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Chickenpox in Pregnancy

Epidemiology

- Risk of primary varicella in pregnancy is 3:1000.
- 90% of reproductive aged women are seropositive to varicella zoster virus (VZV)
- 80% of deaths caused by VZV occur in adult patients

Transmission

VZV transmission	<ul style="list-style-type: none"> • Droplet infection: Significant contact that suggests high risk of transmission includes: <ul style="list-style-type: none"> ▪ Sharing the same room with an infected person for 15 minutes or more ▪ Face-to-face contact • Direct contact with vesicle fluid or indirectly e.g. by fomites
Symptoms of primary infection	<ul style="list-style-type: none"> • Fever, malaise • Maculopapular rash that becomes vesicular and then crusts over before healing <p>The disease is infectious 2 days before appearance of the rash and till vesicles crust over (usually 5 days after appearance of the rash)</p>
Symptoms of recurrent infection	<ul style="list-style-type: none"> • Following primary infection, the virus remains dormant in sensory ganglia • Viral reactivation results in zoster or shingles (erythematous rash which follows dermatomal distribution).
Varicella vaccine	<ul style="list-style-type: none"> • Live attenuated vaccine • 2 separate doses 4-8 weeks apart. • Safe in breast feeding

Management

- **Preconception:**

Offer varicella vaccination to seronegative women (Recommend postponing pregnancy for 4 weeks).

- **Prenatal management:**

Initial antenatal visit

If a pregnant woman has no prior chickenpox/shingles infection or is seronegative

Advise to avoid contact with shingles/chickenpox in pregnancy (vaccine is contraindicated in pregnancy)

If contact occurs

Take full history to determine susceptibility of infection and extent of exposure (Previous history of chickenpox predicts seropositivity in 98-100% of cases)

If the patient has no prior exposure to chickenpox/uncertain

Blood test to assess immunity status (VZIGs is delayed till sero-negativity is confirmed)

If the patient is not immune and she had significant exposure

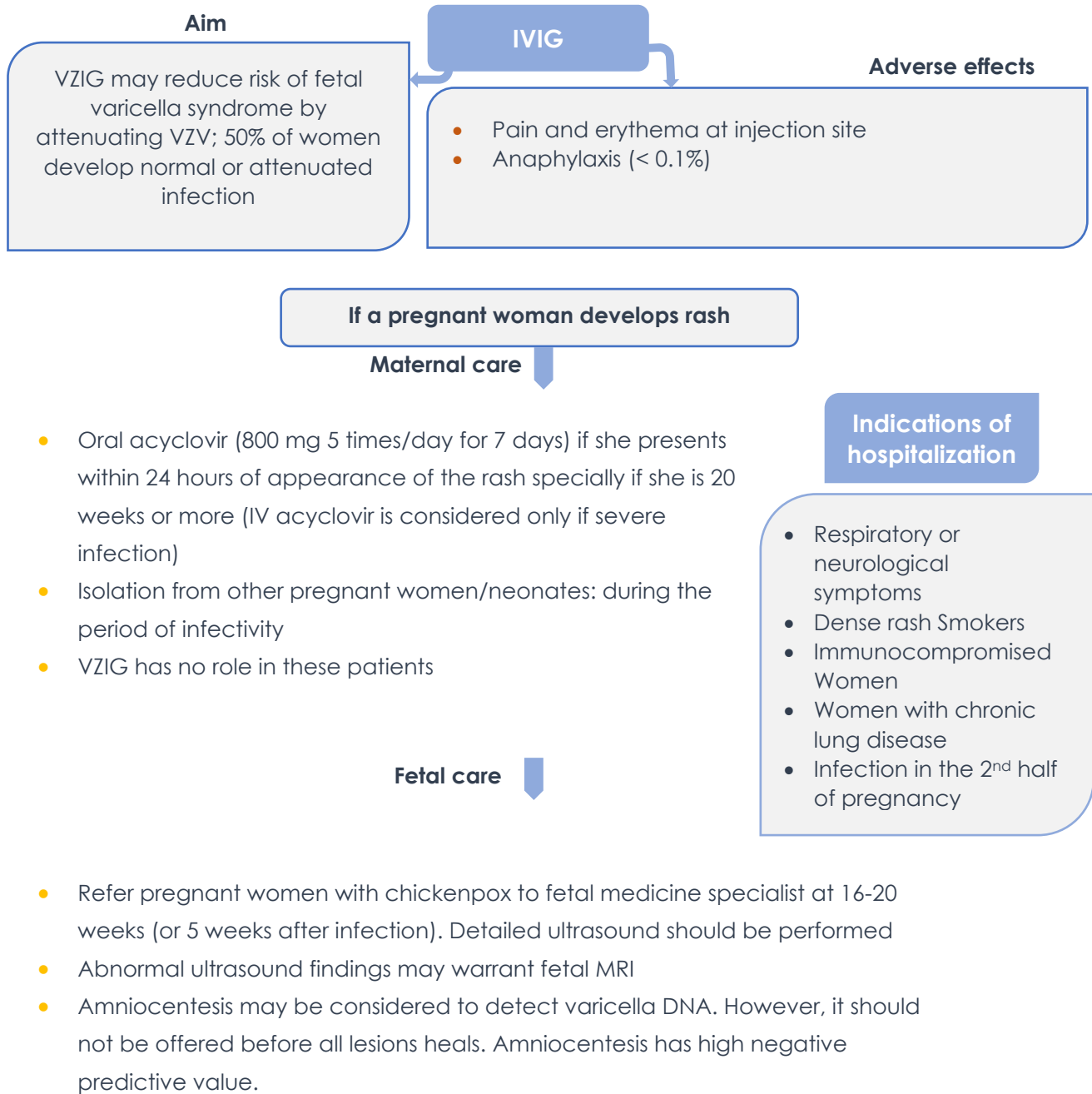
Check availability of VZ immunoglobulins (VZIG). If available, give VZIG as soon as possible for up to 10 days after exposure. A second dose may be given if another exposure is reported beyond 3 weeks of the first dose

If VZIG is given

The patient is considered potentially infectious for 8-21 days

If VZIG is not given

The patient is considered potentially infectious for 8-28 days



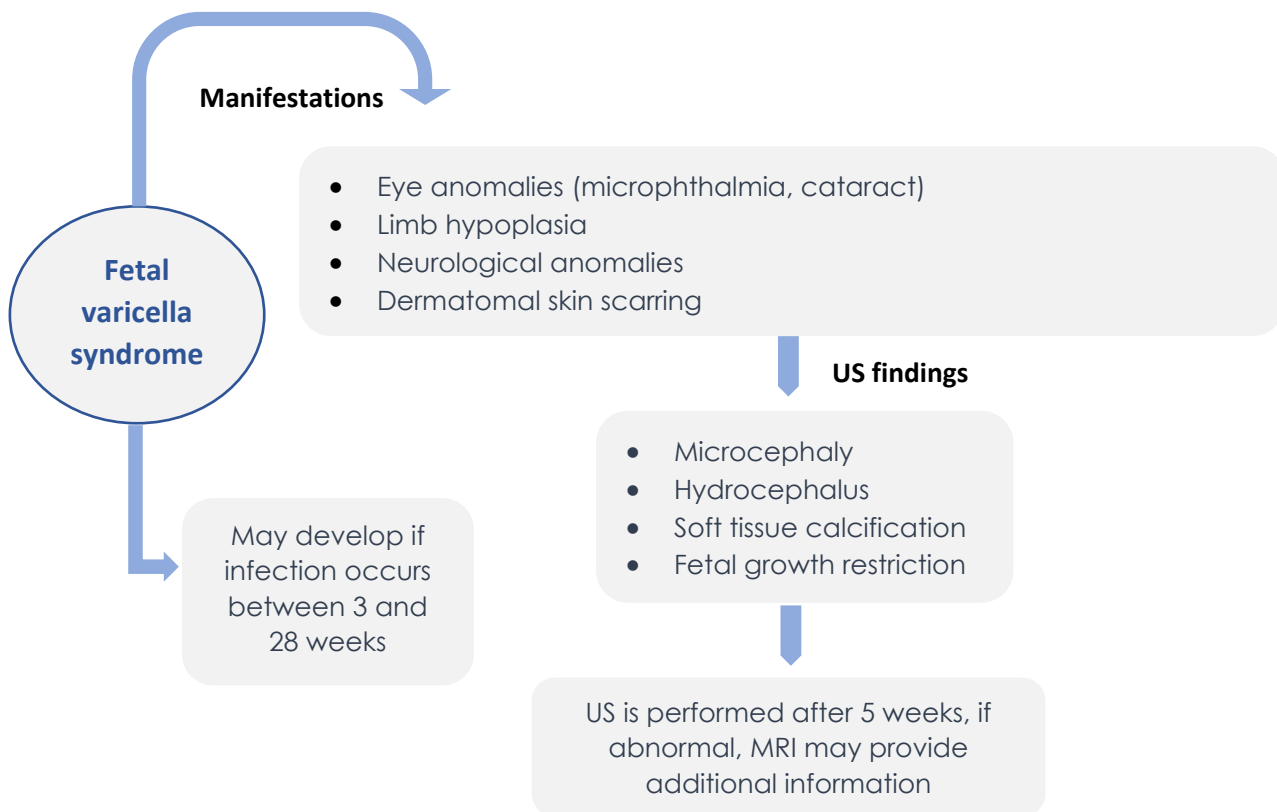
Maternal risks

- **Chickenpox during pregnancy is associated with maternal risk of:**
 - Pneumonia (5-14% in pregnant women with chickenpox; mortality in this subgroup is 0-14%)
 - Encephalitis

- Hepatitis
- Death (rare)

Fetal risks

- Maternal infection in the 1st trimester does not increase risk of miscarriage
- Varicella or seroconversion in the first 28 weeks of pregnancy is associated with small risk of fetal varicella syndrome (approximately 1%)



Neonatal risks

- Varicella infection of the newborn is commonly caused by maternal infection that occurs within 4 weeks of delivery
- Delivery within 1 week of appearance of rash or appearance of rash within 1 week of delivery carries the highest risk. If clinically

Infection occurs within 4 weeks of delivery:

- 50% of newborns will be infected
- 23% develops clinical varicella

appropriate, postponing elective delivery beyond 1 week after appearance of rash may facilitate passive immunity to the newborn

- These newborns should receive VZIG with or without acyclovir

Cytomegalovirus in Pregnancy

Epidemiology

- It is the most common virus that causes congenital infection
- It is the most common non-genetic cause of sensorineural hearing loss
- It affects 0.2-2.2% of live births
- 10-15% of infected neonates are symptomatic at birth
- 10-15% of infected neonates develop complications during childhood
- Approximately 2/3 of congenital CMV occurs with secondary infection, if CMV is highly prevalent in the population

Virology

Types of CMV infection	<ul style="list-style-type: none"> • Primary infection • Secondary infection: which can be either: <ul style="list-style-type: none"> ▪ Reactivation of primary infection (remains dormant primarily in salivary glands) or ▪ Infection with a different CMV strain
Route of transmission	<ul style="list-style-type: none"> • Antenatal (transplacental) • Intrapartum (through birth canal) • Postnatal (through breast milk)
Risk of congenital infection	<ul style="list-style-type: none"> • Risk of transmission with primary infection: 30-40 % (30% in the first trimester and 47% in third trimester) • Risk of transmission with secondary infection: 1-2%. • Infection in early in pregnancy is associated with lower risk of congenital infection but more severe manifestations, compared to late pregnancy

Clinical features

Maternal

- Majority of cases is asymptomatic
- Some has infectious mononucleosis like symptoms (fever, malaise, myalgia, cervical lymphadenopathy)
- Few may have hepatitis and pneumonia

Fetal/neonatal

- 85-90% are asymptomatic. Of these, 6-23% suffers from some hearing loss
- 10-15% is symptomatic. Symptoms include jaundice, petechial rash, hepatosplenomegaly, microcephaly, Small for Gestational Age.

Prenatal diagnosis

Indications of CMV testing

- Routine screening during pregnancy is not recommended.
- Suspicious sonographic findings
- Influenza-like symptoms during pregnancy
- Symptoms of glandular fever after exclusion of Epstein Bar virus
- Hepatitis after exclusion of hepatitis A, B and C

Investigatory tests

IgG avidity to diagnose maternal primary infection*

- High avidity index (> 60%) indicates past infection > 3 months
 - Low avidity index (< 30%) indicates recent infection within 3 months
- For secondary maternal infection, only invasive testing can be used



Confirmation of congenital infection

Amniocentesis and PCR should be done after 20 weeks of gestation (to ensure adequate fetal urine in amniotic fluid)



If congenital infection is confirmed

Fetal cerebral MRI at 28-32 weeks is performed with T1, T2, and diffusion sequences. It may be repeated 3-4 weeks later

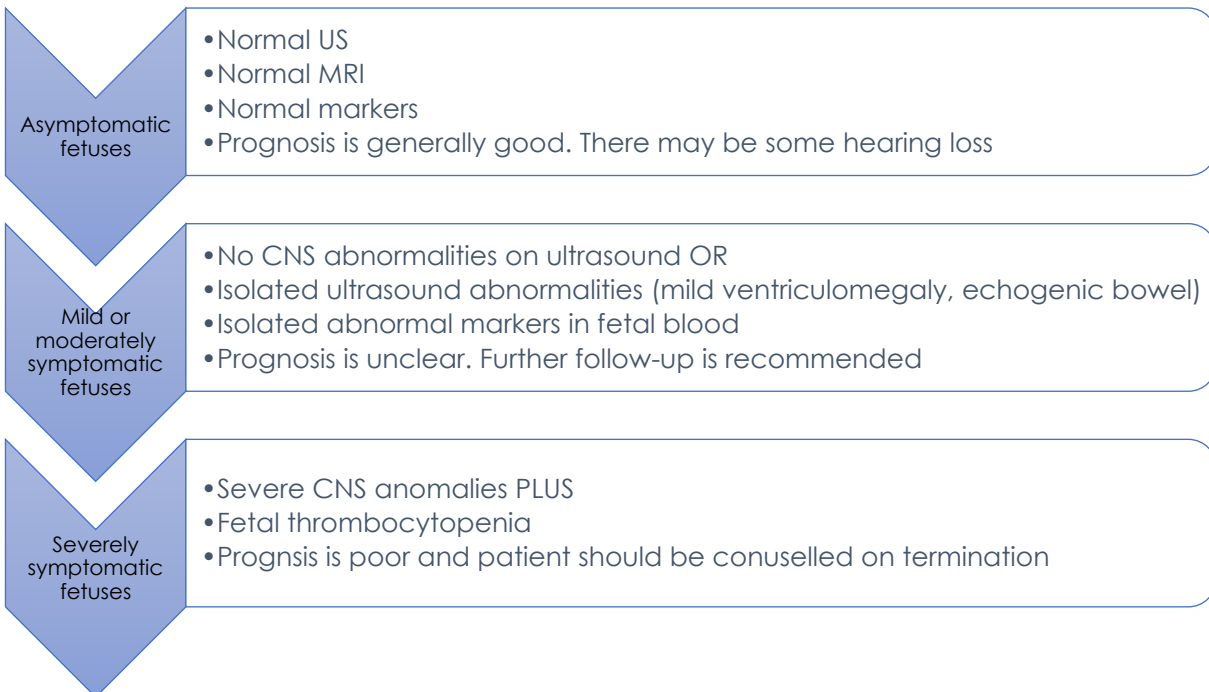
* CMV IgM is not used to diagnose primary infection as it persists for months

Prognosis of congenital CMV

Prenatal prognostic indicators

- ① Timing of infection during pregnancy
- ② Type of infection (primary or secondary)
- ③ Presence of CNS sonographic abnormalities
- ④ Fetal CMV IgM and CMV DNAemia (viral markers) by fetal blood sampling
- ⑤ Fetal beta-2-microglobulin and platelet count (non-viral markers) by fetal blood sampling

Classification of
outcomes of congenital
infection



Management

- **Prenatal treatment:**

- Antiviral drugs:
 - Anti-viral drugs against CMV are teratogenic except valaciclovir.
 - Valaciclovir administration in moderately infected fetuses may result in more fetuses born asymptomatic. Clinical trials may be needed to support routine treatment for this indication
- Hyperimmune globulin (HIG):
HIG is not routinely recommended

- **Neonatal treatment:**

- Neonatal diagnosis is made by CMV PCR from urine or oral swab within 3 weeks of birth
- Valganciclovir/ganciclovir treatment may stop disease progression and improve neurodevelopmental outcome if given within the first 4 weeks of birth

Prevention

- No vaccine available
- Hygiene education is the most effective preventive approach for pregnant women. Incidence of seroconversion is 1% in women who receive such education compared to 8% who do not.

Rubella in Pregnancy

Background

- **Type of virus:** Single-stranded RNA togavirus
- **Mode of transmission:** primarily via the respiratory route
- **Incubation period:** It ranges from 12 to 23 days (average 14 days). Viral replication occurs in the nasopharynx and lymph nodes
- **Infective period:** Women are infectious from 7 days before until 7 days after the onset of the rash

Vertical transmission

- The risk of congenital infection is 90% before 12 weeks, 20% between 12–16 weeks and, thereafter, deafness is a risk up until 20 weeks
- Risk of transmission with congenital infection is approximately 5%.

Diagnosis

- **Clinical picture of maternal rubella infection:**
 - Maternal rubella infection is usually asymptomatic or associated with mild illness of malaise, headache, flu-like symptoms and lymphadenopathy, followed by a diffuse, fine maculopapular rash
 - This clinical picture is similar to maternal parvovirus B19 infection and any pregnant

woman with rash should be investigated for both types of infection regardless of immunity status (vaccination or antibodies)

- **Investigations of maternal rubella infection:**

- Primary rubella infection is confirmed by presence of both rubella IgM and rubella IgG seroconversion or presence of low-avidity antibodies
- Rubella reinfection (or infection in a previously vaccinated woman) is confirmed by the presence of significant increase in baseline rubella IgG titre

- **Diagnosis of congenital rubella syndrome:**

- **Sonographic features:**

- Foetal growth restriction
 - Cardiac defects, primarily pulmonary valvular stenosis and ventricular septal defect
 - peritoneal hyperechogenicity and hyperechogenic foetal bowel
- Neonates may develop cataract and sensorineural hearing loss

- **Amniocentesis:**

Diagnosis can be made by detecting reverse transcriptase PCR (RT-PCR) that is used for the detection of viral nucleic acid in amniotic fluid

Prevention

A live attenuated virus vaccine is used to prevent rubella infection. This vaccine is contraindicated in pregnancy and therefore, it should be considered postpartum in women who are non-immune

Management

There is no specific treatment for rubella infection

- **If infection is diagnosed before 12 weeks:** consider termination of pregnancy.
- **If diagnosis is made between 12 and 16-20 weeks:** ultrasound surveillance to identify features of congenital rubella syndrome are considered if invasive testing of the foetus is positive (55% risk of transmission and a 20% risk of congenital rubella syndrome). Specialist foetal echocardiography should be arranged in addition to foetal growth scans
- **If diagnosis is made after 16-20 weeks:** the risks to the foetus are negligible. Therefore, no further action is required

Toxoplasma in Pregnancy

Mode of transmission

Transmission of infection occurs by ingesting toxoplasma cysts, which may be present in undercooked meat or food contaminated with soil or cat feces

Risk of transmission

As with most congenital infections, risk of transmission is lower with early infection. However, severity of infection and risk of congenital abnormalities is higher compared to late pregnancy infection:

Gestational age	Risk of infection
<4 weeks gestation	<1%
13 weeks gestation	10%
36 weeks gestation	> 60%

Diagnosis

- **Diagnosis of maternal toxoplasmosis:**
 - Clinically, most patients are asymptomatic. Otherwise, they may be present with:
 - Cervical lymphadenopathy
 - low-grade fever
 - muscle ache
 - fatigue
 - headache
 - Maternal infection may be diagnosed by serum IgM and IgG:
 - Both IgM and IgG become positive within 2 weeks of primary infection
 - IgG remains positive for life
 - IgM remains positive for 3 to 18 months
 - IgG avidity may be used to differentiate recent (low avidity) from remote infection (high avidity)

- **Diagnosis of foetal toxoplasmosis (congenital infection):**
 - Amniocentesis for detection of toxoplasma DNA
 - Most common sonographic findings are hydrocephalus, intracranial calcification, and chorioretinitis (the triad is present in approximately 80% of cases)

Management

If maternal infection is confirmed, spiramycin should be given. Maternal treatment may reduce risk of foetal infection by 60-70%

Parvovirus B19 in Pregnancy

Background

- **Type of virus:** Single stranded DNA virus
- **Mode of transmission:** Droplet infection, hand to mouth
- **Incubation period:** 5–7 days following exposure. Women are infectious for 3–10 days post-exposure or until the rash appears.
- **Infectivity period:** 7-10 days before the rash develops to 1 day after the rash appears

Vertical transmission

- If gestational age is less than 15 weeks, risk of vertical transmission is 15%
- If the gestational age is 15 to 20 weeks, risk of vertical transmission is 25%
- If the foetus is term, risk of vertical transmission is 70%

Clinical presentation

- Infected children present with diffuse erythematous facial rash 'slapped cheek' after 5 days of prodromal symptoms
- In adults, infected women are asymptomatic in up to 50% of cases. They may present with no non-specific symptoms e.g. transient fever, malaise and arthralgia.

Investigations

- If a pregnant woman was exposed to Parvovirus or is suspected to have Parvovirus, they should undergo serological testing:

Results	Interpretation
• IgG positive - IgM negative	Immune
• IgG negative - IgM negative	Susceptible to infection
• Positive for IgM (regardless of IgG)	Recent infection

- If suspicion is based on clinical symptoms, rubella should be tested in the same time of the patient is not immune or has unknown immunity to rubella as they can cause similar symptoms

Management

- Urgent referral to a foetal medicine specialist is indicated for serial foetal ultrasound scans and Doppler assessment to detect foetal anaemia, heart failure and hydrops
- The patient should be followed up with serial ultrasound starting 4 weeks after infection and 1- to 2- weekly for up to 12 weeks. This should be combined with middle cerebral artery peak systolic velocity (MCA-PSV) to diagnose anaemia
- If MCA-PSV > 1.5 multiples of the median (MoMs) or if there is ascites or hydrops, Foetal blood sampling and intrauterine blood transfusion may be considered

Syphilis in Pregnancy

Background

- Syphilis is the most common congenital infection worldwide.
- Risk factors for syphilis in pregnancy are:
 - Low socioeconomic status
 - Multiparity
 - History of sexually transmitted infections (STIs)
 - Use of illicit drugs before 18 years or illicit drug use by the current partner
 - Poor antenatal care
 - Three or more sexual partners in the previous 12 months
- Transmission of infection:
 - Most common route is via sexual contact
 - Infection through anal, rectal or oral routes
 - Transplacental transmission during any stage of pregnancy.

Stages of syphilis

Primary syphilis	3 weeks following exposure to infection (9-90 days)
Secondary syphilis	4-10 weeks after primary chancre
Latent syphilis	<ul style="list-style-type: none"> • Early latent syphilis describes infections that occurred within the past year • Late latent syphilis describes infections that occurred > 1 year ago.
Tertiary (late) syphilis	It can present 20 years later and likely in the obstetric population

Syphilis and pregnancy

- Risk of trans-placental transmission starts as early as 14 weeks. This risk increases as the pregnancy progresses towards term
- The stage of syphilis in the mother also influences the risk of transmission to the fetus: it can be as high as 100% in primary syphilis, whereas the risk is much lower in early latent (40%) and late latent syphilis (10%).

Foetal risks

Foetal infection can result in:

- Foetal growth restriction
- Hepatomegaly and intrahepatic calcifications
- Thrombocytopenia
- Anaemia and ascites
- Distorted fetal long bones or foetal hydrops (in more severe cases)
- Preterm birth
- Stillbirth and neonatal death (risk of foetal loss is 30-40%)

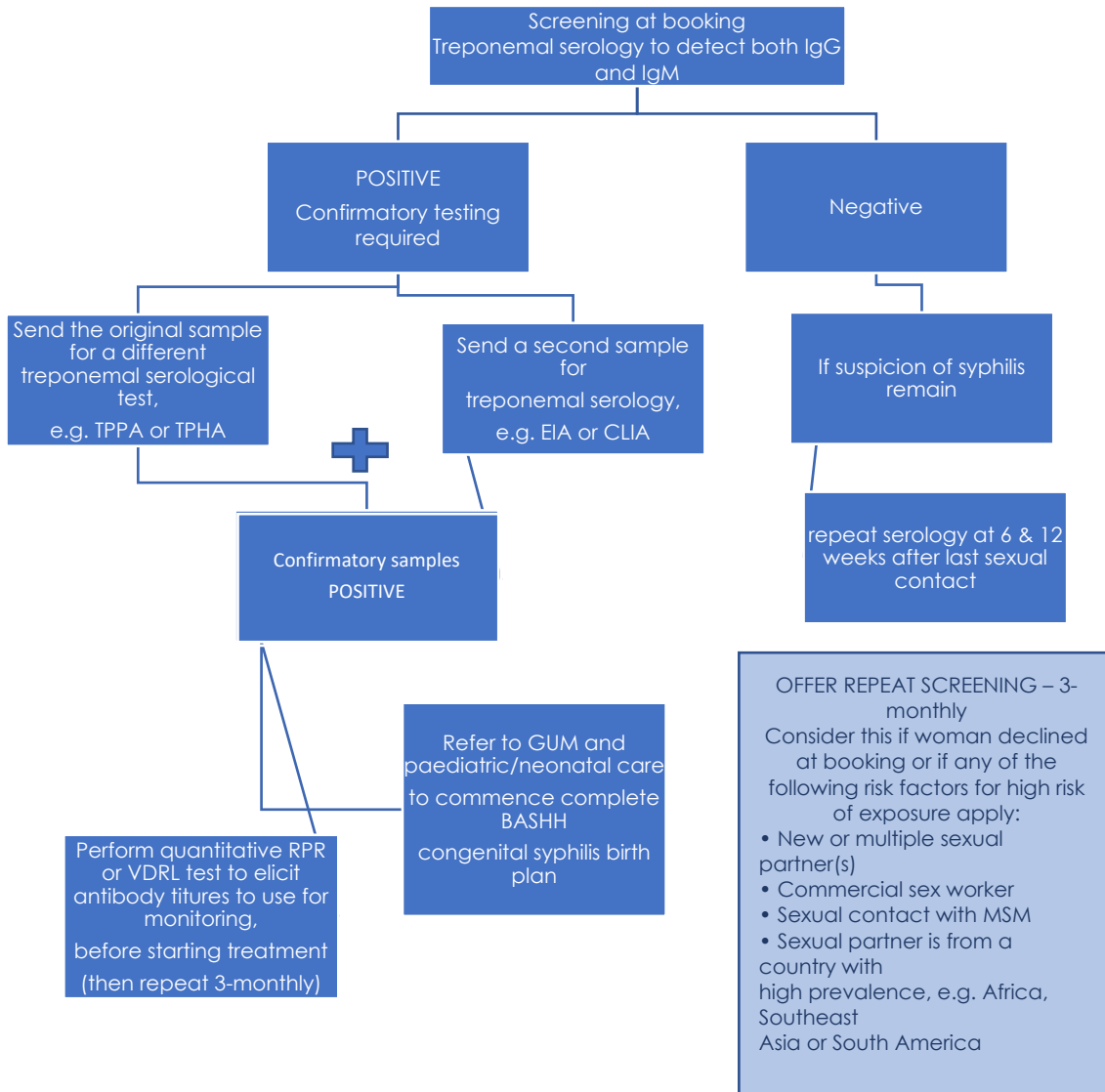
Signs on ultrasound are often general and nonspecific

Diagnosis

- Direct testing methods include dark-field microscopy and polymerase chain reaction (PCR). They are not widely available, but they detect infection quick and early (before a serological response occurs)
- Indirect testing (Serological tests) detects antibodies (such as enzyme immunoassays and T. pallidum particle agglutination assays, which are the most used)
- NICE Recommendations for diagnosis include:
 - Sending a 10-ml clotted blood sample to obtain a full syphilis screen (serological tests)
 - Sending swab from any active lesions with a 'flock/virology' swab to be tested with syphilis PCR and Herpes Simplex testing
 - Screen for other STIs (e.g., chlamydia, hepatitis B/C and HIV) after obtaining a consent

- Women with suspected disease who decline testing, or with confirmed disease who decline treatment, who may transmit infection to other contacts should be counselled that this could result in legal action against them

Suggested screening algorithm for syphilis



Treatment

- Syphilis in pregnancy should be managed by a multidisciplinary team, which involves genitourinary medicine physicians, neonatologists and microbiologists.
- Management should include antimicrobial therapy, counselling, partner notification and safe sex advice.
- Women should be treated as soon as diagnosis is established, preferably in early gestation
- Treatment of maternal syphilis at least 30 days before delivery is the most important factor influencing the risk of congenital infection and perinatal mortality.
- There is increasing macrolide resistance in *T. pallidum* and they are no longer considered a treatment option

Antibiotics used to treat syphilis in each stage of pregnancy				
Trimester	Early disease (Primary/secondary or latent <2 years)	Late disease (Latent/ unknown duration)	Possible sensitivity to penicillin and who can tolerate cephalosporins	unable to tolerate an intramuscular regime
First/second	Benzathine penicillin 2.4 MU IM; single dose	Benzathine penicillin 2.4 MU IM; weekly for 3 weeks/doses	ceftriaxone 500 mg IM, daily for 10 days	amoxicillin 500 mg and probenecid 500 mg, both orally, four times per day for 14 days.
Third	Benzathine penicillin 2.4 mU IM; weekly for 2 weeks/doses	This regimen is used in all stages of pregnancy		

Jarisch–Herxheimer reaction

- It can complicate up to 45% of syphilis treatments in pregnancy.
- Symptoms typically occur within the first 24 hours of treatment and include fever, rigours and a skin rash (or rarely uterine contractions)
- Generally, it is self-limiting; therefore, there is no recommended treatment regimen other than supportive treatment

Congenital syphilis

Epidemiology	Congenital syphilis remains rare in the UK
Classification	<ul style="list-style-type: none"> • Early disease manifests in the first 2 years of life • Late congenital syphilis is apparent after the age of 2 years
Clinical presentation	<ul style="list-style-type: none"> • Around two-thirds are asymptomatic at birth. Two thirds of those demonstrate signs and symptoms from 3–8 weeks of age. Most present before 12 weeks of age • One-third to one-quarter of children presenting over the age of 2 years having asymptomatic neurosyphilis • Clinical manifestations of congenital syphilis include 'Hutchinson's Triad': eighth cranial nerve deafness, interstitial keratitis and 'Hutchinson's Teeth' (notched incisors). • Signs seen in early disease include: <ul style="list-style-type: none"> ▪ Skin rashes ▪ Stigmata of meningitis and jaundice ▪ Hepatosplenomegaly ▪ Anterior bowing of the mid tibia creates the classic 'sabre shins ▪ 'Bloody snuffles', caused by syphilitic rhinitis, create a characteristic pink coloured nasal discharge • Late disease typically presents with bony deformities secondary to chronic inflammation.

Investigations	<ul style="list-style-type: none">• Blood tests: severe anaemia, monocytosis, thrombocytopenia, raised alkaline phosphatase level• X-rays: periostitis, which leads to the development of bone deformity.
Prognosis	<ul style="list-style-type: none">• Congenital syphilis is a multisystem infection that can result in neonatal death and long-term disability• Babies born with congenital syphilis are 10% more likely to die in the first year of life.

Zika Virus in Pregnancy

Background

- Zika virus belongs to the virus family Flaviviridae; genus: Flavivirus. It is a single stranded RNA virus
- Transmission is primarily by Aedes mosquitos. However, it can be sexually transmitted (risk is low)
- Incubation period is 3-12 days

Clinical picture

- Typical symptoms in adults are fever, maculopapular rash, arthralgia, or conjunctivitis. Many women are asymptomatic
- Rash usually resolves within 2 days but may persist up to 1 week

Complications

- Guillain Barre syndrome
- Congenital microcephaly (20-fold increase during the pandemic "1:1000 pregnancies"). It may be associated with other congenital abnormalities

Management

- **Couples planning for conception:**
 - If a male partner has travelled to Zika area, couples should avoid conception for 6 months after return from Zika area

- If a female partner has travelled to Zika area, couples should avoid conception for 8 weeks after return from Zika area if asymptomatic or 8 weeks after recovery if symptomatic
- **Pregnant women:**
Testing is advised for women who report symptoms suggestive of acute Zika infection within 2 weeks of returning from an area with high or moderate risk of Zika infection transmission OR within 2 weeks of sexual contact with a male sexual partner who has recently visited an area with high or moderate risk of Zika infection

Congenital infections during pregnancy

Abstract

Maternal exposure to viral and parasitic infection carries serious risk to the foetus. Although not all viral infections are transmitted to the foetus, maternal symptoms of viral infection are indistinguishable, and they should be assessed for possible congenital infection. Clinical suspicion can guide confirmatory investigations that promote early diagnosis of complications, patient counselling, and interventions, if possible. In this chapter, we will discuss congenital infections during pregnancy and how diagnosis and follow-up should be performed.

Keywords

CMV, Zika, chickenpox, syphilis, toxoplasma, parvovirus

Further readings

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2. Royal college of obstetricians and gynaecologists. Congenital Cytomegalovirus Infection: Update on Treatment. Scientific Impact Paper No. 56: 2017.

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