia, hepatitis B, Lassa fever virus, smallpox, varicella (20% mortality), *Listeria monocytogenes* (infection in first trimester found in Middle East, not in Western Europe, where infection in third trimester occurs), *Haemophilus influenzae*, *Campylobacter fetus* subsp *fetus*, *Campylobacter jejuni*, *Campylobacter coli*, *Leptospira*, *Streptococcus agalactiae*, *Coxiella burnetii*, *Streptococcus equinus*

Diagnosis: serology (complement fixation test, hemagglutination inhibition); bacterial and viral culture of saliva, gastric washings, urine, liver biopsy; post-mortem histology of salivary glands, adenoids, kidneys, liver, lymph glands, myocardium, spleen, pancreas, adrenals; serology

Prophylaxis:

***Listeria monocytogenes* in Pregnancy:** benzylpenicillin 15-20 MU i.v. daily in divided doses for 2 w ± gentamicin 1.3 mg/kg i.v. 8 hourly

***Coxiella burnetii* in Pregnancy:** cotrimoxazole for duration of pregnancy

Rubella: mass immunisation of girls and boys; pre-pregnancy screening for rubella antibodies, followed by immunisation of susceptible women; antenatal screening for rubella antibodies, followed by post-partum immunisation of susceptible women

Varicella: live attenuated vaccine (44-85% effective; do not administer if pregnant)

STILLBIRTH

Agents: 14% parvovirus B19, rubella virus, *human cytomegalovirus*, hepatitis B, *Treponema pallidum*, *Toxoplasma gondii*, *Listeria monocytogenes*, *Campylobacter fetus* subsp *fetus*

Diagnosis: bacterial and viral culture of lymph nodes, lung, spleen, other tissues; serology (rubella: hemagglutination inhibition, complement fixation test)

Parvovirus B19: ELISA (IgM, IgG (kits using recombinant protein more sensitive and specific than those using a synthetic peptide)), PCR of maternal serum or amniotic fluid

***Toxoplasma gondii*:** isolation from placenta, umbilical cord or infant blood; PCR of white blood cells, CSF or amniotic fluid (reference laboratory); IgM and IgA serology; IgG avidity (urea dissociable)

Prophylaxis:

***Listeria monocytogenes* in Pregnancy:** benzylpenicillin 15-20 MU i.v. daily in divided doses for 2 w ± gentamicin 1.3 mg/kg i.v. 8 hourly

***Coxiella burnetii* in Pregnancy:** cotrimoxazole for duration of pregnancy

***Toxoplasma gondii* in Pregnancy:** spiramycin 3 g orally in divided doses

Rubella: see under **ABORTION**

Syphilis: routine antenatal screening and treatment of infected women

TERATOGENIC EFFECTS

Agents: rubella (transient common: intrauterine growth retardation, large anterior fontanelle; transient uncommon: cloudy cornea; permanent common: sensorineural deafness, spastic diplegia, patent ductus arteriosus, pulmonic stenosis, cataract and microphthalmia, retinopathy; permanent uncommon: glaucoma, inguinal hernia, cryptorchidism; permanent developmental common: central language disorders, mental retardation, behavioural disorders; permanent development uncommon: severe myopia), *human cytomegalovirus*, human immunodeficiency virus, lymphocytic choriomeningitis virus (from pet rodents)

Diagnosis: serology (rubella specific IgM present or infant's IgG titre does not fall off at expected rate of 1 doubling dilution per month); viral culture of throat swab and urine; ELISA, Western blot

Prophylaxis (Rubella): see under **ABORTION**

PRENATAL GENERALISED DISEASE

Agents: *human cytomegalovirus* (3-15% of pregnancies, 0.4-7% of live births; multisystem involvement (cytomegalic inclusion disease), usually a sequel of primary maternal infection; microcephaly, seizures, mental retardation, periventricular calcification, deafness (inner ear involvement), chorioretinitis, hepatosplenomegaly, jaundice, thrombocytopenia, petechial rash; sequelae in 90% of survivors—70% microcephaly, 60% mental retardation; most disappear within 4 y, but 29% IQ < 90, 16% IQ < 80, 16% microcephaly, 12% bilateral hearing loss, 2% chorioretinitis), *simplexvirus* (5% of neonatal herpes, 1 in

300,000 deliveries; 10% risk if infection > 32 w gestation; if mother has first episode, 50% infected at birth; during recurrent episode, 3-5%; most transmission occurs while mother has no symptoms), rubella (0.1-4% of pregnancies, 0.05-3% of live births; transient common: thrombocytopenic purpura, hepatosplenomegaly, meningoencephalitis, bone lesions; transient uncommon: generalised adenopathy, hepatitis, hemolytic anemia, pneumonia, myocarditis), *Neisseria gonorrhoeae*, *Treponema pallidum* subsp *pallidum*, varicella-zoster (malformations, 18% disseminated infections), *Listeria monocytogenes* (neonatal disseminated listeriosis (disseminated infantile listeriosis, granulomatosis infantiseptica, listeriosis of the newborn) contracted transplacentally and widely distributed in the fetus, resulting in abortion, premature birth, stillbirth or death shortly after delivery), *Plasmodium*, *Candida* (low birth weight, pneumonia and skin rash), *Campylobacter fetus* subsp *fetus*, *Campylobacter jejuni*, *Toxoplasma gondii* (meningitis)

Diagnosis: cultures of blood and urine; Giemsa stain of blood film; demonstration of specific IgM antibody in cord or neonatal serum (hemagglutination inhibition, passive hemagglutination, immunofluorescence, ELISA); serology of CSF; viral culture of throat swab, saliva, gastric washings, urine

Congenital Human cytomegalovirus Disease: hepatomegaly in 100%, splenomegaly in 100%, mental retardation in 80%, microcephaly in 80%, motor disability in 75%, jaundice in 66%, petechiae in 55%, chorioretinitis in 30%, cerebral calcification in 25%; increased cord serum IgM in 85%, atypical lymphocytosis in 80%, increased SGOT in 80%, thrombocytopenia in 60%, increased bilirubin in 60%, increased CSF protein in 45%; viral culture positive at birth or within 1-2 w, characteristic inclusions seen on cytological examination of urine, IgG antibody; early marker of fetal infection is depression of cellular immunity in mother during pregnancy when exposed to primary *human cytomegalovirus* infection

Maternal Rubella Infection during Pregnancy: rising titres in hemagglutination and complement fixation tests; high titres of specific IgM

Congenital Malaria: platelet count 32,500/ μ L, serum bilirubin 4.1 mg/dL, white cell count 6900/ μ L, haematocrit 28%

Congenital Syphilis (Antenatal Syphilis, Foetal Syphilis, Prenatal Syphilis): syphilis arising in a neonate, infant or child as a result of intrauterine infection of fetus; fetus is infected transplacentally as early as the ninth to tenth week of gestation in 2/3 or more of pregnancies; incidence 13/100,000 live births in USA; CSF analysis for VDRL, cell count and protein; complete blood count, differential and platelet count; long bone radiographs; other tests as clinically indicated

Early (Not Before Third Week Postpartum in 80% of Infants): rhinitis (snuffles; early congenital/prenatal syphilitic coryza; obstruction and discharge—often bloody; one of most characteristic features of early congenital syphilis; severe cases may lead to permanent cracks or fissures (rhagades) about nose or mouth); laryngitis causing characteristic aphonic cry; often fatal pneumonia (early congenital syphilitic pneumonia, indurative syphilitic pneumonia of the newborn, pneumonia alba, primary congenital syphilitic pneumonia) in about 20% of cases, with diffuse interstitial fibrosis and fatty degeneration of lung parenchyma; bullae and vesicles; diffuse maculopapular or papulosquamous desquamative rash, most commonly on palmar, plantar, facial and anal areas; mucous patches; condylomata lata; osteitis (syphilitic osteitis of the newborn; nasal osteitis may cause destruction of vomer and saddle nose), osteomyelitis, periostitis (a hypertrophic, progressive condition affecting tibia leads to sabre shin), osteochondritis (syphilitic osteochondritis of the newborn, Wegner disease, Wegner osteochondritis; femur and humerus most frequently affected; severe osteochondritis may lead to epiphysal separation, causing early congenital syphilitic paralysis—Bednar-Parrot disease, Parrot disease, Parrot pseudoparalysis, syphilitic pseudoparalysis), epiphysitis, chondroepiphysitis, perichondritis may be present at birth; hepatosplenomegaly; jaundice; thrombocytopenia, leucocytosis, anemia; paroxysmal cold hemoglobinuria; nephropathy (mild, acute nephritis, nephrotic syndrome or both); neurologic signs; lymphadenopathy

Latent Congenital Syphilis: serum is serologically positive and CSF negative and there are no symptoms

Late Congenital Syphilis (Syphilis Hereditaria Tarda): 2-30 y; interstitial keratitis gives cornea ground-glass appearance, becomes bilateral and leads to blindness; nerve deafness ('eight nerve deafness' affecting vestibulomandibular (eighth cranial) nerve); recurrent arthropathy (hydrarthrosis; Clutton joint, Clutton syndrome; most frequently knee); odontopathy (notched incisors—Hutchinsonian teeth, Hutchinson's incisors, Hutchinson teeth; domed front molars—Moon molars, Moon teeth; first molars with botryoidal occlusal surface—mulberry molars, mulberry teeth); frontal bosses a common result of hypertrophic periostitis; poor maxillary development; protruding mandible; high palatal arch; rhagades; thickening of inner part of right clavicle (clavicular sign, Higouménakis sign); flaring scapulas; neurosyphilis; gumma; (Hutchinson triad = congenital syphilitic keratitis with eighth nerve deafness and notched incisors); rising VDRL titre diagnostic; positive FTA-ABS-IgM suggestive but not diagnostic (10% false positive); negative FTA-ABS-IgM does not

exclude diagnosis (35% false negative); results for both improved using 19S reagent; DFA Tp monoclonal; EIA IgM; immunoblot IgM of serum; PCR of serum or blood

Listeria monocytogenes: respiratory distress, vomiting, diarrhoea, maculopapular skin lesions, hepatosplenomegaly, meningitis; blood cultures, CSF examination

Toxoplasma gondii: mostly few symptoms at birth; later, generally develop mental retardation, severely impaired eyesight, cerebral palsy, seizures unless treated; isolation from placenta, umbilical cord or infant blood; PCR of white blood cells, CSF or amniotic fluid (reference laboratory); IgM and IgA serology; IgG avidity (urea dissociable) on mother in pregnancy

Herpes: scarring, active lesions, hypopigmentation, hyperpigmentation, aplasia cutis, erythematous macular exanthem, microphthalmia, retinal dysplasia, optic atrophy, chorioretinitis, microcephaly, encephalomalacia, hydranencephaly, intracranial calcification; PCR of CSF, blood

Treatment:

Gonorrhoea: benzylpenicillin 45-60 mg/kg i.v. daily in 4 divided doses for 7-10 d

Syphilis:

Mother Adequately Treated Before 28 w Gestation and Not Reinfected:

benzathine penicillin 37.5mg/kg i.m. as a single dose

Not As Above or Symptoms Present: benzylpenicillin 50 mg/kg i.m. or i.v. 12 hourly for 10 d, procaine penicillin 50 mg/kg i.m. daily for 10 d

Listeria monocytogenes: benzylpenicillin 50 000-1 MU daily i.v. for 2 w

Candida: amphotericin B

Simplexvirus: aciclovir

Rubella: none; consider abortion if infection detected during pregnancy

Plasmodium: chloroquine

Toxoplasma (in Pregnancy): spiramycin 3 g orally daily in divided doses + sulphadoxine-pyrimethamine 500/75 mg orally every 10 d + folinic acid; spiramycin 3 g orally in divided doses for 3 w, alternating with pyrimethamine-sulphadiazine 50 mg/3 g orally daily for 3 w + folinic acid

Prophylaxis:

Listeria monocytogenes in Pregnancy: benzylpenicillin 15-20 MU i.v. daily in divided doses

Prevention and Control:

Rubella: mass immunisation of girls and boys; pre-pregnancy screening for rubella antibodies, followed by immunisation of susceptible women; antenatal screening for rubella, followed by postpartum immunisation of susceptible women

Human cytomegalovirus: viral isolation from amniotic fluid

Syphilis: routine antenatal screening and treatment of infected women

Gonorrhoea: Gram stain and culture of cervical swab of pregnant women in population groups in which gonorrhoea is more common, with symptoms suggestive of gonococcal infection or in a high risk group for STD

Varicella: live attenuated vaccine (44-85% effective; do not administer if pregnant)

PERINATAL GENERALISED DISEASE: 25% of perinatal deaths

Agents: *Staphylococcus epidermidis* (16% of neonatal sepsis/meningitis), *Klebsiella pneumoniae* (15% of neonatal sepsis/meningitis), *Streptococcus agalactiae* (12-25% of neonatal sepsis/meningitis; early onset pneumonia, septicemia, late onset meningitis, endocarditis, abscess, myocarditis, osteomyelitis), *Escherichia coli* (10-16% of neonatal sepsis/meningitis), *Staphylococcus aureus* (7% of neonatal sepsis/meningitis), viridans streptococci (6% of neonatal sepsis/meningitis; *Streptococcus mitis* 0-5%), *Enterobacter cloacae* (5% of neonatal sepsis/meningitis), *Enterococcus* (4% of neonatal sepsis/meningitis), non-*Enterococcus* group D streptococci (3% of neonatal sepsis/meningitis), group C streptococci (0.6% of neonatal sepsis/meningitis), *Streptococcus milleri* (0-5% of neonatal sepsis/meningitis), other streptococci (2% of neonatal sepsis/meningitis), *Listeria monocytogenes* (2% of neonatal sepsis/meningitis), *Serratia marcescens* (2% of neonatal sepsis/meningitis), *Proteus* (2% of neonatal sepsis/meningitis), *Haemophilus influenzae* (nontypeable strains; 0.6-8% of neonatal sepsis/meningitis; sepsis/respiratory distress syndrome; 83% early postnatal onset, 44-66% associated maternal complications, 83-88% premature, 50-90% mortality), *Corynebacterium* (0.6% of neonatal sepsis/meningitis), *Citrobacter* (0.6% of neonatal sepsis/meningitis), *Candida albicans* (0.6% of neonatal sepsis/meningitis), *Bacteroides fragilis* (0.3-5% of neonatal sepsis/meningitis), *Salmonella* (0.3% of neonatal sepsis/meningitis), *Prevotella disiens* (0-5% of neonatal sepsis/meningitis), *Peptostreptococcus magnus* (0-5% of neonatal sepsis/meningitis), *Clostridium perfringens*, *Neisseria gonorrhoeae*, *Haemophilus arophilus*, coxsackievirus B (myocarditis, hepatitis), *simplexvirus* (1-1.5% of pregnancies, 85% of

neonatal herpes; risk 3-60% if present at delivery; increased risk if maternal primary infection, premature rupture of membranes, delayed delivery; subsp 1 and 2 both of equal severity, subsp 2 most common; maternal genital source in ≈ 75%, also maternal non-genital and non-maternal (indirect transmission from another infant in nursery, ≈ 10% of symptomless hospital staff excrete *simplexvirus* in saliva); mortality 61% in disseminated disease; 50% of survivors have severe sequelae; 43% skin, eye and mouth (complete recovery with rapid antiviral treatment, ≤ 75% untreated advance to CNS or disseminated disease), 34% CNS (≥ 50% mortality), 23% disseminated (70% mortality), *human cytomegalovirus* (10% localised to salivary glands, 1-2% disseminated; 88% kidney, 79% liver, 69% lung, 57% pancreas; 60% of neonates breastfed by mothers excreting *human cytomegalovirus* in breast milk, 55% of neonates born to mothers excreting *human cytomegalovirus* in cervical secretions; no neonates infected by mothers excreting only in urine or saliva; asymptomatic viraemia in 20% of infants of seropositive mothers, 30% of third semester viruric mothers, 57% of postpartum and third semester viruric mothers, viraemia delayed for 6 w; pneumonia in premature or (uncommonly) full term infants—'gray pallor', hepatosplenomegaly, respiratory distress, viraemia), echovirus 6, 11, 14, 19 (hepatitis), HIV (transmission rate from 15% in Europe to 50% in Africa), *Streptococcus pneumoniae*, *Hafnia alvei*, *Streptococcus pyogenes*

Diagnosis: Gram stain and culture of gastric aspirate, throat swab, eye swab; Gram stain, immunofluorescence or PCR, electron microscopy, bacterial and viral culture of skin lesions swabs; Gram stain, culture and latex agglutination of CSF; blood cultures; viral culture of saliva, gastric washings and urine; serology; ELISA; C-reactive protein and interleukin levels (combined sensitivity 58-96%)

Listeria monocytogenes: septicemia, often with meningitis; white cell count 13,600/μL, 36% neutrophils, 4% bands, 55% lymphocytes, 3% monocytes, 0.4% eosinophils

Human cytomegalovirus: culture negative specimens at birth but positive specimens at ≥ 4 w; IgG antibody

HIV: ELISA, Western blot (immunoblot)

Enteroviruses, Simplexvirus: virus isolation; PCR; 1/3 herpes cases with CNS disease, 23% disseminated

Treatment:

Streptococcus, Peptostreptococcus, Corynebacterium and Clostridium: benzylpenicillin

Other Anaerobes: metronidazole

Coliforms: gentamicin, chloramphenicol

Neisseria gonorrhoeae: benzylpenicillin 75,000-100,000 U/kg i.v. daily in 4 divided doses for

7-10 d

Penicillinase-producing: cefotaxime or gentamicin

Staphylococcus aureus: cloxacillin

Listeria monocytogenes: benzylpenicillin 500,000-1 MU daily i.v. for 2 w or ampicillin + gentamicin 5 mg/kg daily in divided doses for 14-21 d

Haemophilus influenzae:

β-lactamase Negative: ampicillin for 7 d

β-lactamase Positive: ceftriaxone or cefotaxime

Simplexvirus: aciclovir 20 mg/kg i.v. every 8 h (preterm: 12 h) for at least 14 d (localised) or 21 d (disseminated) (adjust dose for renal function)

Prevention and Control:

Neonatal simplexvirus: good hygiene (soap and water inactivate *simplexvirus*); monitor patients with history of herpes genitalis or with a history of sexual contact with a *simplexvirus*-infected partner; culture cervix and any recurrence site at 32, 34 and 36 w and once a week subsequently and tell patient to report any prodrome to her physician; patients with active disease (lesion visible) or positive culture should have elective caesarean section before membrane rupture

Streptococcus agalactiae: screening of pregnant women at 35-37 w gestation by culture of combined vaginal and rectal swabs or by PCR at time of labour, and administration of benzylpenicillin (1.2 g i.v. stat, then 600 mg i.v. 4 hourly until delivery), or clindamycin (450 mg i.v. 8 hourly until delivery) or lincomycin (600 mg i.v. 8 hourly until delivery) if penicillin hypersensitive, to carriers

HIV: zidovudine 2 mg/kg i.v. over 1 h to mother 4 h before caesarean section before membrane rupture (reduces transmission rate to 2%), then 1 mg/kg per hour i.v. until the umbilical cord is clamped; zidovudine 2 mg/kg orally 6 hourly or 4 mg/kg orally 12 hourly to baby after umbilical cord is clamped or within 6-8 h of delivery and continued for first 6 w

POSTNATAL GENERALISED INFECTIONS

Agents: late-developing or postpartum infection with any of the agents listed in **PRENATAL GENERALISED DISEASE** and **PERINATAL GENERALISED DISEASE**

POSTNATAL GASTROENTERITIS

Agent: echovirus

Diagnosis: serology; viral culture of feces

Treatment: rehydration

ABORTIONAL AND PUERPERAL INFECTION: 0.01% of new episodes of illness in UK

Agents: 75% *Peptostreptococcus* + *Bacteroides*, 5% *Bacteroides* alone, 15% *Mycoplasma hominis*, *Streptococcus pyogenes* (produces peritonitis and septicemia), coliforms (post-abortion; produce endotoxic shock), *Staphylococcus aureus* (produces pneumonia and septicemia; derived from hospitalisation, i.v. therapy), *Enterococcus faecalis*, *Pseudomonas* (gives endotoxic shock), *Clostridium* (post-abortion, uterine tumours, complicated deliveries requiring mechanical intervention; endometritis, gross hemolysis, shock, uterine gas gangrene with fulminant septicemia), *Haemophilus influenzae*, *Aeromonas* (incomplete abortion); anaerobes isolated from blood cultures in 76% of cases of septic abortion complicated by bacteremia

Diagnosis: Gram stain and culture of swabs, pus; when possible, use culdocentesis to obtain specimens from the female genital tract after decontaminating the vagina with povidone iodine; double catheter and bronchial brush or sterile swab may be used for specimens from the uterine cavity; blood cultures

Treatment:

Patient Febrile but Not Clinically Ill: amoxicillin-clavulanate 500/125 mg orally 8 hourly for 3 d

Fever > 48 h: as above + erythromycin 500 mg orally 8 hourly or clindamycin 300 mg orally 8 hourly until fever resolves

Severely Ill: see **SEPTICEMIA**

***Clostridium*:** penicillin 20-30 MU/d i.v., chloramphenicol, metronidazole, clindamycin, cefoxitin

AMNIONITIS

Agents: *Streptococcus agalactiae*, *Listeria monocytogenes*, *Haemophilus influenzae*, *Capnocytophaga*, *Gardnerella vaginalis*, *Streptobacillus moniliformis*, anaerobes

Diagnosis: culture of amniotic fluid

Treatment: ampicillin + metronidazole

CHORIOAMNIONITIS

Agents: 22% anaerobes, 17% *Streptococcus agalactiae*, 22% other β -haemolytic streptococci, 17% coliforms, 6% *Mycoplasma hominis*, 6% *Ureaplasma urealyticum*, 6% *Haemophilus influenzae*, 6% *Gardnerella vaginalis*, *Corynebacterium striatum* (rare), *Capnocytophaga* (rare)

Diagnosis: culture of membrane

Treatment:

***Mycoplasma*, *Ureaplasma*:** erythromycin

Others: amoxicillin-clavulanate, cefotaxime

ENDOMETRITIS: early (\leq 48 h) postpartum following caesarean section, late (48 h - 6 w) postpartum usually following vaginal delivery

Agents: *Gardnerella vaginalis*, *Peptococcus*, *Staphylococcus epidermidis*, *Streptococcus agalactiae*, *Mycoplasma hominis* (34% of post-caesarean sections), *Ureaplasma urealyticum*, *Chlamydia trachomatis*, *Streptococcus pneumoniae*; also non-postpartum due to *Bacteroides*, *Prevotella bivia*, *Haemophilus influenzae* and *Actinomyces israelii* (IUD-related), *Vibrio vulnificus* (in a woman engaging in sex in sea water)

Diagnosis: protected, triple lumen transcervical culture (double catheter and bronchial brush or sterile swab specimens are not suitable because of contamination with vaginal flora)

Treatment: piperacillin, cefoxitin