AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

Management of Perinatal Infections

THIRD EDITION

CHLAMYDIA TRACHOMATIS
CYTOMEGALOVIRUS
ENTEROVIRUS
GROUP B STREPTOCOCCUS
HEPATITIS B VIRUS
HEPATITIS C VIRUS
HERPES SIMPLEX VIRUS
HUMAN IMMUNODEFICIENCY VIRUS
LISTERIA
MYCOBACTERIUM TUBERCULOSIS
NEISSERIA GONORRHOEAE
PARVOVIRUS
RUBELLA
SYPHILIS (TREPONEMA PALLIDUM)
TOXOPLASMA GONDII
VARICELLA ZOSTER VIRUS
ZIKA VIRUS

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Management of Perinatal Infections
Third edition, 2022

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MANAGEMENT OF PERINATAL INFECTIONS

EDITORS' NOTE

Infections in pregnancy represent a unique medical challenge as the management of both the infected woman and the developing fetus must be considered. Perinatal counselling requires a discussion of risks of transmission, interventions to prevent transmission in-utero or postnatally if possible or available, diagnosis of infection in the fetus or newborn and finally, postnatal management of the infant. Many congenital infections are asymptomatic at birth, but some can be associated with significant long-term sequelae. Some congenital infections can be successfully prevented provided adequate strategies are implemented in a timely manner. The anxiety for parents cannot be underestimated. Informed counselling aims to assist parents with the process.

These algorithms were developed to assist medical practitioners, including general practitioners, obstetricians, infectious diseases physicians and paediatricians, involved in the care of pregnant women and/or their newborn infants. The organisms were chosen as they represent infectious agents in pregnancy where information on transmission risks and maternal and perinatal management exist. Where possible, they each follow 4 themes: antenatal diagnosis, antenatal management, transmission risk and available interventions, and management of the newborn.

The algorithms are evidence based and, where data are limited, recommendations are by consensus. We sought feedback prior to finalisation from the Australasian Society for Infectious Diseases (ASID), the Australian and New Zealand Paediatric Infectious Diseases (ANZPID) group and the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG). They are only intended as guidelines. As this is a highly specialised area of obstetric and perinatal medicine, consultation of experts is recommended.

The first edition of this set of comprehensive, contemporary algorithms was published in 2002, with emendations in 2006 and a second edition in 2014. This third edition now includes three additional infections, *Chlamydia trachomatis*, *Neisseria gonorrhoea* and Zika virus. It has been revised by the current editors, and after sourcing feedback from ASID/ANZPID and RANZCOG.

We are grateful for feedback and continued input from colleagues whose contributions have enriched this edition. The publication has stood the test of time and remains a unique and valuable resource. We hope that it will continue to be of use.

ACKNOWLEDGEMENTS

We wish to acknowledge the original contributing authors: Prof Jim Buttery (hepatitis B and C), A/Prof Andrew Daley (*Treponema pallidum*), Prof Sue Garland (cytomegalovirus (CMV), Group B streptococcus (GBS), Prof Lyn Gilbert (parvovirus, *Treponema pallidum*, *Toxoplasma gondii*), Prof Cheryl Jones (CMV, HSV) Prof Alison Kesson (Enterovirus), Dr Anne Marie Heuchan (varicella zoster virus (VZV), Prof David Isaacs (VZV), Prof Clare Nourse (rubella), Prof Pamela Palasanthiran (CMV, human immunodeficiency virus (HIV), A/Prof Mike Starr (*Mycobacterium tuberculosis*, parvovirus, GBS), Dr Lesley Voss (listeria) and the late Dr Allen Yung (*Mycobacterium tuberculosis*).

For this edition, we acknowledge the additional input of Dr Phoebe Williams (*Chlamydia trachomatis* and *Neisseria gonorrhoeae*) as well as Dr Meghan Gunst and Prof Cheryl Jones (Zika virus).

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The Editors: Pamela, Mike, Cheryl and Michelle

Chlamydia trachomatis

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

CHLAMYDIA – ALGORITHM 1

DIAGNOSIS OF SUSPECTED MATERNAL CHLAMYDIA TRACHOMATIS INFECTION

Routine antenatal testing in pregnancy is not recommended[1] but is sometimes done in high risk or high prevalence settings in Australia and New Zealand[1,2,3]

Risk factors for chlamydia infection which may support testing include:

- Age <30 years
- High risk sexual contact
- Use of illicit drugs
- Aboriginal or Torres Strait Islander or Maori or Pacific Peoples background

WOMAN EXHIBITING SYMPTOMS OF CHLAMYDIA INFECTION OR LIVING IN A HIGH PREVALENCE SETTING[a,b]

Vaginal swab (may be self-collected) or
first-void urine for Nucleic Acid Detection (chlamydia PCR)
High sensitivity (> 90%) and specificity (> 99%)

Test for other STIs
including HIV, syphilis and *N. gonorrhoeae*

Swab or
Urine PCR +ve

Swab and
urine PCR - ve

Advise to abstain from sex or use condoms for a week from start of treatment and until 1 week after sexual contact(s) have been treated

IMMEDIATE TREATMENT
Azithromycin 1g orally as a single dose
Alternative regimens include:
Amoxicillin 500mg PO TDS for 7 days[d]
Erythromycin base 500mg PO QID for 7 days

Ongoing antenatal care as planned

TEST OF CURE: 3 – 4 weeks post treatment
(to document chlamydial eradication)
Repeat first-void urine or vaginal swab PCR

RETESTING 3 MONTHS POST-TREATMENT
(to rule out re-infection prior to delivery)[f]

COMMENTS

a. Chlamydia is the most frequently reported sexually transmitted infection (STI) in Australia; and is ~ 10 times more prevalent than *Neisseria gonorrhoeae* infections in women of childbearing age (https://data.kirby.unsw.edu.au/STIs)[4] Similarly, in New Zealand, chlamydia is the commonest reported STI with prevalence about 4 -5 times higher than gonorrhoea (https://www.esr.cri.nz/our-services/consultancy/public-health/sti/)[5]

b. Most infections in women (~80%) are asymptomatic, and examination is normal. The "classic" symptoms include cervicitis, easy cervical bleeding, oedematous ectopy. Dysuria or pyuria from urethritis are uncommon

c. Chlamydia infection in pregnancy is associated with higher risk of preterm birth, low birth weight and perinatal mortality. No clear evidence of increased risk of premature rupture of membranes, miscarriage or postpartum endometritis

d. Cure rates of chlamydia in women who are pregnant are generally lower than in non-pregnant females, particularly with the alternative antibiotic, amoxicillin

e. For this reason, a test of cure is recommended for all women 3 – 4 weeks after treatment is completed

f. Pregnant women should also undergo repeat testing to evaluate for re-infection 3 months following treatment, as recurrent infection could place the infant at risk for chlamydia infection at birth; and epidemiological studies reveal a rate of reinfection of 15% in pregnant women

CHLAMYDIA – ALGORITHM 2

MANAGEMENT OF A NEONATE EXPOSED TO CHLAMYDIA TRACHOMATIS INFECTION

- Infants born to mothers with untreated *C. trachomatis* cervicitis are at high risk of infection from exposure to the infected cervix (~50%)
- Risk for neonatal-acquired conjunctivitis is 20-50% and *C. trachomatis* pneumonia is 15 - 30%
- Prophylactic (oral or topical) antibiotic treatment to an asympotomatic baby born to an untreated mother is not indicated as the efficacy is unknown
- Infants should be monitored to ensure appropriate and prompt treatment if symptoms develop.

MATERNAL HISTORY CONSISTENT WITH RISK FOR CHLAMYDIA INFECTION (SEE ALGORITHM 1) PLUS NEONATE EXHIBITING SYMPTOMS SUGGESTIVE OF CHLAMYDIA INFECTION

Subacute conjunctivitis occurring at 5 –12 days of age (Ophthalmia neonatorum)

Swab collected from everted eyelid for **Nucleic Acid Amplification (PCR) test**

- Concurrently test for *N. gonorrhoeae* to rule-out co-infection

PCR POSITIVE for *C. trachomatis*:
TREATMENT
Azithromycin 20 mg/kg/day PO daily for 3 days
- Ophthalmology review
- There is no evidence for topical therapy

FOLLOW-UP:
The efficacy for azithromycin in treating *C. trachomatis* is extrapolated to be ~90%; a second course of therapy may be required.

AND/OR
(may co-occur in up to 50% of neonates)

Subacute, afebrile pneumonia presenting at age 1 – 3 months

SYMPTOMS:
- Repetitive staccato cough
- Tachypnoea
- Peripheral eosinophilia (>400 cells/m^3)

Nasopharyngeal swab for:
Nucleic acid testing (*C. trachomatis* PCR)

RADIOLOGY EXAMINATION: CXR
- Bilateral diffuse infiltrations
- Hyperinflation

PRE-EMPTIVE TREATMENT[a]
Initiate for all infants aged 1-3 months with above clinical and radiological findings where the risk of chlamydia infection in the mother is deemed to be high (do not wait for test results)
Azithromycin 20 mg/kg/dose
PO daily for 3 days

COMMENTS

a. An association between erythromycin and azithromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported in infants aged <6 weeks. Infants treated with either of these antimicrobials should be followed for signs and symptoms of IHPS

b. Mothers of infants with infection caused by *C. trachomatis* and their sexual partners must be evaluated and treated presumptively for *C. trachomatis* and *N. gonorrhoeae* – contact local sexual health service (counselling and further management)

CHLAMYDIA TRACHOMATIS APPENDIX AND REFERENCES

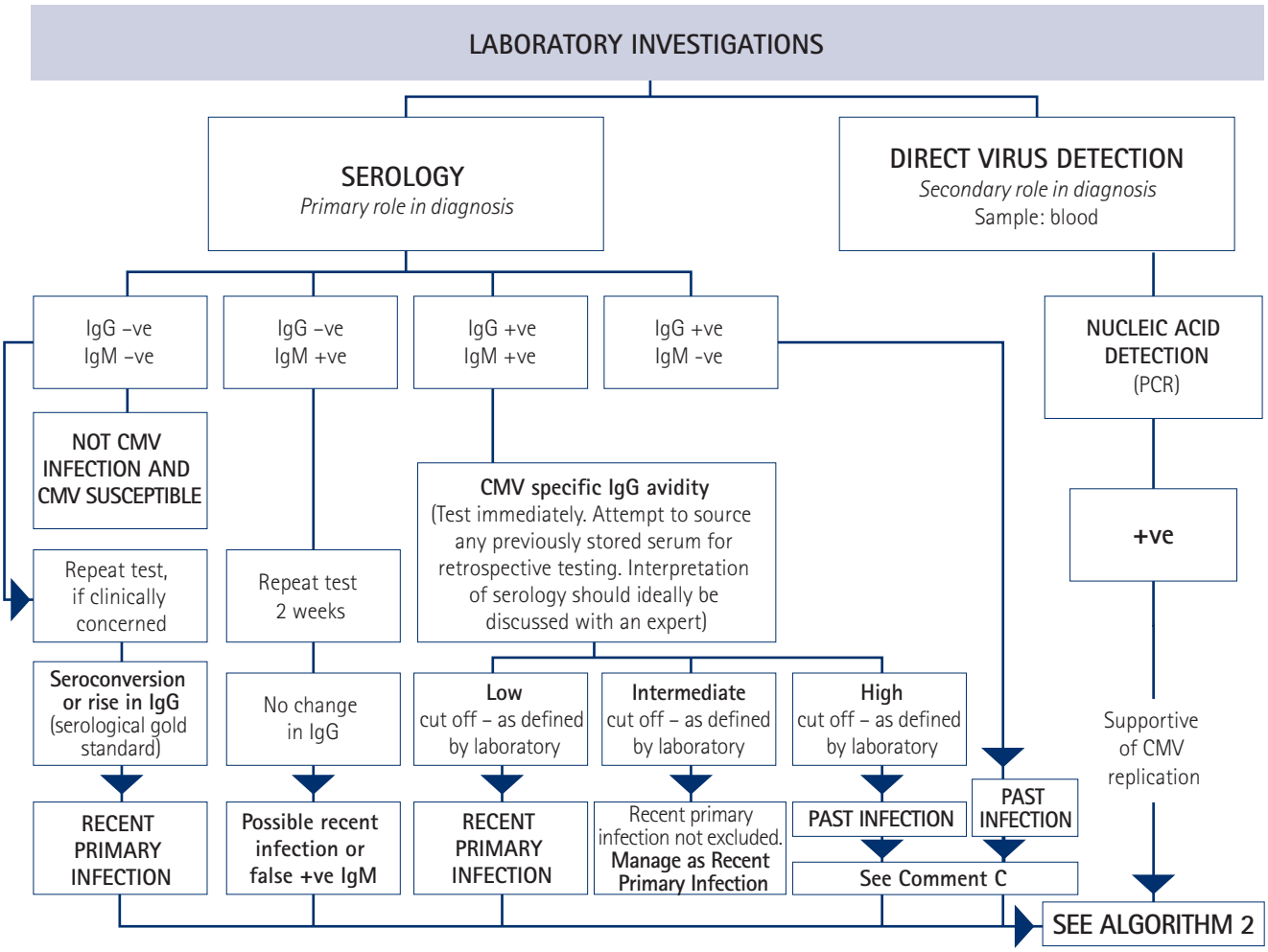
1. RANZCOG. Routine antenatal assessment in the absence of pregnancy complications (C-Obs 3b). 2022. https://ranzcog.edu.au/wp-content/uploads/2022/05/Routine-antenatal-assessment-in-the-absence-of-pregnancy-complications.pdf
2. https://sti.guidelines.org.au/sexually-transmissible-infections/chlamydia/
3. https://sti.guidelines.org.nz/infections/gonorrhoea/
4. https://kirby.unsw.edu.au/report/asr2018
5. https://www.esr.cri.nz/our-services/consultancy/public-health/sti/
6. Hoover KW, Tao G, Nye MB, Body BA. Suboptimal adherence to repeat testing recommendations for men and women with positive Chlamydia tests in the United States, 2008-2010. Clin Infect Dis; (2013), 56(1).
7. American Academy of Paediatrics. Chlamydia trachomatis. In: Red Book: 2018 Report of the Committee on Infectious Diseases. 31st edition. Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds). American Academy of Paediatrics, Itasca, IL 2018.
8. Silva MJ, Florencio GL, Gabiatti JR, Amaral RL, Eleuterio Junior J, Goncalves AK. Perinatal morbidity and mortality associated with chlamydial infection: a meta-analysis study. Braz J Infect Dis. 2011;15(6):533-9.
9. Workowski KA, Bachmann LH, Chan PA et al. Sexually transmitted infections treatment guidelines. MMWR Recomm Rep 2021;70(4):1 - 187
10. Lochner HJ, 3rd, Maraqa NF. Sexually Transmitted Infections in Pregnant Women: Integrating Screening and Treatment into Prenatal Care. Paediatr Drugs. 2018;20(6):501-9.

Cytomegalovirus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

CYTOMEGALOVIRUS (CMV) – ALGORITHM 1

MATERNAL DIAGNOSIS[1]



Routine antenatal CMV screening not generally recommended in Australia but is sometimes done.[1,7] Possible indications for antenatal testing are:

- History suggestive of CMV illness
- Abnormalities on routine antenatal ultrasound (SEE ALGORITHM 2)
- Exposure to known CMV infected individual e.g. partner with acute CMV infection

Note that the majority of primary CMV infections are asymptomatic

COMMENTS

a. CMV is the leading cause of congenital infections with an overall birth prevalence of 0.64%.[2,3] The incidence of congenital CMV (cCMV) in Australia is estimated to be 3.85/100 000 live births, a likely underestimate [4]

b. Knowledge about CMV and cCMV is suboptimal among health care workers and pregnant women with only ~ a quarter reporting knowledge highlighting the importance of education/information [5,6]

c. Note that up to 75% of cases of cCMV occur in non-primary maternal CMV infection. In-utero transmission in non-primary infection may be less likely, but if infected, the full range of features of cCMV is possible

d. Education about preventing CMV infection, including hygienic measures to minimise CMV acquisition should be provided to all pregnant women antenatally.[8]

Table 1: Recommendations for pregnant women to reduce CMV infection[1,8]

- Do not share food, drinks, or utensils used by young children (less than 3 years of age)
- Do not put a child's dummy in your mouth
- Avoid contact with saliva when kissing a child
- Attention to hand hygiene, when changing nappies or when in contact with urine. Thoroughly wash hands with soap and water for 15–20 seconds, especially after changing nappies/feeding a young child, or wiping a young child's nose or saliva
- Clean toys, countertops, and other surfaces that come into contact with children's urine or saliva,. Do not share a toothbrush with a young child

e. Major risk factor for maternal CMV acquisition is frequent, prolonged contact with young children, especially children who are shedding CMV.[9,10] Groups at higher risk of primary CMV and annual seroconversion rates are [9,10]

– Day care workers (pooled incidence of 7.4 per 100 person-years)[9]

– Parents with child in day care (2% p.a. for non-CMV shedding children, 24% p.a. for CMV shedding children)[10]

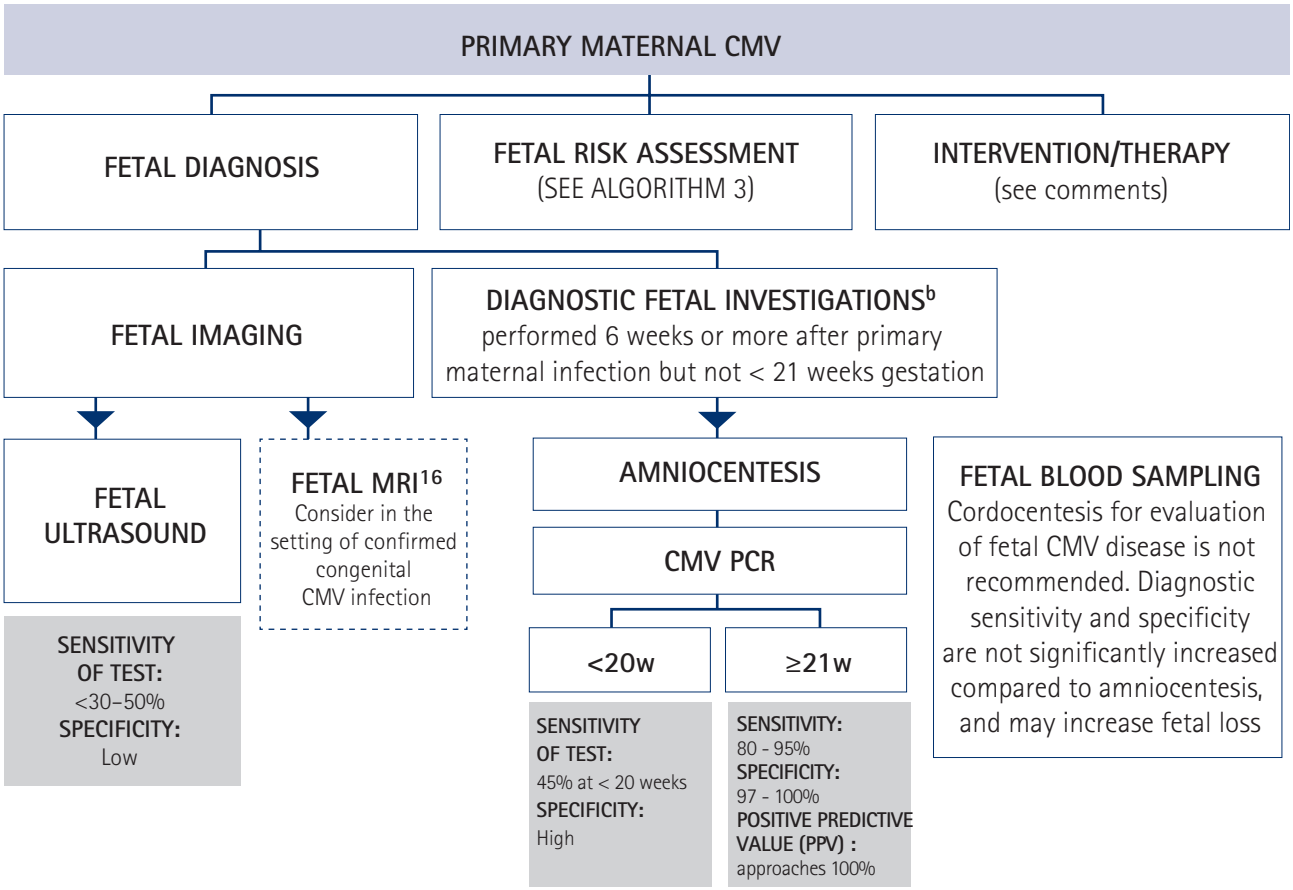
Health care workers seroconvert at a rate comparable to the general population i.e. 2-3% p.a.

Transmission is commonly from salivary shedding and environmental sources [11, 12]

f. Anti CMV IgM is an appropriate screening antibody in pregnancy but caution is needed in interpretation. CMV IgM can persist for months after primary infection or reappear with reactivation or reinfection. False positives occur with cross reactivity with other herpes viruses or autoimmune disorders. Primary CMV infection is eventually diagnosed in a minority of women with positive CMV IgM (20–25%) [13]

CYTOMEGALOVIRUS – ALGORITHM 2

ANTENATAL MANAGEMENT OF MATERNAL CMV INFECTION



COMMENTS

a. Fetal ultrasound:[14,15] Features associated with congenital CMV infection (cCMV) include
- Microcephaly
- Cerebral ventriculomegaly
- Intrauterine growth restriction (IUGR)
- Ascites
- Intracranial calcification
- Pleural or pericardial effusions
- Amniotic fluid abnormalities (oligohydramnios or polyhydramnios)
- Hydrops fetalis
- Hepatomegaly
- Abdominal calcification
- Pseudomeconium ileus
- Hyperechoic bowel

Caution is advised in interpretation of findings as presence of signs not always predictive of degree of fetal damage. The sensitivity of fetal ultrasound is difficult to evaluate from the literature, with an overall estimate of ~30–50% sensitivity for detecting symptomatic congenitally infected infant. The risk of severe sequelae may be significantly reduced if antenatal ultrasounds and MRI are normal [15,16]

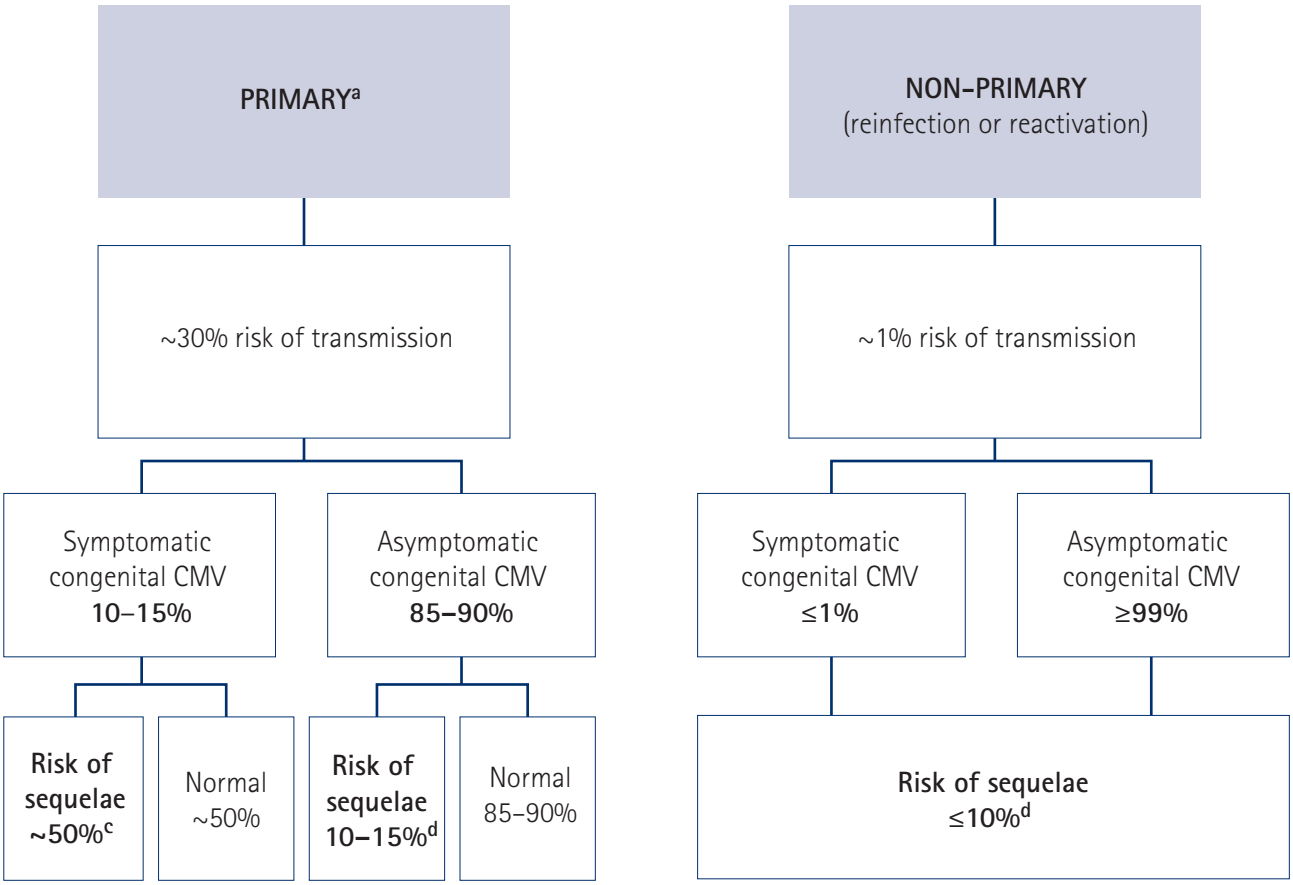
b. Fetal (in-utero) investigations: amniocentesis [1,15]
- Sensitivity is increased by waiting ≥ 6 weeks after maternal infection
- The timing of amniocentesis: If performed ≥21 weeks of gestation and ≥ 6 after maternal infection, sensitivity is high (85 - 95%) and specificity approaches 100%. Reports of cCMV after a negative CMV PCR are uncommon (possible later CMV transmission) and significant sequelae in newborns unlikely.[17] Testing for CMV at birth is recommended
- Diagnosis is best achieved by a combination of fetal ultrasound + amniocentesis (for CMV PCR)
- Positive results cannot predict degree of fetal damage
- The value of quantitative PCR to predict severity of cCMV has not been established

c. Intervention/therapy: Prevention of fetal CMV transmission (reviewed in reference 19)
- **Seek expert advice**
- Behavioural interventions such as providing cCMV information, CMV awareness and counselling, infection prevention and control measures (hand hygiene, avoiding kissing young child on mouth) are effective measures for preventing primary maternal infection[17,18]
- **Prevention of in-utero transmission:** CMV Hyperimmuneglobulin (HIG): Observational studies with differing HIG protocols report significant reduction in transmission. Two randomised controlled trials (RCTs) [20, 21] however report no reduction (29.5 % HIG vs 44% placebo (95% CI – 3 to 31%, p =0.13)[20] with a higher rate of obstetric event (mainly prematurity) in the HIG arm (13% vs 2%). Trial NCT01376778 was stopped prematurely as no difference in transmission was shown (22.7% HIG vs. 19.4% placebo (rel. risk RR 1.17; 95% CI 0.80 – 1.72; p=0.42); there was no increase in obstetric events.[21] HIG is currently not routinely recommended for prevention, but may be considered on a case by case basis for fetal treatment (see section on Therapeutic Intervention below)
- **Prevention of in-utero transmission with antivirals:** Data on valaciclovir for prevention are emerging. A recent RCT reports reduction of transmission when high dose valaciclovir (4g BD) was used early in primary maternal CMV infection. [22] Valaciclovir is currently not routinely recommended but can be considered in primary maternal CMV infection, in the first trimester, given as early as possible from infection [22, 23]
- There is no data to support the combined use of antenatal CMV hyperimmune globulin and valaciclovir

d. Therapeutic intervention for infected fetus [1, 19, 24, 25]
- **Seek expert advice**
- Termination of pregnancy is an option by informed choice if cCMV is confirmed in-utero, with the knowledge that a positive PCR is not predictive of fetal damage
- Observational studies from antenatal use of CMV immunoglobulin in pregnancy report a benefit for neonatal cCMV outcome.[24] Consideration could be given for use antenatally when fetal infection is confirmed (CMV +ve PCR on amniocentesis). Data on valaciclovir use for fetal treatment awaits further studies[25]

CYTOMEGALOVIRUS – ALGORITHM 3

RISK ESTIMATES OF FETAL TRANSMISSION



Overall risk of long term sequelae in a congenitally infected child is ~**10–20%**

SEE ALGORITHM 4

COMMENTS

a. Primary CMV during pregnancy has the highest risk of fetal transmission (~30%).[2] However, peri-conceptional primary CMV (CMV acquired around the time of conception) carries a small increment in risk of 5 –16%,[26,27,28] with risks decreasing with time. Pooled data from [17] studies report a materno-fetal transmission rate of 5.5 % with maternal infection in the "periconception" period (3 months before last menstrual period (LNMP), 21% in the "periconception" period (4 weeks before and 6 weeks after LNMP), 36.5% in first trimester, 40.3% in second trimester and 66% in third trimester.[27]
The optimal interval between infection and conception remains to be defined, with a year after primary infection suggested as the highest 'risk' period. It is important to note that 'reactivation' of CMV occurs, meaning there is never a zero risk of in-utero transmission, no matter how far out from primary CMV infection.

b. Transmission of CMV occurs across the trimesters
   - Risk of severe adverse neurological outcome more likely with primary infection in the first trimester [27,29]
   - A fetus infected late in pregnancy is unlikely to have significant neurological sequelae [27]

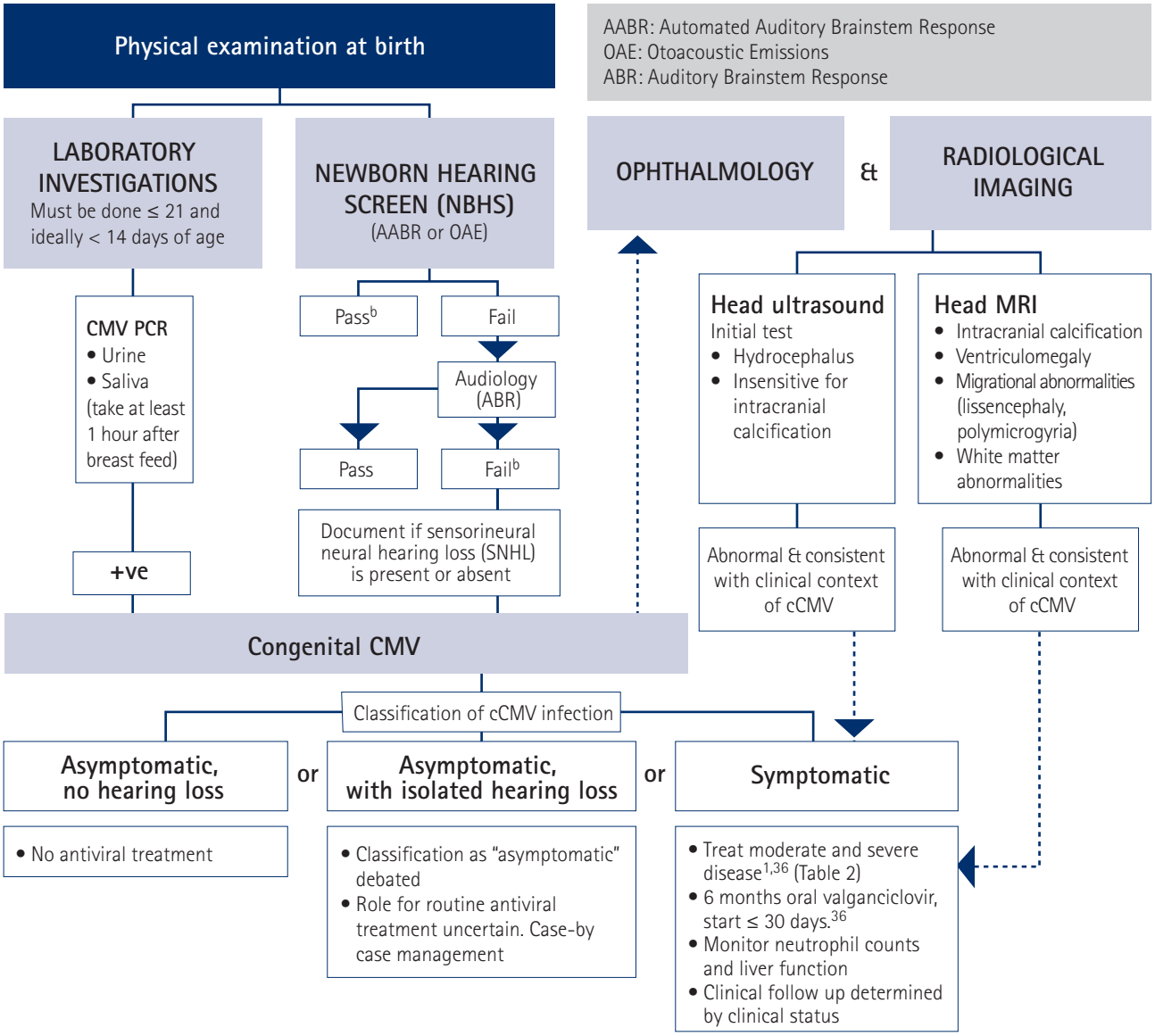
c. Main concerns of symptomatic cCMV infection [30,31]
   - Early mortality (first 3 months) rate between rate 5-10%
   - Neurological sequelae of microcephaly (35–50%), seizures (10%), chorioretinitis (10–20%), developmental delay (70%)
   - Sensorineural hearing loss (SNHL, 25–50%), with progression expected in about half (mainly in the first 2 years of life)

d. Main concerns of asymptomatic congenital CMV are
   - Sensory neural hearing loss (SNHL): ~10% of asymptomatic babies will have SNHL at birth, with cumulative incidence of late onset hearing loss is 7 -10% in asymptomatic cCMV and ~ 34 -41% in symptomatic cCMV infants [30]
   - Neurodevelopmental: Reported later onset neurodevelopmental concerns (case series). In case control studies, neurodevelopment of infants with asymptomatic cCMV appears to be similar when compared with healthy controls [32,33]
   - Chorioretinitis: 2%

Normal development by 12 months is associated with higher likelihood of normal development long term, and progression after the second year of life is uncommon. Emerging concerns about accompanying vestibular dysfunction and subsequent impact on motor development in congenital CMV is emerging and warrant further attention e.g awareness, testing, referral to physiotherapy if present. [34]

CYTOMEGALOVIRUS – ALGORITHM 4

NEONATAL DIAGNOSIS AND MANAGEMENT[1,35]



Suggested clinical follow-up:

- Audiological assessments (6 monthly year till age 2 years then annually till age 6)
- Ophthalmology: Annual review till age 6 years
- Paediatric review: 3 – 6 monthly, first 2 years then annually till age 6
- Assessments to include neurological status, head circumferences & neurodevelopmental assessments

COMMENTS

a. Other tests at birth: CMV IgM may be helpful if positive but generally not done (low sensitivity test). The standard test is the urine CMV PCR +/- saliva CMV PCR FBE & differential, LFT if there are clinical concerns

b. In about half of cCMV infections, SNHL will not be identified at birth, but the infant is at risk of later onset SNHL

c. cCMV infected babies are high CMV shedders (urine), particularly in the first year of life

Table 2 : Symptoms associated with congenital CMV [1,35,36]

Moderately to severely symptomatic congenital CMV disease

- Multiple manifestations attributable to congenital CMV infection: thrombocytopenia, petechiae, hepatomegaly, splenomegaly, intrauterine growth restriction, hepatitis (raised transaminases or bilirubin), or
- Central nervous system involvement such as microcephaly, radiographic abnormalities consistent with CMV central nervous system disease (ventriculomegaly, intracerebral calcifications, periventricular echogenicity, cortical or cerebellar malformations), abnormal cerebrospinal fluid indices for age, chorioretinitis, sensorineural hearing loss, or the detection of CMV DNA in cerebrospinal fluid

Mildly symptomatic congenital CMV disease

- Might occur with one or two isolated manifestations of congenital CMV infection that are mild and transient (eg, mild hepatomegaly or a single measurement of low platelet count or raised levels of alanine aminotransferase). These might overlap with more severe manifestations. However, the difference is that they occur in isolation

Asymptomatic congenital CMV infection with isolated sensorineural hearing loss

- No apparent abnormalities to suggest congenital CMV disease, but sensorineural hearing loss (≥21 decibels)

Asymptomatic congenital CMV infection

- No apparent abnormalities to suggest congenital CMV disease, and normal hearing

CYTOMEGALOVIRUS REFERENCES

References

1. Rawlinson WD, Boppana SB, Fowler KB, et al. Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. The Lancet Infectious Diseases 2017; 17(6): e177-e88.
2. Dollard SC, Grosse SD, Ross DS. New estimates of the prevalence of neurological and sensory sequelae and mortality associated with congenital cytomegalovirus infection. Reviews in Medical Virology 2007; 17(5): 355-63.
3. Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. Rev Med Virol 2007; 17(4): 253-76.
4. McMullan BJ, Palasanthiran P, Jones CA, et al. Congenital cytomegalovirus--time to diagnosis, management and clinical sequelae in Australia: opportunities for earlier identification. Medical Journal of Australia 2011; 194(12): 625-9.
5. Shand AW, Luk W, Nassar N, Hui L, Dyer K, Rawlinson W. Cytomegalovirus (CMV) infection and pregnancy-potential for improvements in Australasian maternity health providers' knowledge. Journal of Maternal-Fetal & Neonatal Medicine 2018; 31(19): 2515-20.
6. Lazzaro A, Vo ML, Zeltzer J, et al. Knowledge of congenital cytomegalovirus (CMV) in pregnant women in Australia is low, and improved with education. Aust N Z J Obstet Gynaecol 2019; 26: 26.
7. RANZCOG. Routine antenatal assessment in the absence of pregnancy complications. C-Obs 3b. 2022. https://ranzcog.edu.au/wp-content/uploads/2022/05/Routine-antenatal-assessment-in-the-absence-of-pregnancy-complications.pdf
8. RANZCOG. Prevention of congenital cyromegalovirus (CMV) infection. C-Obs 64 https://ranzcog.edu.au/wp-content/uploads/2022/05/Prevention-of-congenital-cytomeglovirus-CMV-infection-C-Obs-64.pdf
9. Balegamire SJ, McClymont E, Croteau A, et al. Prevalence, incidence, and risk factors associated with cytomegalovirus infection in healthcare and childcare worker: a systematic review and meta-analysis. *Systematic reviews* 2022; 11(1): 131
10. Hyde TB, Schmid DS, Cannon MJ. Cytomegalovirus seroconversion rates and risk factors: implications for congenital CMV. Reviews in Medical Virology. 2010;20(5):311-26.
11. Cannon MJ, Stowell JD, Clark R, et al. Repeated measures study of weekly and daily cytomegalovirus shedding patterns in saliva and urine of healthy cytomegalovirus-seropositive children. BMC Infectious Diseases 2014; 14: 569.
12. Amin MM, Stowell JD, Hendley W, et al. CMV on surfaces in homes with young children: results of PCR and viral culture testing. BMC Infectious Diseases 2018; 18(1): 391.
13. Lazzarotto T, Guerra B, Gabrielli L, Lanari M, Landini MP. Update on the prevention, diagnosis and management of cytomegalovirus infection during pregnancy. Clinical Microbiology & Infection 2011; 17(9): 1285-93.
14. Leruez-Ville M, Stirnemann J, Sellier Y, et al. Feasibility of predicting the outcome of fetal infection with cytomegalovirus at the time of prenatal diagnosis. American Journal of Obstetrics & Gynecology 2016; 215(3): 342.e1-9.
15. Hui L, Wood G. Perinatal outcome after maternal primary cytomegalovirus infection in the first trimester: a practical update and counseling aid. Prenatal Diagnosis 2015; 35(1): 1-7.
16. Lipitz S, Hoffmann C, Feldman B, Tepperberg-Dikawa M, Schiff E, Weisz B. Value of prenatal ultrasound and magnetic resonance imaging in assessment of congenital primary cytomegalovirus infection. Ultrasound Obstet Gynecol 2010; 36(6): 709-17.
17. Barber V, Calvert A, Vandrevala T, et al. Prevention of Acquisition of Cytomegalovirus Infection in Pregnancy Through Hygiene-based Behavioral Interventions: A Systematic Review and Gap Analysis. *Pediatr Infect Dis J* 2020; 39(10): 949-54.
18. Billette de Villemeur A, Tattevin P, Salmi LR. Hygiene promotion might be better than serological screening to deal with Cytomegalovirus infection during pregnancy: a methodological appraisal and decision analysis. *BMC Infect Dis* 2020; 20(1): 418.
19. Bartlett AW, Hamilton ST, Shand AW, Rawlinson WD. Fetal therapies for cytomegalovirus: What we tell prospective parents. Prenat Diagn. 2020;40(13):1681-92
20. Revello MG, Lazzarotto T, Guerra B, Spinillo A, et al. A randomized trial of hyperimmune globulin to prevent congenital cytomegalovirus. New England Journal of Medicine. 2014;370(14):1316-26
21. Hughes BL, Clifton RG, Rouse DJ, et al. A Trial of Hyperimmune Globulin to Prevent Congenital Cytomegalovirus Infection. N Engl J Med 2021; 385(5): 436-44.
22. Shahar-Nissan K, Pardo J, Peled O, et al. Valaciclovir to prevent vertical transmission of cytomegalovirus after maternal primary infection during pregnancy: a randomised, double-blind, placebo-controlled trial. Lancet. 2020;396(10253):779-85.
23. Faure-Bardon V, Fourgeaud J, Stirnemann J, Leruez-Ville M, Ville Y. Secondary prevention of congenital cytomegalovirus infection with valacyclovir following maternal primary infection in early pregnancy. Ultrasound Obstet Gynecol 2021; 58(4): 576-81.
24. Visentin S, Manara R, Milanese L, et al. Early primary cytomegalovirus infection in pregnancy: maternal hyperimmunoglobulin therapy improves outcomes among infants at 1 year of age. Clin Infect Dis 2012; 55(4): 497-503.
25. Leruez-Ville M, Ghout I, Bussieres L, et al. In utero treatment of congenital cytomegalovirus infection with valacyclovir in a multicenter, open-label, phase II study. American Journal of Obstetrics & Gynecology 2016; 215(4): 462.e1-.e10.
26. Fowler KB, Stagno S, Pass RF. Interval between births and risk of congenital cytomegalovirus infection. Clinical Infectious Diseases 2004; 38(7): 1035-7.
27. Chatzakis, C., et al., Timing of primary maternal cytomegalovirus infection and rates of vertical transmission and fetal consequences. Am J Obstet Gynecol, 2020. 223(6): p. 870-883.e11.
28. Feldman B, Yinon Y, Tepperberg Oikawa M, Yoeli R, Schiff E, Lipitz S. Pregestational, periconceptional, and gestational primary maternal cytomegalovirus infection: prenatal diagnosis in 508 pregnancies. American Journal of Obstetrics & Gynecology 2011; 205(4): 342.e1-6.
29. Picone O, Vauloup-Fellous C, Cordier AG, et al. A series of 238 cytomegalovirus primary infections during pregnancy: description and outcome. Prenat Diagn. 2013;33(8):751-8.
30. Ross SA, Kimberlin D. Clinical outcome and the role of antivirals in congenital cytomegalovirus infection. Antiviral Res 2021; 191: 105083.
31. Dreher AM, Arora N, Fowler KB, et al. Spectrum of disease and outcome in children with symptomatic congenital cytomegalovirus infection. J Pediatr 2014; 164(4): 855-9.
32. Bartlett AW, McMullan B, Rawlinson WD, Palasanthiran P. Hearing and neurodevelopmental outcomes for children with asymptomatic congenital cytomegalovirus infection: A systematic review. Reviews in Medical Virology 2017; 06: 06.
33. Lopez AS, Lanzieri TM, Claussen AH, et al. Intelligence and Academic Achievement With Asymptomatic Congenital Cytomegalovirus Infection. Pediatrics 2017; 140(5).
34. Shears A, Yan G, Mortimer H, et al. Vestibular and balance dysfunction in children with congenital CMV: a systematic review. Arch Dis Child Fetal Neonatal Ed 2022.
35. Luck SE, Wieringa JW, Blazquez-Gamero D, et al. Congenital Cytomegalovirus: A European Expert Consensus Statement on Diagnosis and Management. Pediatric Infectious Disease Journal 2017; 36(12): 1205-13.
36. Kimberlin DW, Jester PM, Sanchez PJ, et al. Valganciclovir for symptomatic congenital cytomegalovirus disease. New England Journal of Medicine 2015; 372(10): 933-43.

Enterovirus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

ENTEROVIRUS AND PARECHOVIRUS – PERINATAL INFECTION

Enteroviral infections generally cause insignificant illness, and perinatal transmission of enteroviruses leading to significant symptomatic disease in infants is rare. There are case reports of stillbirth related to maternal and/or fetal infection with coxsackieviruses, echoviruses, and enterovirus 71.

Cases of congenital anomalies such as urogenital anomalies, gastrointestinal tract anomalies, cardiovascular defects and pulmonary hypoplasia have also been described after maternal and/or fetal infection with enteroviruses during pregnancy. Fetal deaths and congenital anomalies have not been associated with parechovirus infection.

Epidemics of human parechovirus (HPeV) occur in a 2-yearly pattern, causing illness in infants <3 years of age. HPeV genotype 3 causes sepsis-like illness and CNS infection.

Infection in adults

- More than 90% of enteroviral infections are either asymptomatic or cause a non-specific febrile illness. Accompanying symptoms may include sore throat, flu-like symptoms and vomiting. Diarrhoea is less common.
- Meningoencephalitis occurs far less commonly.
- Peak incidence is in spring/summer months in non-tropical regions.

Infection in pregnancy

- The risk of complications is greatest when infection occurs near term:
  - sudden onset of fever and severe abdominal pain mimicking placental abruption - attributed to mesenteric adenitis
  - intrauterine fetal death

Transmission

- In-utero transmission in late gestation has been described, but is less common than intra or postpartum acquisition
- Intrapartum exposure to maternal blood, genital secretions and stool
- Postnatal exposure to oropharyngeal secretions from mother and other contacts
- Possible transmission via breast milk

Neonatal infections

Enterovirus

- Wide spectrum of clinical presentations, from non-specific febrile illness to fatal multisystem disease
- Fever, irritability, poor feeding, lethargy
- Maculopapular rash in 50%
- Respiratory symptoms in 50%
- Gastrointestinal symptoms in 20%
- Hepatitis in 50%
- Myocarditis, meningoencephalitis

HPeV

- Often asymptomatic or mild symptoms including gastroenteritis or influenza-like illness.
- Fever, irritability +/- diffuse rash (described as "red, hot and angry" babies)
- Meningoencephalitis
- Sepsis-like presentation (incl. septic shock)
- Signs of surgical abdomen (uncommon)
- Adverse neurodevelopmental outcomes seen in 15-20%

Diagnosis

- Tissue culture is slow and requires expertise; it is now rarely used
- Serology is insensitive
- RT-PCR - rapid, sensitive and specific – separate assays are available for enterovirus and parechovirus
- Isolation from stool is highly sensitive but not specific as virus is shed in stool for several weeks
- Detection in blood, CSF and tissue is most reliable as follows:
  – Diagnosis in pregnancy - blood, amniotic fluid, stool
  – Diagnosis in neonate - blood, CSF +/- stool
- Genotyping is possible by PCR sequencing of structural protein genes
- CSF pleocytosis and elevated CSF protein appear to occur more commonly in enterovirus infection than parechovirus infection

Treatment in neonates

- Although there is evidence for safety and possible efficacy of two antiviral agents, pleconaril and pocapavir, neither are currently available
- IVIG may be of benefit – one small RCT showed subtle clinical benefits and faster resolution of viraemia[1]

Prevention

- Nursery epidemics have been described
- Handwashing/infection control contact precautions
- Prophylactic IVIG may reduce disease severity in some exposed neonates

ENTEROVIRUS REFERENCES

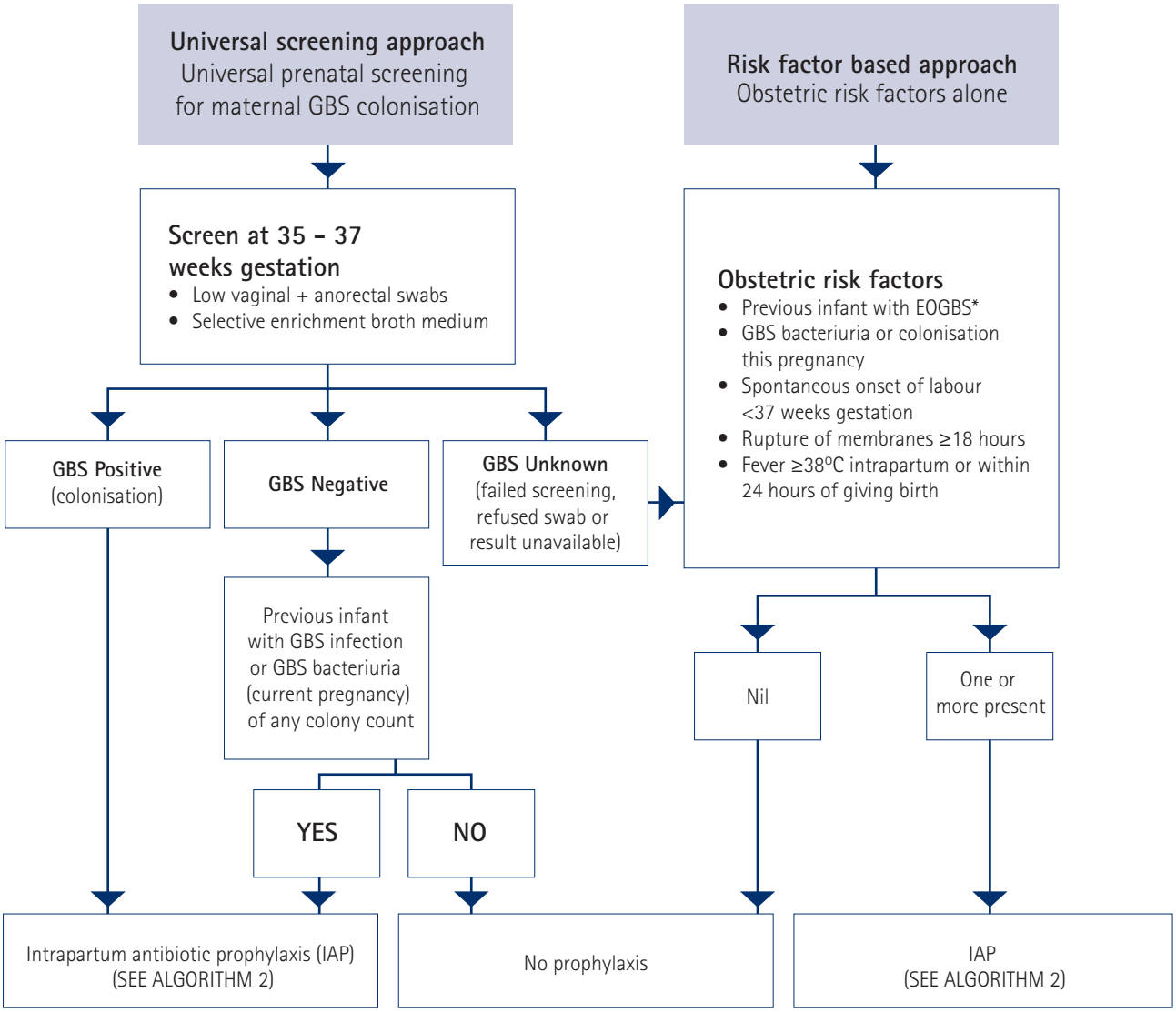
1. Abzug MJ, Keyserling HL, Lee ML, Levin MJ, Rotbart HA. Neonatal enterovirus infection: virology, serology, and effects of intravenous immune globulin. Clin Infect Dis 1995;20:1201–6.
2. Britton PN, Jones CA, Macartney K, Cheng AC. Parechovirus: an important emerging infection in young infants. Med J Aust. 2018;208:365-369.
3. Harik N, DeBiasi R. Neonatal nonpolio enterovirus and parechovirus infections. Semin Perinatol. 2018;42:191-197.
4. Haston J, Dixon T. Nonpolio Enterovirus Infections in Neonates. Pediatr Ann. 2015;44:e103-7.
5. Modlin J, Polk B, Horton P, Etkind P, Crane E, Spiliotes A. Perinatal echovirus infection: risk of transmission during a community outbreak. N Engl J Med 1981;305:368–71.
6. Tebruegge M, Curtis N. Enterovirus infections in neonates. Semin Fetal Neonatal Med. 2009;14:222-7.

Group B streptococcus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

GROUP B STREPTOCOCCUS (GBS) – ALGORITHM 1

MANAGEMENT OF PREGNANCY WITH RESPECT TO GBS INFECTION

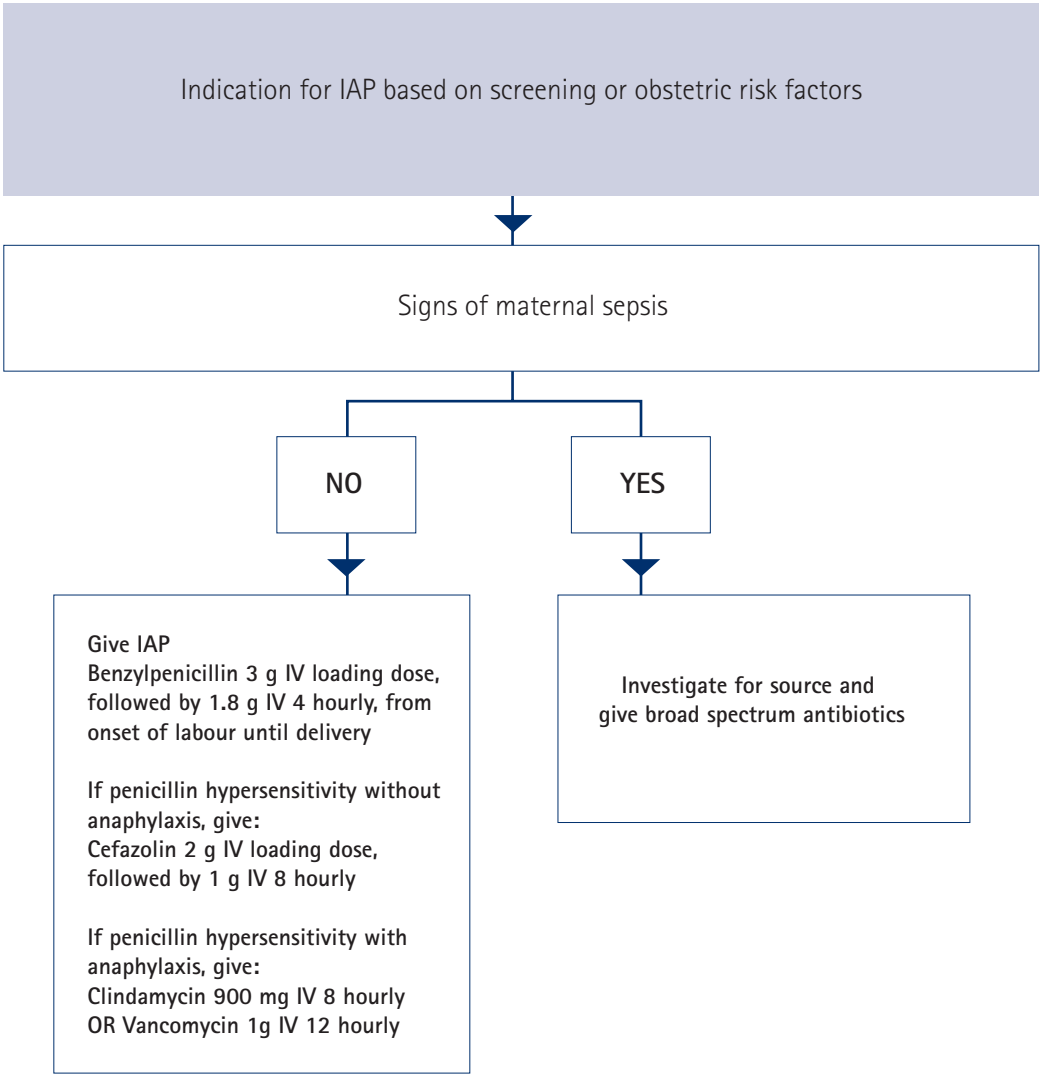


COMMENTS

- Colonisation of the genital tract with GBS occurs in 10-30% of women. Up to 70% of infants born to colonised women are themselves colonised, but early onset GBS disease* (EOGBS) within the first week of life occurs at a rate of <1 per 1000 live births.[1, 2]
- IAP is highly effective in reducing neonatal colonisation with GBS and preventing EOGBS.[3, 4]
- A systematic review & meta-analysis reports screening is associated with a reduced risk for EOGBS disease compared with either risk-based protocols (RR 0.43, 95% CI 0.32–0.56) or with no policy (RR 0.31, 95% CI 0.11–0.84), without overexposing women to antibiotics[5]
  A prospective Australian study supports this.[1]
- In New Zealand, the obstetric risk-based strategy is generally recommended. [6, 7]
- The later in pregnancy (after 35 weeks gestation) that cultures are performed, the better the correlation with culture results at delivery (particularly within 5 weeks of delivery).[1,5,8]
- Detection of GBS is increased by up to 25% by collecting an anorectal swab in addition to a low vaginal swab.[4] A single swab may be used, provided the vagina is swabbed prior to the anorectal area. Samples may be obtained by the patient.
- Most mothers of neonates with late onset GBS disease are identified at diagnosis with anogenital GBS carriage.[9]
- IAP does not have an impact on late onset GBS disease[10]
- PCR based rapid tests may become the standard of care in labour because of their high sensitivity, specificity and rapid turnaround time. However, they are not yet available in routine practice in Australia. Moreover, data on currently available assays do not support their use in replacement of antenatal culture or risk-based assessment of women with unknown GBS status.[4]
- The obstetric factors listed are associated with increased risk for EOGBS.[3] However, 25-30% of cases are not associated with maternal risk factors.[3]
- Babies born to women with GBS bacteriuria (any colony count) during pregnancy are more frequently and more heavily colonised with GBS, increasing the risk of EOGBS.

GROUP B STREPTOCOCCUS – ALGORITHM 2

INTRAPARTUM ANTIBIOTIC PROPHYLAXIS (IAP) FOR PREVENTION OF EARLY ONSET NEONATAL GBS SEPSIS

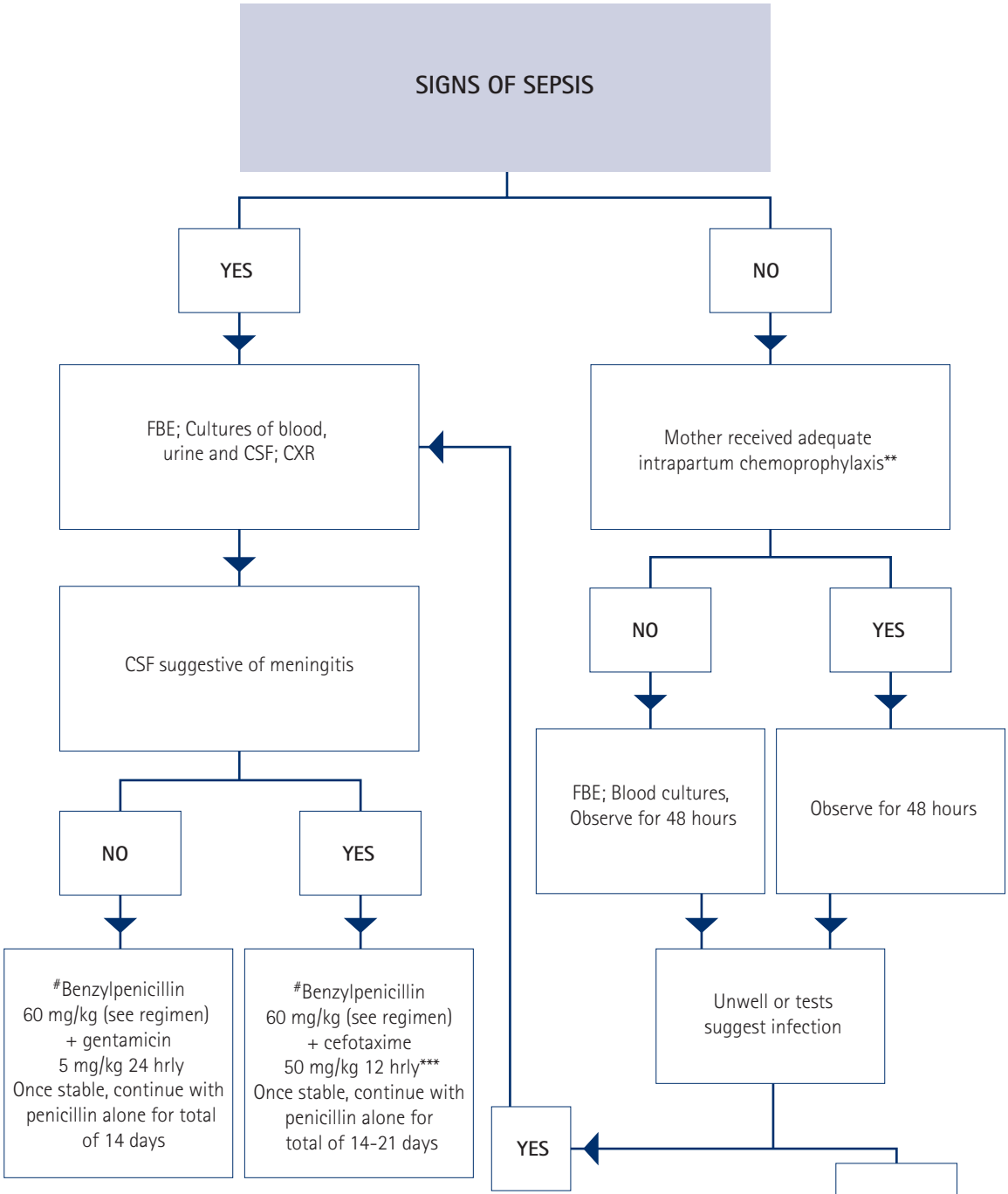


COMMENTS

- 90% of neonates with EOGBS have onset of signs within 12 hours of birth (suggesting intrauterine transmission), so intrapartum antibiotic prophylaxis is the most effective means of prevention.
- The rate of fatal maternal anaphylaxis to penicillin is estimated at 1 in 100 000. Less severe reactions occur in 7-10%.
- Clindamycin and erythromycin resistance amongst GBS is increasingly being reported (up to 20% and 30% respectively for invasive GBS isolates).[4, 8]
- Clindamycin and erythromycin susceptibility testing should be performed on prenatal GBS isolates from penicillin-hypersensitive women.
- Penicillin-hypersensitive women who do not have a history of anaphylaxis following administration of a penicillin or cefazolin should receive cefazolin 2 g IV loading dose, followed by 1 g IV 8 hourly.
- Women with penicillin hypersensitivity at high risk for anaphylaxis should receive clindamycin or vancomycin depending on susceptibility testing [4]
- Erythromycin is no longer an acceptable alternative
- Pathogens responsible for chorioamnionitis include GBS, anaerobic cocci, and enteric Gram-negative bacilli (often polymicrobial).

GROUP B STREPTOCOCCUS – ALGORITHM 3

MANAGEMENT OF INFANT AT RISK OF GBS SEPSIS*



#Benzylpenicillin 60 mg/kg, IV, 12 hourly for the first 7 days of life, then 6 hourly therafter

* Maternal GBS positive status or obstetric risk factors (spontaneous labour at <37 weeks or ROM >18 hours or maternal fever >38°C)
** Adequate intrapartum prophylaxis is defined as ≥4 hours of appropriate IV antibiotics
*** Ceftriaxone may be substituted for cefotaxime in neonates, unless premature or jaundiced.

COMMENTS

- GBS has been cultured from breast milk, but the role of infected breast milk in neonatal infection is uncertain. It is difficult to make concrete recommendations based on current available evidence.[11]

GROUP B STREPTOCOCCUS REFERENCES

1. Angstetra D, Ferguson J, Giles WB. Institution of universal screening for Group B streptococcus (GBS) from a risk management protocol results in reduction of early-onset GBS disease in a tertiary obstetric unit. Aust N Z J Obstet Gynaecol. 2007;47:378-82.
2. Trends in perinatal group B streptococcal disease – United States, 2000-2006. Centers for Disease Control and Prevention (CDC). MMWR Morb Mortal Wkly Rep. 2009;58:109-12.
3. Boyer KM, Gotoff SP. Prevention of early-onset neonatal group B streptococcal disease with selective intrapartum chemoprophylaxis. N Engl J Med. 1986;314:1665-9.
4. Prevention of Perinatal Group B Streptococcal Disease – Revised Guidelines from CDC, 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases. MMWR Recomm Rep. 2010;59(RR-10):1-36.
5. Hasperhoven GF, Al-Nasiry S, Bekker V, Villamor E, Kramer B. Universal screening versus risk-based protocols for antibiotic prophylaxis during childbirth to prevent early-onset group B streptococcal disease: a systematic review and meta-analysis. *Bjog* 2020; 127(6): 680-91.
6. Darlow B, Voss L, Lennon D, Grimwood K. Early-onset neonatal group B streptococcus sepsis following national risk-based prevention guidelines. Aust N Z J Obstet Gynaecol. 2016;56(1):69-74.
7. Darlow B, Campbell N, Austin N, Chin A, Grigg C, Skidmore C, Voss L, Walls T, Wise M, Werno A. The prevention of early-onset neonatal group B streptococcus infection: New Zealand Consensus Guidelines 2014. N Z Med J. 2015;128(1425):69-76.
8 Verani JR, Schrag SJ.Group B streptococcal disease in infants: progress in prevention and continued challenges. Clin Perinatol. 2010;37:375-92.
9. Berardi A, Rossi C, Lugli L, Creti R, Bacchi Reggiani ML, Lanari M, Memo L, Pedna MF, Venturelli C, Perrone E, Ciccia M, Tridapalli E, Piepoli M, Contiero R, Ferrari F; GBS Prevention Working Group, Emilia-Romagna. Group B streptococcus late-onset disease: 2003-2010. Pediatrics. 2013;131:e361-8.
10. Li S, Huang J, Chen Z, Guo D, Yao Z, Ye X. Antibiotic Prevention for Maternal Group B Streptococcal Colonization on Neonatal GBS-Related Adverse Outcomes: A Meta-Analysis. Front Microbiol. 2017;8:374.
11. Filleron A, Lombard F, Jacquot A, Jumas-Bilak E, Rodière M, Cambonie G, Marchandin H. Group B streptococci in milk and late neonatal infections: an analysis of cases in the literature. Arch Dis Child Fetal Neonatal Ed. 2014;99:F41–F47.

FURTHER READING

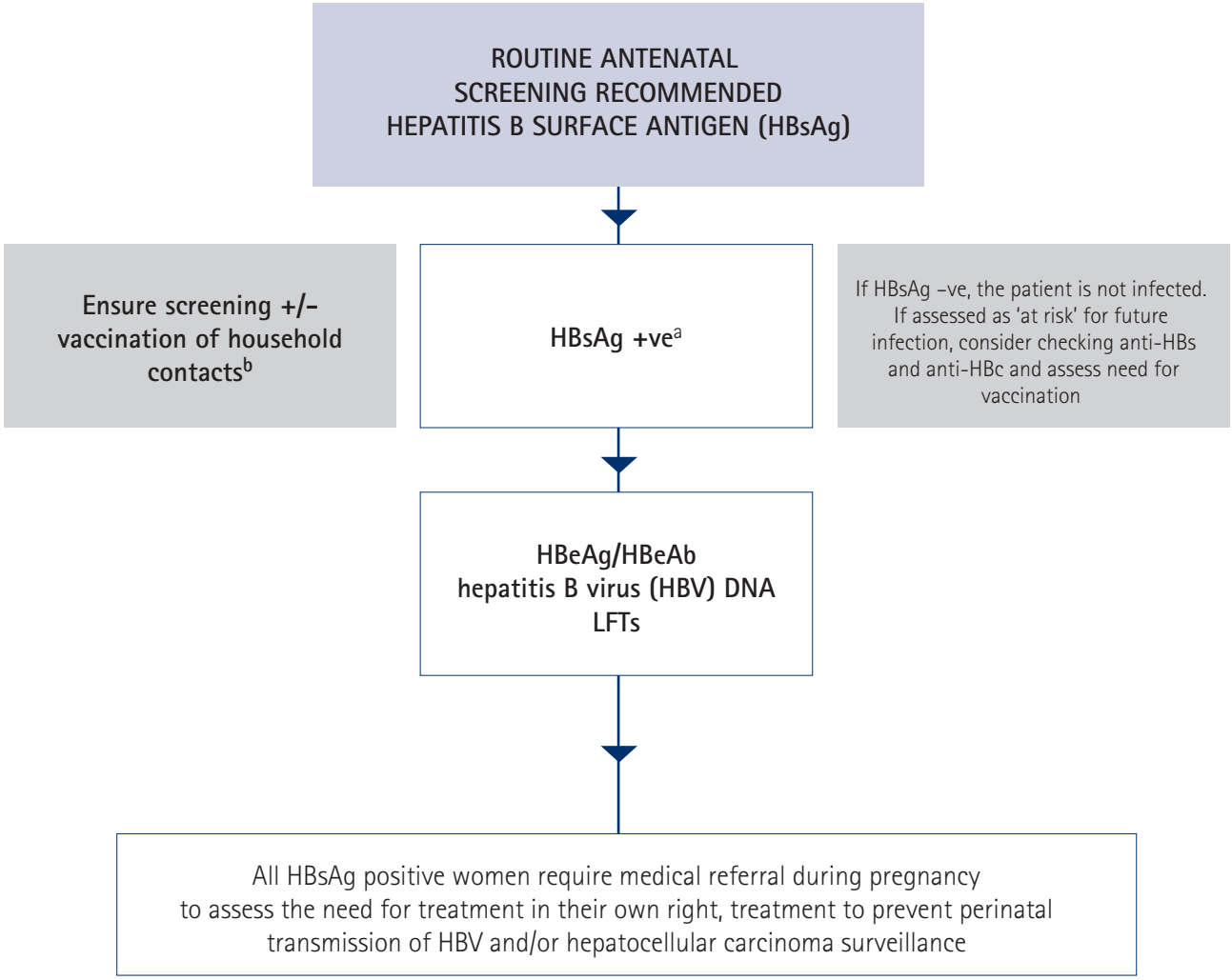
- Screening and Treatment for Group B Streptococcus in Pregnancy. RANZCOG College Statement: C-Obs 19. July 2019.
- Van Dyke MK, Phares CR, Lynfield R, Thomas AR, Arnold KE, Craig AS, Mohle-Boetani J, Gershman K, Schaffner W, Petit S, Zansky SM, Morin CA, Spina NL, Wymore K, Harrison LH, Shutt KA, Bareta J, Bulens SN, Zell ER, Schuchat A, Schrag SJ. Evaluation of universal antenatal screening for group B streptococcus. N Engl J Med. 2009;360:2626-36.
- Puopolo K, Lynfield R, Cummings J; Committee on Fetus and Newborn; Committee on Infectious Diseases. Management of Infants at Risk for Group B Streptococcal Disease. Pediatrics. 2019;144:e20191881.
- Vornhagen J, Adams Waldorf K, Rajagopal L. Perinatal Group B Streptococcal Infections: Virulence Factors, Immunity, and Prevention Strategies. Trends Microbiol. 2017;25:919-931.
- Madrid L, Seale A, Kohli-Lynch M, Edmond K, Lawn J, Heath P, Madhi S, Baker C, Bartlett L, Cutland C, Gravett M, Ip M, Le Doare K, Rubens C, Saha S, Sobanjo-Ter Meulen A, Vekemans J, Schrag S; Infant GBS Disease Investigator Group. Infant Group B Streptococcal Disease Incidence and Serotypes Worldwide: Systematic Review and Meta-analyses. Clin Infect Dis. 2017;65(suppl_2):S160-S172.
- Russell N, Seale A, O'Sullivan C, Le Doare K, Heath P, Lawn J, Bartlett L, Cutland C, Gravett M, Ip M, Madhi S, Rubens C, Saha S, Schrag S, Sobanjo-Ter Meulen A, Vekemans J, Baker C. Risk of Early-Onset Neonatal Group B Streptococcal Disease With Maternal Colonization Worldwide: Systematic Review and Meta-analyses. Clin Infect Dis. 2017;65(suppl_2):S152-S159.
- Hall J, Adams N, Bartlett L, Seale A, Lamagni T, Bianchi-Jassir F, Lawn J, Baker C, Cutland C, Heath P, Ip M, Le Doare K, Madhi S, Rubens C, Saha S, Schrag S, Sobanjo-Ter Meulen A, Vekemans J, Gravett M. Maternal Disease With Group B Streptococcus and Serotype Distribution Worldwide: Systematic Review and Meta-analyses. Clin Infect Dis. 2017;65(suppl_2):S112-S124.

Hepatitis B virus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

HEPATITIS B VIRUS – ALGORITHM 1

MATERNAL DIAGNOSIS AND ASSESSMENT

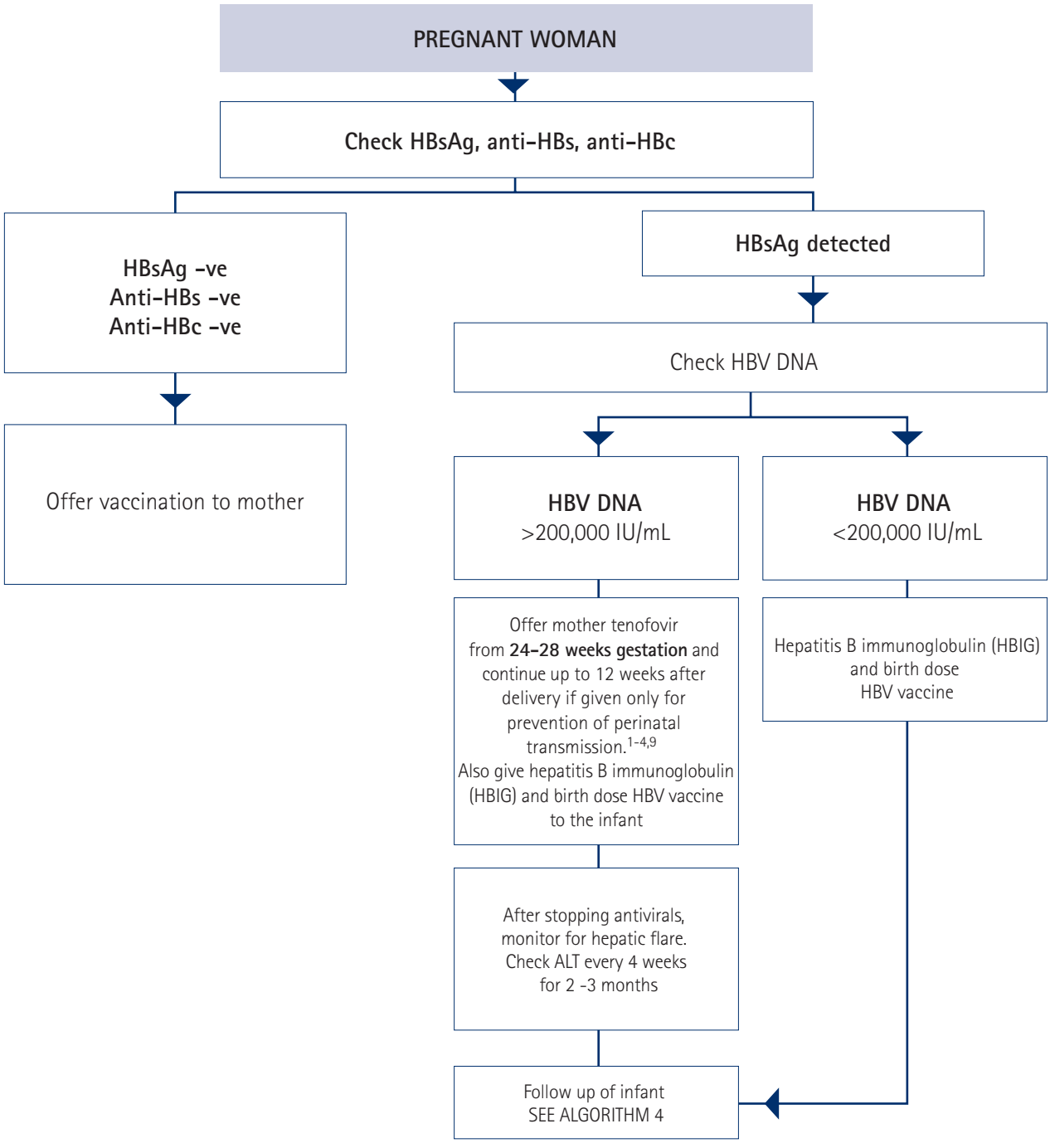


COMMENTS

a. Check maternal hepatitis A IgG. If non immune offer vaccination
b. Ensure screening of household contacts (HBsAg and anti-HBs) +/- vaccination as required

HEPATITIS B VIRUS – ALGORITHM 2

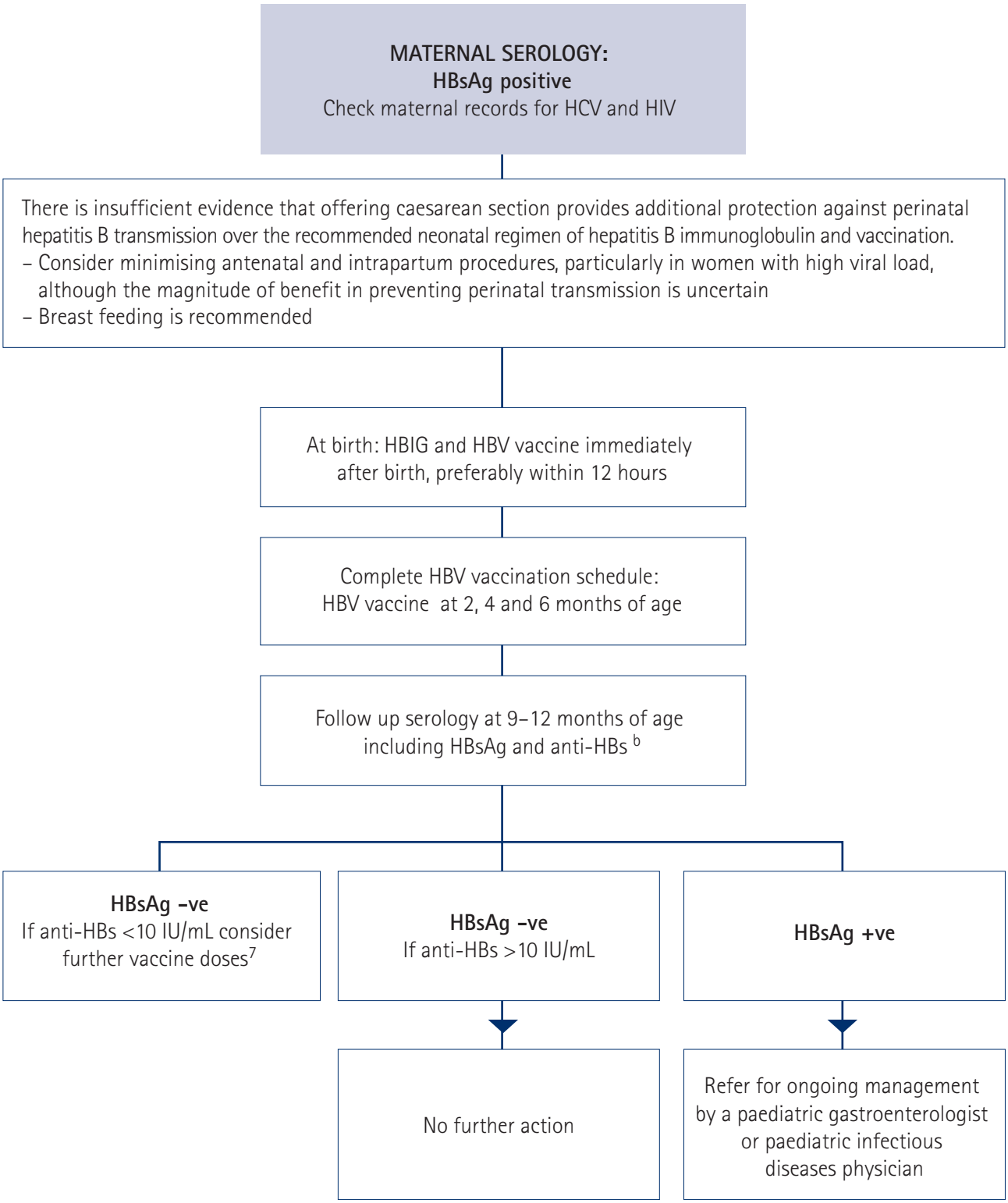
ANTENATAL MANAGEMENT OF HEPATITIS B INFECTION



Acute hepatitis B in pregnancy:
Acute hepatitis B in pregnancy is not associated with an increased risk of fulminant hepatitis or mortality. Lamivudine has been used in pregnant women with fulminant hepatic failure due to acute hepatitis B and also in women with an acute exacerbation of chronic hepatitis B during pregnancy[5,6] There are no data regarding optimal mode of delivery in acute hepatitis. The infant should receive HBIG (100 IU IM) immediately after birth, preferably within 12 hours and monovalent hepatitis B vaccine in the other limb at the same time. Do not delay beyond 7 days of life. [7]

HEPATITIS B VIRUS – ALGORITHM 3

NEONATAL DIAGNOSIS AND MANAGEMENT



COMMENTS

a. Low birth weight preterm newborn infants do not respond as well to hepatitis B containing vaccines as full-term infants. Thus, for low-birth-weight infants (<2000 gm) and/or infants born at <32 weeks gestation (irrespective of weight), it is recommended to give the vaccine in a 4-dose schedule at 0 (birth), 2, 4 and 6 months of age followed by either:
   - measuring the anti-HBs level at 7 months of age, and if the antibody titre is <10 IU/mL, giving a booster at 12 months of age (due to a better immunogenic response at this age compared with a younger age); or
   - giving a booster of a hepatitis B containing vaccine at 12 months of age (without measuring the antibody titre)

b. Test at least 2 months after last hepatitis B vaccine (transient hepatitis B antigenemia described after hepatitis B vaccine) [9]

HEPATITIS B REFERENCES

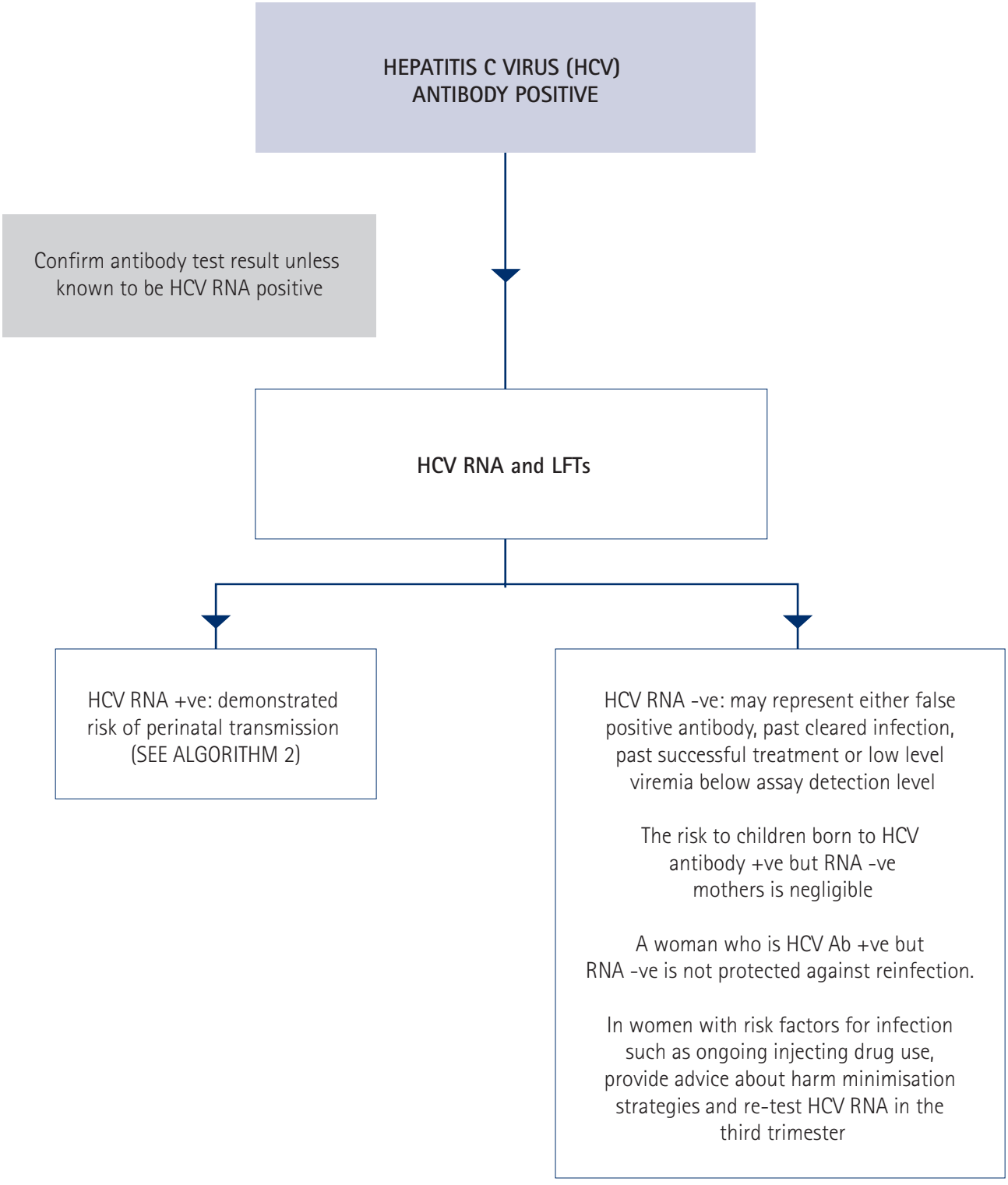
1. Pan CQ, Duan Z, Dai E, Zhang S, Han G, Wang Y, et al. Tenofovir to prevent hepatitis B transmission in mothers with high viral load. N Engl J Med 2016;374:2324–2334.
2. Jourdain G et al Tenofovir versus placebo to prevent perinatal transmission of Hepatitis B N Engl J Med 2018 Mar 8;378(10): 911-923
3. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection Journal of Hepatology 2017 Vol 67 370-398
4. Funk AL, Lu Y, Yoshida et al. Efficacy and safety of antiviral prophylaxis during pregnancy to prevent mother-to-child transmission of hepatitis B virus: a systematic review and meta-analysis Lancet Infect Dis 2022 Jan;21(1):70-84
5. Han YT et al Clinical features and outcomes of acute hepatitis B in pregnancy BMC Infectious Diseases 2014; 14:368
6. Hung JH et al. Lamivudine therapy in the treatment of chronic hepatitis B with acute exacerbation during pregnancy. J Chin Med Assoc 2008 71:155-8
7. Potthoff A et al. Successful treatment of fulminant hepatitis B during pregnancy. Z Gastroenterol 2009 47:667-70
8. The Australian Immunisation Handbook is now updated to online version https://immunisationhandbook.health.gov.au
9. Lubel JS, Strasser SI, Thompson AJ, et al. Australian consensus recommendations for the management of hepatitis B. *Med J Aust* 2022; 216(9): 478-86

Hepatitis C virus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

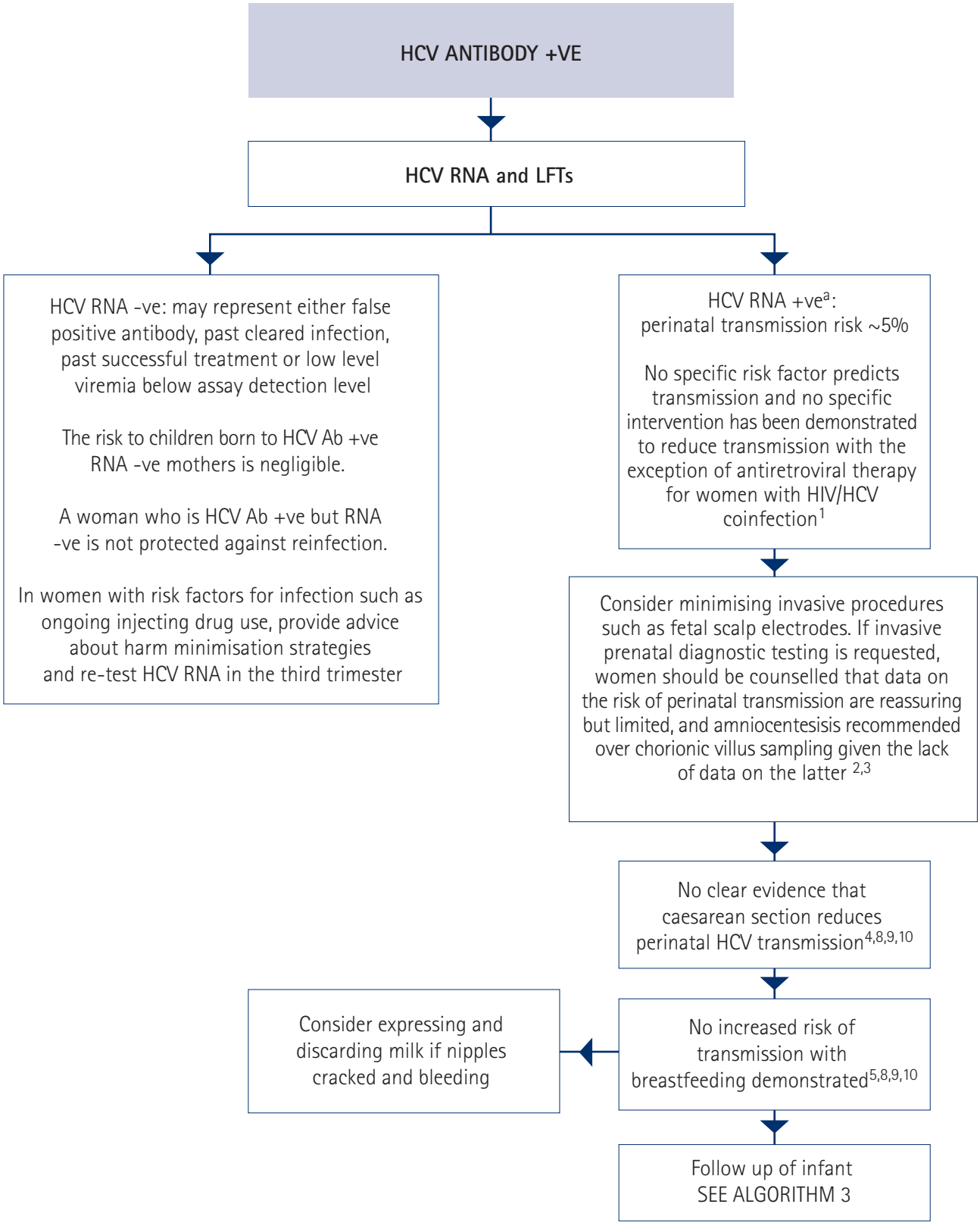
HEPATITIS C VIRUS – ALGORITHM 1

ANTENATAL DIAGNOSIS OF HEPATITIS C



HEPATITIS C VIRUS – ALGORITHM 2

ANTENATAL MANAGEMENT OF HEPATITIS C INFECTION



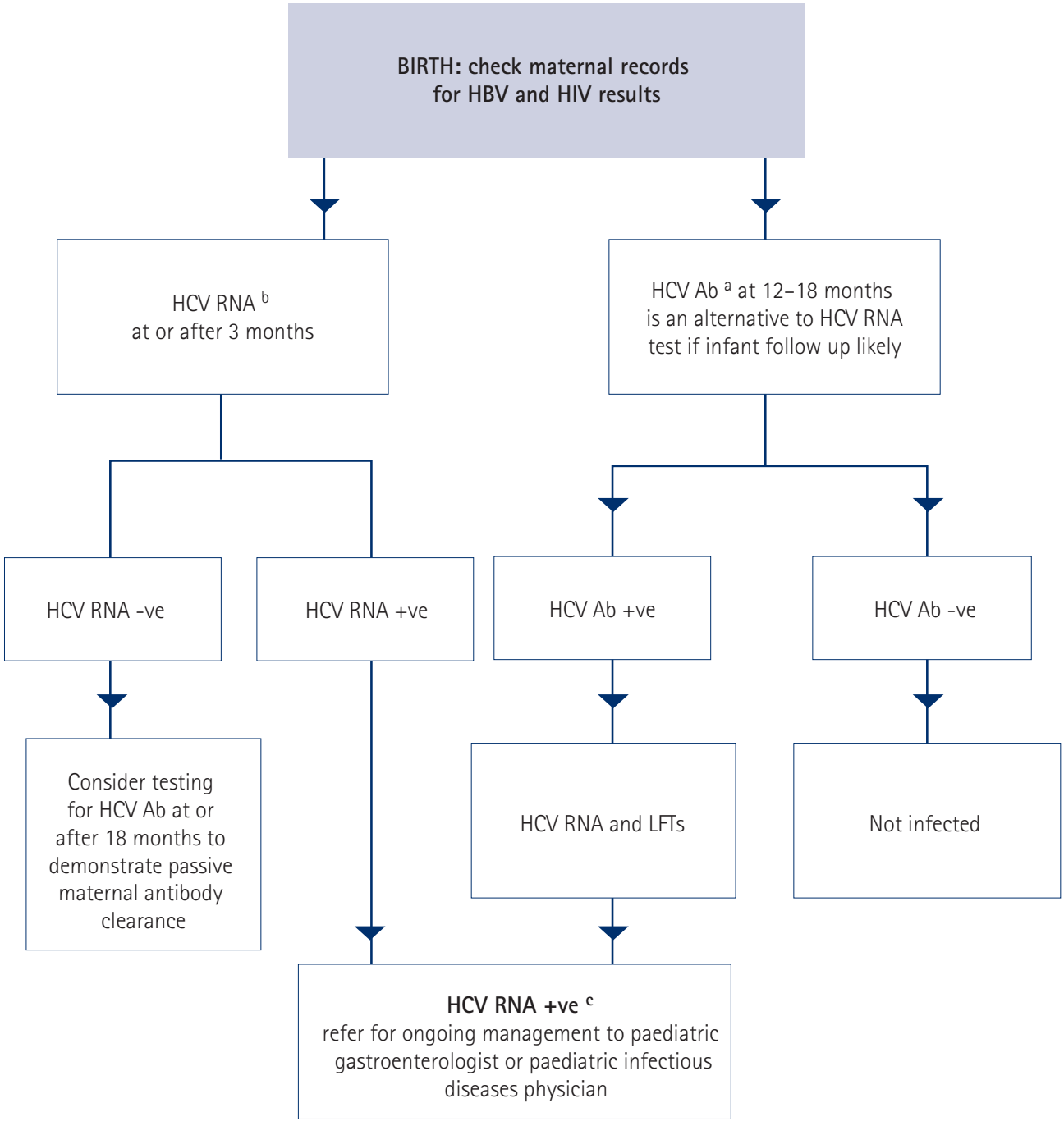
COMMENTS

a. Treatment during pregnancy and during breastfeeding with direct-acting antivirals (DAA) is currently contraindicated due to a lack of safety, efficacy and pharmacokinetic data. Women who become pregnant while on DAA therapy should discuss the risks versus benefits of continuing treatment with their physician. HCV RNA +ve women should be referred to an infectious diseases physician or gastroenterologist for consideration of treatment post partum

b. Data on fetal monitoring are conflicting, with some studies reporting an association with increased risk of HCV transmission and no associated risks in others [6,7]

HEPATITIS C VIRUS – ALGORITHM 3

MANAGEMENT AND FOLLOW UP OF INFANTS OF HEPATITIS C INFECTED MOTHERS



COMMENTS

a. Most uninfected infants are antibody negative by 12 months. In a prospective study on uninfected infants, anti-HCV antibodies were still present in 15% of infants at 12 months and 1% of infants at 24 months [6] If HCV antibody is still positive at 18 months, either repeat at 24 months to ensure clearance of maternal antibodies or perform a HCV RNA PCR before considering them infected

b. HCV RNA testing for the sole purpose of diagnosis of vertically transmitted HCV is not an approved item on the current Medicare Benefits Schedule

c. ~ 20% of HCV RNA +ve infants clear the infection at a median age of 15 months, with 80% having chronic infection.[11] Thus HCV RNA should be monitored beyond the second year of life to document persistence (chronic infection)

HEPATITIS C REFERENCES

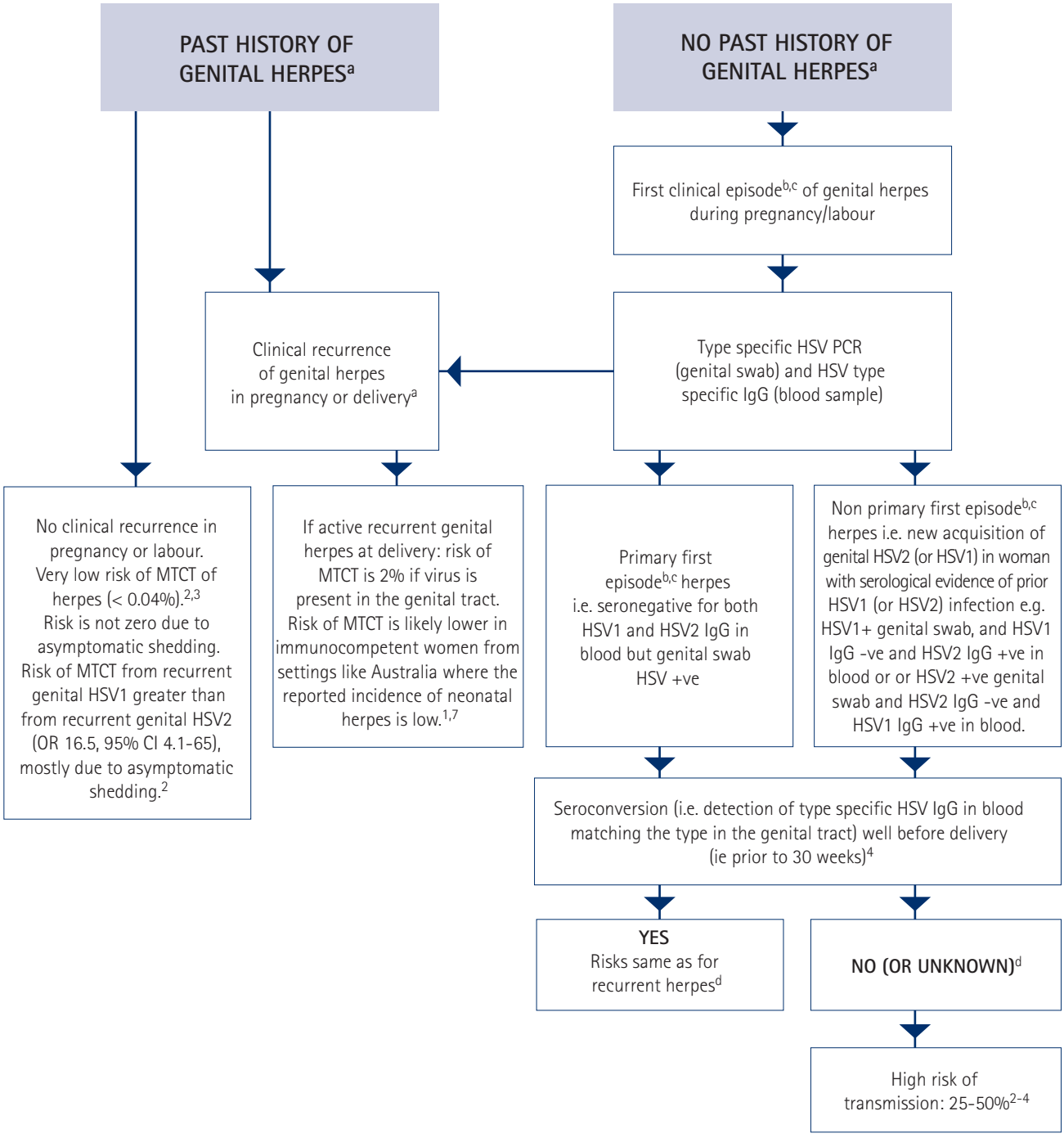
1. Checa-Cabot CA et al. Mother-to-child Transmission of Hepatitis C Virus (HCV) Among HIV/HCV-Co-infected Women. Journal of Pediatric Infectious Diseases Society 2013;2(2):126-135
2. Society for Maternal-Fetal Medicine; Hughes BL, Page CM, Kuller JA. Hepatitis C in pregnancy: screening, treatment and management. Society for Maternal-Fetal Medicine Consult Series #43 smfm.org
3. Gagnon A et al. Prenatal invasive procedures in women with hepatitis B, hepatitis C and or human immunodeficiency virus infections. J Obstet Gynaecol Can 2014;36:648-53
4. Ghamar Chehreh M et al. Effect of caesarean section on the risk of perinatal transmission of hepatitis C virus from HCV RNA+/HIV- mothers: a meta-analysis. Arch Gynecol Obstet 2011 283:255-260
5. European Paediatric Hepatitis C Virus Network. Effects of mode of delivery and infant feeding on the risk of mother-to-child transmission of hepatitis C virus. European Paediatric Hepatitis C Virus Network. BJOG 2001 108:371-7
6. Mast EE et al. Risk factors for perinatal transmission of hepatitis C virus (HCV) and the natural history of HCV infection acquired in infancy J Infect Dis 2005;192:1880-9
7. Garcia-Tejedor A et al Risk factors for vertical transmission of hepatitis C virus: a single center experience with 710 HCV-infected mothers Eur J Obstet Gynecol Reprod Biol 2015;194:173
8. European Pediatric Hepatitis C Virus Network. Effects of mode of delivery and infant feeding on the risk of mother-to-child transmission of hepatitis C virus Br J Obstet Gynaecol 2001;108:371
9. Benova L et al. Vertical transmission of hepatitis C virus: systematic review and meta-analysis. Clin Infect Dis 2014;59:765-73
10. Cottrell EB et al. Reducing risk for mother-to-infant transmission of hepatitis C virus: a systematic review for the US Preventive Services Task Force. Ann Intern Med 2013;158:109-13
11. European Paediatric Hepatitis C Virus Network. Three broad modalities in the natural history of vertically acquired hepatitis C virus infection. Clin Infect Dis. 2005;41(1):45-51

Herpes simplex virus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

HERPES SIMPLEX VIRUS (HSV) – ALGORITHM 1

GENITAL HSV IN PREGNANCY: RISK OF MOTHER TO CHILD TRANSMISSION (MTCT)



COMMENTS

a. In Australia, the reported incidence of neonatal HSV disease is very low (approx. 3 per 100,000 live births). The majority (>65%) of neonatal HSV infections are due to HSV1 and are acquired during delivery through an infected birth canal.[1] True intrauterine infection accounts for <5% of reported cases. Postnatal infection occurs in approximately 10% of cases from an infected care giver. Breast milk transmission has not been reported, but neonatal disease after contact with maternal breast herpes lesions has been reported

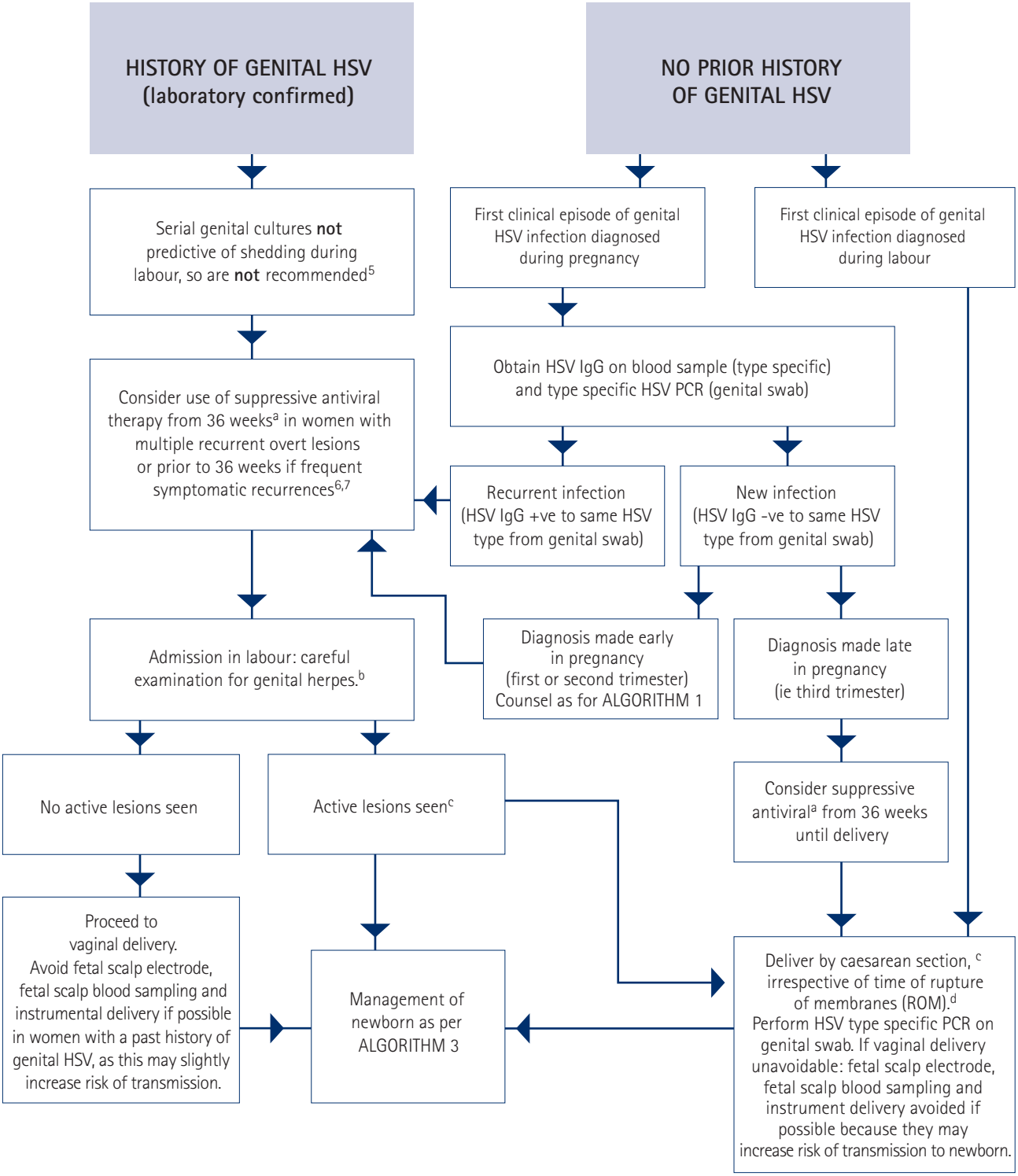
b. Most genital HSV infections (primary, non-primary or recurrent HSV1 or HSV2) are asymptomatic. i.e. most mothers of infants with neonatal HSV disease were previously unaware of their own infection before the baby's diagnosis[1 -4]

c. Primary first episode refers to new acquisition of either HSV serotype without prior exposure (i.e. neither HSV1 or HSV2 IgG detected in blood). Non primary first episode refers to new acquisition of the another HSV serotype, with evidence of exposure to the other type (i.e. HSV IgG +ve to the other serotype)

d. Risk of neonatal infection is determined by the type of maternal infection (primary versus recurrent), the presence of maternal type specific IgG, the use of devices that break skin integrity e.g. fetal scalp electrodes, fetal scalp blood sampling, or instrument delivery, the type of delivery (vaginal >caesarean section). If virus is detected in the genital tract, use of scalp electrodes increases risk of transmission (OR 6.8)[2] and caesarean delivery reduces risk of transmission (OR 0.14).[2,4] However, in clinical practice this is not often known at delivery

HERPES SIMPLEX VIRUS – ALGORITHM 2

MANAGEMENT OF GENITAL HSV IN PREGNANCY AND LABOUR



COMMENTS

a. Suppressive oral aciclovir 400 mg po tds or valaciclovir 500 mg po bd reduces clinical recurrences, asymptomatic shedding, rate of caesarean section and virus in genital tract. Use must be balanced with risks of medication to newborn[6,7]. Clinical trials underpowered to evaluate efficacy of preventing transmission to the newborn[6,7] and neonatal disease has been reported after maternal suppression [8]

b. Most women are unaware of geniral herpes (recurrent or acute). Therefore the Royal Australia and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) recommend careful examination for genital herpes for all women when admitted in labour.

c. Caesarean section reduces risk of HSV transmission in women shedding HSV at the time of birth, but does not provide complete protection against neonatal HSV disease. [1, 2] The low risk of MTCT of HSV after vaginal delivery in women with recurrent genital herpes lesions need to be balanced against the risks of caesarean section.

d. Caesarean section is still recommended if ROM has already occurred, and genital lesions are present. Data from 50 years ago suggesting reduced benefit if ROM >4 h is not high quality.

HERPES SIMPLEX VIRUS – ALGORITHM 3

MANAGEMENT OF ASYMPTOMATIC NEONATE BORN TO MOTHER WITH ACTIVE GENITAL HERPES[a] AT DELIVERY

ASYMPTOMATIC INFANT WITH VERY LOW RISK OF HSV EXPOSURE AND DISEASE (< 2% in Australia)[2,7]

– Mother with active recurrent genital herpes due to HSV2 at delivery, or
– Mother who had primary genital HSV2 and who has now developed HSV type specific IgG

The predictive value of surface swabs has not been shown in settings where the incidence of neonatal herpes is low, like in Australia. [9] The consensus view in Australia, NZ and the UK (in contrast to the US) [16] is that collection of surface swabs from well babies born to mothers with recurrent genital herpes is not indicated.[b] All families should monitor the baby closely for symptoms and signs of HSV disease.[c]

Newborn develops symptoms and signs (see Algorithm 4) of clinical disease while monitored. Investigate for HSV disease as shown.

ASYMPTOMATIC INFANT WITH POSSIBLE HIGH RISK OF EXPOSURE AND HSV DISEASE(~25–57%)[8,9]

– Mother with primary genital or systemic infection close to delivery, or
– Infant born to mother with active genital herpes and no known past history of genital HSV, or
– Preterm infant born to mother with active genital herpes, or
– Infant born to immunocompromised mother with active genital herpes

Perform:
- LP (CSF analysis, viral culture HSV PCR)
- FBE (for low platelets),
- LFTs
- HSV PCR on blood (if available)
- Surface swabs - eye, throat, umbilicus, rectum, urine (if not collected already), skin vesicle[9]

Commence IV aciclovir immediately. The duration will depend on surface culture and CSF results

ACICLOVIR 20 mg/kg IV over 1–2 hours, 8 hourly[10]
- Laboratory confirmed infection or clinical disease confined to skin, eye, mouth: 10-14 days
- Encephalitis, disseminated disease: 21 days
- Pre-emptive therapy for high risk asymptomatic infant with HSV confirmed on surface swab, but CSF and blood PCR negative and CSF and LFTs normal: 10 days.[13]

CSF HSV PCR positive:
Some experts advise to repeat LP and HSV PCR towards end of treatment to confirm clearance of viral DNA[15]. Not all experts advise this routinely as the value of an end of therapy HSV CSF PCR test after 21 days of aciclovir with clinical response has not been demonstrated. If performed and the HSV PCR remains positive, extend treatment duration or consider alternate antiviral agent e.g. foscarnet.

All cases of laboratory confirmed infection

SEE ALGORITHM 4

COMMENTS

a. This algorithm is for use in settings where the prevalence of genital herpes and neonatal HSV disease is low. It does not refer to asymptomatic infants born to mothers with a history of genital herpes but no active lesions at delivery
b. Experts from the US, where the prevalence of genital and neonatal HSV disease is higher, recommend surface swabs on well infants after possible exposure to HSV [10,11]
c. Monitor for skin, eye, mouth disease, lethargy/irritability, poor feeding

HERPES SIMPLEX VIRUS – ALGORITHM 4

HSV INFECTIONS IN PREGNANCY: NEONATAL MANAGEMENT

Signs of congenital (*in utero*) HSV
Triad of:
Skin - (active herpes, scarring, pigmentation changes)
CNS - (microcephaly, intracranial calcifications)
Eye - (chorioretinitis, optic atrophy, microphthalmia)

Newborn develops symptoms or signs of HSV disease

- Vesicular skin lesions or atypical pustular or bullous lesions, especially on presenting part (note: may be absent)
- Seizures
- Unexplained sepsis with -ve blood cultures not responding to antibiotics
- Low platelets
- Elevated LFTs
- DIC (Disseminated intravascular coagulation (DIC))
- Respiratory distress (after day 1 of life)
- Corneal ulcer/keratitis

Perform:

- LP (CSF analysis, viral culture, HSV PCR)
- FBE (for low platelets)
- LFTs
- HSV PCR on blood (if available). A positive blood HSV PCR implies infection but does not imply disseminated disease.[13]
- Surface swabs - eye, throat, umbilicus, rectum, urine (if not collected already), skin vesicle[9]

Commence IV aciclovir immediately from birth (for suspected HSV disease). Duration will depend on surface culture and CSF results

ACICLOVIR 20 mg/kg IV over 1–2 hours, 8 hourly[11]

- Laboratory confirmed infection or clinical disease confined to skin, eye, mouth: 10-14 days
- Encephalitis, disseminated disease: 21 days
- Pre-emptive therapy for high risk asymptomatic infant with HSV confirmed on surface swab, but CSF and blood PCR negative and CSF and LFTs normal: 10 days.[13]

CSF HSV PCR positive:

Some experts advise to repeat LP and HSV PCR towards end of treatment to confirm clearance of viral DNA.[15] Not all experts advise this routinely as the value of an end of therapy HSV CSF PCR test after 21 days of aciclovir with clinical response has not been demonstrated. If performed and the HSV PCR remains positive, extend treatment duration or consider alternate antiviral agent e.g. foscarnet.

All cases of laboratory confirmed infection[b]

Infected infants should be monitored closely for recurrences, eye disease, hearing impairment and neurological sequelae.

ACICLOVIR TO PREVENT CNS SEQUELAE

Neonatal HSV CNS disease +/– disseminated infection.[11] *Recommended for all infants with HSV encephalitis* - Oral aciclovir (300 mg/m^2 BSA/ dose = approximately 20 mg/kg, three times daily) for 6 months after completion of IV treatment shown to improve CNS outcomes (data mostly from HSV2 CNS disease).[12]

Skin, eye, mouth or disseminated infection without CNS involvement: Some experts also recommend oral aciclovir to suppress troublesome cutaneous recurrences after skin, eye, mouth disease or to reduce early reactivation after all forms of disease in any infant; or in very preterm infants. This is not routinely recommended as it has not been shown to alter neurological outcome.[12]

COMMENTS

a. Oral aciclovir therapy **is not** recommended for therapeutic or pre-emptive treatment of HSV in the neonates. The role of oral valaciclovir has not been evaluated in this context

b. There are few data to guide management of herpes recurrences after neonatal HSV disease. Most experts recommend performing investigations for HSV disease including LP and HSV PCR and treating empirically with IV aciclovir for the following: herpes recurrence (any site) in infants under 3 months; herpes recurrence (any site and any age) after previous neonatal encephalitis, presentation at any age with neurological signs +/- fever

HERPES SIMPLEX VIRUS REFERENCES

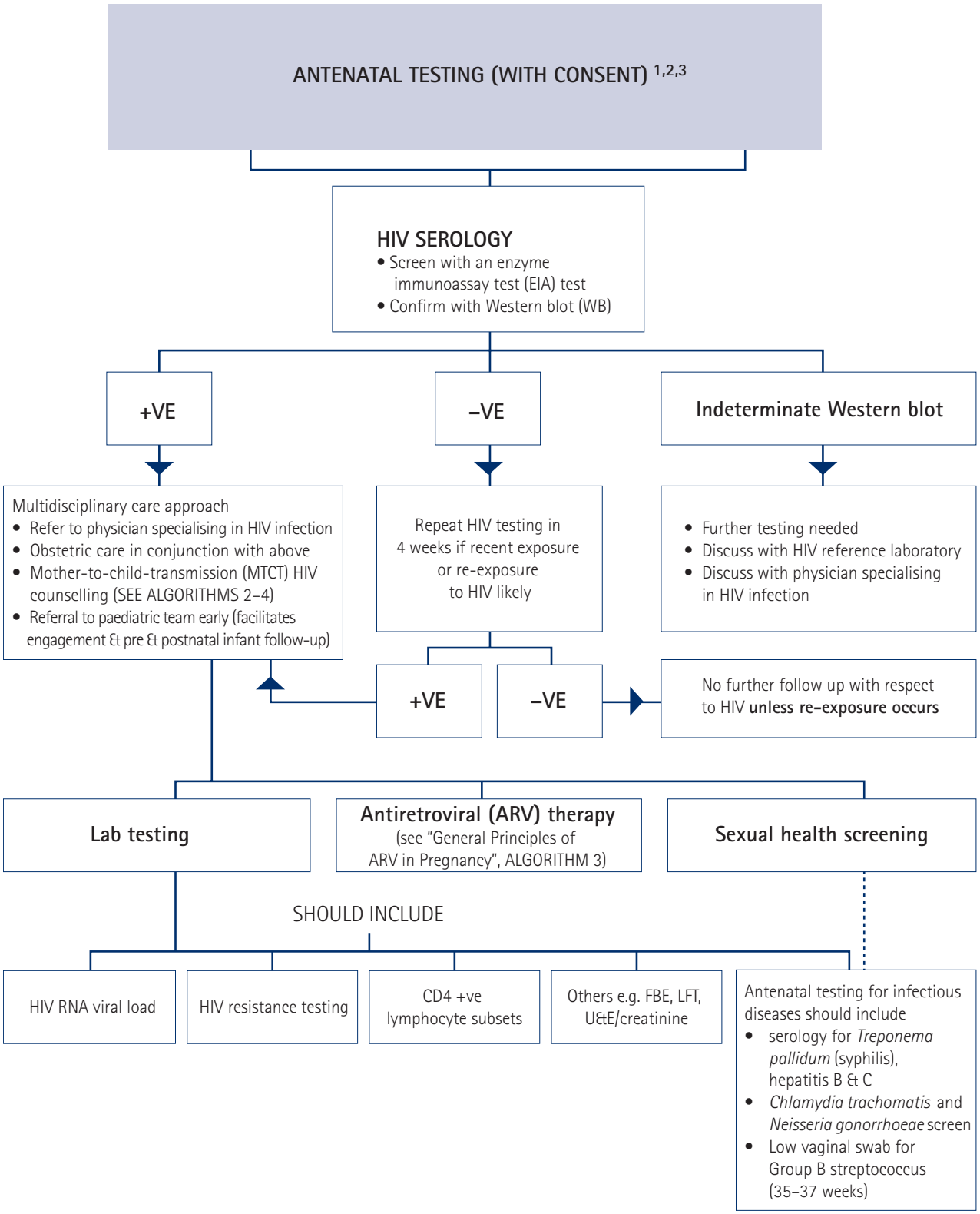
1. Jones CA, Raynes Greenow C, Isaacs D, on behalf of APSU HSV study team and contributors. Population-based surveillance of neonatal HSV infection in Australia (1997-2011). Clin Infect Dis. 2014 Aug 15;59(4):525-31.
2. Brown ZA, Wald A, Morrow RA, Selke S, Zeh J, Corey L. Effect of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant JAMA.289(2):203-9, 2003.
3. Brown ZA, Benedetti J, Ashley R, et al. Neonatal herpes simplex virus infection in relation to asymptomatic maternal infection at the time of labour. New Engl J Med, 1991; 324: 1247-52.
4. Brown ZA, Selke A, Zeh J et al. The acquisition of herpes simplex virus during pregnancy. New Engl J Med, 1997; 337: 509-15.
5. Arvin AM, Hensleigh PA, Prober CG et al. Failure of antepartum maternal cultures to predict the infant's risk of exposure to herpes simplex virus at delivery. New Engl J Med, 1986; 315: 796-800.
6. Hollier LM, Wendel GD.Third trimester antiviral prophylaxis for preventing maternal genital herpes simplex virus (HSV) recurrences and neonatal infection. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD004946. doi: 10.1002/14651858.CD00494
7. Sénat MV, Anselem O2, Picone O3. Prevention and management of genital herpes simplex infection during pregnancy and delivery: Guidelines from the French College of Gynaecologists and Obstetricians (CNGOF). Eur J Obstet Gynecol Reprod Biol. 2018 May;224:93-101.
8. Pinniniti S et al. Neonatal Herpes Disease following Maternal Antenatal Antiviral Suppressive Therapy: J Pediatr 2012; 161: 134-138
9. Berkout A, Nourse, C, Jones CA, Kappor V, Heney C, Lai, M. Herpes simplex virus infection in infants - 13 year evaluation (2005-2017) of labroatory confirmed cases in Queensland Australia. The Pediatric Infectious Disease Journal, 40(3), 209-214 - November 2020 https://doi.org/10.1097/inf.0000000000002970
10. Kimberlin DW, Lin CY, Jacobs RF, et al. Safety and efficacy of high-dose intravenous acyclovir in the management of neonatal herpes simplex virus infections. National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. Pediatrics 2001;108:230-8.
11. James SH, Sheffield JS, Kimberlin DW. Mother-to-Child Transmission of Herpes Simplex Virus. J Pediatric Infect Dis Soc. 2014;3(Suppl 1):S19-23.
12. Kimberlin DW, Whitley RJ, Wan W et al. Oral Acyclovir Suppression and Neurodevelopment after Neonatal Herpes. N Engl J Med 2011;365:1284-92.
13. Kimberlin DW, Bailey J, Guidance on Management of Asymptomatic Neonates Born to Women With Active Genital Herpes Lesions Pediatrics 2013;131 e635-e646.
14. Kimberlin DW, Lakeman FG, Arvin AM et al.Application of the polymerase chain reaction to the diagnosis and management of neonatal herpes simplex virus disease. National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group J Infect Dis, 174 (1996), pp. 1162-1167
15. Kimberlin DW, Lin CY, Jacobs RF et al. Natural history of neonatal herpes simplex virus infections in the acyclovir era Pediatrics, 108 (2001), pp. 223-229
16. Royal College of Obstetricians and Gynaecologists. Management of genital herpes in pregnancy 2014. www.rcog.org.uk/globalassets/documents/guidelines/management-genital-herpes.pdf;

Human immunodeficiency virus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

HUMAN IMMUNODEFICIENCY VIRUS (HIV) – ALGORITHM 1

DIAGNOSIS OF HIV INFECTION IN PREGNANCY

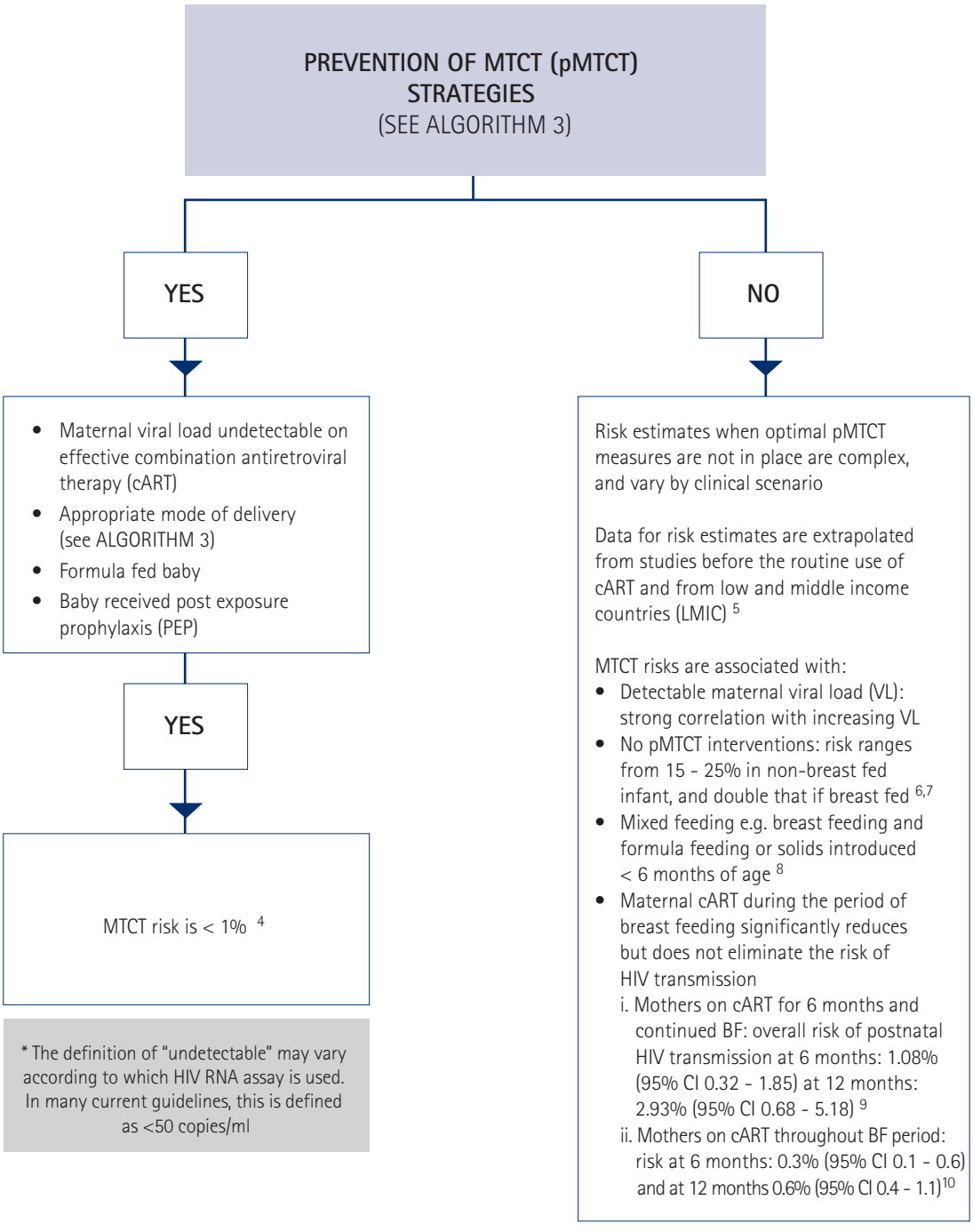


COMMENTS

a. Antenatal testing for HIV is recommended to allow for the opportunity to implement MTCT prevention strategies

HUMAN IMMUNODEFICIENCY VIRUS – ALGORITHM 2

MOTHER-TO-CHILD-TRANSMISSION (MTCT) HIV RISK ASSESSMENT



COMMENTS

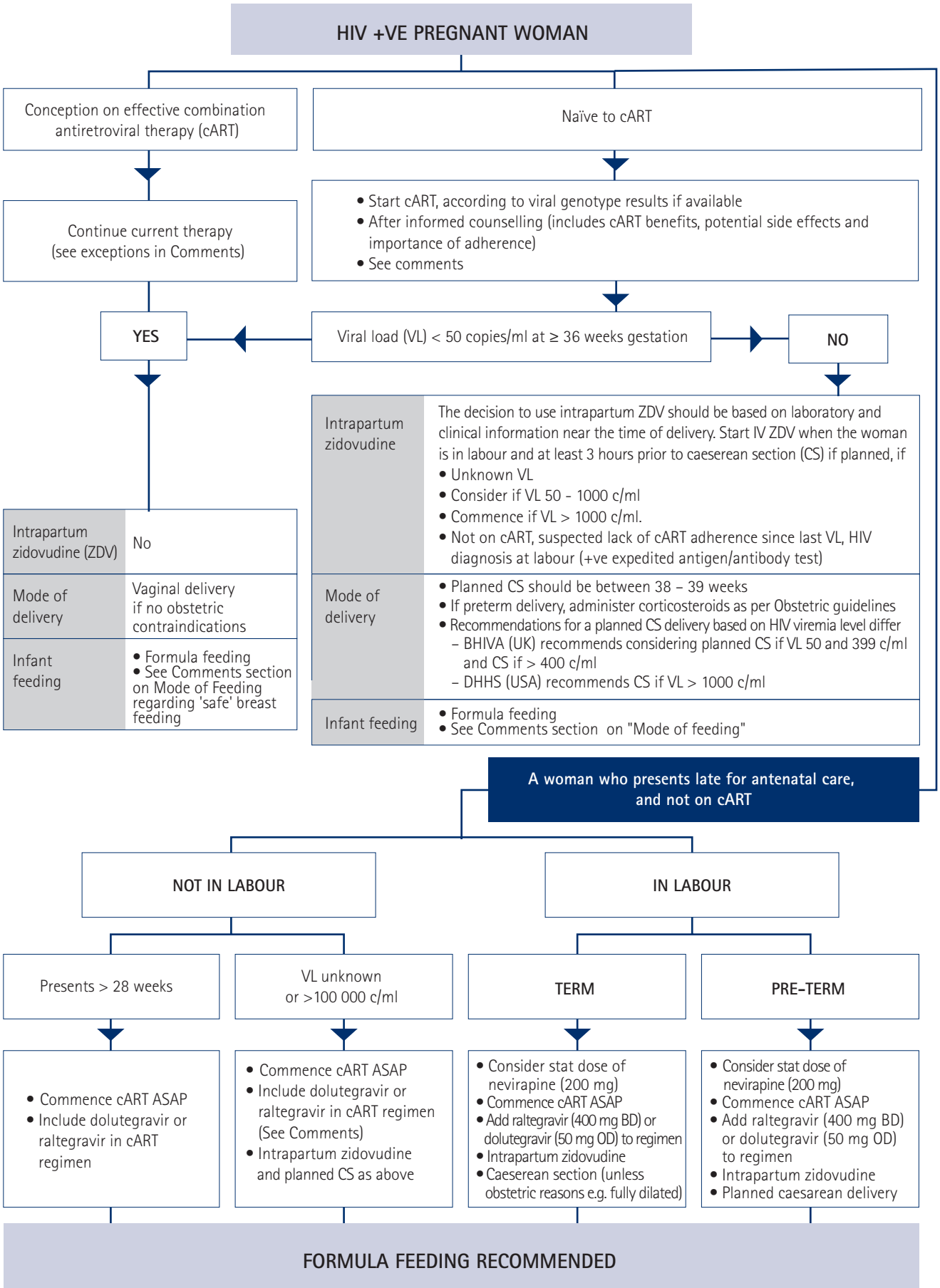
a. Perinatal counselling should include
   - MTCT risks
   - strategies to prevent transmission (SEE ALGORITHM 3)
   - management of baby at birth, including ARV prophylaxis (ALGORITHM 4)
   - testing schedule and clinical follow-up of baby (ALGORITHM 4)

b. The approach should be multi-disciplinary (HIV care team, obstetric and midwifery/ward and paediatric team, and psychosocial supports)

c. A "Care Plan" that includes the antenatal, peripartum and post-natal management of the pregnancy, delivery and infant is recommended

HUMAN IMMUNODEFICIENCY VIRUS – ALGORITHM 3

STRATEGIES TO MINIMISE MTCT HIV



HUMAN IMMUNODEFICIENCY VIRUS – ALGORITHM 3

STRATEGIES TO MINIMISE MTCT HIV

COMMENTS

- All women should have commenced cART by 24 weeks. Earlier virologic suppression is associated with a lower risk of HIV transmission to fetus
- Guidance on the use of antiretroviral therapy in pregnancy is available on the Department of Health and Human Services (DHHS), USA and the British HIV Association (BHIVA), UK sites and are constantly updated. Commentary is provided to the DHHS guidelines by ASHM (Australian Society for HIV Medicine) Minor variations in practice exist, but the principles concur
  1. Department of Health and Human Services (DHHS), USA https://clinicalinfo.hiv.gov/en/guidelines/perinatal/whats-new-guidelines [11]
  2. British HIV Association (BHIVA) https://www.bhiva.org/file/5f1aab1ab9aba/BHIVA-Pregnancy-guidelines-2020-3rd-interim-update.pdf [12]
  3. ASHM commentary, DHHS Guidelines https://arv.ashm.org.au
- If on a once daily raltegravir regimen (1200 mg once daily (OD)), dosing should be changed to 400mg twice daily (BD)
- Preliminary concerns about increased risks of neural tube defects (NTD) with dolutegravir (DTG) in the periconceptional period have been revised based on the estimated rate of ~ 2:1000 NTD with peri-conceptional DTG which is not dissimilar to that reported with other anti-retrovirals in pregnancy. Once daily DTG is well tolerated and produces durable viral suppression
  Recommendations differ:
  DHHS
  – Recommends DTG as the 'Preferred ARV' irrespective of trimester or women trying to conceive (based on risk vs. benefits, like quicker viral suppression)
  – The recommendation for folic acid use in pregnancy is emphasised. The dosing is as for any other pregnancy where there are no / NTD risk factors (at least 400 mcg/day)
  BHIVA
  – Recommends not starting DTG if planning conception or if ≤ 6 weeks gestation
  – If already on DTG and < 6 weeks, swap to another ARV (e.g. efavirenz or atazanavir)
  – Continue if > 6 weeks post conception
  – High dose folic acid (5 mg, once daily) is recommended if on DTG and trying to conceive, or in the first trimester
- Once cART is commenced, the recommendation is to continue cART life long
- Nevirapine, raltegravir and tenofovir readily cross the placenta and are added to 'pre-load' the fetus prior to delivery in late presenters.
- Intrapartum zidovudine: 2 mg/kg, intravenously, for the first hour, then follow by a continuous infusion at 1 mg/kg/hour
- **Mode of feeding**
  - Formula feeding is recommended as this ensures there is no further risk for HIV transmission. Affordable and safe access to formula is an important part of the plan and should be addressed prior
  - In recognition of circumstances where a woman may wish to breast feed, a supportive and transmission risk reduction approach, working openly together with the mother is supported and outlined inthe BHIVA, (the 2020 third interim update https://www.bhiva.org/pregnancy-guidelines) and the Australasian Society for HIV Medicine (ASHM) BF Guidance document https://ashm.org.au/resources/the-optimal-scenario-context-of-care-guidance-for-healthcare-providers-regarding-infant-feeding-options-for-people-living-with-hiv/
  - This is a complex area and multi-disciplinary approach with optimal supports for the mother and baby is recommended (includes HIV specialist, paediatric HIV team, lactation consultant, social supports)
  - The optimal scenario for 'safe breast feeding' includes strong maternal engagement with health care, strong adherence to cART and suppressed maternal VL, continuing maternal cART during breast feeding, exclusive breast feeding ≤ 6 months, avoiding mixed feeding (giving both breast and formula milk), or solids before 6 months of age, attention to breast health and avoiding breast milk from both breasts during any episode of mastitis (use stored expressed breast milk during this time or formula feed; once formula feeding is commenced, breast feeding should not be recommenced), and suspending breast feeding if the mother has gastroenteritis (as ARVs may not be absorbed optimally) and use stored EBM or formula feed. If the infant has gastroenteritis, stop breast feeding and formula feed. Note that once formula feeding is commenced, breast feeding should not recommence
  - 1 - 2 monthly maternal and baby clinic visits for viral load monitoring is recommended to ensure viral load suppression is maintained
  - HIV testing of the baby should include an HIV PCR test 2 months after cessation of breast feeding

HUMAN IMMUNODEFICIENCY VIRUS – ALGORITHM 4

MANAGEMENT OF INFANT AT RISK OF MTCT HIV [11,12]

ASSESSMENT AT BIRTH

CLINICAL

- Clinical examination, growth parameters & neurodevelopmental assessments
- Routine childhood immunisation as per the Australian National Immunisation Program (NIP)* or the NZ childhood immunisation programme**

"HIV exposed uninfected children" (HEUC): follow-up, at least for the first 5 years, uninfected infants to determine any health or developmental issues

LABORATORY TESTING

HIV RNA or HIV DNA PCR

- An HIV antibody test should not be used for diagnosis in infants < 18 months of age (transplacentally acquired maternal HIV antibodies can persist till this age)
- See table below for timing of tests

ANTIRETROVIRAL POST EXPOSURE PROPHYLAXIS (PEP)

Duration of PEP by MTCT risk stratification

VERY LOW RISK

- Maternal cART > 10 weeks.
- At least 2 maternal VL <50 c/mL during pregnancy, ≥ 4 weeks apart
- With one VL <50 copies/mL at ≥ 36 weeks gestation

→ 2 weeks zidovudine monotherapy
- Start within 4 hours of delivery

LOW RISK

- Maternal VL <50 copies/mL at ≥ 36 weeks gestation
- Other 'low risk' criteria not met OR
- Infant born < 34 weeks gestation and most recent maternal VL < 50 c/ml

→ 4 weeks zidovudine monotherapy
- Start within 4 hours of delivery

HIGH RISK

- Maternal HIV VL at delivery anticipated to be or documented > 50 c/ml or unknown
- Uncertainty about recent maternal adherence to cART

→ Triple ARV
- Zidovudine + lamivudine (4 weeks) + 2 weeks nevirapine (Table 1)

Pneumocystis jirovecii pneumonia (PJP) prophylaxis is not required unless HIV infection is confirmed

Testing and clinical follow up

TIME OF TEST (AGE)	TEST	
	PCR: either proviral PCR or HIV RNA PCR	HIV Antibody
First week, <48 hours ideally	+	Recommended at 18 months to demonstrate clearance of maternal HIV antibodies and exclude late infection (rare)[a]
6 weeks	+	
3 months	+	
6 months	-	
12 months	-	
18 months	-	

Is recommended

- Any positive PCR must be confirmed with a repeat sample
- Clinical review at all above time points
- Routine childhood immunisations as per Australian National Immunisation Program schedule

[a] An added benefit of the 18 month review is the opportunity for a baby review where emergent paediatric concerns may be identified

* https://www.health.gov.au/health-topics/immunisation/when-to-get-vaccinated/national-immunisation-program-schedule#national-immunisation-program-schedule-from-1-july-2020
** https://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/new-zealand-immunisation-schedule

HUMAN IMMUNODEFICIENCY VIRUS – ALGORITHM 4

MANAGEMENT OF INFANT AT RISK OF MTCT HIV [11,12]

Table 1: Neonatal ARV Dosing [Start within 4 hours of birth] [11,12, 14]

<table>
<tr><th>DRUG NAME</th><th colspan="6">DOSE</th></tr>
<tr><td>Zidovudine</td><td colspan="3">ORAL (Paediatric formulation)
(concentration: 10 mg/ml)</td><td colspan="3">INTRAVENOUS
(concentration: 10 mg/ml)</td></tr>
<tr><td rowspan="5">Dosing from the Australasian Neonatal Medicines Formulary (Neomed).[14] adapted from BHIVA[12]</td><td>Gestation at birth</td><td>Dose*</td><td>Interval</td><td>Gestation at birth</td><td>Dose*</td><td>Interval</td></tr>
<tr><td>< 30 weeks</td><td>2 mg/kg/dose</td><td>12 hourly</td><td>< 33 +6 weeks</td><td>1.5 mg/kg/dose</td><td>12 hourly</td></tr>
<tr><td>30+0- 33+6 weeks</td><td>2 mg/kg/dose</td><td>12 hourly for 2 weeks, and then 8 hourly</td><td>≥34 weeks</td><td>1.5 mg/kg/dose</td><td>6 hourly</td></tr>
<tr><td>≥34 weeks</td><td>4 mg/kg/dose</td><td>12 hourly</td><td colspan="3" rowspan="2">- *round up to the nearest 0.5 mg to assist administration
- Switch to oral once tolerating oral feeds</td></tr>
<tr><td colspan="3">*round up to the nearest 0.5 mg to assist administration</td></tr>
<tr><td>Lamivudine (3TC)
Oral solution concentration: 10 mg/ml</td><td colspan="6">• 2mg/kg/dose, 12-hourly</td></tr>
<tr><td>Nevirapine (NVP)
Oral suspension concentration: 10 mg/ml</td><td colspan="6"><u>No maternal NVP in the peripartum period</u>
• 2 mg/kg/dose, once daily for first week
• 4 mg/kg/dose, once daily for second week
• Stop after week 2 (NB: "tail" of AZT + 3TC needs to continue after for 2 weeks)
<u>If mother has had >3 days of antenatal NVP</u>
• 4 mg/kg/dose, once daily for 2 weeks (NB: "tail" of AZT +3TC needs to continue after for 2 weeks)

NVP has a long half-life. This regimen allows for a 2 week "tail" cover with the other 2 ARVs (AZT + 3TC)</td></tr>
<tr><td colspan="7">NOTE: Lopinavir/ritonavir (Kaletra) is contraindicated in term newborns ≤14 days old or in premature babies until ≥14 days past their due date (due to reports of adrenal dysfunction).</td></tr>
</table>

HUMAN IMMUNODEFICIENCY VIRUS REFERENCES

1. RANZCOG. Routine antenatal assessment in the absence of pregnancy complications. C-Obs 3b. 2022. https://ranzcog.edu.au/wp-content/uploads/2022/05/Routine-antenatal-assessment-in-the-absence-of-pregnancy-complications.pdf
2. Australian Government Department of Health. Fourth National Sexually Transmissible Infections Strategy. 2018-2022.
3. ASHM. National HIV testing policy. 2017.
4. Townsend CL, Cortina-Borja M, Peckham CS, de Ruiter A, Lyall H, Tookey PA. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000-2006. Aids. 2008;22(8):973-81.
5. Rollins N, Mahy M, Becquet R, Kuhn L, Creek T, Mofenson L. Estimates of peripartum and postnatal mother-to-child transmission probabilities of HIV for use in Spectrum and other population-based models. Sex Transm Infect. 2012;88(2):2012-050709.
6. Nduati R, John G, Mbori-Ngacha D, Richardson B, Overbaugh J, Mwatha A, et al. Effect of breastfeeding and formula feeding on transmission of HIV-1: a randomized clinical trial. Jama. 2000;283(9):1167-74.
7. White AB, Mirjahangir JF, Horvath H, Anglemyer A, Read JS. Antiretroviral interventions for preventing breast milk transmission of HIV. Cochrane Database Syst Rev. 2014(10):CD011323.
8. Coovadia HM, Rollins NC, Bland RM, Little K, Coutsoudis A, Bennish ML, et al. Mother-to-child transmission of HIV-1 infection during exclusive breastfeeding in the first 6 months of life: an intervention cohort study. Lancet. 2007;369(9567):1107-16.
9. Bispo S, Chikhungu L, Rollins N, Siegfried N, Newell ML. Postnatal HIV transmission in breastfed infants of HIV-infected women on ART: a systematic review and meta-analysis. Journal of the International AIDS Society. 2017;20(1):21251.
10. Flynn PM, Taha TE, Cababasay M, Fowler MG, Mofenson LM, Owor M, et al. Prevention of HIV-1 Transmission Through Breastfeeding: Efficacy and Safety of Maternal Antiretroviral Therapy Versus Infant Nevirapine Prophylaxis for Duration of Breastfeeding in HIV-1-Infected Women With High CD4 Cell Count (IMPAACT PROMISE): A Randomized, Open-Label, Clinical Trial. Journal of Acquired Immune Deficiency Syndromes: JAIDS. 2018;77(4):383-92.
11. Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Recommendations for the use of antiretroviral drugs in pregnant women with HIV Infection and Interventions to reduce perinatal HIV Transmission in the United States. 2020.https://clinicalinfo.hiv.gov/en/guidelines/perinatal/overview-2?view=full
12. BHIVA. British HIV Association guidelines for the management of HIV in pregnancy and postpartum 2018. (2020 third interim update) https://www.bhiva.org/pregnancy-guidelines
13. Shepherd K, Giles M, Blyth K, O'Keeffe F, Bordun L, Connell TG, et al. Follow-up and Clinical Outcomes of Human Immunodeficiency Virus (HIV)-Exposed Infants in A Low-Prevalence Setting in A Multidisciplinary Model of Care in Australia: The Children's HIV Exposure Study 1. J Pediatric Infect Dis Soc. 2022;10(1):14-21.
14. The Australasian Neonatal Medicince Formulary. Version 1.1. Published, November 16, 2020. https://www.seslhd.health.nsw.gov.au/sites/default/files/groups/Royal_Hospital_for_Women/Neonatal/Neomed/neomed20zidovudinefull.pdf

Listeria

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

LISTERIA – ALGORITHM 1

DIAGNOSIS OF SUSPECTED MATERNAL LISTERIOSIS AND MANAGEMENT OF PROVEN MATERNAL INFECTION

MATERNAL ILLNESS [1,2,3]

- unwell febrile pregnant woman, observed most often in third trimester (includes 'flu-like' illness).
- ~ 30% asymptomatic
  ~ 30% flu-like illness
  ~ 80% fever

There is no role for maternal screening, even in community outbreaks of listeriosis.

LISTERIOSIS

PERINATAL RISK [1,2,3,6]

- Most transmissions are reported in third trimester
- High rate of transmission (96% in one prospective study (MONALISA)[2]
- High rate of fetal or neonatal complications (83%)
- Fetal loss/miscarriage/stillbirth (13-24%)
- >29 weeks gestation or maternal hospital admission >2 days associated with fetal survival
- Overall perinatal mortality ~50%

Laboratory investigations

Inform lab of clinical suspicion for listeriosis (may assist microbiological yield)

- Culture from sterile site (e.g. blood culture (55% positive[2]), CSF, placenta (if delivering)
- Genital tract swab: Gram stain and culture (interpret with caution as asymptomatic carriage occurs in up to 16%)

Negative for *Listeria monocytogenes*

Consider other infections and empiric antibiotics

The route and duration of antibiotics will be guided by the clinical entity and severity of illness e.g. Blood stream infection: at least 14 days Meningitis: at least 21 days

Positive for *Listeria monocytogenes*

Amoxicillin/Ampicillin[3,8]
(2 g IV 4-6 hourly)
Penicillin allergy:* Trimethoprim/sulfamethoxazole (TMP/SMX, 5/25 mg (max 480/2800) IV 8 hourly)

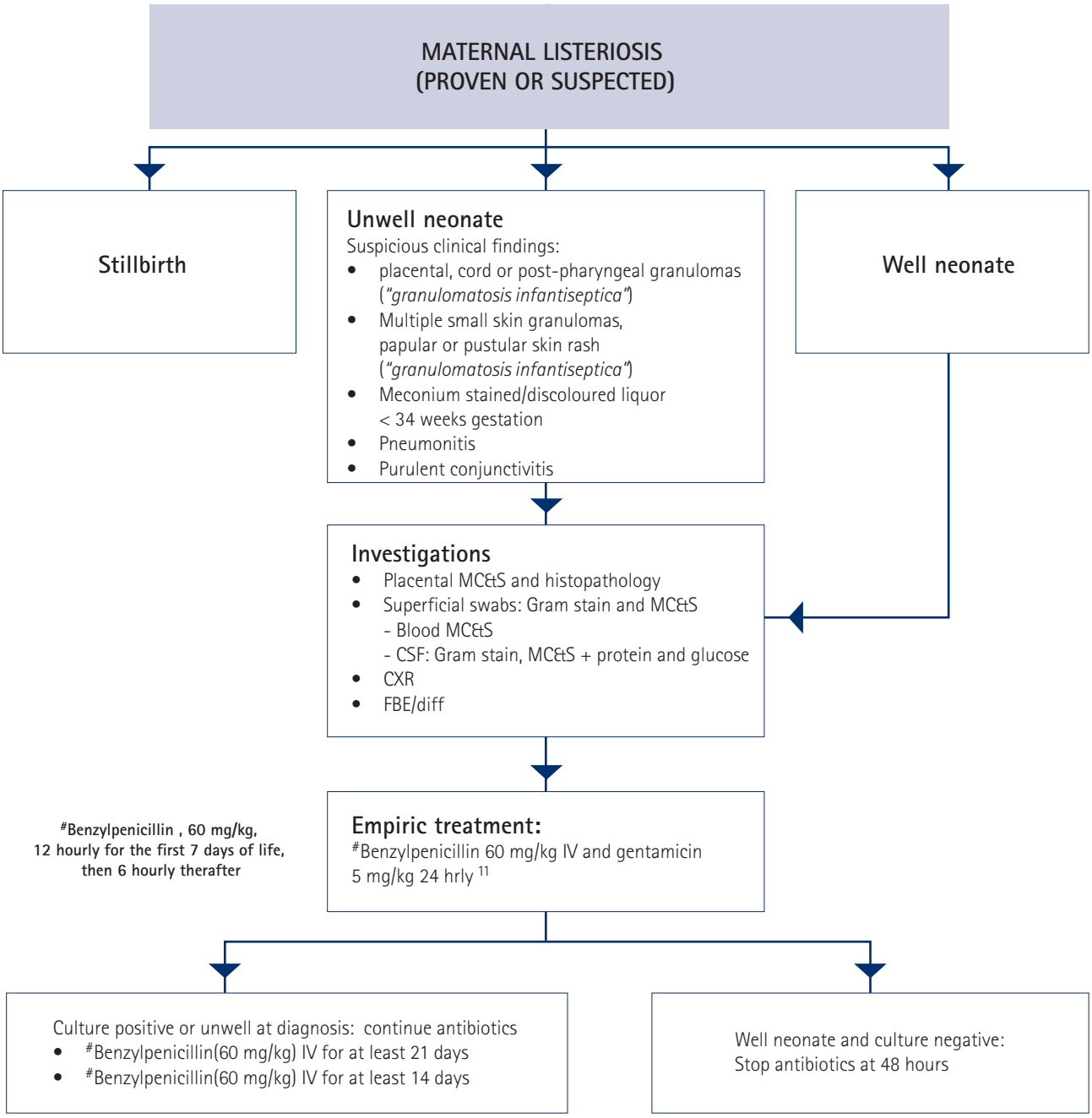
Urgent delivery depends on severity of maternal illness and gestation

COMMENTS

- Listeriosis is a foodborne infection and uncommon in Australia and New Zealand. An incidence of 0.3 and 0.56 cases per 100 000 population is reported respectively.[4,5] Global incidence is 1 to 11.3 per million of the population.[3,6] However, listeriosis is significantly more common in pregnancy than in non pregnancy (~ 18 times) and accounted for 14% of cases in one Australian report[1] and12.3 per100 000 births in New Zealand [5]
- Measures to minimise listeria infection are readily available from local Public Health Department publications / fact sheets. (Appendix 1)
- Transmission is highest in the third trimester. Maternal listeriosis in second/third trimester results in fetal mortality of 25-50% [3,6]
- Past history of listeriosis: There is no role for vaginal cultures or intrapartum antibiotics
- Faecal carriage of *L. monocytogenes* is found in 0.6-16% of the population. Transient colonisation of the GI tract is common but invasive disease is rare. The significance of maternal faecal excretion of listeria in perinatal infection is uncertain [6]
- Laboratory investigations e.g. blood or stool cultures and treatment are not indicated in asymptomatic pregnant women who have consumed food implicated in outbreaks. Return for review if symptoms occur (within 2 months of suspected risk). Fetal surveillance is not indicated. Management is 'expectant' for those with 'mild symptoms' and no fever. Monitor up to 2 months to cover the incubation period. All symptomatic, febrile women should be investigated, and treatment commenced, pending results [7]
- The estimated incubation period (IP) for invasive listeria infection ranges from 0 – 70 days (median 10 days), with longer IP for pregnancy associated cases (≤ 5 weeks in > 75% and ≤ 6 weeks in 90%) [9,10]
- An effective anti-listeria antibiotic should penetrate and maintain a high intracellular concentration, cross the placenta, and should be given for a prolonged period (at least 2 weeks). The recommended treatment regimens above are based on case reports. No randomised controlled trials have been performed to establish optimal treatment regimens or to support efficacy of penicillin over ampicillin, but at high doses for placental penetration, are generally considered the preferred agents [1, 2, 3]
- Synergy of penicillin or ampicillin with aminoglycosides has only been reported in vitro[3] and combination therapy has not been shown to be beneficial.[11]
- Antibiotics to avoid: cephalosporin, chloramphenicol as efficacy is limited
- Use if options exhausted: vancomycin, fluroquinolone [6,11]
- Giving corticosteroids for fetal lung maturation in women with any suspicion of CNS listeria is not recommended. Survival was reported to be lower in a prospective observational cohort study (the MONALISA study) for patients with neurolisteriosis receiving adjunctive dexamethasone therapy vs not (54% vs 73% (p = 0.024) [2]

LISTERIA – ALGORITHM 2

DIAGNOSIS AND MANAGEMENT OF INFANT AT RISK OF PERINATAL LISTERIOSIS



COMMENTS

- Preterm delivery is common. Mortality rates range from 20-60% in infected neonates born alive [2,6]
- Perinatal listeria infection can present as **early onset disease** (within 7 days of birth, mean 1.5 days) often associated with prematurity and fulminant disease. Mortality is high (20–60%) [6]
- **Late onset disease** occurs typically in term infants (4 - 6 weeks, mean onset ~14 days), often presenting with meningitis, but can be more non-specific sepsis (fever, irritability, anorexia, diarrhoea, lethargy). Mortality is 10–20% [3,6]
- Gram stain and MC&S of swabs of the placenta, meconium, rectum and external ear canal have a high yield in identifying the organism [12]
- Optimal antimicrobial therapy for various manifestations of listeriosis has not been established in controlled clinical trials and remains controversial. No controlled trials available to establish a drug of choice or duration of therapy [3,4,10]
- Alternative antibiotics: Trimethoprim/sulfamethoxazole reserved in the event of lack of response to standard therapy; Rifampicin effective in vitro but inadequate clinical information available; Erythromycin should not be used in meningitis as macrolides penetrate the blood brain barrier poorly
- Linezolid and quinolones are not recommended in pregnancy or newborns
- There is no role for cephalosporins as listeria is resistant to this class of antibiotics

LISTERIA
APPENDIX AND REFERENCES

APPENDIX

Avoid high risk foods

These foods include:

- Unpasteurised milk or food made from raw milk
- Pate, dips and soft cheeses
- Chilled precooked seafoods
- Precooked meats and meat products which are eaten without further cooking or heating
- Uncooked or smoked seafood
- Pre-prepared and pre-packed fruits salads and coleslaws
- Rockmelon
- Cold delicatessen meats
- Soft serve ice-cream
- Sprouted seeds and raw mushrooms

AND

Use safe food handling practices

- Wash hands before preparing foods
- Thoroughly wash raw fruit and vegetables
- Thoroughly cook raw food from animal sources including seafood
- Keep uncooked meat separate from vegetables, cooked foods and ready-to-eat foods
- Eat freshly cooked foods
- Avoid eating dips and salads in which raw vegetables may have previously been dipped
- Reheat left-over or ready-to-eat food until steaming hot
- Use separate cutting boards for raw meats and foods that are ready to eat e.g. cooked foods and salads

Further material: Local public health resources are readily available for information in pregnancy
e.g. NSW Health - Listeria Fact Sheet: http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-listeria-fs.htm
-Foods to eat or avoid when pregnant: http://www.foodauthority.nsw.gov.au/foodsafetyandyou/life-events-and-food/pregnancy/ foods-to-eat-or-avoid-when-pregnant

REFERENCES

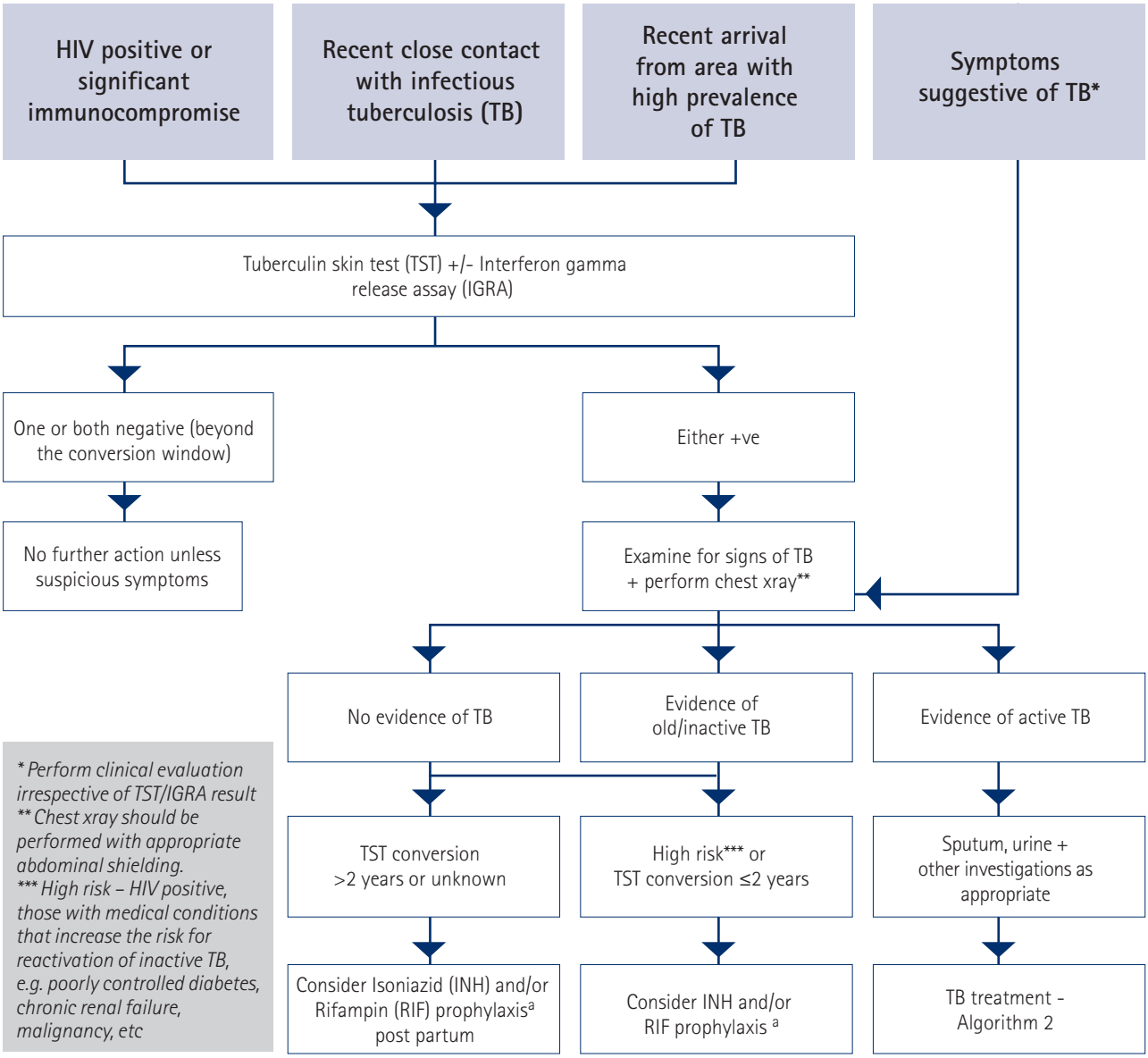
1. Dalton CB, Merritt TD, Unicomb LE, et al. A national case-control study of risk factors for listeriosis in Australia. Epidemiology & Infection 2011;139:437-45.
2. Charlier C, Perrodeau E, Leclercq A, et al. Clinical features and prognostic factors of listeriosis: the MONALISA national prospective cohort study.[Erratum appears in Lancet Infect Dis. 2017 Sep;17(9):897; PMID: 28729165]. The Lancet Infectious Diseases 2017;17:510-9.
3. Khsim IEF, Mohanaraj-Anton A, Horte IB, et al. Listeriosis in pregnancy: An umbrella review of maternal exposure, treatment and neonatal complications. *Bjog* 2022; 129(9): 1427-33.
4. Kirk M, Ford L, Glass K, Hall G. Foodborne illness, Australia, circa 2000 and circa 2010. Emerg Infect Dis 2014;20:1857-64.
5. Jeffs E, Williman J, Brunton C, Gullam J, Walls T. The epidemiology of listeriosis in pregnant women and children in New Zealand from 1997 to 2016: an observational study. BMC Public Health. 2020;20(1):116.
6. Madjunkov M, Chaudhry S, Ito S. Listeriosis during pregnancy. Arch Gynecol Obstet 2017;296:143-52.
7. American College of Obstetrics and Gynaecologist (ACOG). Management of pregnant women with presumptive exposure to Listeria monocytogenes. Committee Opinion on Obstetric Practice 2014, December 2014.
8. Temple ME, Nahata MC. Treatment of listeriosis. Annals of Pharmacotherapy. 2000;34(5):656-61.
9. Goulet V, King LA, Vaillant V, de Valk H. What is the incubation period for listeriosis? BMC Infect Dis 2013;13:1471-2334.
10. Angelo KM, Jackson KA, Wong KK, Hoekstra RM, Jackson BR. Assessment of the Incubation Period for Invasive Listeriosis. Clinical Infectious Diseases 2016;63:1487-9.
11. Craig AM, Dotters-Katz S, Kuller JA, Thompson JL. Listeriosis in Pregnancy: A Review. Obstet Gynecol Surv. 2019;74(6):362-8.
12. Osfay-Barbe KM, Wald ER. Listeriosis. Semin Fetal Neonatal Med 2009;14:228-33.

Mycobacterium tuberculosis

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

MYCOBACTERIUM TUBERCULOSIS [MTB] – ALGORITHM 1

ANTENATAL DIAGNOSIS: MANAGEMENT OF PREGNANT WOMAN



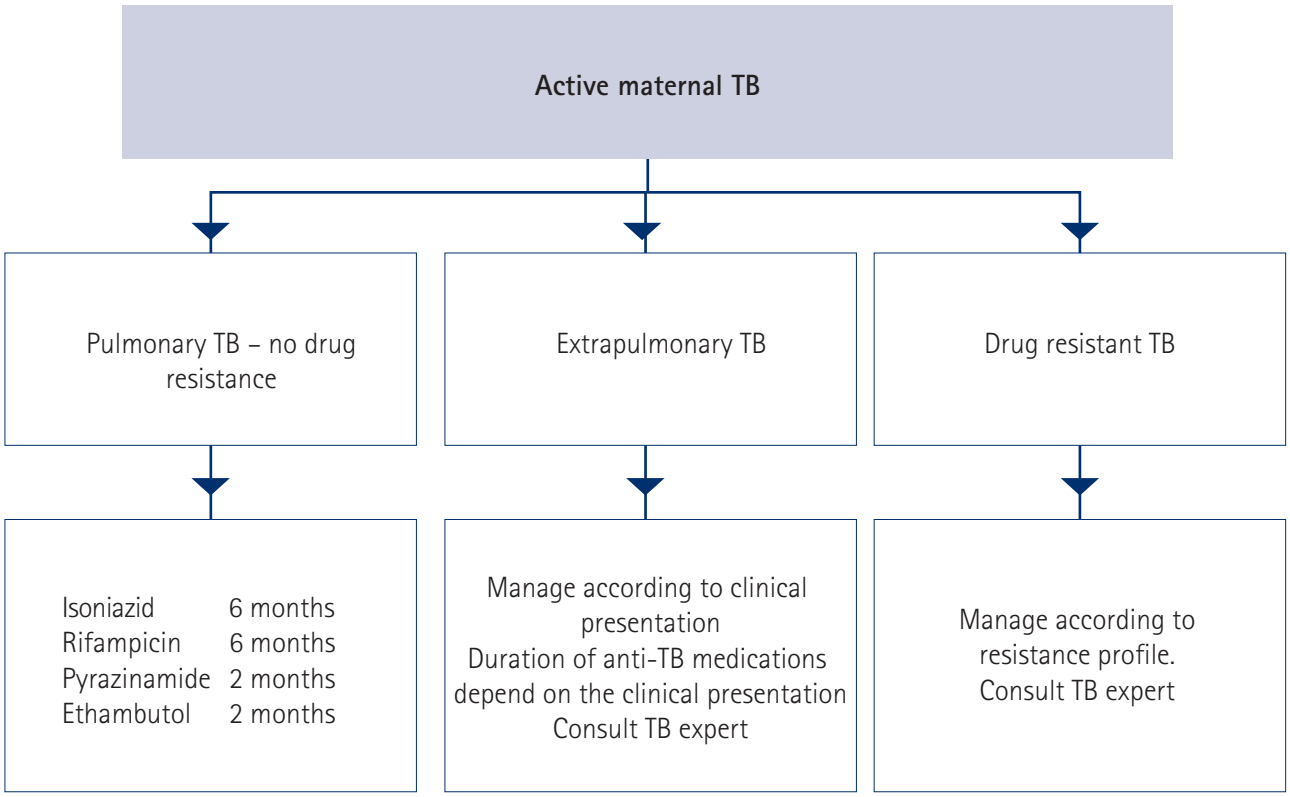
COMMENTS

- The development, clinical presentation and progression of TB are not altered by pregnancy
- The symptoms of extrapulmonary TB are frequently non-specific, and may be attributed to physiological changes of pregnancy
- Areas with high prevalence of TB include South East Asia, Pacific Islands, Africa, Eastern Europe, Latin America
- Screening with a Tuberculin skin test (TST) or T cell interferon gamma release assay (IGRA) is usually reserved for those with an increased risk of TB, particularly those at high risk for progression of latent TB infection (LTBI) to active disease***
- All women with symptoms suggestive of active TB must be fully investigated
- IGRA and TST have been shown to perform equally well in each trimester of pregnancy with comparable results to non pregnant females. IGRA and TST can be performed safely in pregnant women
- Both tests have limited specificity and sensitivity, particularly in HIV-infected individuals. IGRA has improved specificity in BCG vaccinated patients
- TST testing of contacts is usually performed by local health authorities, and may need to be repeated at 12 weeks after break of contact. (conversion window). See guide to interpretation below
- INH is safe in pregnancy
- Pyridoxine should be given with INH to pregnant and breast feeding women (50 mg/day)

a. Prophylaxis of latent TB infection: regimens include INH (for 6 or 9 months), or RIF (for 4 months), or INH + RIF (for 3 months)

MYCOBACTERIUM TUBERCULOSIS – ALGORITHM 2

MANAGEMENT OF PROVEN MATERNAL TB

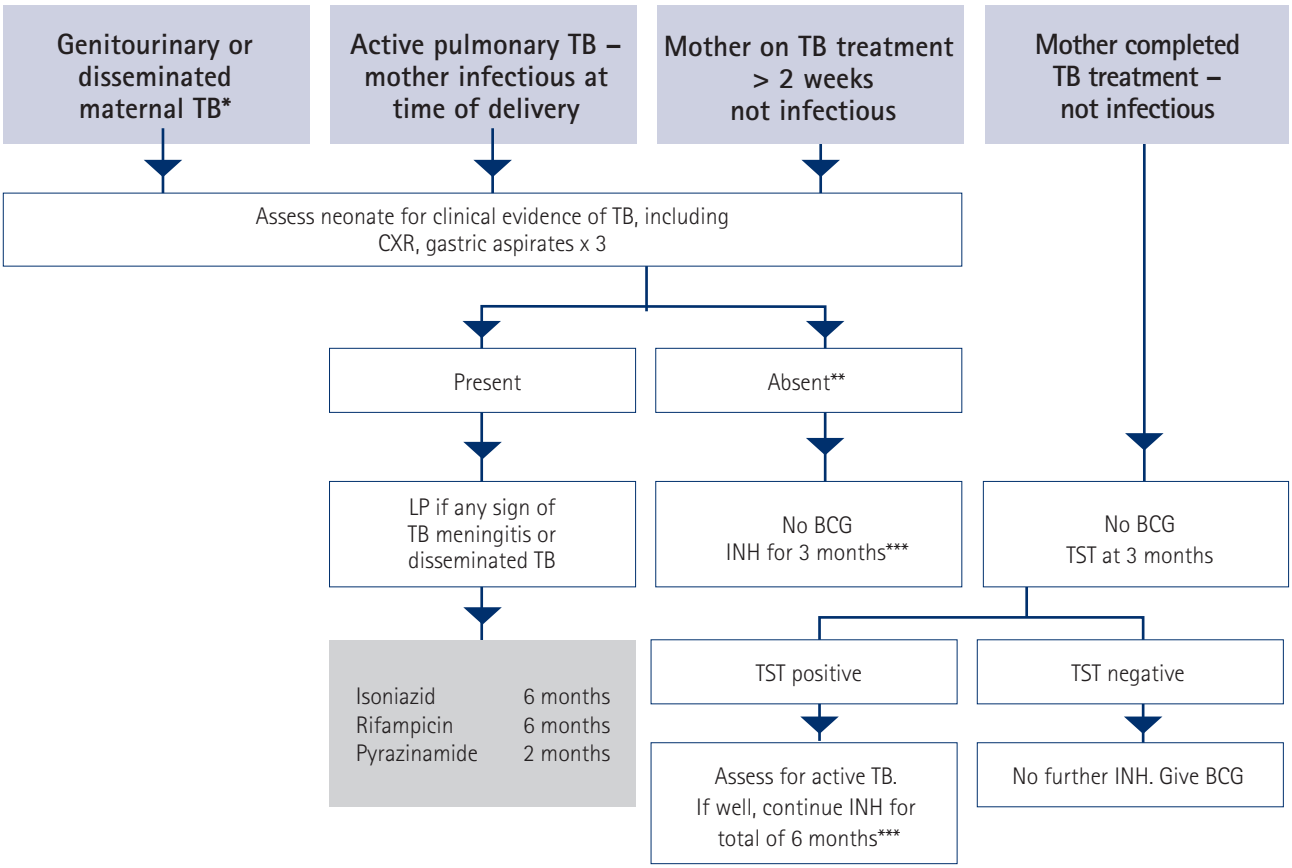


COMMENTS

- Active TB during pregnancy must be treated immediately. This is true for cases in which TB has not been confirmed, but is considered likely on clinical grounds
- TB does not affect the course of pregnancy or type of delivery required
- Culture confirmation and drug susceptibility testing should be undertaken in all cases
- Duration of therapy for extra-pulmonary TB may vary according to the presentation (e.g. longer for TB meningitis)
- TB is a notifiable disease and all TB treatment should be coordinated by the local TB program. Appropriate contact tracing should be performed
- All TB drugs cross the placenta and reach a low concentration in fetal tissues. Isonaizid (INH), rifampicin and ethambutol are all safe in pregnancy. There are less safety data for pyrazinamide, but it is recommended by the World Health Organisation during all trimesters of pregnancy
- Isoniazid – 300 mg po daily (give with pyridoxine 50 mg daily – note increased dose in pregnant and breast feeding women)
- Rifampicin - 450 mg oral daily (< 50 kg)
  - 600 mg oral daily (> 50 kg)
- Ethambutol – 15 mg/kg oral daily
- Pyrazinamide – 25-35 mg/kg (max 2 g) oral daily
- The risk of INH-induced hepatotoxicity appears to be higher in women, and may be more so in the perinatal period. Women should be monitored for hepatotoxicity with monthly ALT/AST

MYCOBACTERIUM TUBERCULOSIS – ALGORITHM 3

MANAGEMENT OF THE NEONATE



**Transplacental spread leading to congenital TB is rare, but can occur with disseminated (miliary) TB or recent primary infection as indicated by a pleural effusion. Aspiration of infected secretions at the time of delivery is possible if the mother has genitourinary TB.*
***If symptoms or signs suspicious of TB develop at any time, reinvestigate for TB*
**** Daily INH + Rif for 3 months is an alternative regimen, particularly for high risk infants.*

COMMENTS

- Most cases of neonatal TB occur as a result of airborne spread after delivery. However, separation of mother and neonate is only necessary if the mother has drug resistant TB. If the mother has active TB, other family members and close contacts should be assessed for TB infection or disease
- Respiratory distress, hepatosplenomegaly, fever, lymphadenopathy and poor feeding are the most common presenting features of neonatal TB
- If congenital infection is suspected, the placenta should be examined, and microscopy, culture and histology performed
- The TST is likely to be negative for the first few weeks of life, even if the neonate has TB
- IGRA performance in children is less well understood than in adults. Indeterminate IGRA results are common in young children; TST is preferred

DRUG TREATMENT

- The decision regarding number and choice of drugs for management of neonates and infants with TB warrants specialist advice. Routine treatment will include:
- Isoniazid 10 mg/kg po daily for 6 months (Pyridoxine 10 mg oral daily must be added for breast fed infants)
- Rifampicin 15 mg/kg oral daily for 6 months
- Pyrazinamide 35 mg/kg oral daily for 2 months
- Additional drugs are only required in cases with extra-pulmonary involvement or drug resistance

MYCOBACTERIUM TUBERCULOSIS REFERENCES

1. Adhikari M. Tuberculosis and tuberculosis/HIV co-infection in pregnancy. Semin Fetal Neonatal Med. 2009;14:234-40.
2. Bothamley G. Drug treatment for tuberculosis during pregnancy: safety considerations. Drug Saf. 2001;24:553.
3. Connell TG, Curtis N, Ranganathan SC, Buttery JP. Performance of a whole blood interferon gamma assay for detecting latent infection with Mycobacterium tuberculosis in children. Thorax. 2006;61:616-20.
4. Guidelines for treatment of drug-susceptible tuberculosis and patient care, 2017 update. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.
5. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management.
6. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO.
7. Lighter-Fisher J et al. Performance of an interferon-gamma release assay to diagnose latent tuberculosis infection during pregnancy. Obstet Gynecol 2012;119:1088-95.
8. Marais BJ, Schaaf HS. Childhood tuberculosis: an emerging and previously neglected problem. Infect Dis Clin North Am. 2010;24:727-49.
9. Mathad J, Gupta A. Tuberculosis in pregnant and postpartum women: epidemiology, management, and research gaps. Clin Infect Dis. 2012;55:1532-49.
10. Mazurek M, Jereb J, Vernon A, LoBue P, Goldberg S, Castro K; IGRA Expert Committee; Centers for Disease Control and Prevention (CDC). Updated guidelines for using Interferon Gamma Release Assays to detect Mycobacterium tuberculosis infection - United States, 2010. MMWR Recomm Rep. 2010;59(RR-5):1-25.
11. Menzies D, Adjobimey M, Ruslami R, et al. Four Months of Rifampin or Nine Months of Isoniazid for Latent Tuberculosis in Adults. N Engl J Med. 2018;379:440-453
12. Mnyani C, McIntyre J. Tuberculosis in pregnancy. BJOG. 2011;118:226–231.
13. Rendell N, Batjargal N, Jadambaa N, Dobler C. Risk of tuberculosis during pregnancy in Mongolia, a high incidence setting with low HIV prevalence. Int J Tuberc Lung Dis. 2016;20:1615-1620.
14. Schaaf H, Collins A, Bekker A, Davies P. Tuberculosis at extremes of age. Respirology. 2010;15:747-63.
15. Sugarman J, Colvin C, Moran A, Oxlade O. Tuberculosis in pregnancy: an estimate of the global burden of disease. Lancet Glob Health. 2014;2:e710-6.
16. Swaminathan S, Rekha B. Pediatric tuberculosis: global overview and challenges. Clin Infect Dis. 2010;50 Suppl 3:S184-94.
17. Worjoloh A et al. Interferon Gamma Release Assay Compared with Tuberculin Skin Test for Latent Tuberculosis Detection in Pregnancy. Obstet Gynecol 2011;118:1363-1370.
18. Zenner D, Kruijshaar M, Andrews N, Abubakar I. Risk of tuberculosis in pregnancy: a national, primary care-based cohort and self-controlled case series study. Am J Respir Crit Care Med. 2012;185:779-84.
19. Ministry of Health. 2019. Guidelines for Tuberculosis Control in New Zealand, 2019. Wellington: Ministry of Health.

GUIDE TO INTERPRETATION OF THE TST

	LOW RISK	MODERATE RISK	HIGH RISK
	No risk factors	• Ethnic origin from high prevalence population • Locally identified high risk populations • Adult HIV patient with CD4 count >500/mL • Children aged 1-5 years	• Recent close contact with infectious TB • HIV-infected or other immunosuppression (including steroids, equivalent of >1mg/kg/day for >4 weeks) • CXR: fibrotic changes suggestive of past TB • Children under 1 year
0-4 mm	Negative	Negative	Negative
5-9 mm	Negative	Negative	**Positive**
10-14 mm	Negative	**Positive**	**Positive**
15 mm	**Positive**	**Positive**	**Positive**

Neisseria gonorrhoeae

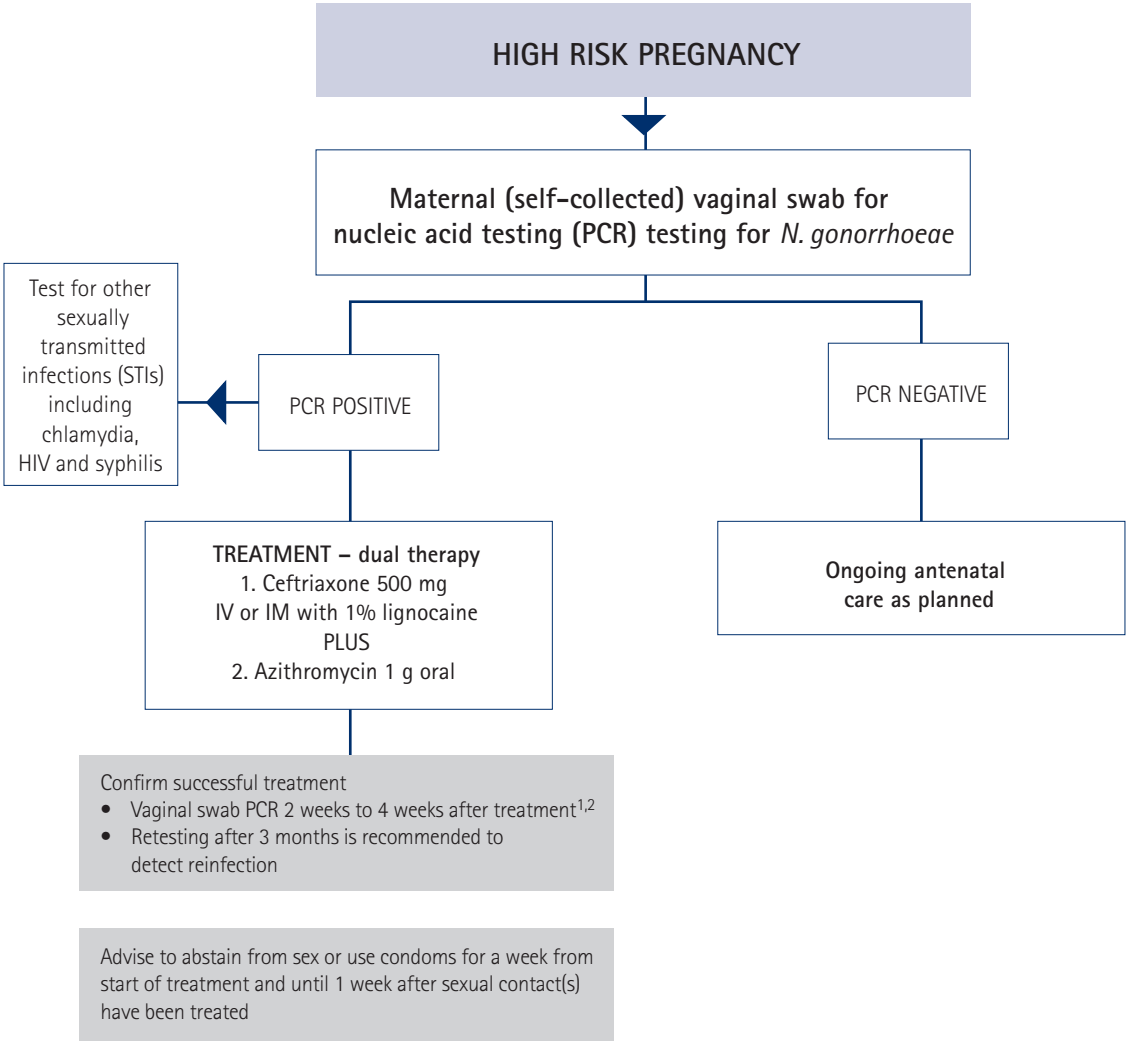
AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

NEISSERIA GONORRHOEAE – ALGORITHM 1

MANAGEMENT OF A WOMAN WITH SUSPECTED MATERNAL NEISSERIA GONORRHOEAE INFECTION

Routine antenatal testing in pregnancy is not recommended[1] but is sometimes done in high risk or high prevalence settings in Australia and New Zealand[1,2] Almost all infections are asymptomatic in women.
Risk factors for *N. gonorrhoeae* infection include:

- Age < 30 years
- High risk sexual contacts (e.g. multiple partners, consistent non-use of condoms)
- Sexually active women of reproductive age residing or returning from a high prevalence country
- Aboriginal or Torres Strait Island or Maori or Pacific peoples population



COMMENTS

- Dual therapy is recommended due to the changing patterns of antimicrobial resistance in *N. gonorrhoeae*
- Urogenital gonococcal infections have been associated with chorioamnionitis, premature rupture of membranes and prematurity, low birth weight infants, and spontaneous abortions in pregnant women
- The risk of these complications in the setting of gonococcal infection is 2-5 times greater than in uninfected controls
- Transmission of *N. gonorrhoeae* from an untreated infected mother to her baby may occur in 30-50% of cases
- Chlamydia and *N. gonorrhoeae* infections are the commonest STIs in Australia. The prevalence of *N. gonorrhoeae* infections in women of child bearing age in Australia is about 10 times less than *Chlamydia trachomatis* infections (data: https://data.kirby.unsw.edu.au/STIs)[3] and similarly in NZ[4]

NEISSERIA GONORRHOEAE – ALGORITHM 2

POSTNATAL MANAGEMENT OF AN INFANT BORN TO A MOTHER WITH N. GONORRHOEAE INFECTION (OR HIGH-RISK UNTREATED MOTHER)

INFANT BORN TO A MOTHER WITH KNOWN *N. GONORRHOEAE* INFECTION (OR HIGH-RISK UNTREATED MOTHER)

ASYMPTOMATIC INFANTS

born to mothers with known untreated *N. gonorrhoeae*

- Risk of perinatal transmission: 30-40%

Oropharyngeal swab for *N. gonorrhoeae* PCR

Treat prophylactically
Ceftriaxone 25-50 mg/kg (max 125 mg) IV or IM as a single dose*

LOCALISED INFECTION OF MUCOSAL SURFACES

Pharynx, vagina, urethra, anus

Mucosal swab: pharynx, vagina, urethra, anus for *N. gonorrhoeae* PCR

Treat empirically
Ceftriaxone 25-50 mg/kg (max 125 mg) IV or IM as a single dose*

PLUS
Azithromycin
20 mg/kg
oral daily for 3 days

OPHTHALMIA NEONATORUM

- Most common site of *N. gonorrhoeae* infection in neonates
- Presents on day 2-5
- Visual impairment results if untreated

Conjunctival exudate swabs for Gram stain, culture and *N. gonorrhoeae* PCR

Treat empirically
Ceftriaxone 25-50 mg/kg (max 125 mg) IV or IM as a single dose*

Topical therapy is not effective

OPHTHALMOLOGY REVIEW

- Rule out disseminated infection
- Hospitalise to observe response to therapy
- Frequent saline irrigation until purulence subsides
- *C. trachomatis* co-infection should be ruled out with chlamydia PCR testing

INFECTION AT SITE OF SCALP ELECTRODE

(*N. gonorrhoeae* scalp abscess)

Swab of scalp abscess for Gram stain and culture

DISSEMINATED INFECTION:

- Arthritis
- +/- sepsis
- +/- meningitis

INVESTIGATIONS
Identify site(s) of infection:

- M/C/S: Blood, CSF, joint aspirate (if arthritis present)
- PCR:Joint aspirate (if arthritis), mucosal swab of conjunctiva, vagina, oropharynx.

Note the importance of checking susceptibilities

Treat (start empirically)
Ceftriaxone 25-50 mg/kg (max 125 mg) IV or IM daily
OR
Cefotaxime
(see local guidelines for age-dependent dosing and frequency) for 7 days
(10-14 days for meningitis)

COMMENTS

- In some health settings, prophylactic topical antibiotics (erythromycin ointment) are applied to prevent gonococcal ophthalmia neonatorum; this is not advocated in Australia where the prevalence of *N. gonorrhoeae* is low and the emphasis is screening for STIs in pregnancy as a prevention strategy
- *One dose of ceftriaxone is adequate therapy for gonococcal conjunctivitis. A maximum dose of 125mg should be used and a lower dose used in premature or hyperbilirubinaemic infants, since it displaces bilirubin from albumin and may increase the risk of encephalopathy. Avoid ceftriaxone in infants receiving calcium-containing IV fluids (including TPN) due to risk of precipitation. Treatment with other classes of antibiotics is not indicated due to high resistance rates
- Azithromycin is used concomitantly in *N. gonorrhoeae* conjunctivitis to delay cephalosporin resistance and because co-infection with *C. trachomatis* is possible
- Mothers of infants with ophthalmia neonatorum caused by *N. gonorrhoeae* should be evaluated, tested and presumptively treated for *N. gonorrhoeae*, along with their sexual partners

NEISSERIA GONORRHOEAE REFERENCES

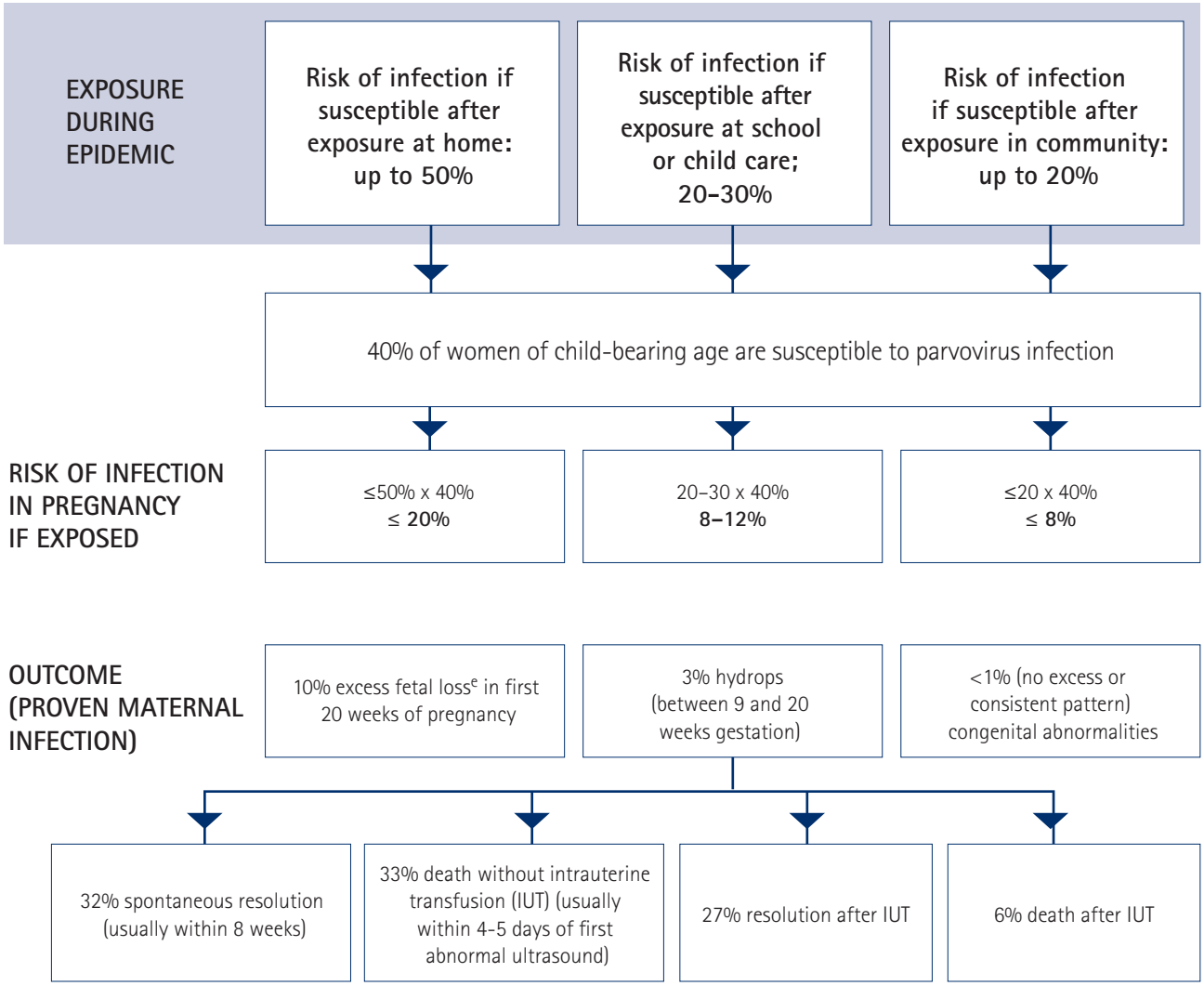
1. Australian STI Management Guidelines http://www.sti.guidelines.org.au/sexually-transmissible-infections/gonorrhoea
2. NZ STI guidelines: https://sti.guidelines.org.nz/infections/gonorrhoea/
3. Kirby Institute, Annual Surveillance Report 2018: Sexually transmissible infections https://kirby.unsw.edu.au/sites/default/files/kirby/report/KI_Annual-Surveillance-Report-2018.pdf#page=134
4 NZ STI Surveillance https://www.esr.cri.nz/our-services/consultancy/public-health/sti/
5. Liu B, Roberts CM, Clarke M, Jorm L, Hunt J, Ward J. Chlamydia and gonorrhea infections and the risk of adverse obstetric outcomes: A retrospective cohort study. Sex Transm Infect (2013); 89(8) 672-8.
6. Woods, CR. Gonococcal infections in neonates and children. Semin Pediatric Infect Dis (2005). 16(4), 258-70.
7. American Academy of Pediatrics. Gonococcal infections. In: Red Book: 2018 Report of the Committee on Infectious Diseases, 31st ed, Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds), American Academy of Pediatrics, Itasca, IL 2018. p.355.
8. Workowski KA, Bachmann LH, Chan PA et al. Sexually transmitted infections treatment guidelines. MMWR Recomm Rep 2021;70(4):1 - 187
9. RANZCOG. Routine antenatal assessment in the absence of pregnancy complications (C-Obs 3b). 2022. https://ranzcog.edu.au/wp-content/uploads/2022/05/Routine-antenatal-assessment-in-the-absence-of-pregnancy-complications.pdf

Parvovirus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

PARVOVIRUS – ALGORITHM 1

RISK ASSESSMENT



OVERALL RISKS:

	Any pregnant woman exposed to parvovirus	Pregnant woman with proven recent infection
Excess fetal loss in first 20 weeks	0.4-1% (1 in 100-1 in 250)	10% (1 in 10)
Death from hydrops or its treatment	0.05-0.1% (1 in 850-1 in 2000)	0.6% (1 in 170)

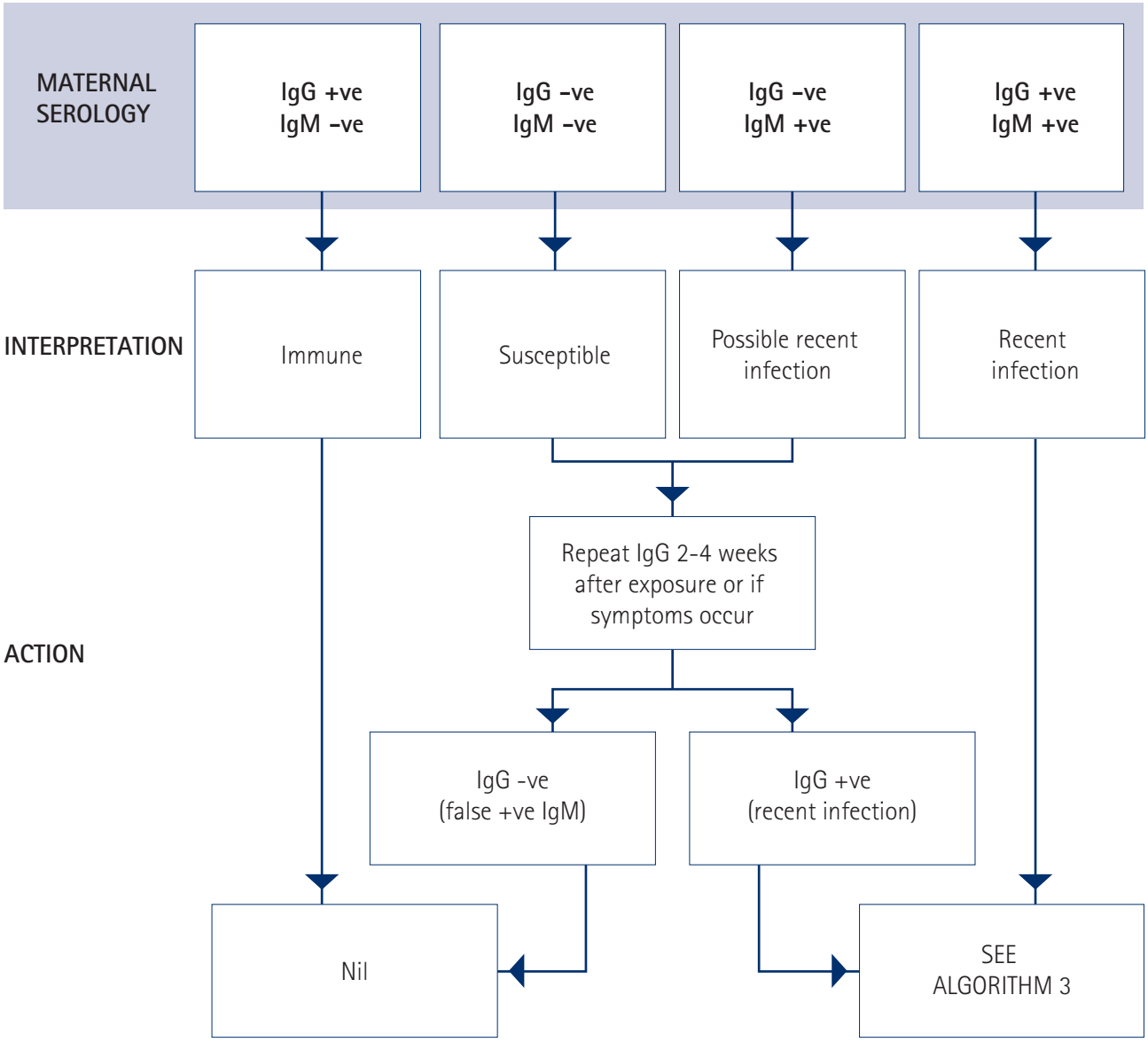
Pregnant women who are exposed should be informed of risks, and offered serological testing.

COMMENTS

a. It is not practicable to prevent exposure at home
b. Exclusion from work of pregnant school teachers or child care workers **is not recommended** during parvovirus epidemics, which are often very prolonged (nor is exclusion of infected children)
c. Routine antenatal screening is **not** indicated
d. There is a 50% risk of transmission from an infected mother to her fetus
e. Fetal loss = 15%, compared with 5% overall (i.e. excess loss = 10%)
f. Onset of hydrops 2-17 weeks (average 5 weeks) after maternal infection
g. Congenital abnormalities – anecdotal reports only (less than rate of major malformations in newborns of 2%)
h. The risk of intrauterine death is higher in fetuses affected by hydrops. Spontaneous resolution of infection occurs in about half of cases without hydrops but in only about 5% of those with hydrops. Resolution of infection after IUT is achieved in about half of cases affected and in all cases not affected by hydrops. Intrauterine death after IUT occurs in ~30% of hydropic and in ~5% of non-hydropic fetuses

PARVOVIRUS – ALGORITHM 2

ANTENATAL DIAGNOSIS & MANAGEMENT



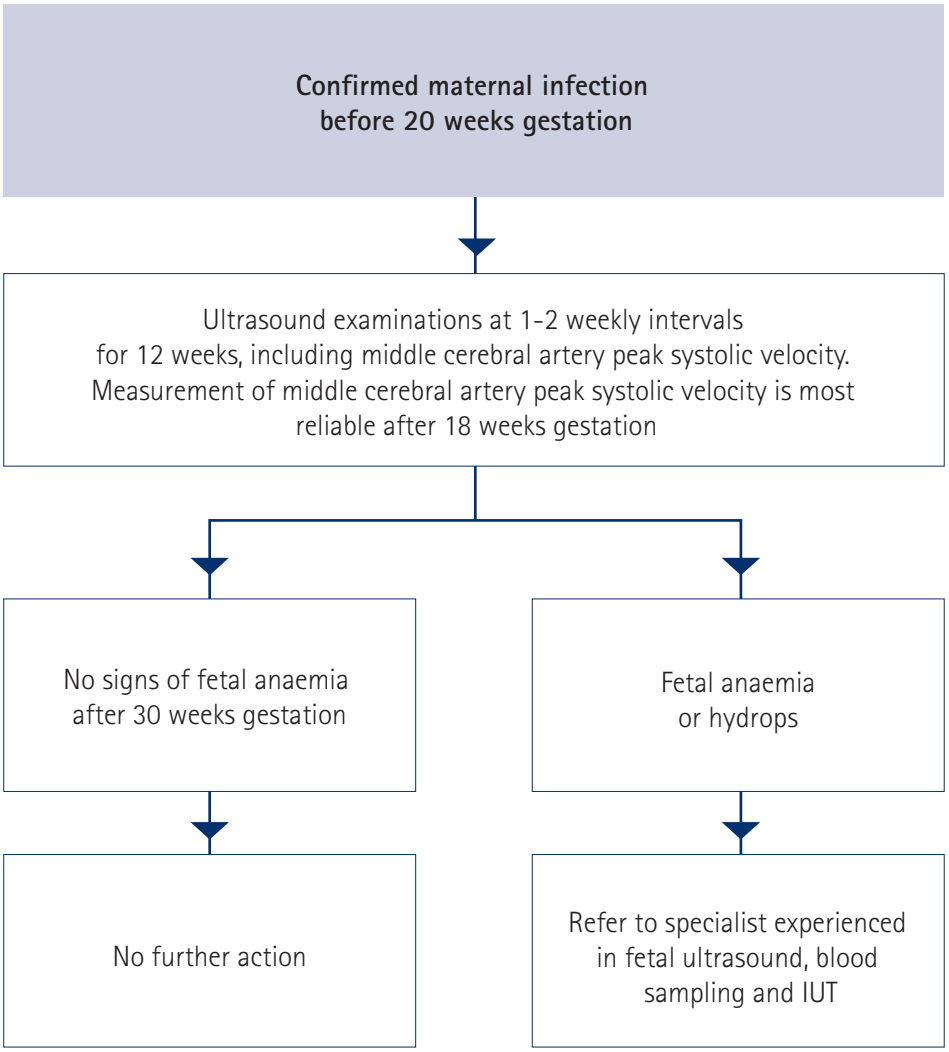
COMMENTS

- IgM is detectable within 1-3 weeks of exposure and usually remains detectable for 2-3 months
- Commercial IgM test kits (EIA or IF):
  - sensitivity: 70-80% overall (100% in adults with arthropathy; lower in children)
  - specificity: 92-97% overall (70-85% in patients with other infections, including rubella)

  Note: absence of IgM does not exclude recent infection
- Newer diagnostic techniques, such as IgG avidity and epitope-type specificity assays may be more sensitive, specific and can more reliably identify acute versus persistent infection. However, they are not widely available. PCR can be performed on plasma, but is generally unlikely to be positive after onset of symptoms
- Symptoms include non-specific illness, rash, and/or arthralgia/arthritis

PARVOVIRUS – ALGORITHM 3

MANAGEMENT OF PROVEN MATERNAL INFECTION



COMMENTS

- No intervention is available to prevent fetal infection or damage
- Amniocentesis for diagnosis of asymptomatic intrauterine fetal infection is not recommended
- α fetoprotein levels are not helpful – previous reports that increased levels predict poor outcome have not been confirmed
- Fetal infection may be identified by using (non-quantitative) PCR on amniotic fluid or fetal cord blood
- Pregnancy should be monitored by serial ultrasound examination to detect fetal anaemia
- A fetus with mild hydrops may be profoundly anaemic
- Fetal blood sampling may be required to monitor for anaemia and thrombocytopenia
- Doppler assessment of the fetal middle cerebral artery peak systolic velocity is an accurate tool for the determination of fetal anemia from 16-34 weeks gestation, providing a noninvasive alternative to cord blood sampling
- If anaemia and/or thrombocytopenia reach a critical level, IUT may be required
- Infants in whom hydrops has occurred and resolved should be monitored for evidence of anaemia
- No specific investigation is indicated in normal infants

PARVOVIRUS REFERENCES

1. Attwood LO, Holmes NE, Hui L. Identification and management of congenital parvovirus B19 infection. Prenat Diagn. 2020;40:1722-1731.
2. Bascietto F, Liberati M, Murgano D, Buca D, Iacovelli A, Flacco M, Manzoli L, Familiari A, Scambia G, D'Antonio F. Outcome of fetuses with congenital parvovirus B19 infection: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2018;52:569-576.
3. Crane J, Mundle W, Boucoiran I; Maternal Fetal Medicine Committee. Parvovirus B19 infection in pregnancy. J Obstet Gynaecol Can. 2014;36:1107-1116.
4. de Jong EP, de Haan TR, Kroes AC, Beersma MF, Oepkes D, Walther FJ. Parvovirus B19 infection in pregnancy. J Clin Virol 2006; 36:1–7.
5. Enders M, Weidner A, Rosenthal T, Baisch C, Hedman L, Söderlund-Venermo M, Hedman K. Improved diagnosis of gestational parvovirus B19 infection at the time of nonimmune fetal hydrops. J Infect Dis. 2008;197:58-62.
6. Harger JH, Adler SP, Koch WC, Harger GF. Prospective evaluation of 618 pregnant women exposed to parvovirus B19: risks and symptoms. Obstet Gynecol 1998;91:413-20.
7. Keighley C, Skrzypek H, Wilson A, Bonning M, Gilbert G. Infections in pregnancy. Med J Aust. 2019. doi: 10.5694/mja2.50261.
8. Lamont R, Sobel J, Vaisbuch E, Kusanovic J, Mazaki-Tovi S, Kim S, Uldbjerg N, Romero R. Parvovirus B19 infection in human pregnancy. BJOG. 2010;Oct
9. Morgan-Capner P, Crowcroft NS. Guidelines on the management of, and exposure to, rash illness in pregnancy (including consideration of relevant antibody screening programmes in pregnancy). Commun Dis Public Health 2002;5:59–71.
10. Ornoy A, Ergaz Z. Parvovirus B19 infection during pregnancy and risks to the fetus. Birth Defects Res. 2017;109:311-323.
11. Sarfraz AA, Samuelsen SO, Bruu AL, Jenum PA, Eskild A. Maternal human parvovirus B19 infection and the risk of fetal death and low birthweight: a case-control study within 35 940 pregnant women. BJOG. 2009;116:1492-8.

Rubella

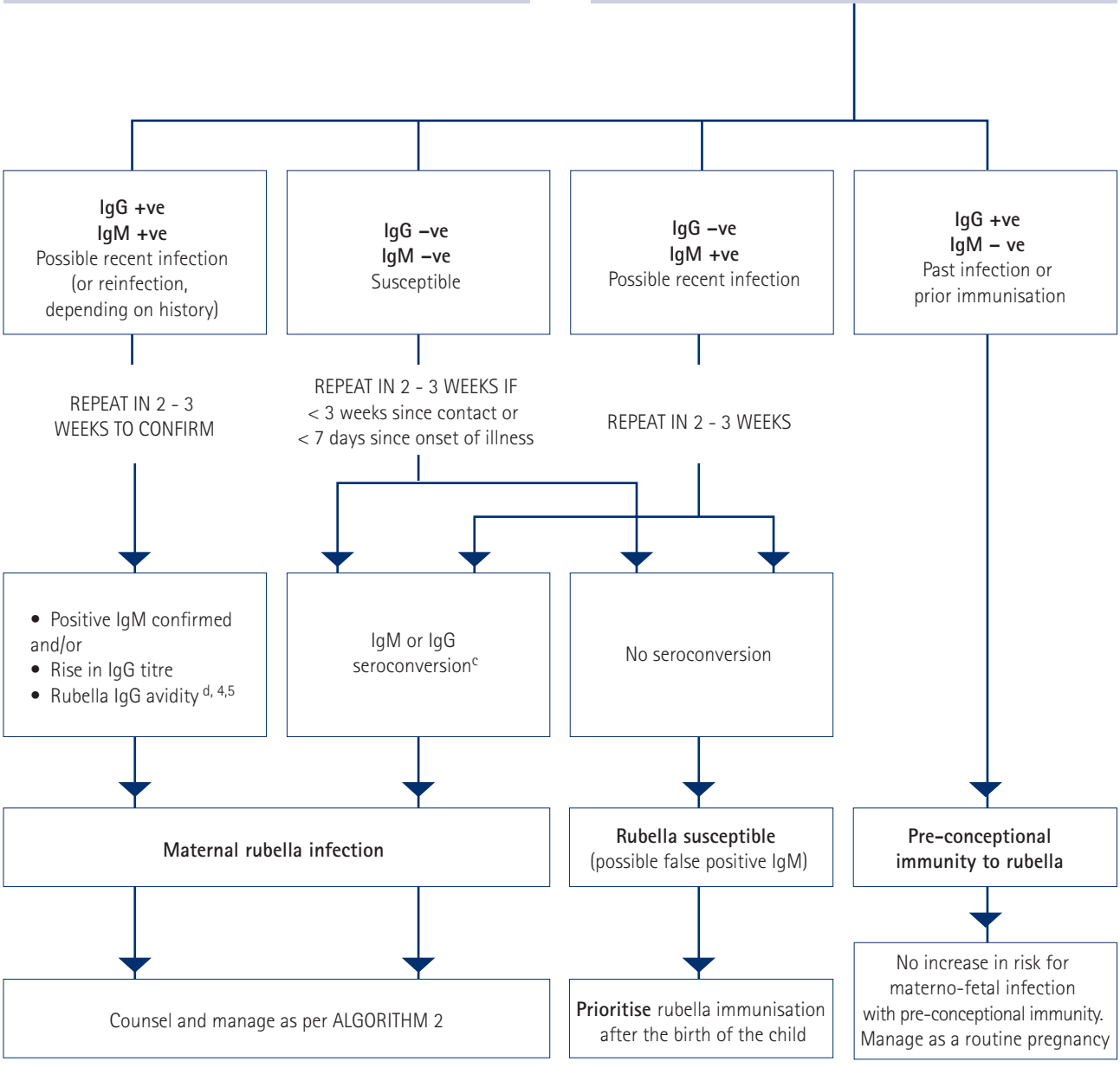
AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

RUBELLA – ALGORITHM 1

DIAGNOSIS OF SUSPECTED MATERNAL RUBELLA INFECTION

Routine antenatal screening (IgG only)[a] [1,2,3]
- If IgG –ve, prioritise rubella immunisation after delivery
- If IgG +ve at 10 - 15 IU/mL: potential risk of reinfection
  Consider re-immunisation after delivery
- If > 15 IU/mL: re-immunisation not needed

Rubella testing (IgG/IgM)[b] because of
(i) contact with rubella
(ii) rubella-like illness (fever, erythematous rash, arthralgia)
Serum should be obtained 7 - 10 days after onset of rash



COMMENTS

a. Rubella serological tests are expressed as IU/ml (WHO International reference)[6] and lack standardisation. Different laboratories use varying cut-offs for reporting low IgG levels (ranging from 5 - 10 IU/mL). The WHO levels corresponding to protection from reinfection are imprecise, but only a small proportion of women are affected by reinfection [1,2]

b. IgM +ve results should be interpreted within the clinical context. IgM can be positive in re-infection, or persist after rubella vaccination or represent a false positive result [6]

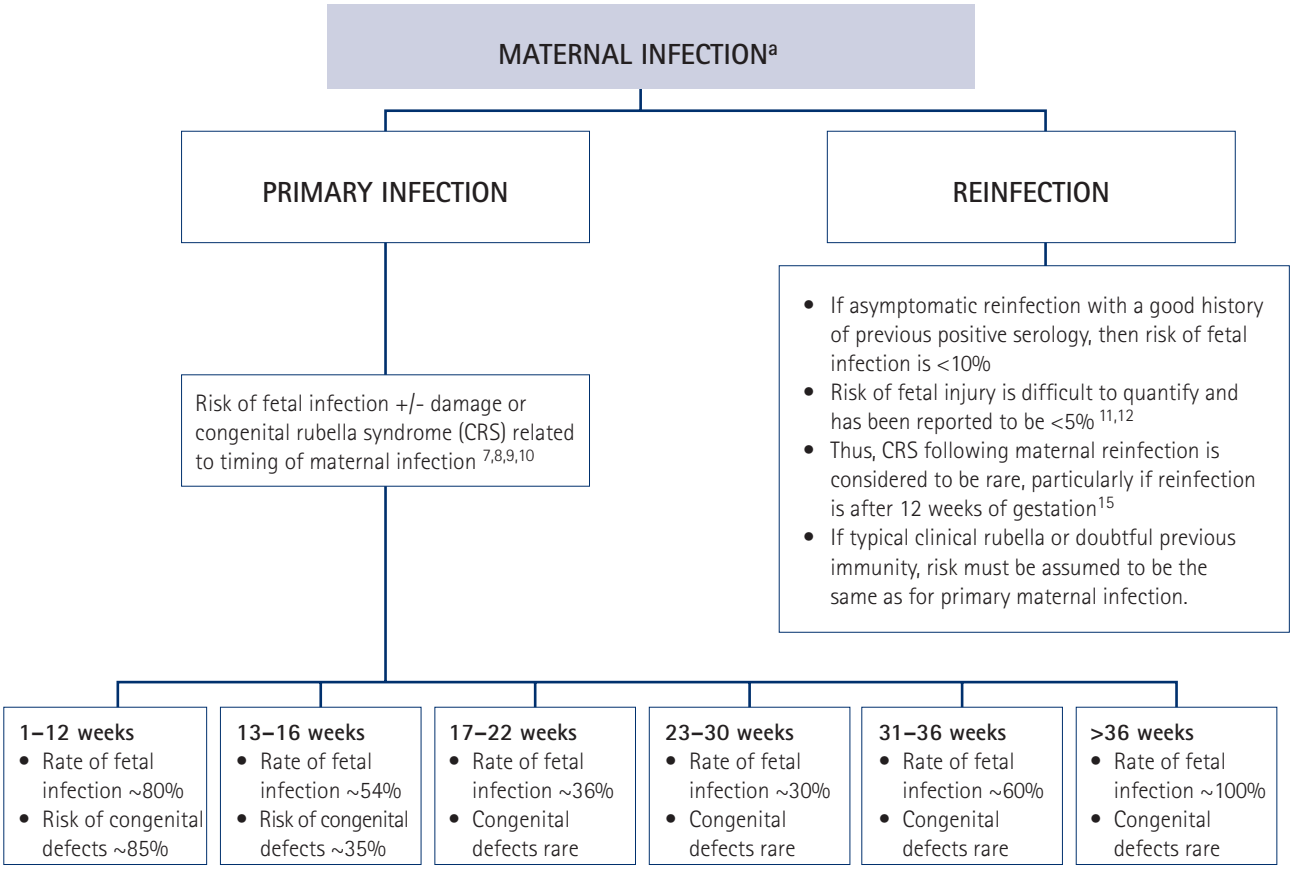
c. Seroconversion should be checked by testing the sera in parallel

d. Rubella IgG avidity may assist in determining primary infection, with low avidity indicating recent primary infection and high avidity against primary infection [4, 5]

e. Prevention: Women who are planning pregnancy who have not received rubella vaccination should be tested for immunity (rubella IgG). Non-immune women should receive rubella vaccination before they conceive, but should avoid pregnancy for 28 days after vaccination

RUBELLA – ALGORITHM 2

MANAGEMENT OF PROVEN MATERNAL RUBELLA INFECTION



- Counsel about materno-fetal transmission risks and expected outcomes
- Discuss the role of fetal testing and options for termination of pregnancy if maternal infection occurred prior to 20 weeks of gestation
- Maternal infection after 20 weeks is rarely associated with congenital rubella syndrome

Prenatal fetal diagnosis/testing

- Rubella virus PCR or culture can be performed on chorionic villous samples (CVS) or on amniotic fluid obtained by amniocentesis, or rubella IgM can be performed by fetal blood sampling (by cordocentesis), with CVS enabling diagnosis at an earlier gestation.[10, 13, 14]
- The timing of prenatal testing is recommended for at least 6 weeks after known maternal infection[15]

However

- CVS can be associated with risk of contamination with maternal tissue giving false positive PCR.
- PCR is not widely available and sensitivity is generally not well validated. However, a positive result will be helpful[15] (assuming that contamination can be excluded).[13]
- False negative fetal IgM is common until late in pregnancy. [16,17]

COMMENTS

a. Normal human immunoglobulin (NHIG) as post-exposure prophylaxis in non-immune pregnant contacts may modify disease symptoms in the mother, and may marginally reduce rubella infection to the fetus[17,18,19] In such cases, intramuscular administration of 20 mL of NHIG within 72 hours of rubella exposure might reduce, but will not eliminate, the risk for rubella. Serological follow-up of NHIG recipients is essential and should continue for up to 2 months
b. Transmission risks and details of incidence and type of abnormalities can be found in textbooks [9,10] and reviews. [15]
c. Contact your local virology laboratory for information about the availability of rubella culture or PCR
d. Infection control: Women with acute rubella infection should be isolated and contact and droplet precautions apply. Women who present with rubella infection > 4 days after rash onset do not need isolation. Newborns being investigated for CRS or with confirmed CRS should be isolated in hospital with contact and droplet precautions

RUBELLA – ALGORITHM 3

MANAGEMENT AND FOLLOW UP OF THE INFANT AT RISK OF INFECTION

ASSESSMENT OF THE NEWBORN

Examine infant for evidence of Congenital Rubella Syndrome (CRS)*

Investigate infant

- Serology (IgM)
- PCR (urine and throat swab); note NEGATIVE PCR does not exclude infection
- Culture urine and throat swabs, tears (conjunctival swab), lens tissue (if available); results can take several weeks

Clinical features of CRS present[a]	**No clinical features of CRS**	
• IgG ≥ maternal IgG titre (measured in parallel) • IgM +ve • PCR +ve	• IgM +ve • PCR +ve	• IgG ≤ maternal IgG titre (measured in parallel) • IgM -ve • PCR -ve
Symptomatic, infected infant	Asymptomatic, infected infant (risk of late onset disease months or years after birth)	Infant probably not infected
• No specific management • Breast feeding not contraindicated • Ensure ophthalmology, cardiac and hearing assessments at birth • Regular assessments (3 - 6 monthly) necessary in the first few months and years of life to detect the emergence of late abnormalities related to persisting infection • Infants are infectious for at least 12 months after birth and a potential infection risk to susceptible female staff and pregnant contacts • Infant should be isolated (droplet and contact) while in hospital • Ensure all hospital contacts/caregivers are rubella immune		• Reassure • Breast feeding not contraindicated • Confirm absence of infection with falling/absent IgG, 6 - 9 months post birth (before first MMR childhood vaccination)

COMMENTS

a. **Features of CRS** [6, 20, 21]

At birth or early manifestations

- Deafness (sensorineural hearing loss, 60–75%), central nervous system dysfunction (10–25%, intellectual disability, developmental delay, microcephaly), cardiovascular defects (10–20%, patent ductus, pulmonary artery stenosis, pulmonary stenosis), ophthalmological abnormalities (10–25%, cataracts, microophthalmos, retinopathy, glaucoma, strabismus, cloudy cornea), Others: growth restriction, haematological abnormalities, GI tract abnormalities, pneumonitis and osteitis

Late manifestations

- Deafness (sensorineural hearing loss), neurological deficiencies, epilepsy, cataracts, retinopathy, tooth defects, growth retardation, insulin dependent diabetes mellitus (up to 50 times the rate in the general population), thyroid dysfunction and panencephalitis

RUBELLA REFERENCES

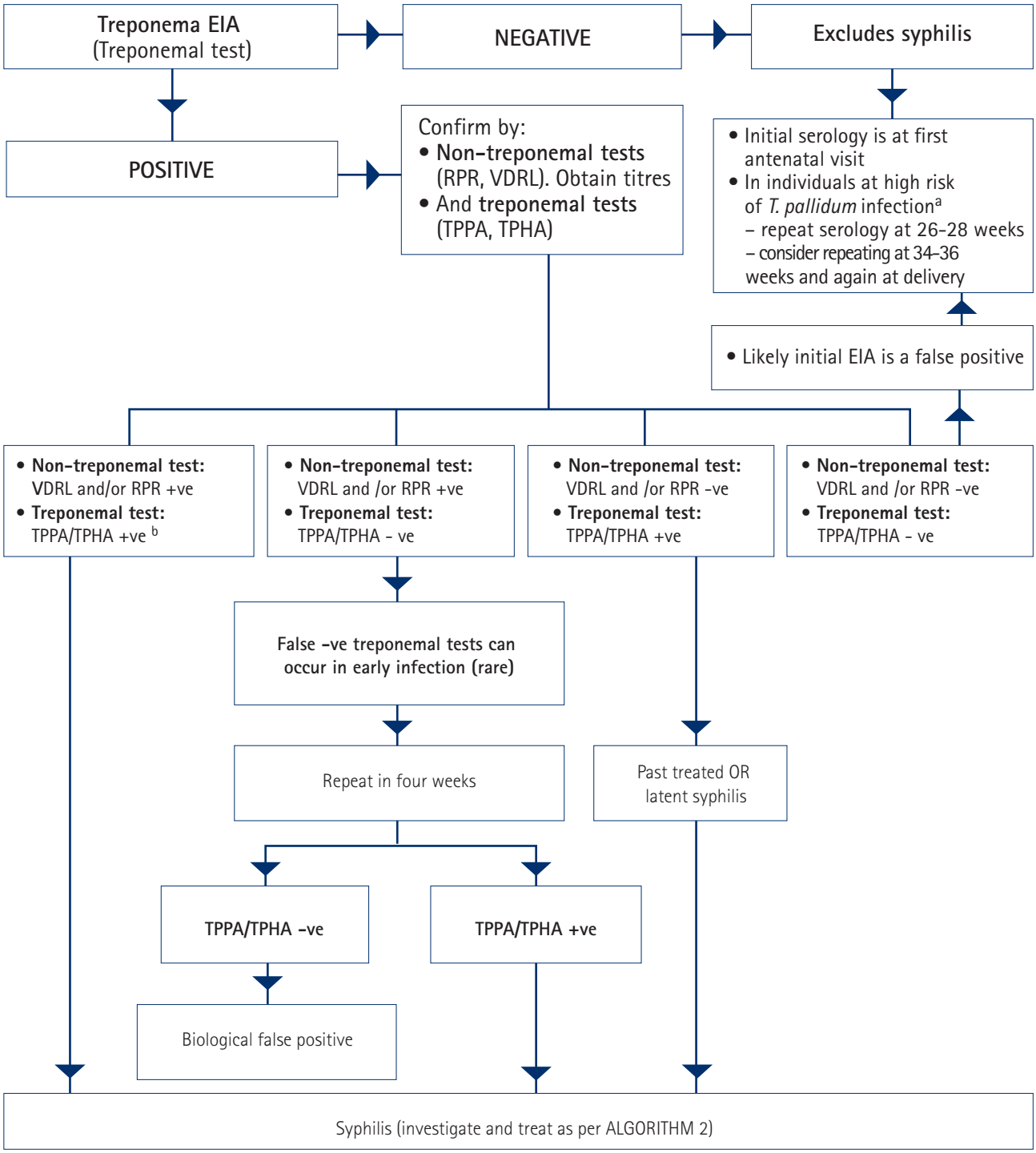
1. Dimech W, Grangeot-Keros L, Vauloup-Fellous C. Standardization of Assays That Detect Anti-Rubella Virus IgG Antibodies. Clinical Microbiology Reviews 2016;29:163-74.
2. Bouthry E, Furione M, Huzly D, et al. Assessing Immunity to Rubella Virus: a Plea for Standardization of IgG (Immuno)assays. Journal of Clinical Microbiology 2016;54:1720-5.
3. RANZCOG. Routine antenatal assessment in the absence of pregnancy complications (C-Obs 3b). 2022. https://ranzcog.edu.au/wp-content/uploads/2022/05/Routine-antenatal-assessment-in-the-absence-of-pregnancy-complications.pdf
4. Vauloup-Fellous C, Ursulet-Diser J, Grangeot-Keros L. Development of a rapid and convenient method for determination of rubella virus-specific immunoglobulin G avidity. Clinical & Vaccine Immunology: CVI 2007;14:1416-9.
5. Mubareka S, Richards H, Gray M, Tipples GA. Evaluation of commercial rubella immunoglobulin G avidity assays. Journal of Clinical Microbiology 2007;45:231-3.
6. Bouthry E, Picone O, Hamdi G, Grangeot-Keros L, Ayoubi JM, Vauloup-Fellous C. Rubella and pregnancy: diagnosis, management and outcomes. Prenatal Diagnosis 2014;34:1246-53.
7. Miller E, Cradock-Watson JE, Pollock TM. Consequences of confirmed maternal rubella at successive stages of pregnancy. Lancet 1982;2:781-4.
8. Enders G, Nickerl-Pacher U, Miller E, Cradock-Watson JE. Outcome of confirmed periconceptional maternal rubella. Lancet 1988;1:1445-7.
9. Peckham CS. Clinical and laboratory study of children exposed in utero to maternal rubella. Archives of Disease in Childhood 1972;47:571-7.
10. Remington and Klein's Infectious Diseases of the Fetus and the Newborn Infant. 8 ed: Saunders; 2015.
11. Cradock-Watson JE, Ridehalgh MK, Anderson MJ, Pattison JR. Outcome of asymptomatic infection with rubella virus during pregnancy. J Hyg (Lond) 1981;87:147-54.
12. Morgan-Capner P, Miller E, Vurdien JE, Ramsay ME. Outcome of pregnancy after maternal reinfection with rubella. Communicable Disease Report 1991;1:R57-9.
13. Revello MG, Baldanti F, Sarasini A, Zavattoni M, Torsellini M, Gerna G. Prenatal diagnosis of rubella virus infection by direct detection and semiquantitation of viral RNA in clinical samples by reverse transcription-PCR. Journal of Clinical Microbiology 1997;35:708-13.
14. Ho-Terry L, Terry GM, Londesborough P. Diagnosis of foetal rubella virus infection by polymerase chain reaction. Journal of General Virology 1990 71:1607-11.
15. Mace M, Cointe D, Six C, et al. Diagnostic value of reverse transcription-PCR of amniotic fluid for prenatal diagnosis of congenital rubella infection in pregnant women with confirmed primary rubella infection. Journal of Clinical Microbiology 2004;42:4818-20.
16. Daffos F, Forestier F, Grangeot-Keros L, et al. Prenatal diagnosis of congenital rubella. Lancet 1984;2:1-3.
17. Young MK, Cripps AW, Nimmo GR, van Driel ML. Post-exposure passive immunisation for preventing rubella and congenital rubella syndrome. Cochrane Database Syst Rev 2015:CD010586.
18. The Australian Immunisation Handbook - on-line access (current) https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/rubella
19. Centers for Disease Control and Prevention (CDC), Zimmerman LA, Reef SE, McCauley MM. Control and prevention of rubella: evaluation and management of suspected outbreaks, rubella in pregnant women, and surveillance for congenital rubella syndrome. MMWR. Recommendations and Reports 2001;50(RR-12):1-23.
20. Yazigi A, De Pecoulas AE, Vauloup-Fellous C, Grangeot-Keros L, Ayoubi JM, Picone O. Fetal and neonatal abnormalities due to congenital rubella syndrome: a review of literature. Journal of Maternal-Fetal & Neonatal Medicine 2017;30:274-8.
21. Best JM. Rubella. Seminars In Fetal & Neonatal Medicine 2007;12:182-92.

Syphilis (Treponema pallidum)

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

SYPHILIS (TREPONEMA PALLIDUM) – ALGORITHM 1

ANTENATAL SCREENING FOR SYPHILIS

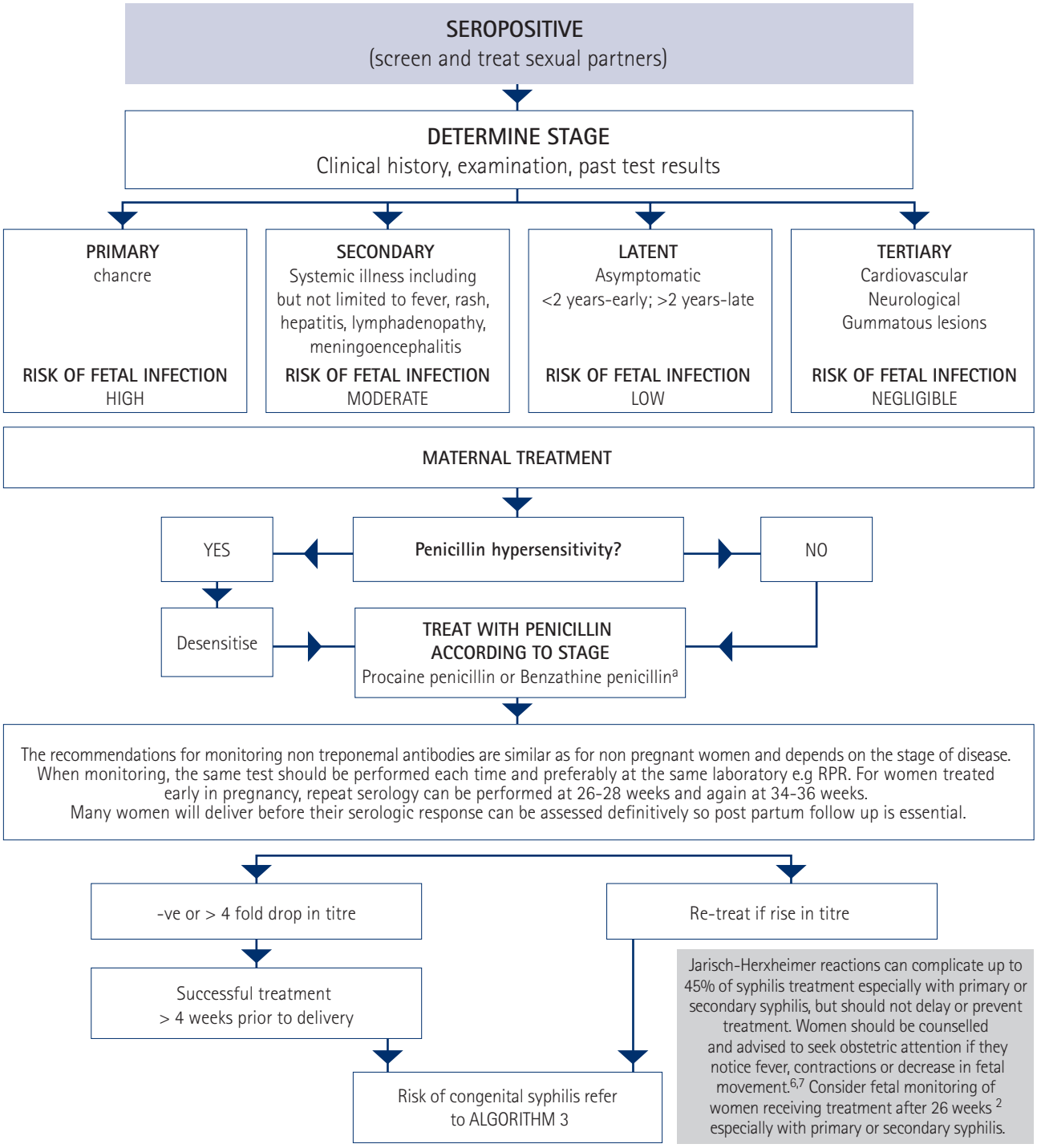


a Individuals at "high risk of *T. pallidum*" infection may include
- a woman who has had sexual contact with an infectious syphilis case
- a women or partner who identify as Aboriginal or Torres Strait Islander
- a woman with substance abuse particularly metamphetamines
- a women whose partner is a man who also has sex with men
- a woman with late, limited or no antenatal care
- a women who engages in high risk sexual activity
- a woman diagnosed with an STI in the current pregnancy or in the last 12 months

b Discuss all cases with a clinician with specialist knowledge and experience in testing, serology interpretation, management and treatment of syphilis in pregnancy

SYPHILIS (TREPONEMA PALLIDUM) – ALGORITHM 2

INVESTIGATION AND TREATMENT OF MATERNAL SYPHILIS



COMMENTS

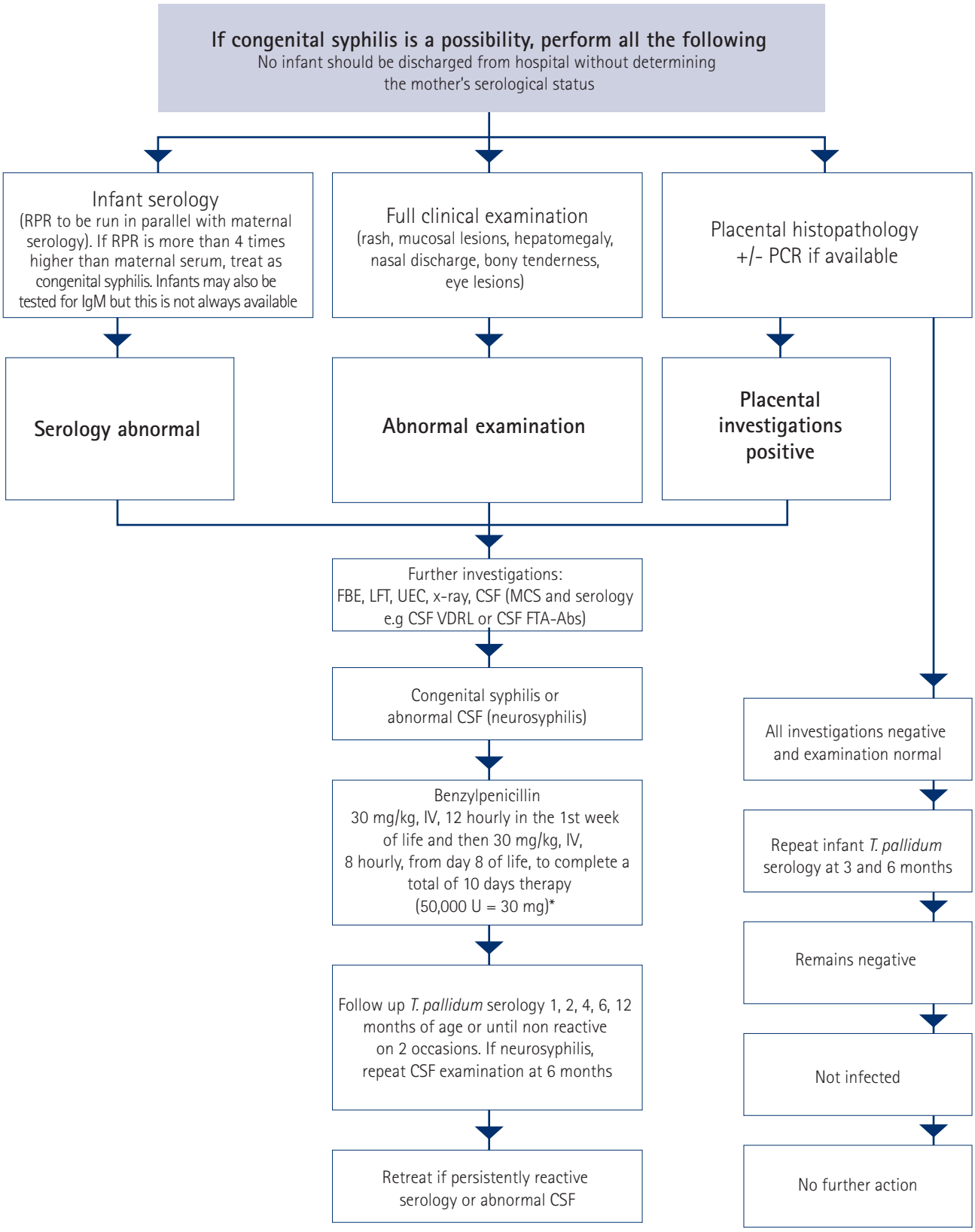
a. Early syphilis (primary, secondary or early latent syphilis) treatment:
- Benzathine penicillin 1.8 g (= 2.4 million units) IM as a single dose OR
- Procaine penicillin 1.5 g IM daily for 10 days
- For women with primary or secondary syphilis, a second dose can be given one week after the first.

Late syphilis (>2 years or unknown duration) treatment:
- Benzathine penicillin 1.8 gm (= 2.4 million units) IM once weekly for 3 weeks. If a dose is missed for more than 14 days, the full three dose course of treatment should be re-started.
- An alternative treatment regimen for late syphilis is procaine penicillin 1.5 g IM daily for 15 days

Treatment failure despite maternal treatment has been associated with early syphilis, prematurity, high titres of RPR or VDRL at time of treatment and/or at delivery and a short interval between treatment and delivery[3,4]. Therefore some experts recommend a second dose of benzathine penicillin one week after the initial dose if primary, secondary or early latent syphilis, high RPR/VDRL titres or late treatment in pregnancy. Although penicillin is extremely effective in the treatment of syphilis in pregnancy and the prevention of congenital syphilis, there are no randomised trials comparing different doses of penicillin or in combination with other antibiotics in the setting of pregnancy [1]

SYPHILIS (TREPONEMA PALLIDUM) – ALGORITHM 3

INVESTIGATION AND MANAGEMENT OF THE NEONATE BORN TO A MOTHER WITH SYPHILIS



* Procaine penicillin (50 mg/kg per dose), IM, daily may be an option if IV access is not feasible.

SYPHILIS (TREPONEMA PALLIDUM) REFERENCES

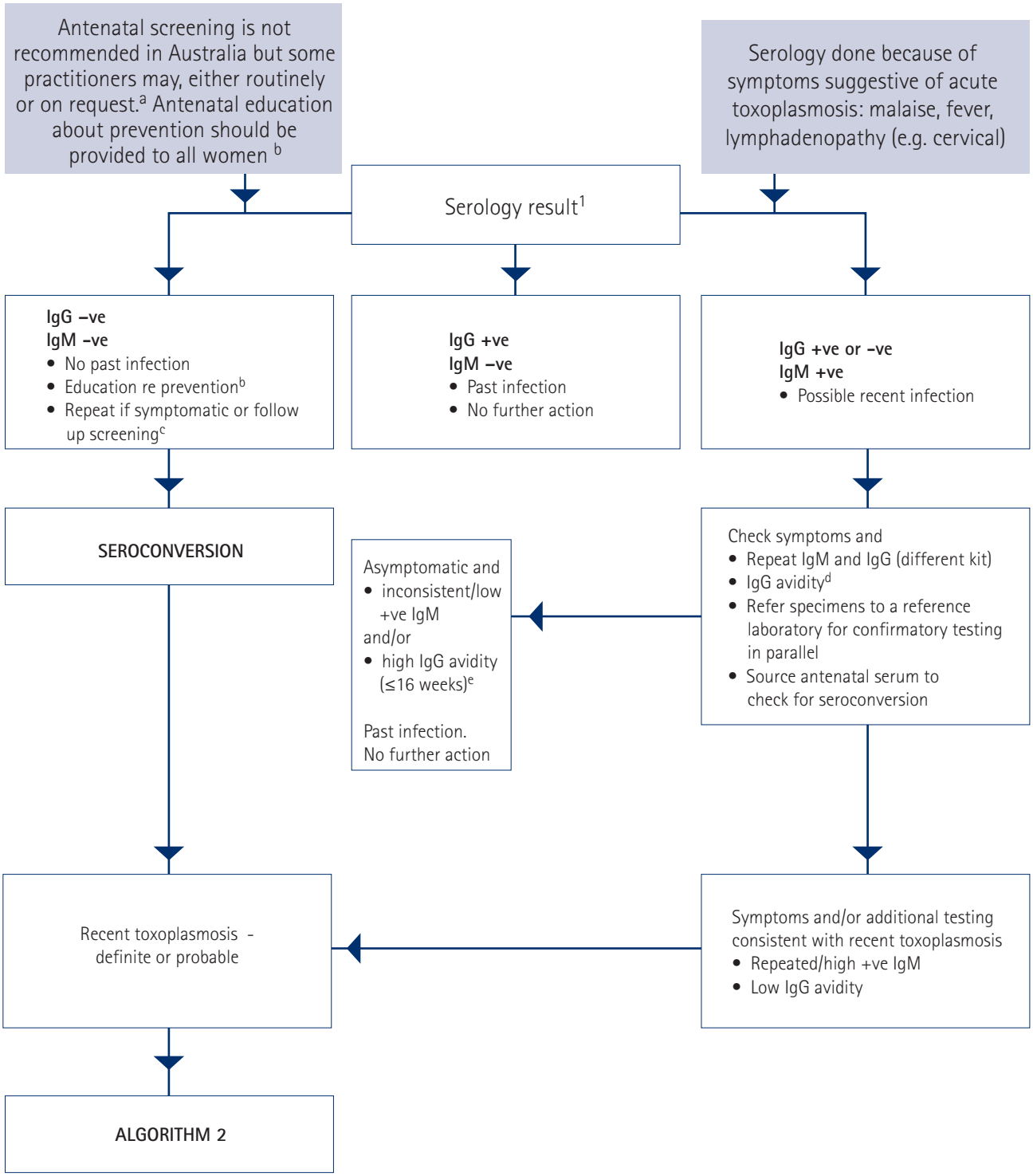
1. Walker GJA Antibiotics for syphilis diagnosed during pregnancy. Cochrane Database of Systematic Reviews Issue 3 2009
2. Myles TD et al The Jarisch-Herxheimer reaction and fetal monitoring changes in pregnant women treated for syphilis Obstet Gynecol 1999 93(4):631-2
3. Sheffield JS et al. Congenital syphilis after maternal treatment for syphilis during pregnancy. Am J Obstet Gynecol 2002 186(3):569-73
4. Alexander JM et al. Efficacy of treatment for syphilis in pregnancy Obstet Gynecol 1999 93(1):5-8
5. Guideline: Syhpilis in pregnancy - Queensland Health (first published 2018, amended 2021) https://www.health.qld.gov.au/__data/assets/pdf_file/0035/736883/g-sip.pdf
6. Workowski KA, Bachmann LH, Chan PA et al. Sexually transmitted infections treatment guidelines. MMWR Recomm Rep 2021;70(4):1 - 187
7. Macumber S, Singh AE, Gratrix J, et al. Retrospective Cohort Study of the Incidence and Outcomes of Jarisch-Herxheimer Reactions Following Treatment for Infectious Syphilis in Late Pregnancy. Sex Transm Dis 2022 doi: 10.1097/OLQ.0000000000001610.

Toxoplasma gondii

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

TOXOPLASMA GONDII – ALGORITHM 1

ANTENATAL EVALUATION

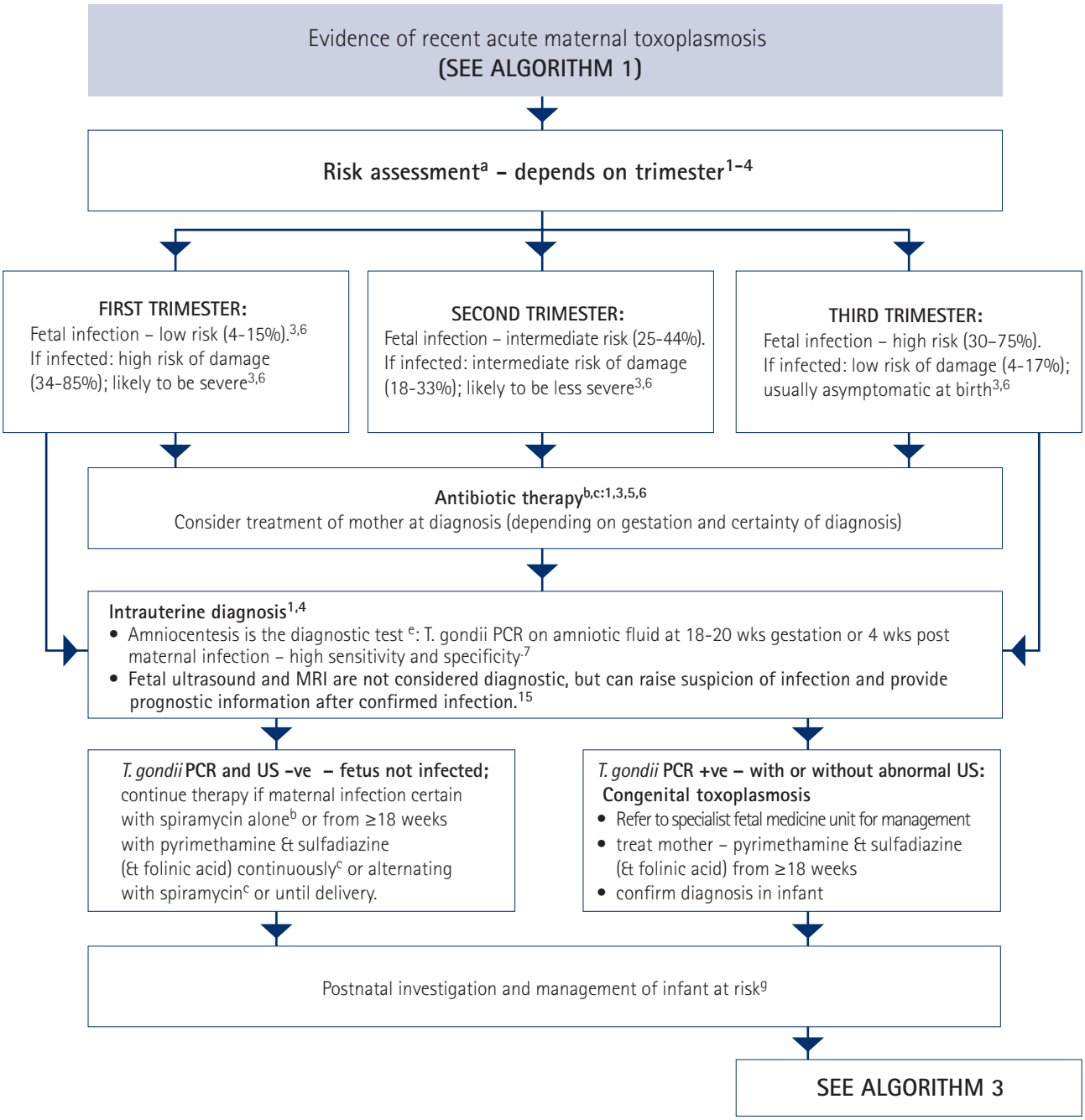


COMMENTS

a. Pros and cons of antenatal screening are complex; if done, there should be an appropriate management plan. European centres screen seronegative women throughout pregnancy every 4-6 weeks and offer antenatal therapy if infection occurs
b. Avoid raw/undercooked meat; wash hands after gardening; wash raw vegetables; minimise contact with young kittens and their litter etc [1]
c. Various protocols recommend repeat testing after 1-6 months or at delivery, to identify seroconversion
d. IgM can remain +ve for months or years; rising IgG level and/or low IgG avidity are more specific for "recent" infection (within ~3 months)[1]
e. High IgG avidity after 16 weeks does not exclude infection in early pregnancy

TOXOPLASMA GONDII – ALGORITHM 2

INVESTIGATION AND MANAGEMENT OF MATERNAL TOXOPLASMOSIS



COMMENTS

a. Estimated risks also vary according to the methods of diagnosis, duration of follow-up and treatment, the availability of antental screening programs, and possibly *T. gondii* strains in different geographic location (USA and France)[14,16]

b. **≤ 18 weeks:** Consider spiramycin[c] to prevent vertical transmission until intrauterine diagnosis. Spiramycin is not routinely available in Australia, but can be imported on request. Does not readily cross placenta and therefore does not treat infected fetus. Efficacy has not been confirmed in randomised controlled trials. Some experts continue spiramycin +/- other drugs until term if *T.gondii* PCR a negative on aminiotic fluid [1,4-7]

c. **≥ 18 weeks** with prenatal diagnosis (i.e. fetal infection confirmed by PCR), or if maternal infection acquired >18 weeks (as fetal transmission rate high): consider pyrimethamine + sulfadiazine[d] + folinic acid to treat fetus. Efficacy remains unconfirmed[1,4-6,7] Pyrimethamine and sulfadiazine: potentially toxic in first trimester. A recent cohort study from Brazil showed reduction in severity of congenital infection with prenatal treatment [11,13]

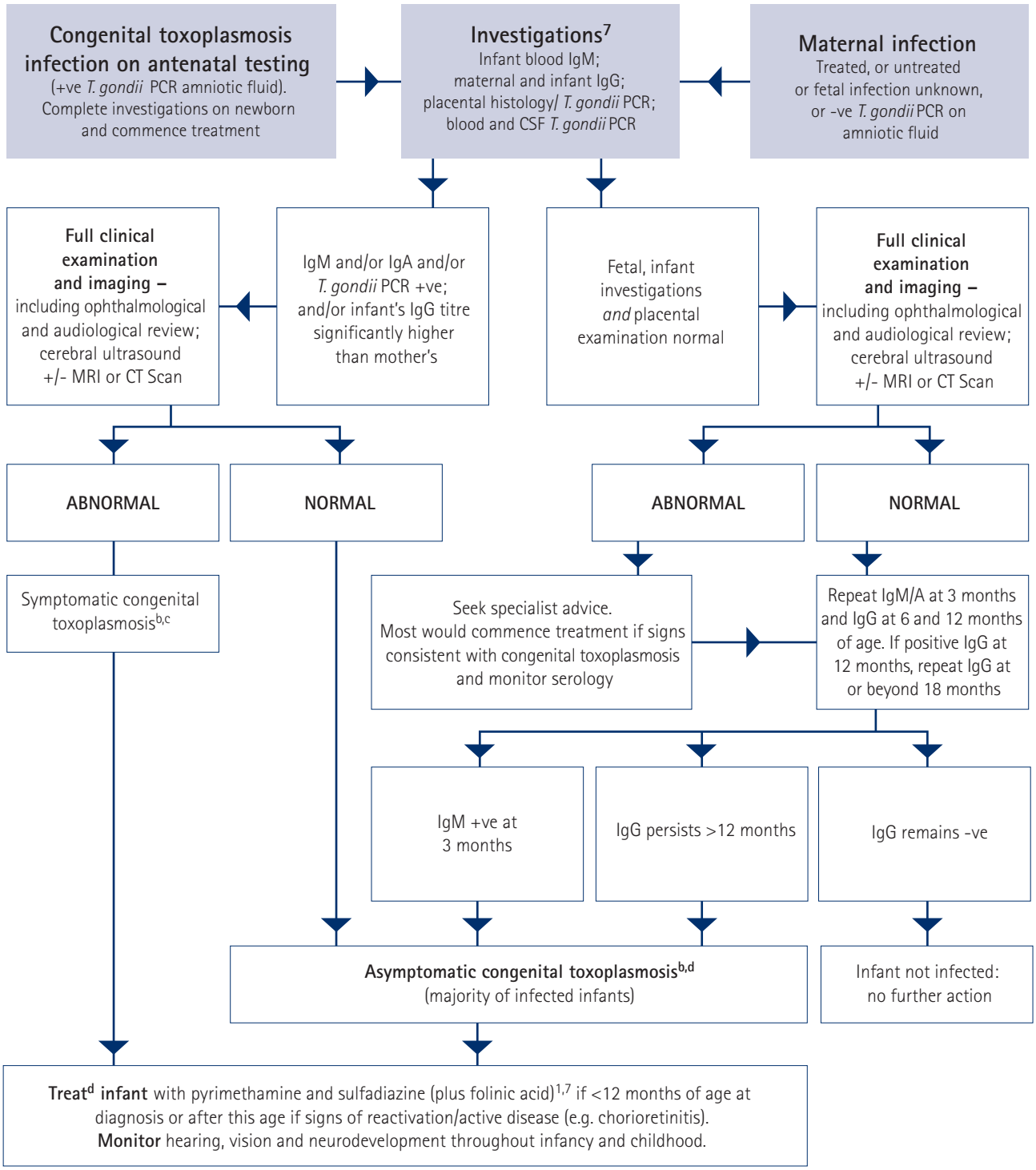
d. Ultrasound findings not specific for toxoplasmosis; include hydrocephalus, brain or hepatic calcification, ascites, splenomegaly

e. PCR sensitivity and negative predictive value (NPV) vary with gestation of maternal infection[1,4,11]: NPV ≤ 20 weeks high (90-100%), sensitivity high 17-21 weeks, but low <17 weeks (20-60%) or > 21 weeks (50-60%); culture of *T. gondii* is now rarely, if ever done for diagnosis; it requires mouse inoculation; no additional benefit from fetal blood testing

f. Local laws need to be taken into account when considering late termination

TOXOPLASMA GONDII – ALGORITHM 3

INVESTIGATION AND MANAGEMENT OF INFANT AT RISK OF TOXOPLASMOSIS



COMMENTS

a. Neonatal screening not often done, but is an alternative to antenatal screening to detect infected infants for treatment [7]
b. Proportion of infants infected and severity depends on when maternal infection occurred and if/how treated [9,10]
c. Chorioretinitis/retinal scarring; intracranial calcification; hydrocephalus; hepatosplenomegaly; pneumonia; thrombocytopenia; lymphadenopathy; myocarditis and IgM +ve +/or abnormal placenta +/- CSF abnormality (PCR +ve). Toxo CSF PCR can assist with confirming diagnosis in symptomatic infants when IgM negative [13]
d. High incidence of long term sequelae (e.g. chorioretinitis) in untreated infants even if asymptomatic at birth - can be reduced by treatment
e. Recommended duration of treatment 12 months. Studies to evaluate shorter durations under evaluation in randomized controlled trials [1,8]
f. Dose: pyrimethamine: 1 mg/kg, every 12 hours for 2 days followed by 1 mg/kg daily for 6 months followed by the same dose, three times a week to complete 12 months; sulfadiazine: 50 mg/kg, every 12 hours; and folinic acid (10 mg three times a week for 12 months). Folinic acid should be administered until 1 week following cessation of pyrimethamine treatment [9]

TOXOPLASMA REFERENCES

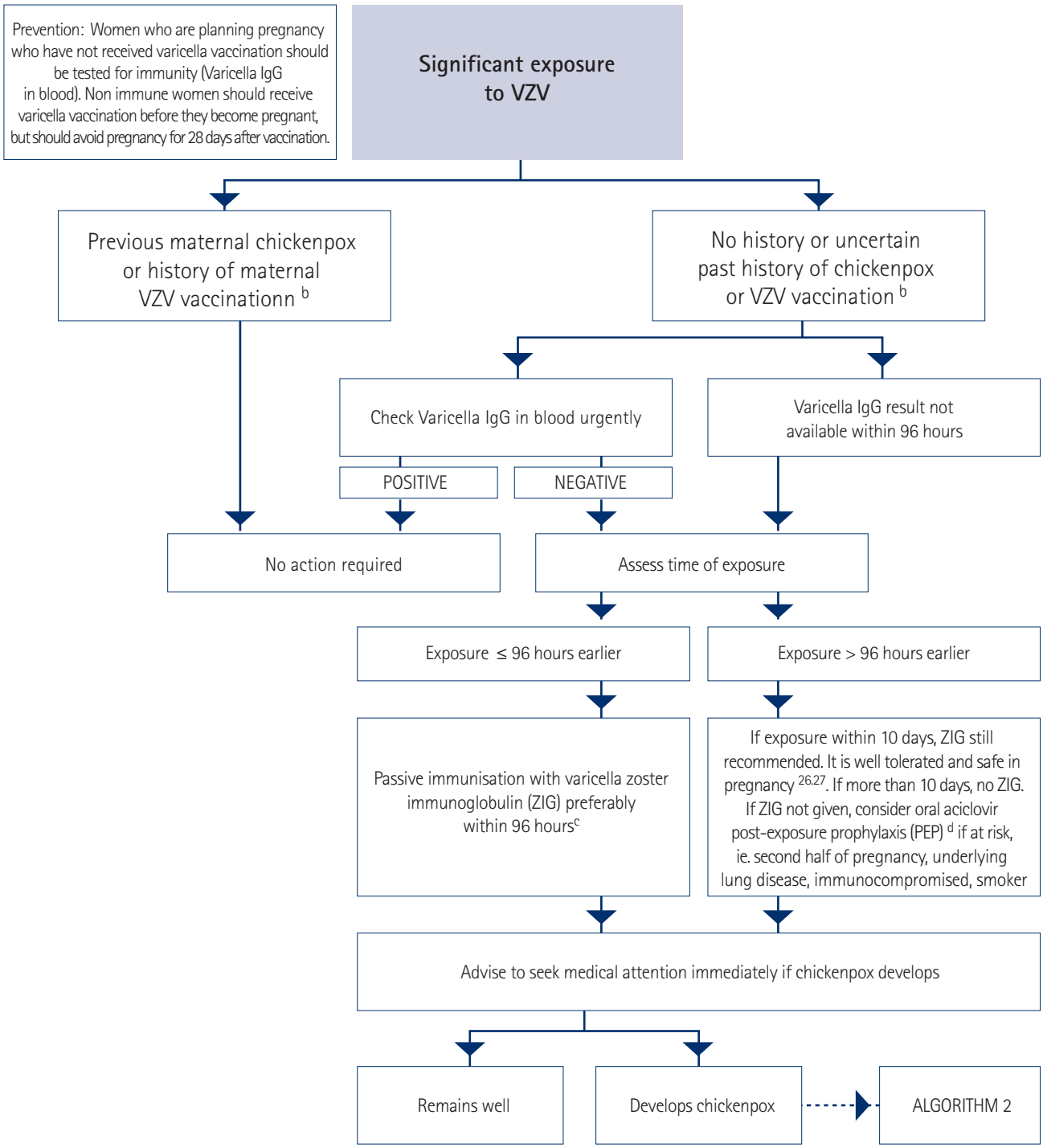
1. Jose G. Montoya and Jack S. Remington Management of Toxoplasma gondii Infection during Pregnancy Clinical Infectious Diseases 2008; 47:554–66
2. Dunn D, Wallon M, Peyron F, Petersen E, Peckham C, Gilbert R Mother-to-child transmission of toxoplasmosis: risk estimates for clinical counselling. Lancet 1999 May 29;353:1829-33
3. Thiébaut R, Leproust S, Chêne G, Gilbert R; SYROCOT (Systematic Review on Congenital Toxoplasmosis) study group.Effectiveness of prenatal treatment for congenital toxoplasmosis: a meta-analysisof individual patients' data. Lancet 369(9556), 115–122 (2007).
4. Wallon M, Franck J, Thulliez P et al. Accuracy of real-time polymerase chain reaction for Toxoplasma gondii in amniotic fluid. Obstet. Gynecol. 115(4), 727–733 (2010).
5. Wallon M, Liou C, Garner P, Peyron F. Congenital toxoplasmosis: systematic review of evidence of efficacy of treatment in pregnancy.BMJ. 1999 Jun 5;318(7197):1511-4.
6. Cortina-Borja M, et al. Prenatal Treatment for Serious Neurological Sequelae of Congenital Toxoplasmosis: An Observational Prospective Cohort Study. PLoS Med 2010; 7:e1000351
7. Yamada H, et al Prospective Study of Congenital Toxoplasmosis Screening with Use of IgG Avidity and Multiplex Nested PCR Methods. J Clin Microbiol 2011;49:2552-62.
8. Mandelbrot L, Kieffer F, Sitta R, Laurichesse-Delmas H, Winer N, Mesnard L, et al. Prenatal therapy with pyrimethamine + sulfadiazine vs spiramycin to reduce placental transmission of toxoplasmosis: a multicenter, randomized trial. Am J Obstet Gynecol. 2018;219(4):386. e1-.e9.
9. Berrebi A, Bardou M, Bessieres MH, et al. Outcome for children infected with congenital toxoplasmosis in the first trimester and with normal ultrasound findings: a study.Eur J Obstet Gynecol Reprod Biol 2007; 135:53–7.
10. Moncada PA, Montoya JG. Toxoplasmosis in the fetus and newborn: an update on prevalence, diagnosis and treatment Expert Rev. Anti Infect. Ther. 10(7), 815–828 (2012)
11. Peyron F, Garweg JG, Wallon M, Descloux E, Rolland M, Barth J. Long-term impact of treated congenital toxoplasmosis on quality of life and visual performance. Pediatr Infect Dis J. 2011 Jul;30(7):597-600.
12. Rajapakse S, Weeratunga P, Rodrigo C, de Silva NL, Fernando SD5.Prophylaxis of human toxoplasmosis: a systematic review. Pathog Glob Health. 2017 Oct;111(7):333-342.
13. Olariu TR1, Remington JS, Montoya JG. Polymerase chain reaction in cerebrospinal fluid for the diagnosis of congenital toxoplasmosis. Pediatr Infect Dis J. 2014 Jun;33(6):566-70.
14. Yvonne A. Maldonado, Jennifer S. Read, COMMITTEE ON INFECTIOUS DISEASES. From the American Academy of Pediatrics Technical Report Diagnosis, Treatment, and Prevention of Congenital Toxoplasmosis in the United States Pediatrics 2017; 139 (2)
15. Khalil A, et al. ISUOG Practice Guidelines: role of ultrasound in congenital infection. Ultrasound Obstet Gynecol. 2020 Jul;56(1):128-151. doi: 10.1002/uog.21991. Epub 2020 May 13. PMID: 32400006.
16. Mandelbrot, L. Congenital toxoplasmosis: What is the evidence for chemoprophylaxis to prevent fetal infection? Prenatal Diagnosis. 2020; 40: 1693– 1702. https://doi.org/10.1002/pd.5758

Varicella zoster virus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

VARICELLA ZOSTER VIRUS – ALGORITHM 1

EXPOSURE TO VARICELLA ZOSTER VIRUS DURING PREGNANCY



COMMENTS

a. Significant exposure to varicella or zoster [1,2]
   - Living in the same household as a person with active chickenpox or herpes zoster
   - Face-to-face contact with a case of chickenpox or zoster for at least 5 minutes or being in the same room for at least one hour.[1]

   Chickenpox cases are infectious from 2 days before rash until lesions crusted

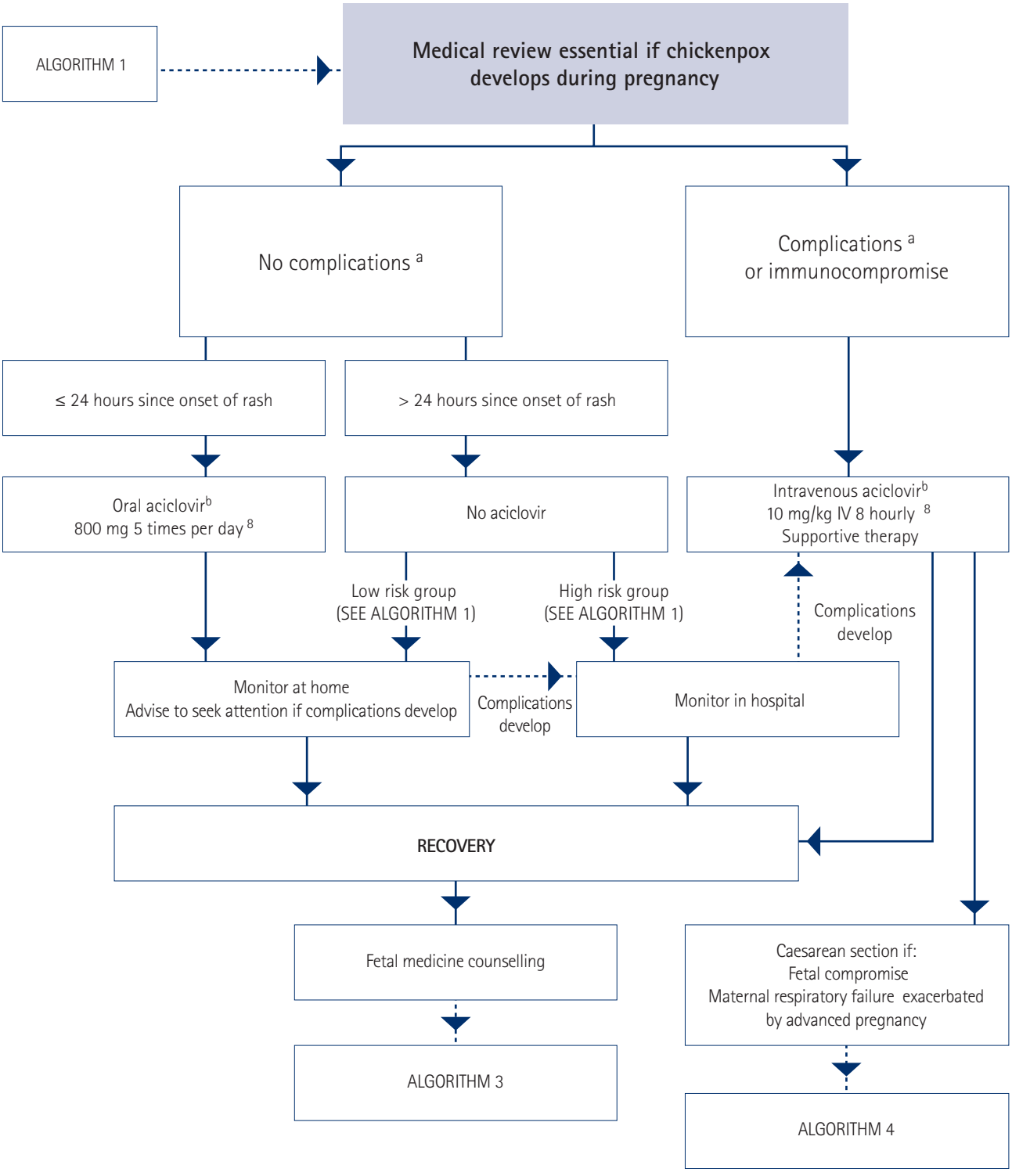
b. VZV vaccine not recommended during pregnancy. Women should avoid pregnancy for 28 days after varicella vaccination. However, inadvertent administration of VZV vaccine to pregnant women has not been shown to be associated with fetal infection [3]

c. ZIG should be given early in the incubation period (within 96 hours of exposure) but may have some efficacy if administered out to as late as 10 days post exposure. Dose is based on weight and given IM. [1,4] High titre varicella zoster immune globulin (ZIG) is available from the Red Cross Blood Transfusion Service in Australia. Each vial contains 200 international units VZV in /2 mL. Recommended dose: 2 mL (200 units) for 0-10 kg, 4 mL for 11-30 kg and 6 mL for >30 kg. Normal human immunoglobulin can be used if ZIG unavailable.[1]

d. Efficacy of aciclovir PEP in pregnancy has not been tested in controlled trials. Testing for seroconversion to varicella after vaccination is not recommended as antibody levels are often lower than with natural immunity. Dose is 800 mg orally five times per day. [4-8] Duration 7 days. Unlikely to be effective if started 14 days post exposure

VARICELLA ZOSTER VIRUS – ALGORITHM 2

MANAGEMENT OF CHICKENPOX IN PREGNANCY



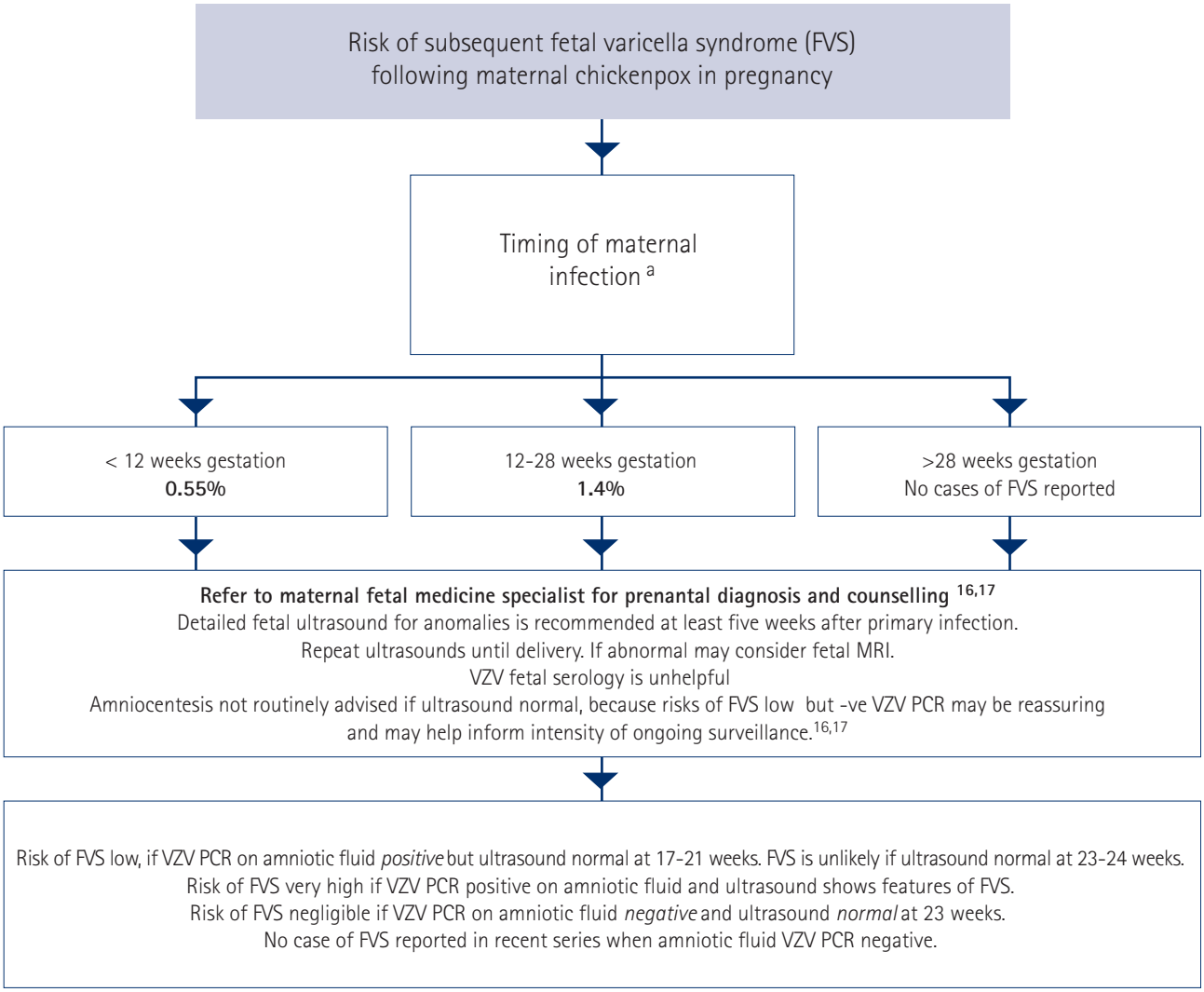
COMMENTS

a. Complications [4]:
- Respiratory symptoms
- Haemorrhagic rash or bleeding
- New lesions developing >6 days
- Persistent fever >6 days
- Neurological symptoms

b. Aciclovir is not licensed for use in pregnancy, but data from large registries suggest it is safe[8]. Limited data suggest valaciclovir safe. Insufficient data to support use of famciclovir in pregnancy. Dose of aciclovir is on pre-pregnancy weight

VARICELLA ZOSTER VIRUS – ALGORITHM 3

FETAL MEDICINE COUNSELLING FOLLOWING CHICKENPOX IN PREGNANCY



Varicella Syndrome manifestations

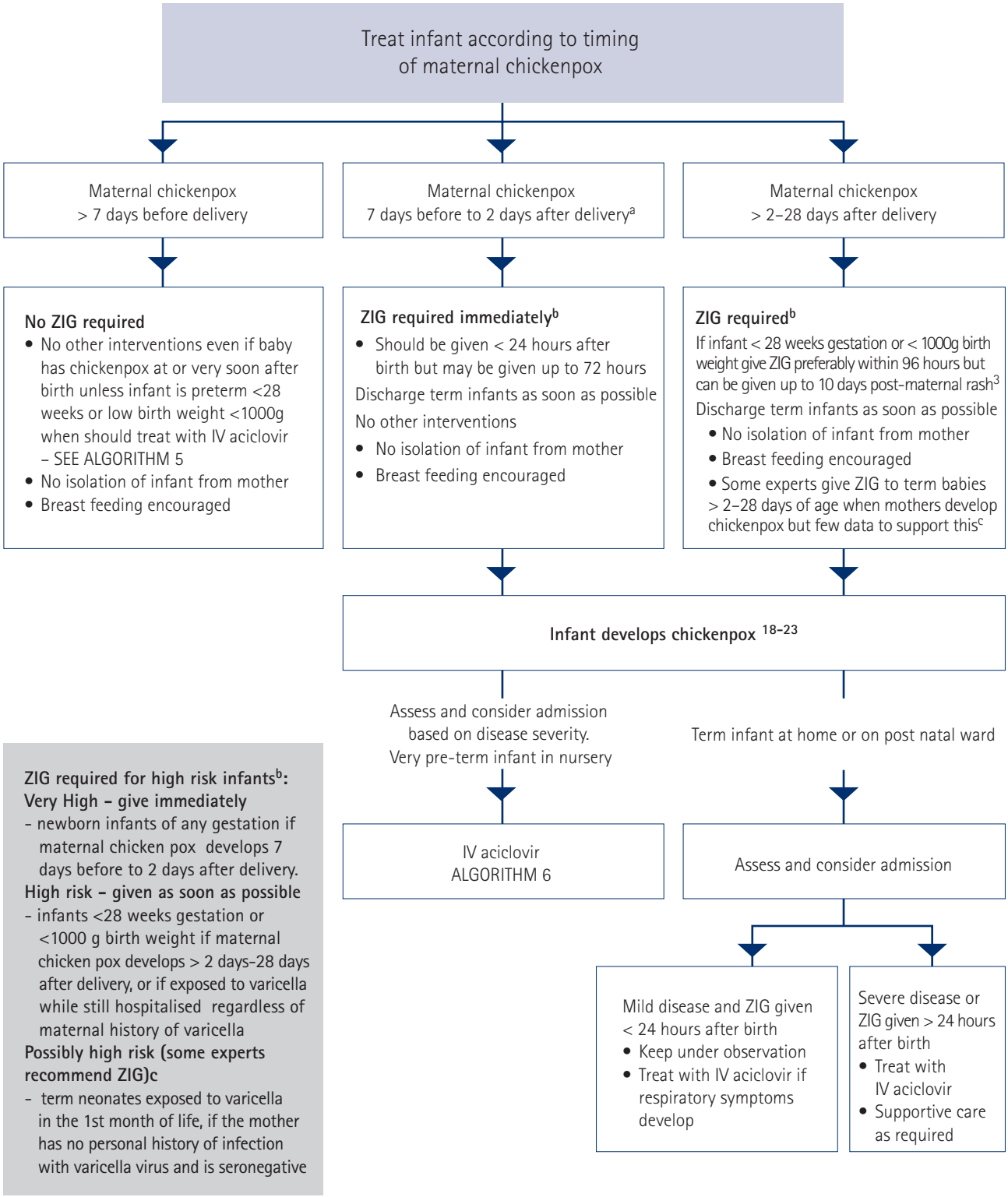
Abnormalities	Frequency
Skin scars	78%
Eye abnormalities	60%
Limb abnormalities	68%
Prematurity, low birth weight	50%
Cortical atrophy, intellectual disability	46%
Poor sphincter control	32%
Early death	29%

COMMENTS

a. Majority of reported cases occurred < 20 weeks, [9-13] but isolated cases up to 28 weeks have been reported [14]

VARICELLA ZOSTER VIRUS – ALGORITHM 4

MANAGEMENT OF INFANTS FROM MOTHERS WITH PERINATAL CHICKENPOX

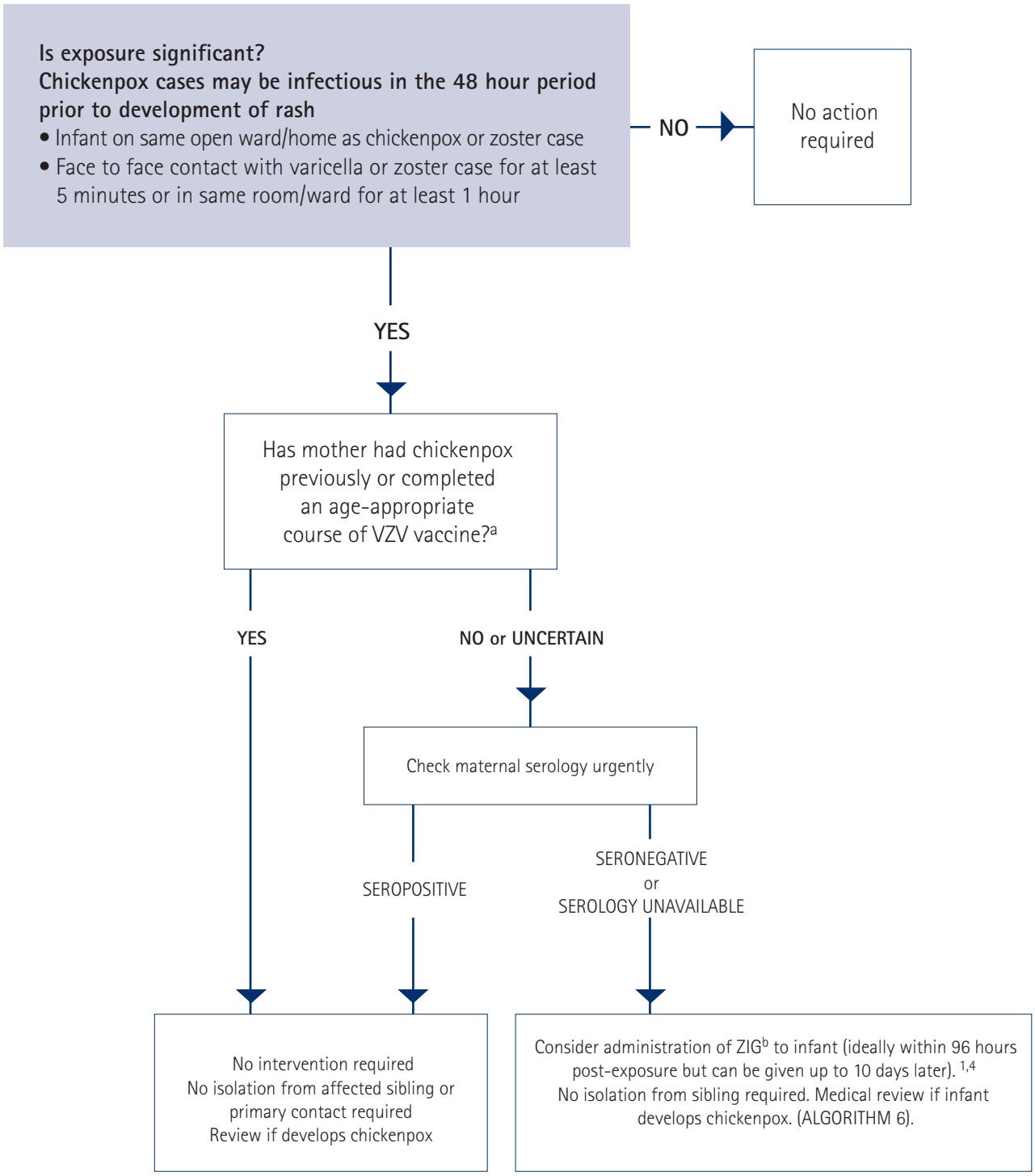


COMMENTS

a. Transplacentally acquired VZV is high-risk and severity reduced by ZIG
b. High titre varicella zoster immune globulin (ZIG) is available from the Red Cross Blood Transfusion Service in Australia. Each vial contains 200 international units VZV in /2 mL. Recommended dose: 2 mL (200 units) for 0-10 kg, 4 mL for 11-30 kg and 6 ml for > 30 kg. Normal human immunoglobulin can be used if ZIG unavailable [1]
c. Opinions vary as to need to administer ZIG to term infants whose mothers develop chickenpox > 2 days after delivery, as there is limited evidence to suggest increased risk of severe disease even if mother VZV seronegative

VARICELLA ZOSTER VIRUS – ALGORITHM 5

MANAGEMENT OF TERM NEONATES EXPOSED TO VZV IN THE POSTNATAL WARDS OR AT HOME



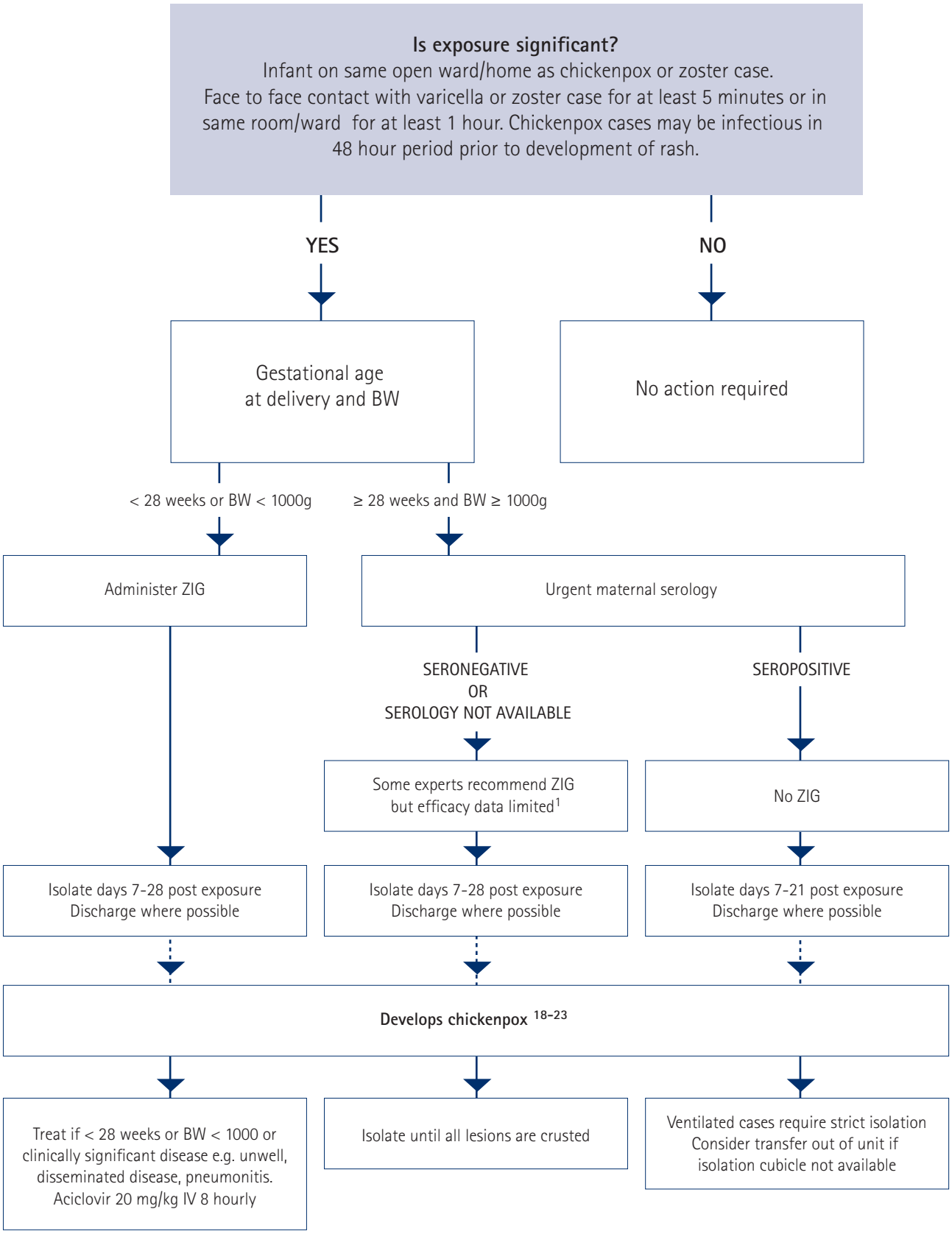
COMMENTS

a. Evidence to inform protection conferred to the newborn by maternal VZV vaccination is limited. Expert opinion is that if a mother has a history of a complete course of age-appropriate doses of VZV vaccine, she is considered immune and thought to confer protection to the newborn irrespective of measured antibody levels. Most experts would not recommend ZIG be given to the newborn in this setting

b. Opinions vary as to the need to administer ZIG to term infants of seronegative mothers who are exposed to chickenpox, as there is limited evidence to suggest increased risk of severe disease

VARICELLA ZOSTER VIRUS – ALGORITHM 6

TREATMENT AND ISOLATION OF INFANTS EXPOSED TO VZV WITHIN THE NEONATAL UNIT



VARICELLA ZOSTER VIRUS REFERENCES

1. Australian Technical Advisory Group on Immunisation (ATAGI). Australian Immunisation Handbook, Australian Government Department of Health, Canberra, Varicella (chickenpox) immunisationhandbook.health.gov.au/vaccine-preventable-diseases/varicella-chickenpox
2. Centers for Disease Control and Prevention. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices. MMWR 1996;45:1–25.
3. Enders G Mille E. Varicella and herpes zoster in pregnancy and the newborn, In: Arvin AM, Gershon AA. editors: Varicella Zoster Virus Virooogy and Clinical Management. Cambridge: Cambridge Unviersity Press, 2000, p 317-47.
4. Wilson E, Goss MA, Marin M, et al. Varicella vaccine exposure during pregnancy: data from 10 years of the pregnancy registry. Journal of Infectious Diseases 2008;197 Suppl 2:S178-84.
5. Grayson ML, Newton-John H. Smoking and varicella pneumonia. J Infect 1988; 16: 312.
6. Rice P, Simmons K, Carr R, Banatvala J. Near fatal chickenpox during prednisolone treatment. Br Med J 1994; 309: 1069-70.
7. Balfour HH. Intravenous aciclovir therapy for varicella in immunocompromised children. J Pediatr 1984; 104: 134.
8. Andrews EB, Yankasksas BC, Cordero JF, Schoeffler K, Hamp S. Aciclovir in pregnancy registry : 6 years experience. The aciclovir in pregnancy registry advisory committee. Obstet Gynecol 1991; 78: 1112-6.
9. Haake DA, Zakowski PC, Haake DL, Bryson YJ. Early treatment with acyclovir for varicella pneumonia in otherwise healthy adults. Rev Infect Dis 1990; 12: 788-97.
10. Tan MP, Koren G. Chickenpox in pregnancy: revisited.Reprod Toxicol 2005; 21: 410–20
11. Joseph CA, Noah ND. Epidemiology of chickenpox in England and Wales, 1967-85. Br Med J 1988; 296: 673-76.
12. Enders G, Miller E, Cradock-Watson J, Bolley I, Ridehalgh M. Consequences of varicella and herpes zoster in pregnancy; prospective study of 1739 cases. Lancet 1994; 343: 1548-51.
13. Preblud SR, Cochi SL, Orenstein WA. Varicella zoster infection in pregnancy. N Engl J Med 1986;315: 1416-7.
14. Chant KG, Sullivan EA, Burgess MA et al. Varicella-zoster virus infection in Australia. ANZ J Public Health 1998; 22:413-8.
15. Nathwani D, Maclean A, Conway S. Varicella innfections in pregnancy and the newborn J Infection 1998; 36 (suppl 1): 59-71.
16. Pretorius DH, Hayward I, Jones KL, Stamm E. Sonographic evaluation of pregnancies with maternal varicella infection. J Ultrasound Med 1992; 11: 459-63.
17. Mouly F, Mirlesse V, Meritet J, Rozenberg F, Poissonier M, Lebon P, Daffos F. Prenatal diagnosis of fetal varicella zoster virus infection with polymerase chain reaction of amniotic fluid in 107 cases. Am J Obstet Gynecol 1997;177:894-8.
18. Jones KL, Johnson KA, Chambers CD. Offspring of women infected with varicella during pregnancy: a prospective study. Teratology 1994; 49: 29-32.
19. Pastuszak AL, Levy M, Schick B, et al. Outcome after maternal varicella infection in the first 20 weeks of pregnancy. N Engl J Med 1994; 330: 901-5.
20. Miller E, Cradock-Watson JE , Ridehalgh MKS. Outcome of newborn babies given anti varicella zoster immunoglobulin after peronatal maternal infection with varicella zoster virus. Lancet 1989; ii:371-3.
21. Hanngren K, Grandien M, Granstrom G. Effect of zoster immunoglobulin for varicella prophylaxis in the newborn. Scand J infect Dis. 1985; 17: 343-7.
22. Rubin L. Disseminated varicella in the neonate and implications for immuno- prophylaxis in neonates exposed to varicella. Pediatr Infect Dis J 1986; 56: 100-2.
23. Reynolds L, Struik S, Nadel S. Neonatal varicella: varicella zoster immunoglobulin (VZIG) does not prevent disease. Arch Dis Child Fetal Neonatal Ed 1999; 81: F69-F70.
24. Conway SP, Dear PRF, Smith I. Immunoglobulin profile of the preterm baby. Arch Dis Child 1985; 60: 208-12.
25. Lin TY, Huang YC, Ning HC, Hsueh C. Oral aciclovir prophylaxis after intimate contact. Pediatr Infect Disease J 1997; 16 : 1162-5.
26. K.Swamy, Sarah K.Dotters-Katz. Safety and varicella outcomes after varicella zoster immune globulin administration in pregnancy. American Journal of Obstetrics and Gynecology 2019 In Press

Zika virus

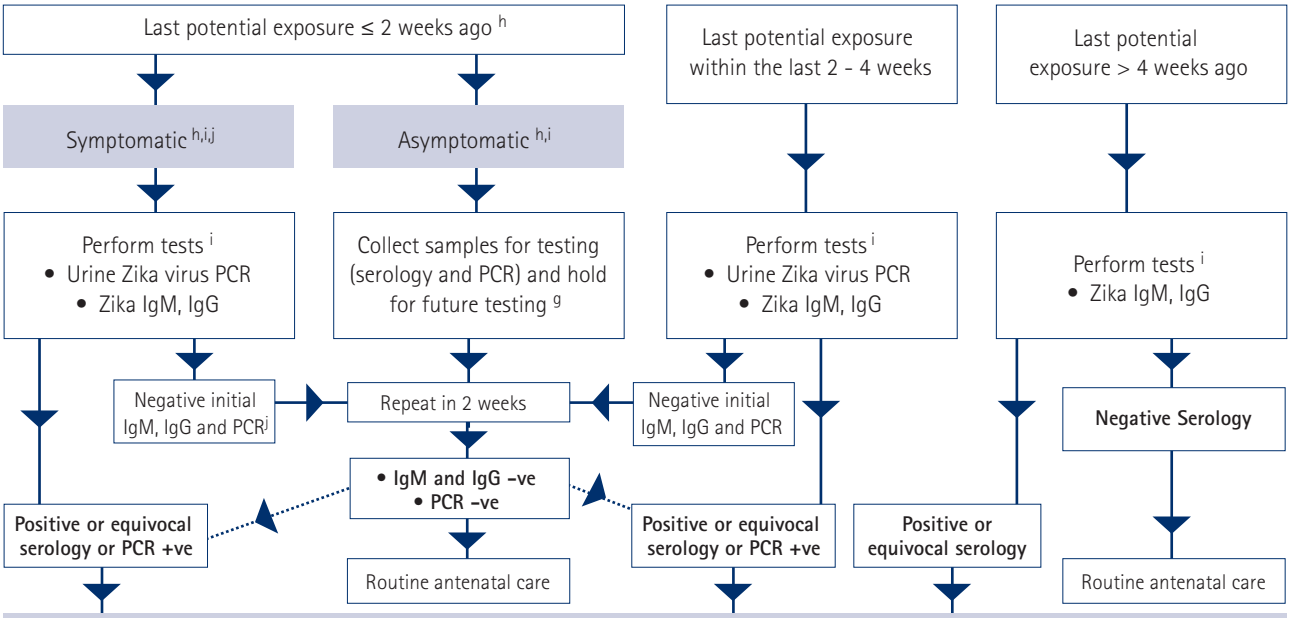
AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2022

ZIKA VIRUS – ALGORITHM 1

ASSESSMENT OF PREGNANT WOMEN WITH POTENTIAL EXPOSURE TO ZIKA VIRUS

- Zika virus can be transmitted by a pregnant woman to the fetus and can cause birth defects (see Algorithm 3).
- Women who are pregnant or planning to become pregnant should be counselled about prevention of Zika virus infection during pregnancy if they or their partner propose travel or live in a Zika endemic area.[a,b,c,d]
- The most common way Zika virus is spread is via mosquitos. It can also be sexually transmitted. In endemic areas, other modes of transmission have been reported.[c]
- The *Aedes aegypti* mosquito which can spread the virus is found in some parts of Queensland, but local transmission has not been demonstrated to date. Refer to Australian Government [b], New Zealand Health [c] and CDC websites for updated exposure risks. [d]
- The virus is endemic in Pacific Island nations. Large populations of Pacific peoples and frequent travel between Australia and New Zealand may be of relevance[1]
- Pregnant women should be asked about possible exposure(s) to Zika virus if they have travelled or lived in an endemic country for part of their pregnancy, or there is antenatal evidence of fetal abnormalities including microcephaly [b,d]
  - Unprotected sexual contact [e] with a person who has recently travelled to or lived in an endemic area
  - Unprotected recent sexual contact [e] with a person infected with Zika virus
  - A laboratory confirmed diagnosis of Zika virus infection before current pregnancy

Potential Zika virus exposure in periconception period [f] or pregnancy
(with permission, Australian Government Department of Health, 2021) [g]
Seek specialist advice early as tests are difficult to interpret and depend on the presence of symptoms and the timing of last exposure.
Refer to the Australian Government Department of Health for site detailed advice

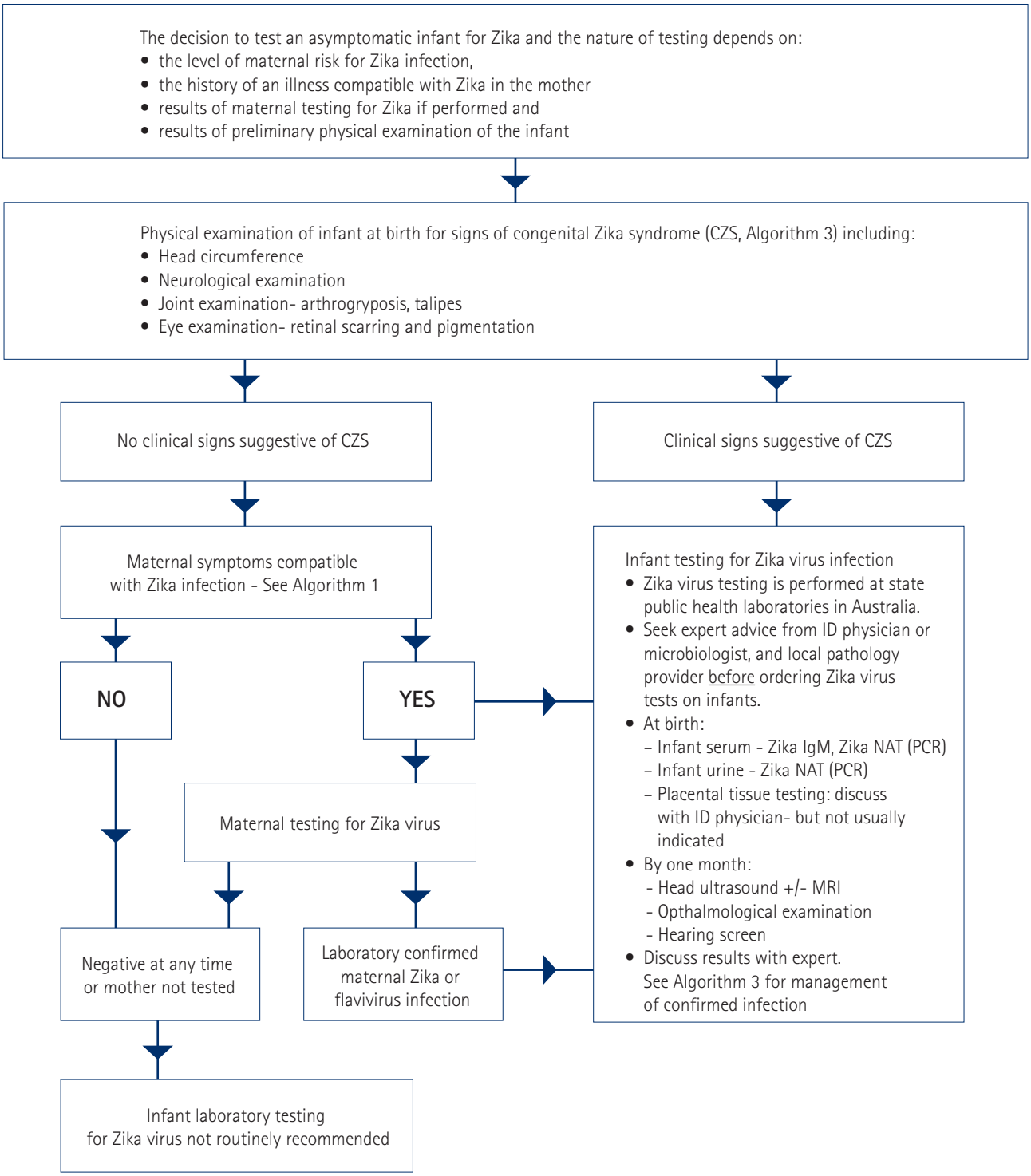


COMMENTS

a. Prevention of Zika infection in pregnancy includes advice to defer travel to areas of risk, avoid mosquito bites, avoid pregnancy during and up to 8 weeks after travel, and avoid unprotected sex during pregnancy with partner who travelled. See up to date advice at b,c
b. Australian Dept. of Health https://www.health.gov.au/diseases/flavivirus-infection-including-zika-virus?utm_source=health.gov.au&utm_medium=callout-auto-custom&utm_campaign=digital_transformation
c. NZ Ministry of Health https://www.health.govt.nz/your-health/conditions-and-treatments/diseases-and-illnesses/zika-virus
d. The Centers for Disease Control and Prevention (CDC) https://wwwnc.cdc.gov/travel/diseases/zika
e. Unprotected sexual contact includes oral/anal/vaginal sex without a condom
f. Periconception period is one month prior to approximate time of conception
g. https://www1.health.gov.au/internet/main/publishing.nsf/Content/ohp-zika-pregnant.htm (2021)
h. Incubation period 2 – 14 days. Most Zika infections are asymptomatic. Symptomatic Zika includes fever, rash, conjunctivitis, arthralgia, malaise or headache. There is no treatment for Zika infection
i. No Zika laboratory assays are currently validated to guide management of pregnant women. Results must be interpreted with caution and with considered in context of clinical and other laboratory data. A negative PCR does not exclude Zika virus infection. Zika IgM alone does not confirm recent infection as prolonged IgM +ve result has been observed (>3 months) after initial infection
j. Other vector borne causes of fever should be considered if the woman is a returned traveller from endemic areas e.g. malaria, dengue, chikungunya. After acute infection: In general, urine PCR clears in 6 weeks to 12 weeks.
k. Zika RNA is detectable in serum for about 2 weeks from infection (longer in whole blood)

ZIKA VIRUS – ALGORITHM 2

ASSESSMENT OF ASYMPTOMATIC INFANTS BORN TO MOTHER WITH POSSIBLE ZIKA VIRUS EXPOSURE DURING PREGNANCY



ZIKA VIRUS – ALGORITHM 3

EVALUATION AND MANAGEMENT OF INFANTS BORN TO MOTHERS WITH POSSIBLE EXPOSURE TO ZIKA DURING PREGNANCY AND CLINICAL FINDINGS SUGGESTIVE OF CONGENITAL ZIKA SYNDROME (CZS)

Infant has signs consistent with CZS or additional findings in presence of high risk of maternal exposure of confirmed infection.

Consult expert for advice re differential diagnosis, testing, follow up as required e.g. paediatric infectious diseases, clinical genetics, paediatric neurology, developmental paediatrics

CZS is a classic pattern of birth defects and disabilities due to intrauterine transmission of Zika[8]

- Severe microcephaly
- Decreased brain tissue with subcortical calcifications
- Common eye abnormalities: macular scarring and retinal focal pigmentation
- Hypertonia
- Joint abnormalities: arthrogryposis, talipes
- Other findings include: dysphagia, seizures, other eye findings (microphthalmia, optic nerve pallor, other brain malformations on neuroimaging (ultrasound or MRI/ autopsy) cerebral calcifications, disrupted brain development (brain atrophy and asymmetry, hydranencephaly, ventriculomegaly), abnormally formed or absent brain structures (e.g., corpus callosum, thalami, pons, cerebellar vermis, brainstem)
- Long term sequelae are not yet fully defined, including risks of adverse outcomes in asymptomatic infected infants

Infant testing for Zika virus

- Zika virus testing is performed at state public health laboratories in Australia.
- Seek expert advice from ID physician or microbiologist, and local pathology provide before ordering Zika virus tests on infants.
- At birth:
  - Infant serum- Zika IgM, Zika NAT (PCR)
  - Infant urine- Zika NAT (PCR)
  - Placental tissue testing: discuss with ID physician - but not usually indicated
- By one month
  - Head ultrasound +/- MRI
  - Ophthalmological examination
  - Hearing screen

There is no available treatment for CZS

Differential diagnosis of CZS:

- Other congenital infections: toxoplasmosis, HSV, VZV, syphilis, rubella, CMV
- Genetic disorders
- Neurodevelopmental disorders
- Fetal Alcohol Spectrum Disorder or other antenal toxin exposure

ZIKA VIRUS REFERENCES

1. Pettersson, J. H., et al. (2018). "Re-visiting the evolution, dispersal and epidemiology of Zika virus in Asia." Emerg Microbes Infect 7(1): 79.
2. Department of Health Zika country classifications https://www1.health.gov.au/internet/main/publishing.nsf/Content/ohp-zika-countries.htm
3. Recommendations for assessment of pregnant women with potential exposure to Zika virus https://www1.health.gov.au/internet/main/publishing.nsf/Content/ohp-zika-pregnant.htm (accessed October 1st 2022)
4. https://www.health.govt.nz/your-health/conditions-and-treatments/diseases-and-illnesses/zika-virus
5. Zika virus – information for clinicians and public health practitioners https://www1.health.gov.au/internet/main/publishing.nsf/content/ohp-zika-health-practitioners.htm
6. Zika Travel Information (CDC): https://wwwnc.cdc.gov/travel/page/zika-information
7. Oduyebo T, Polen KD, Walke HT et al. Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure - United States (Including U.S. Territories), July 2017. MMWR Morb Mortal Wkly Rep. 2017 Jul 28;66(29):781-793. doi: 10.15585
8. Melo, A, de Sales Tavares, J, de Assis Costa, M, et al. Obstetric and perinatal outcomes in cases of congenital Zika syndrome. Prenatal Diagnosis. 2020; 40: 1732– 1740. https://doi.org/10.1002/pd.5831