Non-HIV sexually transmitted infections in pregnancy

Annette Thwaites
Kate Flanagan
Shreelata Datta

Abstract

Sexually transmitted infections (STIs) in pregnancy can have serious consequences for the woman, the fetus and neonate yet may remain asymptomatic throughout. Screening for many STIs is not explicit in UK antenatal guidelines and may be overlooked. Therefore it is essential to consider a woman's risk of STIs regularly throughout pregnancy and know how and when to undertake an appropriate sexual history and relevant testing. Early diagnosis and treatment, partner notification and multi-disciplinary management together with genitourinary physicians and paediatricians are key to securing good outcomes for mother and child. This article reviews the presentation, diagnosis and management of (non-HIV) STIs in pregnancy, highlighting indications for testing and important differences compared with management of non-pregnant women.

Keywords chlamydia; genital herpes; genital warts; gonorrhoea; hepatitis; mycoplasma; pregnancy; sexually transmitted infections; syphilis; trichomonas

Introduction

The World Health Organisation (WHO) estimates more than a million sexually transmitted infections (STIs) are acquired every day with over 357 million new infections of four curable STIs (chlamydia, gonorrhoea, syphilis and trichomonas) per year. STIs have a heterogeneous distribution nationally and globally and can have serious reproductive health consequences. The burden of STIs in women in the UK is largely carried by young women (aged 16–24), black and minority ethnic groups and those living in urban areas and areas of higher deprivation.

The total numbers of STIs in England have remained stable overall over the last ten years, despite interim rises seen 2012–2014, and in 2017 there were over 200,000 new STIs diagnosed in women. There are, however, significant underlying trends. *Mycoplasma genitalium* is now being increasingly recognised as a pathogen. Emerging antimicrobial resistance is a threat to successful management of common STIs, most notably gonorrhoea, which is of increasing incidence with 11,475 cases diagnosed in woman in England in 2017. Conversely, diagnoses of genital warts are falling after the introduction of the quadrivalent HPV vaccine to the immunisation programme in 2012.

Many STIs can be asymptomatic and yet in pregnancy can have catastrophic consequences for the woman and fetus. Ascending infection in pregnancy can lead to chorioamnionitis and subsequent premature rupture of membranes, preterm delivery, low birth weight and maternal sepsis. Fetal infection can arise via transplacental, intrapartum or postpartum transmission.

Initial screening for HIV, syphilis and hepatitis B are part of routine antenatal blood tests, taken ideally before 10 weeks' gestation. However diagnosis of more common STIs such as chlamydia or herpes rely on women self-screening, presenting with symptoms or on history alone. Therefore clinicians must retain a high index of suspicion for STIs throughout antenatal and postnatal care. Risk factors for STIs include age under 25, high number of sexual partners and any new sexual partners in pregnancy, diagnosis of any other STI, country of origin with high prevalence, intravenous drug use, and commercial sex. A careful sexual history should be taken at the start of pregnancy to establish a woman's risk and identify any high risk partners, such as those with known or suspected STIs or men who have sex with men (MSM). This should be revisited regularly and used to initiate further screening tests as appropriate (Table 1).

The key to successfully managing STIs in pregnancy is early diagnosis and effective treatment together with minimising the risk of re-infection and vertical transmission. Partner notification and treatment, abstinence during and post treatment and risk reduction are important and common to the management of all STIs. Management in pregnancy may differ depending on gestation, stage of infection and contraindication to drugs and test of cure (TOC) is often advised. Mode of delivery is not commonly influenced by the presence of an STI with the exception of herpes. Neonatal management may be determined on mode of delivery and the condition of the baby. Multidisciplinary working with genitourinary physicians and paediatricians is therefore vital to optimising outcomes for the mother and child.

Chlamydia

Genital chlamydia infection is caused by the obligate intracellular pathogen *Chlamydia trachomatis* and is the most common bacterial STI in the UK, with over 200,000 new chlamydia diagnoses in England in 2017 with over 60% of these being in 15–24 year olds. The cervix is the most commonly infected site in women but the urethra, throat and rectum may also be infected. Concurrent infection of urogenital and anorectal sites are estimated up to 77% but there is scarce data as to rates of pharyngeal infection in women. Most women with chlamydial infection are asymptomatic although may present with post-coital bleeding, lower abdominal pain, purulent vaginal discharge, cervicitis, proctitis or dysuria. Untreated, chlamydia can persist for years leading to a wide range of complications including pelvic inflammatory disease (PID), ectopic pregnancy, tubal factor infertility and chronic pain.

Annette Thwaites *MEng MA (Cantab) MSc MB BChir MFSRH is an Academic Clinical Fellow in Community Sexual and Reproductive Health (CSRH) at the Institute for Women's Health, University College London and ST4 in CSRH at King's College Hospital, London, UK. Conflicts of interest: none declared.*

Kate Flanagan *BMedSci BMBS MRCP DFSRH is an ST4 in Genitourinary Medicine at King's College Hospital, London, UK. Conflicts of interest: none declared.*

Shreelata Datta *MBBS BSc (Hons) LLM MRCOG is a Consultant Obstetrician and Gynaecologist at King's College Hospital, London, UK. Conflicts of interest: none declared.*

STI Testing: indications and timings

STI	Test and window period	When to Test
Chlamydia	• Nucleic Acid Amplification Test (NAAT) • Vulvovaginal or endocervical swabs (clinician or self-taken) • Window period typically 2 weeks	• At booking in under 25s (signpost to community sexual health services/online self-testing services as part of the national chlamydia screening programme) • If any new sexual partner • Regularly if any high risk partner • Diagnosis of another STI • If symptomatic (focal or signs of sepsis) • After 6 weeks post treatment with azithromycin • After 5 weeks post treatment with alternative regimens • In 3rd trimester if tested positive earlier in pregnancy • Neonatal conjunctivitis or pneumonia
Gonorrhoea	• NAAT • Vulvovaginal or endocervical swabs (clinician or self-taken) • Confirmatory culture and sensitivities • Window period typically 2 weeks	• At booking in under 25s (signpost to community sexual health services/online self-testing services) • If any new sexual partner • Regularly if any high risk partner • Diagnosis of another STI • If symptomatic (focal or signs of sepsis) • After 72 h post treatment if symptoms persist • After 2 weeks post treatment if asymptomatic • In 3rd trimester if tested positive earlier in pregnancy • Neonatal conjunctivitis or neonatal sepsis
Trichomoniasis	• Microscopy of vaginal secretions from posterior fornix mixed with saline • Culture is available and used in some centres • May find on high vaginal self-taken swab • NAAT more sensitive and becoming increasingly available	• Regularly if any high risk partner • Unexplained or new vaginal discharge • Vulvitis or vaginitis on examination

Syphilis	• Ulcerative Lesion:
	  ○ Polymerase Chain reaction (PCR)
	  ○ Dark Ground Microscopy (now less common and limited to experienced clinicians)
	• IgM and IgG serology. Repeat serology 6 and 12 weeks after high risk exposure
	• Cardiolipin RPR/VDRL test to monitor response to treatment
		• <10 weeks' gestation
		• Any genital ulceration
		• If any new sexual partner
		• Diagnosis of another STI
		• Repeat testing at 6 weeks and 3 months if high risk exposure or ulceration and initial testing negative

Genital Warts	• Clinical diagnosis	
Genital Herpes	• PCR of vesicle fluid on viral swab • Herpes Simplex Virus (HSV) type specific antibody test	• Any genital ulceration • Suspected/known HSV positive partner • Genital ulceration in 3rd trimester
Mycoplasma	• NAAT • Vulvovaginal or endocervical swabs (clinician or self-taken)	• Signs and symptoms of PID (muco-purulent cervicitis, postcoital bleeding, pelvic pain) • Sexual contacts of men with proven *M. genitalium* infection

Hepatitis A,B,C	• Serology
	  ○ HAV IgM/IgG
	  ○ HbcAb/HbsAg
	  ○ HCVAb/HCV RNA/combined Ag/Ab test
		• Always consider in high risk groups (sex workers, sexual assault, anal sex, oro-anal sex and sexual acts likely to break mucosal barrier)
		• Prodromal or icteric symptoms or signs of chronic liver disease

HIV	• HIV antibody AND p24 antigen blood test • Point of care test to be considered if late booking of pregnancy • Window period typically 4 weeks	• <10 weeks' gestation • Any new sexual partner • Regularly if high risk • Diagnosis of another STI and retest 4 weeks after last episode of sex without condom use

Table 1

In pregnancy, chlamydia infection can spread from the cervix into the uterine cavity causing chorioamnionitis and subsequent premature rupture of membranes, preterm delivery, low birth weight and maternal sepsis. It is unknown if the risks differ between primary infection or persistent or recurrent infection but there is some evidence to suggest that risks of complications are increased if infection occurs at earlier gestations. Perinatal transmission can also occur with infected babies typically presenting with conjunctivitis, pneumonia or otitis media. Approximately 50% of neonates born to women with untreated chlamydia will develop ophthalmia neonatorum and 15% pneumonitis.

Current NICE guidance on antenatal care recommends informing women under 25 at their booking appointment, and ideally before 10 weeks' gestation, about the high prevalence of chlamydia in their age group, providing details of local screening. However the national chlamydia screening programme, in contrast to other national screening programmes, relies on patients self-presenting. Therefore, if a patient is high risk and unlikely to access testing successfully in the community, testing at booking and regularly in each trimester of pregnancy is advisable.

The recommended treatment of chlamydia has recently been revised due to emerging azithromycin resistance in mycoplasma genitalium. First-line recommendation for treatment of chlamydia in pregnancy is now with a 3 day course of azithromycin where 1 g is taken on day 1 followed by 500 mg on days 2 and 3. Azithromycin is unlicensed for use in pregnancy in the UK and the BNF states that manufacturers advise use only if adequate alternatives are unavailable. However, single dose 1 g azithromycin has been widely used in pregnancy and adverse pregnancy outcomes are thought to be unlikely with the updated total dose of 2 g. First-line treatment of choice in the nonpregnant woman is with a 7-day course of doxycycline, which is contraindicated in pregnancy.

Azithromycin is still considered preferable to the alternative regimens of erythromycin and amoxicillin on the basis of better compliance and side effect profile. Ofloxacin, the only other second line treatment recommended is also contraindicated in pregnancy. Given the lack of data relating to azithromycin use in pregnancy it is recommended that treatment options are discussed with women prior to treatment. Management must also include partner notification and treatment and advice to avoid all sex (including oral sex and sex with a condom) until a week after completion of treatment and avoidance of all sex with current partners until a week after they have also finished treatment.

Due to higher positive chlamydia tests after treatment in pregnancy resulting from either reduced efficacy of treatment in pregnancy, non-compliance or re-infection, TOC is recommended. Current UK guidelines recommend this should be performed no earlier than 3 weeks after completing treatment as residual, non-viable, chlamydial DNA may be detected for 3–5 weeks after treatment. TOC is not routinely recommended in non-pregnant women.

Gonorrhoea

The causative organism is the gram-negative intracellular diplococcus bacterium *Neisseria gonorrhoeae*. Gonorrhoea is the second commonest bacterial STI in the UK and diagnoses in England are increasing with a total of 46,676 new cases in 2017. As for chlamydia, the primary site of infection is most commonly the endocervix but can also be the mucous membranes of the urethra, rectum, pharynx and conjunctiva. Genital gonorrhoea infection can produce the same symptoms as chlamydia and, whilst more often symptomatic than chlamydia, gonorrhoea is still asymptomatic in up to 50% of cases. Without treatment gonorrhoea can also cause PID with associated longer-term complications and haematogenous dissemination, although uncommon, may also occur causing skin lesions, arthralgia, arthritis and tenosynovitis.

As with chlamydia, there are important consequences in pregnancy, which can be severe. Infection can ascend similarly causing chorioamnionitis, premature rupture of membranes, preterm delivery, low birth weight and postpartum infection. There is some recent evidence that infection diagnosed in the first trimester of pregnancy increases the likelihood of preterm birth. *N. gonorrhoeae* is also transmitted to the neonate in 30–50% of cases. This occurs during delivery or, less commonly and in the context of prolonged rupture of membranes, before birth. The most common presentation is gonococcal ophthalmia neonatorum with profuse purulent conjunctival discharge of the newborn. This invariably causes blindness if untreated, so the neonate should receive prophylactic erythromycin ophthalmic ointment at birth regardless of mode of delivery.

Current UK guidelines have recently been revised in response to concerns about antimicrobial resistance and now recommend an increased 1 g dose of ceftriaxone intramuscularly. Co-administration of 1 g azithromycin is no longer recommended, due to limited evidence of benefit, high levels of resistance in gonorrhoea and concerns about driving resistance to other organisms. (The increased dose of ceftriaxone is expected to be effective even in strains of gonorrhoea with reduced ceftriaxone susceptibility). As ciprofloxacin is contraindicated in pregnancy, ceftriaxone is always the first line treatment of choice in pregnancy with an alternative treatment in pregnancy of spectinomycin 2 g IM.

Partner notification, treatment and advice on abstinence is as for chlamydial infection. However TOC, including sensitivities, is recommended in all cases, within and outside of pregnancy, reflecting emergence of resistance to treatment. This should be carried out at 72 h after completion of treatment if the woman remains symptomatic and at 2 weeks if asymptomatic.

Trichomoniasis

Trichomonas vaginalis (TV), a flagellated protozoon, is the commonest non-viral STI worldwide, with WHO estimates in 2012 of 142 million new diagnoses a year globally. However, this infection is less common in the UK, with only around 6000 diagnoses in 2014, mainly among women with highest rates seen in London among black Caribbean ethnic groups and in those with another concurrent STI. Unlike most other STIs, prevalence is not highest in the younger age groups.

In women, the organism can be found in the vagina, urethra and paraurethral glands with vaginal infection almost always spreading to the urethra but sole urethral infection presenting less than 5% of cases. While in men the infection is usually asymptomatic and therefore diagnosed with less frequency, infection in women is asymptomatic in less than half of cases. Common symptoms include offensive vaginal discharge (classically purulent green or frothy yellow), vulvo-vaginitis (associated with itching or dysuria) but infection can also cause pelvic pain or

vulval ulceration. A minority of women will also have a "strawberry" cervix on speculum examination describing the appearance of punctate haemorrhages. Although there is increasing evidence that TV infection is associated with preterm delivery, low birth weight and maternal postpartum sepsis, further research is needed before a causal link is established. There are also studies that suggest infection with TV may increase HIV acquisition and transmission. There is no existing evidence to suggest additional neonatal effects or puerperal infection.

Further research is also needed to inform the management of TV in pregnancy as studies to date have shown little impact of treatment regimens on pregnancy outcomes. A spontaneous cure rate is approximately 20–25%. However, current treatment with metronidazole is currently advised at all stages of pregnancy with a cure rate of over 90%. Historical concerns regarding teratogenicity, as metronidazole readily crosses the placenta, have not been supported by more recent meta-analyses. The *British National Formulary* (BNF) states that manufacturers advise against high dose regimens so 400–500 mg twice daily for 5–7 days is usual and may be associated with fewer side effects compared to a single dose. Women who drink alcohol in pregnancy should be advised not to do so for the duration and at least 48 h after treatment because of the possibility of a disulfiram-like reaction.

Tinidazole, used as an alternative treatment outside of pregnancy is contraindicated in the first trimester and its safety in later pregnancy has also not been well-evaluated. If an alternative to metronidazole is needed, close liaison with genitourinary medicine (GUM) and allergy teams is necessary as treatment options are very limited.

Any sexual partners within the four weeks prior to presentation should be treated simultaneously and patients should be advised to avoid sex for a week after they and their partners have completed treatment. TOC is recommended if the patient remains symptomatic following treatment or if symptoms recur but may be carried out in pregnancy.

Syphilis

Syphilis is caused by infection with the spirochete bacterium *Treponema pallidum*. Since the WHO strategy for global elimination of syphilis in 2007 there has been a one third reduction globally in maternal and infant syphilis. However, last year England saw a 29% increase from 333 new diagnoses (2016) to 430 (2017) and syphilis in pregnancy is associated with a significant adverse pregnancy outcomes. Syphilis is transmitted by sexual contact with an infectious lesion or vertical transmission. Acquired syphilis is categorised into early (primary, secondary and early latent) and late (late latent or tertiary) phases. Late syphilis is not usually infectious to sexual partners. It is not possible to differentiate syphilis from other treponemal infections based on serology (e.g. yaws, pinta and bejel, which can be endemic in some groups).

Signs of infection can vary enormously between individuals and stage of infection and it has been known as "the great imitator" due to its frequent atypical presentations resembling other conditions. Primary syphilis classically presents with a single, painless anogenital ulcer or "chancre" with inguinal lymphadenopathy. Classically lesions present within 9–90 days of exposure. However, any ulcer in this area should be considered to be syphilis until proven otherwise. Secondary syphilis is multisystem involvement within 2 years of infection and often presents with rash (typically non-itchy, macular-papular affecting the palms and soles), condylomata lata and generalized lymphadenopathy but also less commonly with patchy alopecia, anterior uveitis, meningitis, cranial nerve palsies, hepatitis, splenomegaly, periostitis and glomerulonephritis. The latent phase is asymptomatic and split between "early", i.e. less than 2 years from infection and "late" thereafter. Symptomatic late syphilis includes neurosyphilis, cardiovascular and gummatous forms and it has been estimated that, without antibiotic treatment, approximately one third of cases progress to this stage within 15 years of infection.

In pregnancy, syphilis can be transmitted transplacentally at any stage leading to polyhydramnios, miscarriage, preterm labour, stillbirth, hydrops and congenital syphilis. Vertical transmission causes high infant mortality and morbidity worldwide but UK rates are low due to antenatal screening, recommended at booking within the first 10 weeks. Maternal early syphilis and high RPR/VDRL titres are risk factors for congenital syphilis but transmission can also occur in late latent maternal infection. HIV co-infection may also increase transmission risk. Referral to fetal medicine is indicated where maternal syphilis has not been treated by 26 weeks' gestation, where further evaluation by ultrasound and subsequent antepartum care can be planned. Many infected neonates are asymptomatic at birth but may present with rash, hepatosplenomegaly, syphilitic snuffles and periostitis. Signs of late syphilis in infants include keratitis, Hutchinson's incisors, moon's mulberry molars, saddlenose deformity, frontal bossing and deafness.

Treatment of early syphilis is usually with single dose benzathine penicillin 2.4 MU IM. However concentrations may be reduced by the physiological changes of pregnancy and so treatment in the last trimester, which is associated with poorer outcomes, should include a second dose a week after. Three doses are given weekly for late syphilis in pregnancy. Retreatment is advised if syphilis has previously been diagnosed and there is uncertainty over previous treatment, if RPR/VDRL titres have not demonstrated four-fold drop or remains higher than 1:8. Procaine penicillin can also be used but non-penicillin alternatives such as ceftriaxone or macrolides have not been well or favourably evaluated and so skin testing and desensitization should be considered in patients with a history of penicillin allergy. The Jarisch–Herxheimer reaction occurs in approximately 40% of cases of treated syphilis. This is the same in pregnancy as with the general population and maternal and fetal monitoring is no longer recommended. It usually presents within 12 h as an acute febrile illness with headache, myalgia and rigors, resolving within 24 h. It is thought to be caused by the release of endotoxin-like substances when large numbers of *T. pallidum* are killed. This reaction may provoke uterine contractions and fetal heart rate decelerations and therefore a theoretical increased risk of preterm delivery and fetal demise. This should be managed supportively with antipyretics and there is no evidence for steroid therapy although this has been used.

Follow up should include repeat serology to monitor treatment response, re-infection and relapse at 3, 6 and 12 months post-treatment, and if RPR/VDRL is not negative or serofast at this stage, 6 monthly thereafter until it is. Sexual partners must also be tested and partner notification should extend to 3 months

for primary syphilis and 2 years for secondary syphilis. Any previous serology is therefore helpful to stage the disease and inform partner notification, particularly in latency and should be pursued together with sexual health colleagues. Careful paediatric assessment, serial serological testing and consideration of neonatal treatment is also required post-delivery. Treatment for congenital syphilis is indicated based on clinical suspicion, absence or inadequate maternal treatment, non-penicillin regimens or treatment less than four weeks prior to delivery. Older siblings should also be screened for congenital syphilis.

Genital warts

Genital warts are extremely common worldwide and are most commonly caused by the human papillomavirus (HPV) subtypes 6 and 11, with a small minority due to other subtypes. The virus is spread by genital skin-to-skin contact and transmission can occur from partners without visible warts due to asymptomatic viral shedding. The incubation period is on average 3 months but can be much longer and therefore it is often impossible and unhelpful to identify the source of infection. The diagnosis is clinical with typical lesions evident as single or multiple, fleshy, cauliflower—like lumps on the genital or perianal areas.

Studies on HPV infection in pregnant women have produced inconsistent results but there is some evidence that prevalence may be as high as 65% with the majority cleared in pregnancy and low levels of new infections. Key risk factors for HPV acquisition and persistence of HPV infection include young age, smoking, other STIs and immunosuppressive conditions. Since the introduction of the quadrivalent vaccine, which targets both high risk oncogenic subtypes as well as subtypes 6 and 11, as part of the national HPV immunisation programme in 2012 there has been a steep decline in new diagnoses of genital warts. PHE data reports a 90% reduction in new genital warts diagnoses in females aged 15—17 between 2009 and 2017 and, as the proportion of vaccinated women increases over time, rates are expected to fall further.

The vast majority of cases of genital warts cause no problems in pregnancy or labour. They can however enlarge rapidly in the second and third trimesters and are often more resistant to treatment. The management of genital warts is importantly different, with topical treatments such as podophyllotoxin contraindicated due to possible teratogenicity and imiquimod similarly unlicensed in pregnancy. Therefore active treatment in pregnancy should be limited to weekly cryotherapy and consideration of excision or deferred treatment if there is no improvement after four weeks. Some centres will offer hyfrecation (similar to diathermy). Warts often regress spontaneously postpartum.

Vertical transmission can cause genital warts and laryngeal papillomatosis but is very rare and parents should be reassured. The prevalence of laryngeal papillomatosis has been estimated at 4.5 per 100,000 children. Treatment aims to minimise the number of lesions present at delivery to reduce the neonatal exposure to virus. However since the mechanisms of vertical transmission of HPV are poorly understood and the complications are so rare, no treatment and vaginal delivery are considered safe. Caesarean section is only rarely indicated if the vaginal outlet or cervix are grossly obstructed with warts.

Genital herpes

Genital herpes is caused by the herpes simplex virus (HSV) type 1 or type 2 and although most genital herpes globally is caused by type 2, in the UK and other developed countries the cause is equally likely to be either type. In 2017 there were approximately 21,000 new diagnoses of genital herpes in women in England, which has remained stable in recent years. It is roughly twice as common among women as men of the same age and the prevalence is greatest among 20—25 year olds with around 70% of under 25s in the UK already infected with HSV type 1 or 2.

The virus is transmitted by skin-to-skin contact and can occur during vaginal, anal and oral sex, including sex with condoms. The incubation period is usually 5—14 days but can be longer so it is often difficult to ascertain the partner source of infection. The typical lesions of genital herpes are shallow, painful vesicles or ulcers of the genital or perianal area; however, many experience mild or no symptoms. Conversely patients may have systemic features such as malaise, myalgia, headache and lymphadenopathy. Patients may also present with isolated dysuria or constipation so genital examination should be undertaken, particularly in the context of pregnant women with culture negative or persistent "urinary tract infection". Symptomatic episodes usually spontaneously resolve within 3 weeks.

If genital lesions are present there is a high risk of passing on the virus to sexual partners but asymptomatic shedding and transmission also occurs, particularly in the first year after infection. The virus then lies dormant in a dorsal root ganglion and reactivates variably which may lead to recurrent symptomatic episodes, often preceded by a prodrome of localised tingling for a few days. The majority of women with genital herpes will have a recurrence during pregnancy and women can experience more outbreaks when pregnant. HSV-2 typically recurs more frequently than HSV-1. However, clinical diagnosis is neither sensitive nor specific and PCR testing of vesicle fluid and type-specific serological tests are required to distinguish between primary and recurrent infection which has major implications for management.

Primary HSV can cause miscarriage, preterm delivery, low birth weight and neonatal herpes. Neonatal herpes is rare in the UK, occurring in 1—2 out of every 100,000 newborn babies, however, it is almost always symptomatic with high mortality. It is categorized as localized (to skin, eye or mouth), encephalitic or disseminated multi-organ infection. The majority of cases occur as a result of direct contact with maternal secretions at birth but postnatal infection also occurs due to contact with oral herpes. Congenital herpes by transplacental infection in utero is extremely rare.

The risk of transmission is greatest when a woman acquires a new infection in the third trimester, particularly within 6 weeks of delivery, as viral shedding may continue until delivery and the baby is unlikely to have protective transplacental maternal antibodies. Serological testing is required as up to 15% of women presenting with a first episode will actually be recurrence. Testing may be difficult to interpret and women should be referred to genitourinary physicians. However, since results may not be available for some time, primary infection should be assumed in the interim. Serological testing may also be useful in the context of a partner with suspected or known HSV to establish true discordance and advise on how to minimize transmission during pregnancy.

The RCOG/BASHH guidance strongly recommends vaginal delivery for women with primary and recurrent genital herpes in the first or second trimesters with no other indications for caesarean section. Women should be reassured that there is no evidence that recurrent HSV infection is associated with miscarriage or congenital abnormalities. Whilst GUM referral should be made, this should not delay initiation of treatment, in line with clinical condition, to reduce the duration and severity of the episode. Aciclovir, although not licensed in pregnancy, has been used extensively without reported problems. From 36 weeks' gestation, 400 mg three times daily aciclovir should be offered to prevent recurrence at term. This is increased from a twice daily prophylactic dose outside of pregnancy. There is limited data on the neonatal safety of prophylaxis so the risks and benefits should be discussed with women.

In the final trimester vaginal delivery should also be recommended in recurrent cases as the risk of transmission remains low (0–4%), even if lesions are present at delivery. Invasive procedures may be used if necessary and in women with spontaneous rupture of membranes at term, most clinicians expedite delivery to minimise neonatal exposure. However, in primary HSV infection in the third trimester, caesarean section is indicated as the neonatal transmission rate is as high as 41% within 6 weeks of expected delivery. Prophylactic aciclovir should commence and continue until delivery. If caesarean section is declined or vaginal delivery is unavoidable, intravenous aciclovir should be considered and invasive procedures avoided. Babies will need testing and specialist neonatal care with preterm babies most at risk of disseminated HSV infection.

In the context of preterm prelabour rupture of membranes (PPROM) and HSV infection, there is limited evidence to guide management. However current expert opinion suggests that expectant management with oral aciclovir is appropriate for recurrent HSV and PPROM before 34 weeks' gestation. After this time, the management is the same as without HSV. However, when PPROM is complicated by primary HSV infection, there is no evidence base for management and therefore a plan should involve a senior multidisciplinary team. Conservative management should include prophylactic intravenous aciclovir and caesarean section should be considered if delivery is indicated within 6 weeks of primary HSV infection.

Mycoplasma genitalium

Mycoplasma genitalium, a slow growing, fastidious organism is the smallest known self-replicating bacterium and, as it lacks a cell wall, cannot be detected by Gram stain. Prevalence in the UK is estimated at 1–2% and infection is slightly more common in women. Macrolide resistance is an emerging problem and in the UK resistance could be present in up to 40% of cases. Risk factors are similar to those of chlamydia although peak prevalence is seen at an older age. Transmission is via genital–genital contact or penile-anal contact; oropharyngeal carriage is thought to be less common. Co-infection with other STIs has been noted, most commonly with chlamydia.

Current evidence suggests that the majority of those infected with *M. genitalium* do not develop associated disease. However, presentations in women can include dysuria, post-coital bleeding, cervicitis and lower abdominal pain. Complications in women include pelvic inflammatory disease, preterm delivery, sexually acquired reactive arthritis and possibly links to tubal factor infertility. Asymptomatic screening is not recommended due to emerging antimicrobial resistance, limitations to available treatments and limited evidence. Testing in women however is recommended in certain groups: women with signs and symptoms of PID, muco-purulent cervicitis, postcoital bleeding and sexual contacts of men with proven *M. genitalium* infection. Due to its slow growing nature, culture can be very difficult and vulvovaginal NAAT sampling is the recommended investigation.

Uncomplicated infection in pregnancy should be treated, as for chlamydia infection, with a 3-day course of azithromycin, with 1 g on day 1 followed by 500 mg on days 2 and 3. Azithromycin has been widely used in the treatment of chlamydia in pregnancy and therefore adverse pregnancy outcomes are unlikely. Treatment options for complicated disease or macrolide-resistant disease in pregnancy are limited. Moxifloxacin, the first-line treatment outside of pregnancy, is contraindicated; there is no safety data in pregnancy for pristinamycin and doxycycline, although found safe in the first trimester by the US Food and Drug Administration (FDA), the BNF states should not be given to pregnant women. Treatment options should therefore be fully discussed with pregnant women and, if possible, delayed until after pregnancy. Contact tracing should be carried out, partners treated and patients should be advised to abstain from sexual intercourse until they and their partner(s) have completed treatment. Test of cure is recommended no sooner than 3 weeks after treatment.

Hepatitides

Viral hepatitis is caused by several very different viruses and is usually transmitted by the faecal–oral (hepatitis A) or blood-borne routes (hepatitis B and C). However they should be considered as potential STIs in specific high-risk groups. Hepatitis A testing should be offered to people who inject drugs (PWID) and those with known hepatitis B, C or HIV. In pregnant, at-risk women who are not immune vaccination should be considered. Hepatitis B screening should be offered in sex workers, PWID, HIV positive patients, victims of sexual assault and those from endemic countries. In non-immune, pregnant patients with ongoing risk, hepatitis B vaccination should similarly be offered. These vaccines carry no known risks to the developing fetus.

Although often acquired asymptomatically, prodromal or icteric symptoms (loss of appetite, fatigue, abdominal pain, nausea and vomiting, fever, diarrhoea, dark urine and pale stools, jaundice and pruritus) can occur and should prompt serological testing. Pregnant women with a diagnosis of viral hepatitis should be counselled on increased rates of miscarriage and preterm labour, in addition to risk of vertical transmission, most significant in hepatitis B, but also seen in hepatitis C.

Pregnant women diagnosed with hepatitis B should be referred to specialist hepatology services. HIV status must be confirmed prior to Hepatitis B treatment as this may induce resistance to anti-retroviral therapy. All infants born to infectious mothers should be vaccinated at birth, with the addition of hepatitis B specific immunoglobulin if there is high risk of transmission. If mothers have hepatitis B DNA $>10^7$ IU/ml, tenofovir monotherapy in the third trimester can be considered to prevent vertical transmission.

Sexual transmission of hepatitis C is very uncommon in heterosexual relationships although slightly increased in the

presence of HIV. Hepatitis C testing should be offered to similar risk groups for hepatitis B in addition to those receiving blood transfusions prior to 1990, needle stick injury, tattoo recipients, alcoholics, those who snort cocaine and ex-prisoners. Pregnant women diagnosed with hepatitis C should be referred to specialist hepatology services. Treatment of chronic hepatitis C consists of direct acting antivirals, however these are not recommended during pregnancy.

Conclusion

STIs in pregnancy represent a significant risk to the mother and child. Clinicians should consider the risks regularly throughout the pregnancy in order to test, diagnose and manage effectively. Treatment regimens often differ in pregnancy and multidisciplinary teams are needed. The impact on mode of delivery depends on the timing and type of infection in relation to pregnancy gestation. Referral to the fetal medicine team for ultrasound assessment of growth and structural abnormalities must be considered early. Test of cure, partner notification and treatment, risk reduction advice, testing for other STIs and retesting must not be overlooked. ◆

FURTHER READING

Report on global sexually transmitted infection surveillance. 2015. World Health Organisation, http://apps.who.int/iris/bitstream/handle/10665/249553/9789241565301-eng.pdf?sequence=1.

Sexually transmitted infections and screening for Chlamydia in England 2017, vol12 20. 8 June 2018. Public Health England Health. protection report, https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/713944/hpr2018_AA-STIs_v5.pdf.

United Kingdom national guideline on the management of infection with Chlamydia trachomatis. Clinical Effectiveness Group (British Association for Sexual Health and HIV), 2015. Updated 26/09/2018.

British Association for Sexual Health and HIV national guideline for the management of infection with Neisseria gonorrhoeae, 2019.

United Kingdom National Guideline for the Management of Trichomonas Vaginalis. Clinical Effectiveness Group (British Association of Sexual Health and HIV), 2014.

United Kingdom national guideline for the management of syphilis. Clinical Effectiveness Group (British Association for Sexual Health and HIV), 2015.

United Kingdom national guideline on the management of ano-genital warts. Clinical Effectiveness Group (British Association for Sexual Health and HIV), 2015.

British Association for Sexual Health and HIV and Royal College of Obstetricians and Gynaecologists, Management of Genital Herpes in Pregnancy, October 2014.

British Association for Sexual Health and HIV national guideline for the management of infection with Mycoplasma genitalium, 2018.

United Kingdom national guideline on the management of the viral hepatitides A, B & C. Clinical Effectiveness Group (British Association of Sexual Health and HIV), 2008.

Practice points

- Sexually transmitted infections are common in young women, often asymptomatic and can have serious consequences to mother and child in pregnancy.
- Assess and reassess a woman's risk of sexually transmitted infections regularly throughout pregnancy.
- Management should be undertaken jointly with genitourinary physicians and paediatricians.