Management of Perinatal Infections

CYTOMEGALOVIRUS ◻ ENTEROVIRUS ◻ HEPATITIS B VIRUS ◻ HEPATITIS C VIRUS ◻ HERPES SIMPLEX VIRUS ◻ HUMAN IMMUNODEFICIENCY VIRUS ◻ LISTERIA ◻ MYCOBACTERIUM TUBERCULOSIS ◻ PARVOVIRUS ◻ RUBELLA ◻ STREPTOCOCCUS - GROUP B ◻ TOXOPLASMA GONDII ◻ TREPONEMA PALLIDUM (SYPHILIS) ◻ VARICELLA ZOSTER VIRUS ◻

EDITORS Pamela Palasanthiran, Mike Starr, Cheryl Jones and Michelle Giles

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2014

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MANAGEMENT OF PERINATAL INFECTIONS

EDITORS' NOTE

Infections in pregnancy represent a unique medical challenge as there is the management of the infected woman and the developing fetus to consider. Perinatal counselling requires a discussion of risks of transmission, interventions to possibly prevent transmission in-utero or postnatally, 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. They each follow 4 themes (where possible): antenatal diagnosis, antenatal management, transmission risk and interventions where available, and management of the newborn. The organisms were chosen as they represent infectious agents in pregnancy where information on transmission risks and maternal and perinatal management exist.

The algorithms are evidence based and, where data are limited, recommendations are by consensus. They have undergone a review process and have been endorsed by the Australasian Society for Infectious Diseases (ASID) 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.

This set of comprehensive, contemporary algorithms was first published in 2002 and emendations made in 2006. The publication has stood the test of time and remains a unique and valuable resource. This second edition, revised by the current editors, is a welcome and long awaited update.

The Editors: Pamela Palasanthiran, Mike Starr, Cheryl Jones and Michelle Giles

ACKNOWLEDGEMENTS

The Editors wish to acknowledge the original contributing authors: Dr Jim Buttery (Hepatitis B and C), Dr Andrew Daley (*Treponema pallidum*), Professor Sue Garland (CMV, Group B streptococcus), Professor Lyn Gilbert (parvovirus, *Treponema pallidum*, *Toxoplasma gondii*), Professor Cheryl Jones (CMV, HSV) Professor Alison Kesson (Enterovirus), Dr Anne Marie Heuchan (Varicella zoster virus), Professor David Isaacs (Varicella zoster virus), A/Professor Clare Nourse (Rubella), A/Professor Pamela Palasanthiran (CMV, HIV), Dr Mike Starr (*Mycobacterium tuberculosis*, Parvovirus, Group B streptococcus), Dr Lesley Voss (Listeria) and Dr Allen Yung (*Mycobacterium tuberculosis*).

We thank ASID for its support and the funding of this publication. We thank the members of the ASID paediatric speciality interest group, ANZPID and RANZCOG for review and endorsement of these algorithms.

Cytomegalovirus

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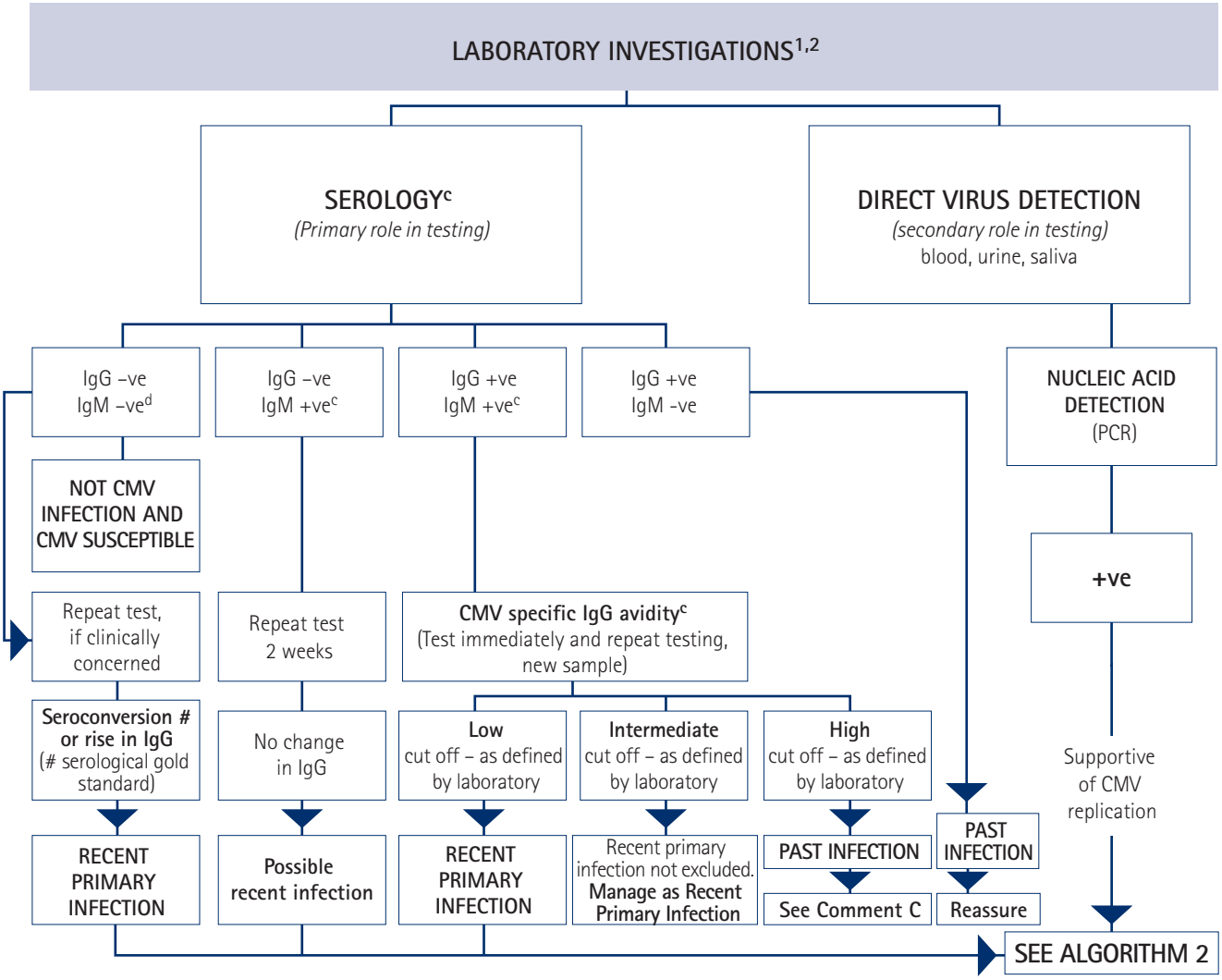
CYTOMEGALOVIRUS – ALGORITHM 1

MATERNAL DIAGNOSIS



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

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

COMMENTS

a. CMV is the leading cause of congenital infections, with a birth prevalence of ~ 0.64 – 0.7%.[3,4] The incidence of congenital CMV in Australia from a surveillance study was estimated to be 3.85/100 000 live births, a likely under estimate.[5]

Antenatal testing is complex.[1] Diagnosis of infection in mothers is potentially difficult, offset by possible and emerging intervention/ treatment for prevention of, or treatment of newborns with CMV disease.

Antenatal counselling for maternal CMV infection and hygienic precautions to minimise CMV acquisition in pregnancy should be part of counselling, particularly for the CMV susceptible woman (SEE APPENDIX 1). Risk groups for CMV infection are included in Comment d.

b. The majority of primary CMV infections are asymptomatic. Primary CMV disease may occur as a viral illness associated with atypical lymphocytosis which is "Monospot" negative (also seen in primary toxoplasmosis) or with clinical syndromes associated with CMV disease.

c. 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 re-infection. False positive IgM occur with cross reactivity with other herpes viruses or autoimmune disorders. CMV IgG avidity may assist in timing of CMV infection. Low avidity indicates a probable recent infection, with progression to high avidity with time.[2] Primary CMV infection is eventually diagnosed in a minority of women with positive CMV IgM (20–25%).[2]

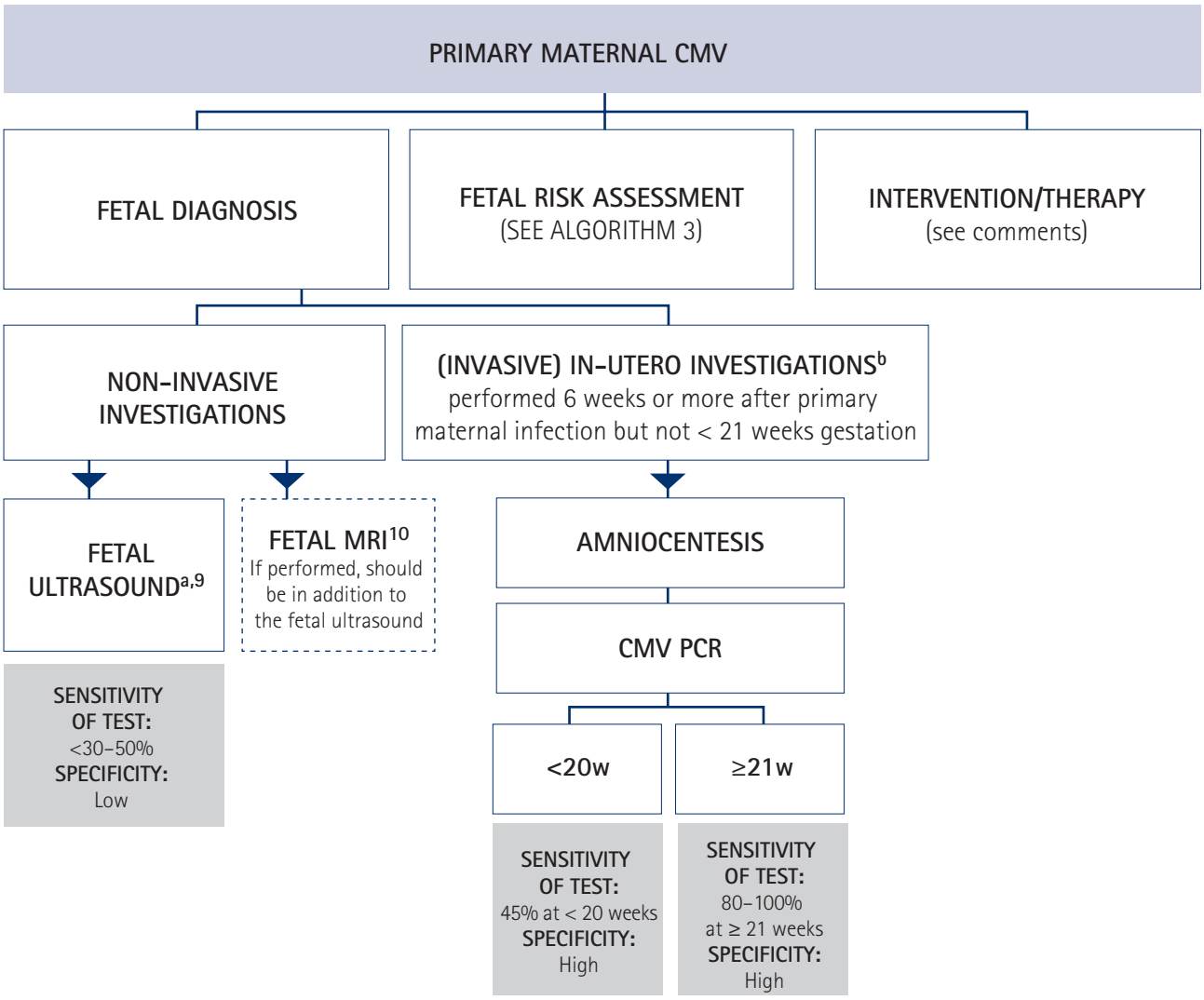
d. Major risk factors for maternal CMV acquisition is frequent, prolonged contact with young children, in particular children who are shedding CMV.[6] Some groups identified at higher risk of primary CMV and annual seroconversion rates are [7,8]

I. Day care workers	up to 12.5% per annum (p.a)
II. Parents with child in day care	2% p.a. for non-CMV shedding children 24% p.a. for CMV shedding children

In comparison, health care workers seroconvert at a rate comparable to the general population i.e. **2–3% p.a.**

CYTOMEGALOVIRUS – ALGORITHM 2

ANTENATAL MANAGEMENT OF PRIMARY MATERNAL CMV INFECTION



COMMENTS

a. **Fetal ultrasound**:[9] Features associated with symptomatic congenital CMV infection include

Microcephaly	Hydrocephalus (ventricular dilation)	Intrauterine growth retardation (IUGR)
Ascites	Intracranial calcification	Pleural or pericardial effusions
Oligo or polyhydramnios	Hydrops fetalis	Hepatomegaly
Abdominal calcification	Pseudomeconium ileus	Hyperechogenic 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 infants.

b. Fetal (*in-utero*) investigations: amniocentesis [2,11]
- Sensitivity is increased by waiting ≥ **6 weeks** after maternal infection
- Diagnosis by amniocentesis testing (PCR and culture) is poor, ~ 45% sensitive if taken < 20 weeks and 80-100% sensitive if taken ≥ 21 weeks gestation. **Specificity approaches 100%.** Diagnosis is best achieved by a combination of fetal ultrasound + amniocentesis (for PCR)
- Positive results **cannot** predict degree of fetal damage
- Quantitative PCR may identify infected fetuses at risk of symptomatic disease but not reliably.

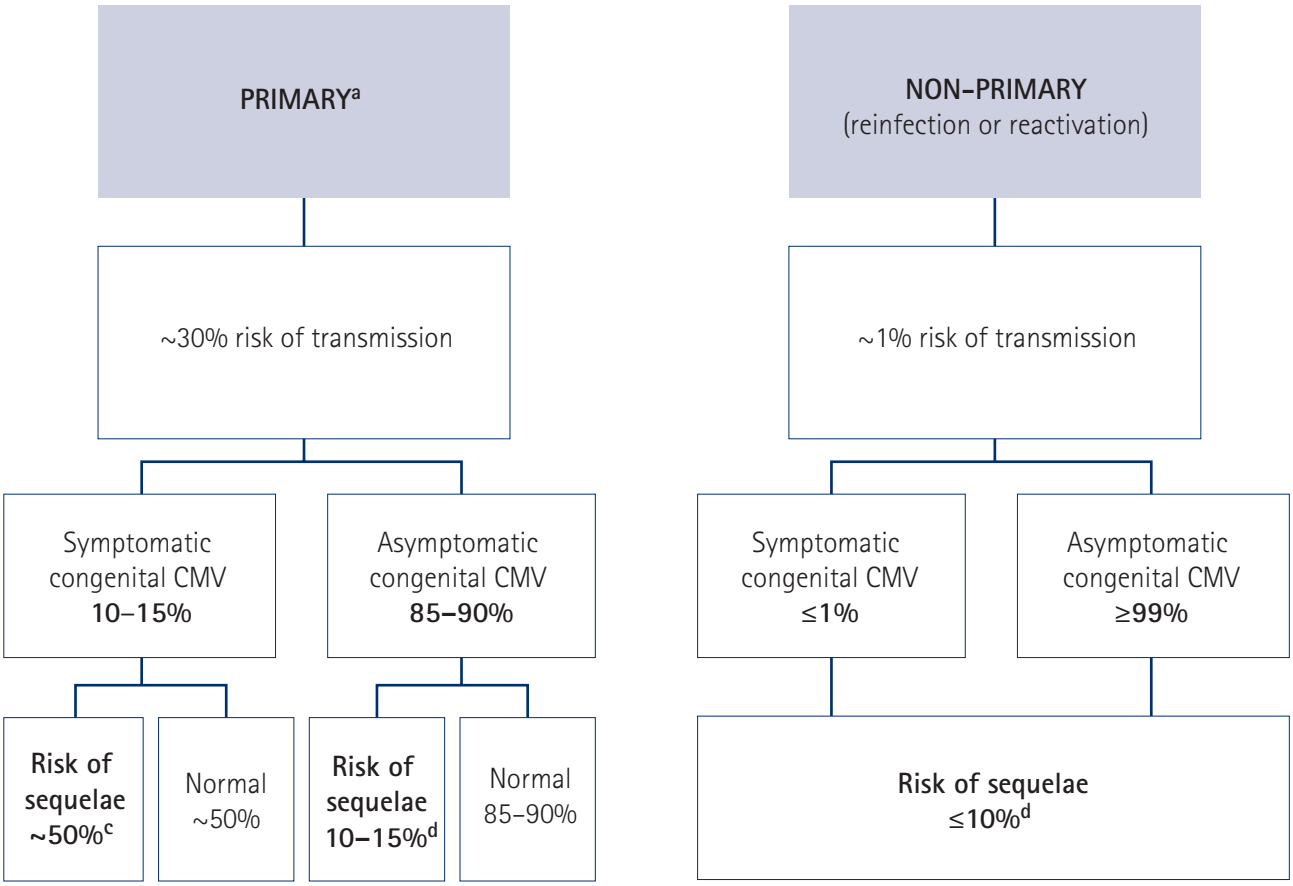
c. Intervention/therapy

Prevention of fetal CMV transmission: seek expert advice
- A non-randomised control trial reporting lower rates of CMV fetal transmission with antenatal CMV hyperimmune globulin has not been confirmed.[12] A recent randomised placebo control trial (RCT) studying CMV hyperimmune globulin in women with primary CMV in pregnancy has shown a lower but non-significant rate of CMV transmission *in-utero* in women who received CMV hyperimmune globulin compared to those who did not (30% in the treatment arm vs 44% in the placebo arm). A higher rate of obstetrical events (mainly prematurity) in the treatment arm was noted (13% vs 2%).[13] Thus, current data does not support a role for CMV immuneglobulin in preventing *in-utero* transmission of CMV. The results of 2 other RCTs are pending.

Therapeutic intervention for infected fetus: seek expert advice
- Termination of pregnancy is an option by informed choice if congenital CMV is confirmed *in-utero*, with the knowledge that a positive PCR is not predictive of fetal damage
- Antenatal use ofCMV immuneglobulin[14] when fetal infection is confirmed (CMV PCR +ve in amniotic fluid) may be a consideration, with better clinical outcomes for infected babies at 1 year reported in one non-RCT.[15]

CYTOMEGALOVIRUS – ALGORITHM 3

RISK ESTIMATES OF FETAL TRANSMISSION[3,4]



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

SEE ALGORITHM 4

COMMENTS

a. Primary CMV during pregnancy is associated with the highest risk of transmission[4]. However, peri-conceptional primary CMV (CMV acquired around the time of conception) carries a small increment in risk of 4–12%[16,17 & 18] compared to the 'baseline' risk of 1–2 %. Risks decrease with time after primary infection. The optimal interval remains to be defined, with a year after primary infection suggested as the highest 'risk' period.

b. Transmission of CMV occurs across the trimesters
   - Risk of severe adverse neurological outcome more likely with primary infection in first half of pregnancy.
   - A fetus infected late in pregnancy is more likely to have acute visceral disease (hepatitis, pneumonia, purpura and severe thrombocytopenia).

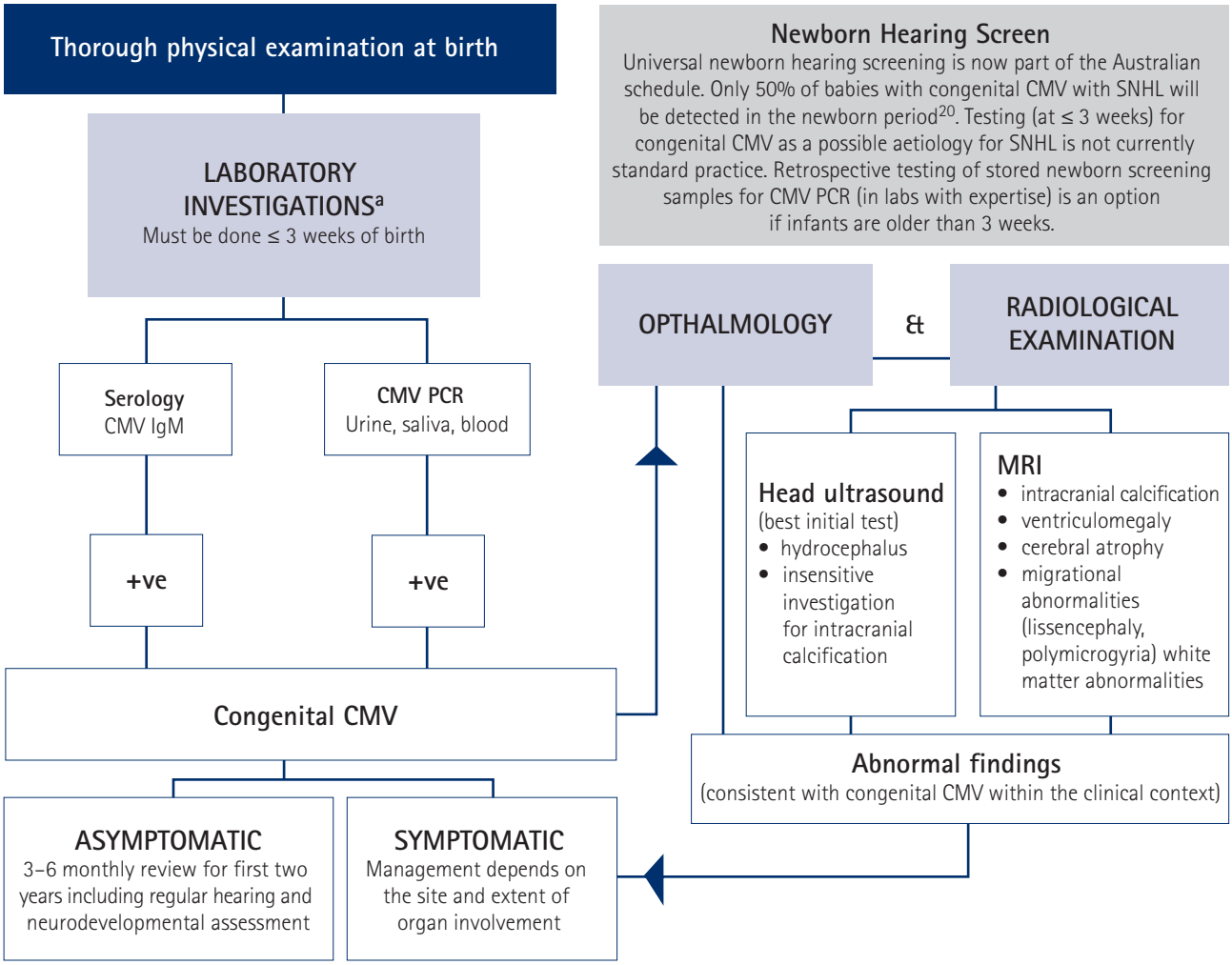
c. Main concerns of symptomatic congenital CMV infection[19]
   - An early mortality (first 3 months) rate between 5% to 10%
   - Neurological sequelae of microcephaly (35–50%), seizures (10%), chorioretinitis (10–20%), developmental delay (≤70%)
   - Sensory neural hearing loss (SNHL, 25–50%), with progression expected in about half (mainly in the first 2 years of life).

d. Main concerns of asymptomatic congenital CMV are[20,21]
   - Sensory neural hearing loss (5%), with progression in about half with time.
   - Chorioretinitis (2%).

   Normal development by 12 months is associated with higher likelihood of a normal development long term, and progression after the second year of life is uncommon. [22]

CYTOMEGALOVIRUS – ALGORITHM 4

NEONATAL DIAGNOSIS AND MANAGEMENT



COMMENTS

a. Other baseline tests at birth: FBE & differential and LFT.

b. Follow-up hearing assessment: Delayed onset of hearing loss (SNHL) is anticipated in a proportion of congenital CMV infants with normal hearing screen at birth. Improved prognosis for speech development is expected if hearing impairments are detected early.[23] Thus, regular hearing testing is recommended. A suggested schedule is 6 monthly till age 2 years, then annually till age 6 years.

c. Ophthalmology assessments: annually for the first 2 years, then close review till age 6 years.

d. Treatment options: seek expert advice
   - A randomised placebo control trial (RCT) trial studying intravenous ganciclovir (GCV), started in the neonatal period for 6 weeks in congenitally infected infants with CNS involvement showed normal, stable or improved hearing in treated children at 6 and 12 months. However, the significant loss to follow-up (~60%) makes interpretation of the data difficult and long term outcomes are not available. ~ 2/3 developed transient neutropenia.[24] Neurodevelopmental benefit for treated children has been reported.[25]
   - Valganciclovir (VGCV) at 16 mg/kg/dose, BD is an acceptable alternative to iv ganciclovir based on a pharmacodynamic/pharmacokinetic study in infants.[26]
   - Preliminary results from a randomised placebo control trial (CASG 112) using oral valganciclovir for 6 weeks vs 6 months report better hearing and neurological outcomes at 12 and 24 months with the longer duration (6 months) of VGCV. [27]
   - Summary: Limitations in interpreting the original RCT need to be recognised, and benefits versus short/long term risks discussed. Oral valganciclovir is an acceptable, practical alternative to iv ganciclovir. The duration of therapy, prior to published details CASG 112, merits discussion and a conclusive recommendation is not possible at this stage.

e. Congenitally infected babies are high CMV shedders for the first years of life. Pregnant women should be aware of this and hygiene measures to minimize CMV infection recommended. (see Appendix 1).[28]

CYTOMEGALOVIRUS APPENDIX AND REFERENCES

Appendix 1: Practices for pregnant women to reduce CMV infection[28]

1. Assume that children under age 3 years in your care have CMV in their urine and saliva
2. Thoroughly wash hands with soap and warm water after
   a. diaper (nappy) changes and handling child's dirty laundry
   b. feeding or bathing child
   c. wiping child's runny nose or drool
   d. handling child's toys, pacifiers, or toothbrushes
3. Do not:
   a. share cups, plates, utensils, toothbrushes, or food
   b. kiss your child on or near the mouth
   c. share towels or washcloths with your child
   d. sleep in the same bed with your child

CDC http://www.cdc.gov/pregnancy/cmv/

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Enterovirus

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ENTEROVIRUS – NEONATAL INFECTION

Enteroviral infections generally cause insignificant illness, and perinatal transmission of enteroviruses leading to significant symptomatic disease in infants is rare.

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.

Transmission

- In-utero transmission in late gestation has been described[1]
- Intrapartum exposure to maternal blood, genital secretions and stool
- Postnatal exposure to oropharyngeal secretions from mother and other contacts

Neonatal infection

- 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%
- May have myocarditis, meningoencephalitis

Diagnosis

- Traditional cell culture/shell vial culture followed by immunofluorescence - slow and insensitive
- Serology – very limited use as no single antigen present in all serotypes. Specimens need to be paired with those of mother for appropriate interpretation.
- RT-PCR - rapid, sensitive and specific (NB Not all enterovirus PCR tests identify parechoviruses, which cause clinical syndromes indistinguishable from enterovirus)
- Isolation from stool not specific, as virus shed in stool for several weeks
- Detection in blood, CSF, tissue most reliable
- Genotyping possible by PCR sequencing of structural protein genes

Treatment in neonates

- No antivirals currently available
- IVIG may be of benefit – one small RCT showed subtle clinical benefits and faster resolution of viraemia[2]

Prevention

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

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Further reading

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Hepatitis B virus

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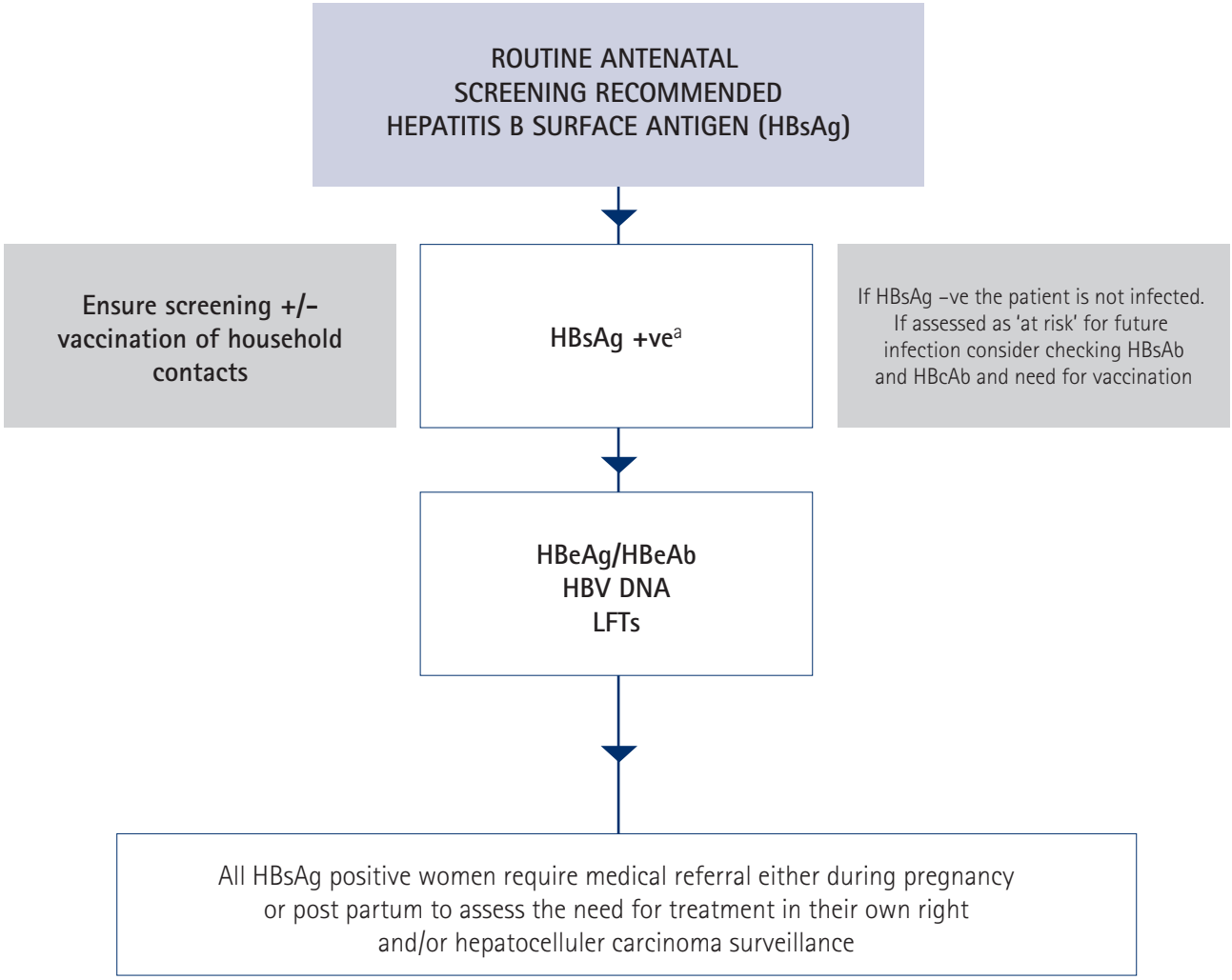
HEPATITIS B VIRUS – ALGORITHM 1

MATERNAL DIAGNOSIS AND ASSESSMENT

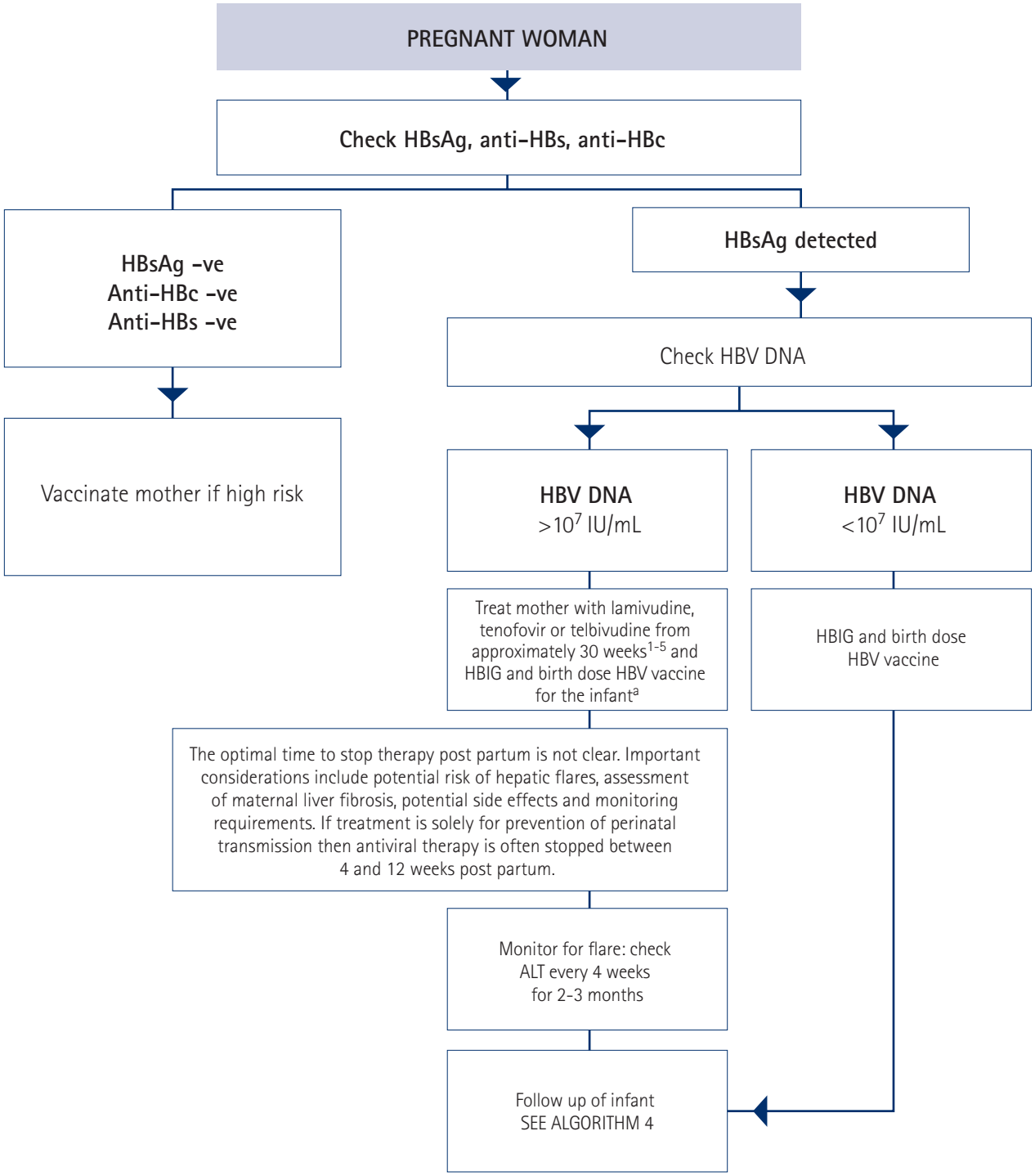


COMMENTS

a. Check maternal hepatitis A IgG. If non immune offer vaccination.

HEPATITIS B VIRUS – ALGORITHM 2

ANTENATAL MANAGEMENT OF HEPATITIS B INFECTION



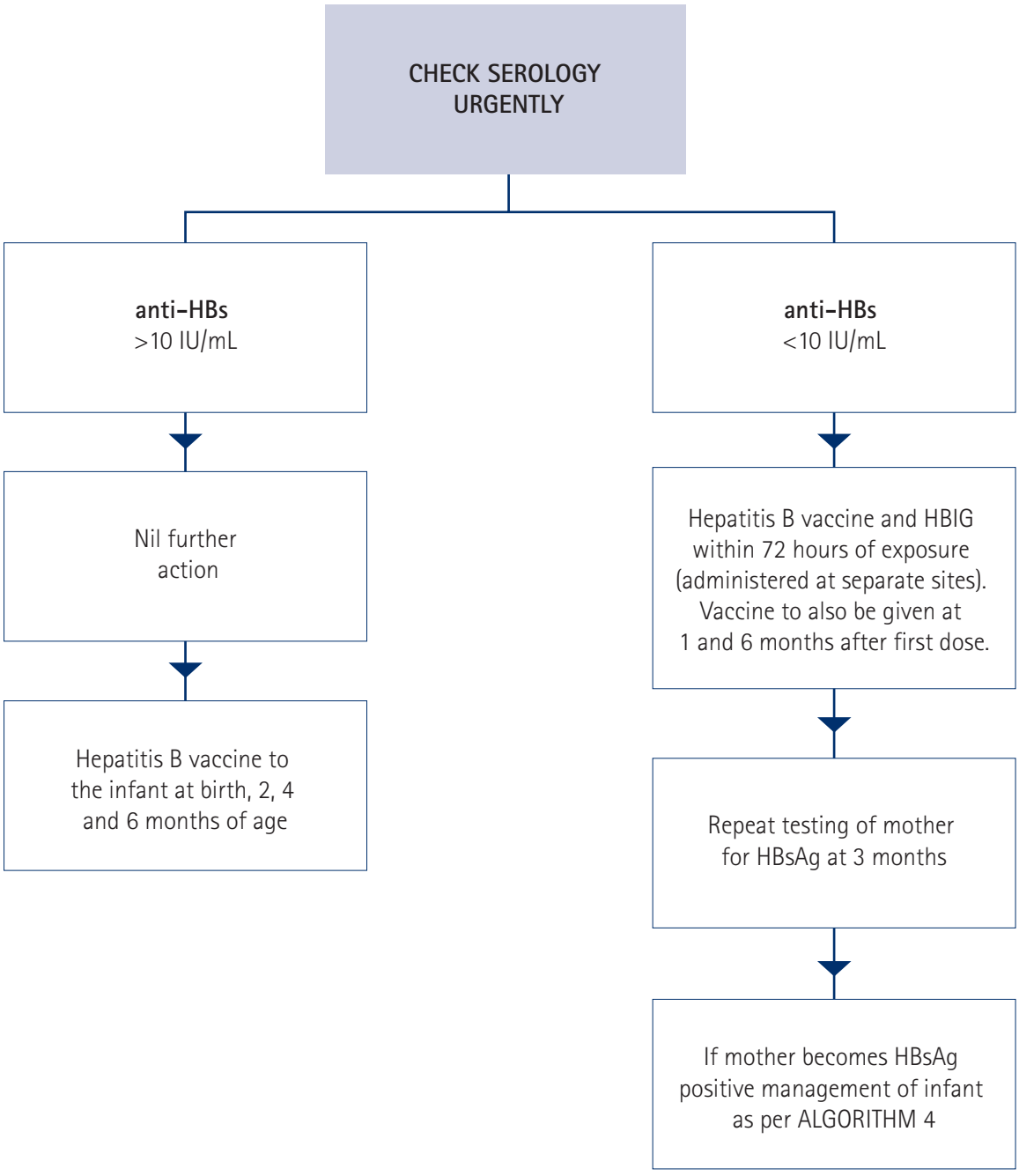
Acute hepatitis B in pregnancy:
Lamivudine has been used in pregnant women with fulminant hepatic failure due to acute hepatitis B and also in women with an acute exacerbation of chronic hepatitis B during pregnancy[6,7] There is no data regarding optimal mode of delivery in acute hepatitis. The infant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

COMMENTS

a. Monotherapy with nucleoside or nucleotide analogues that have been assessed during pregnancy should be considered. To date, no clinical trials of tenofovir to prevent perinatal transmission have been done (unlike lamivudine and telbivudine). However, it is a potent inhibitor of hepatitis B virus and has a high barrier to resistance.

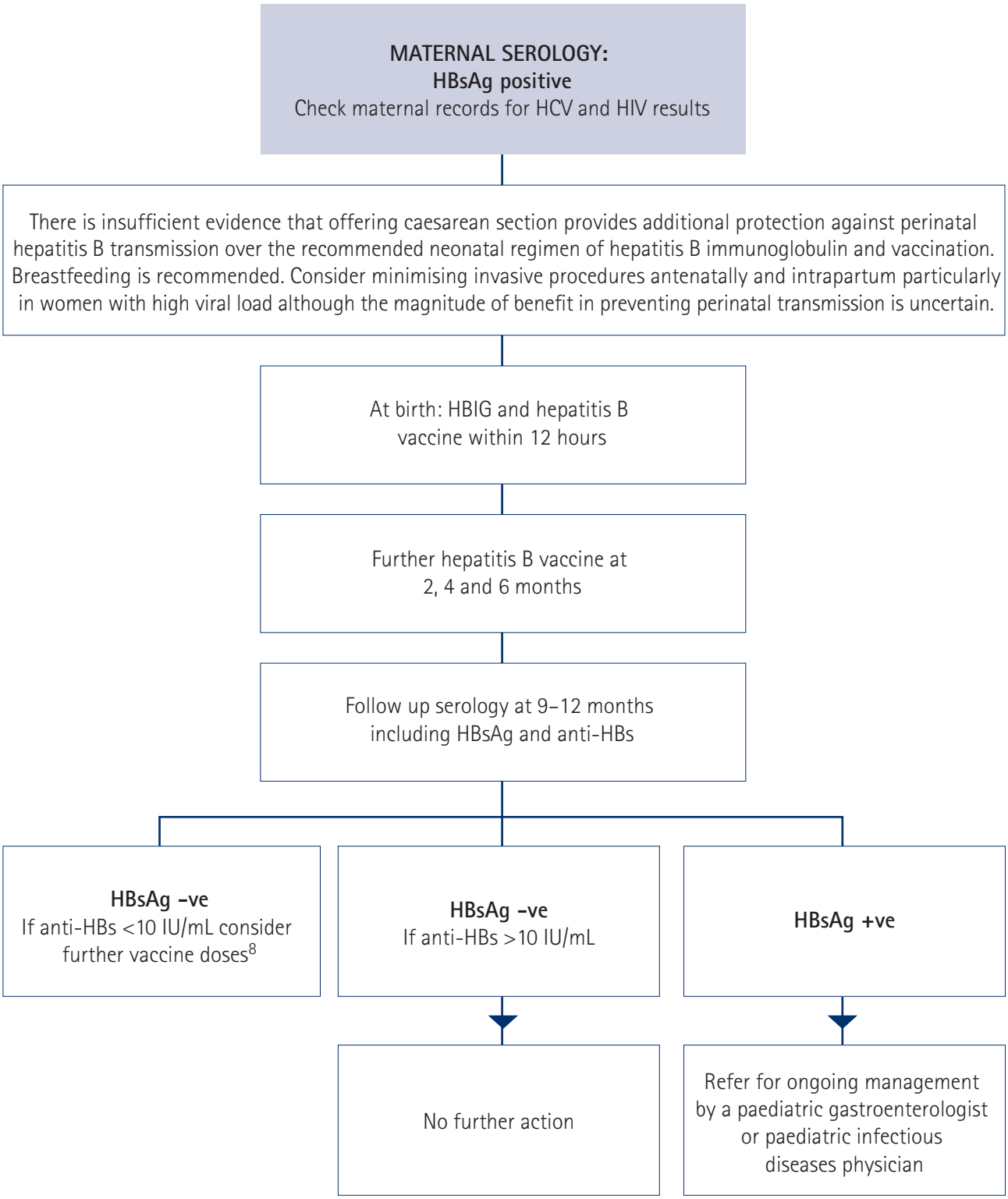
HEPATITIS B VIRUS – ALGORITHM 3

MANAGEMENT OF POTENTIAL EXPOSURE TO HEPATITIS B DURING PREGNANCY



HEPATITIS B VIRUS – ALGORITHM 4

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).

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Hepatitis C virus

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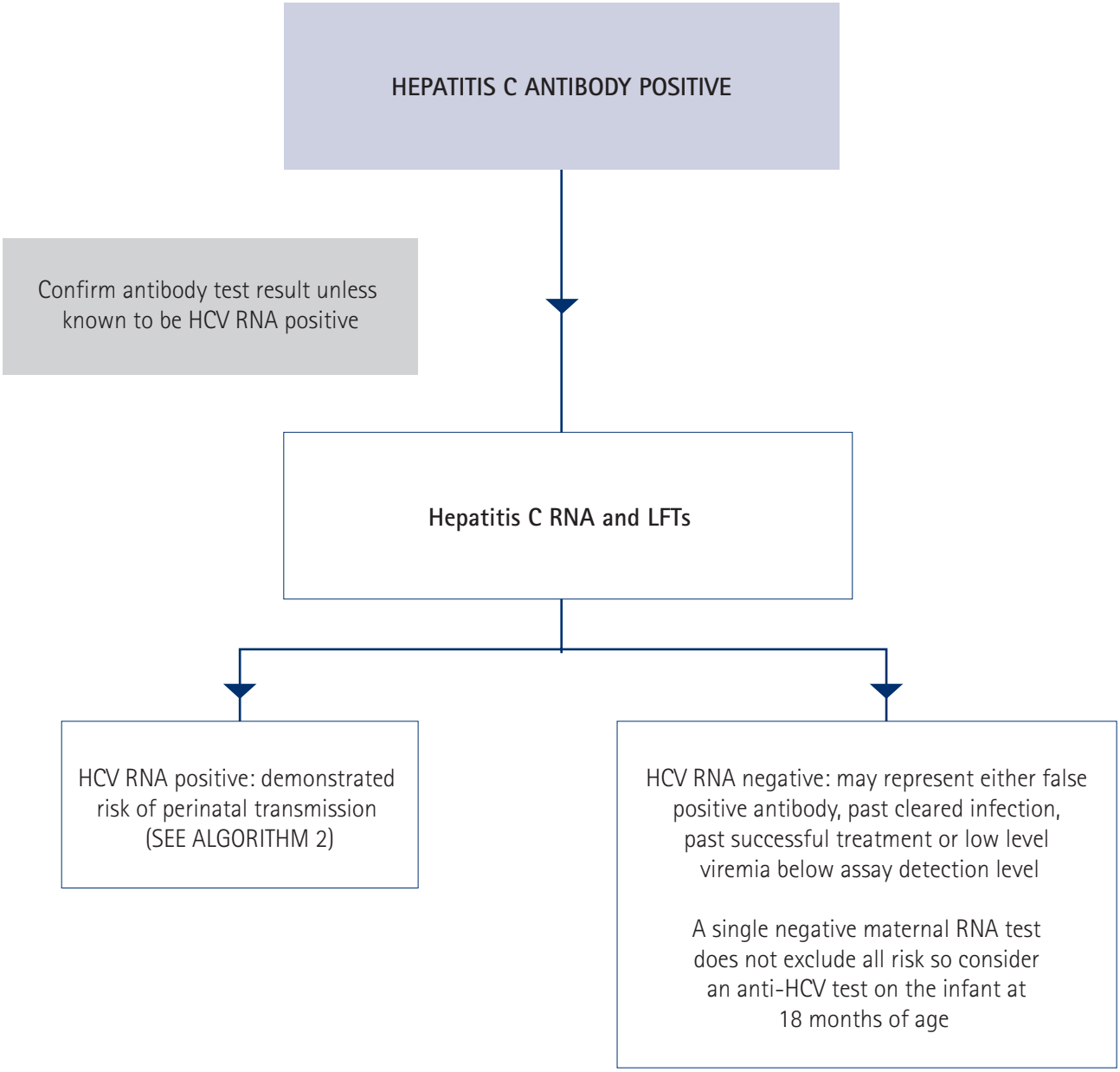
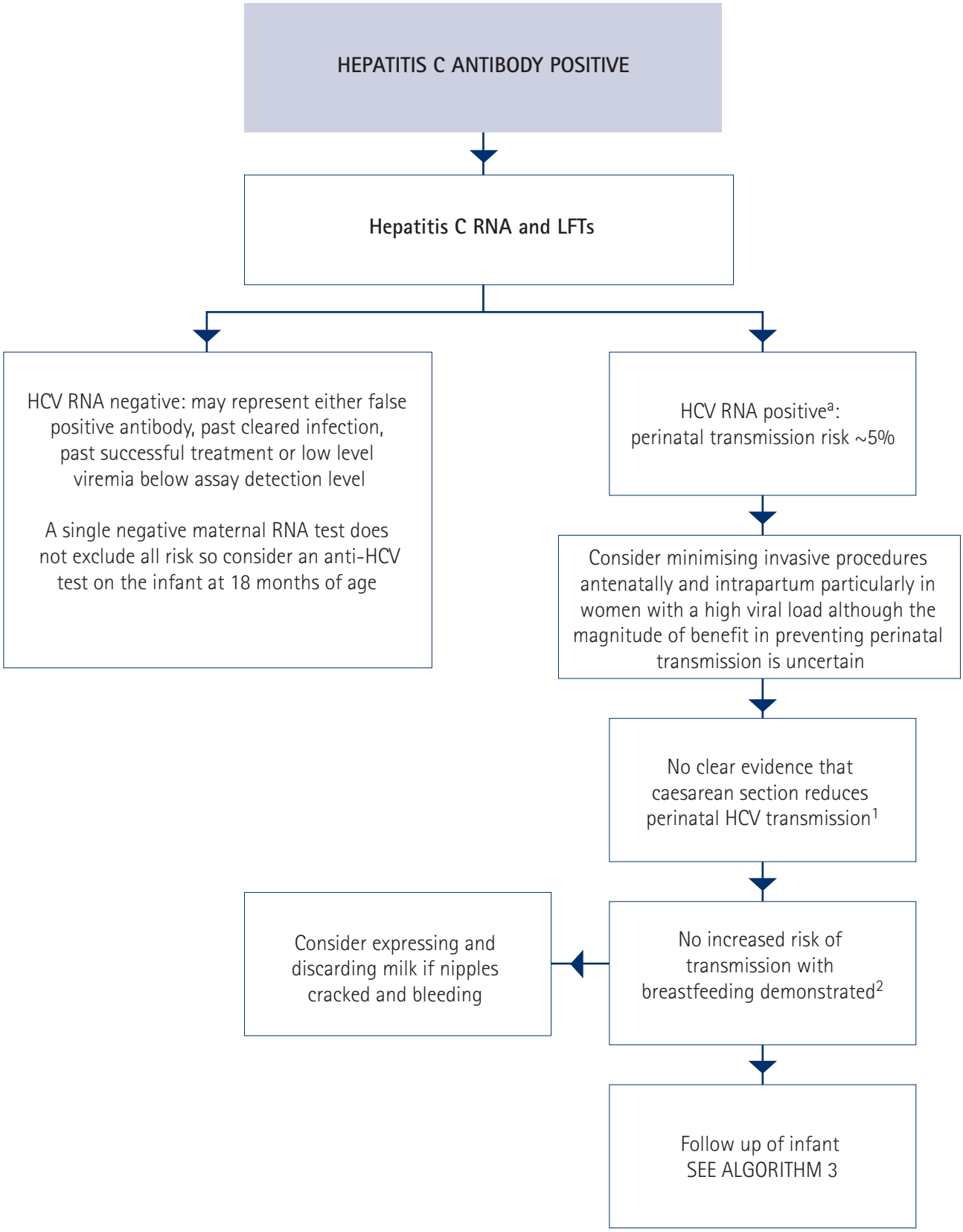
HEPATITIS C VIRUS – ALGORITHM 1

ANTENATAL DIAGNOSIS OF HEPATITIS C



HEPATITIS C VIRUS – ALGORITHM 2

ANTENATAL MANAGEMENT OF HEPATITIS C INFECTION

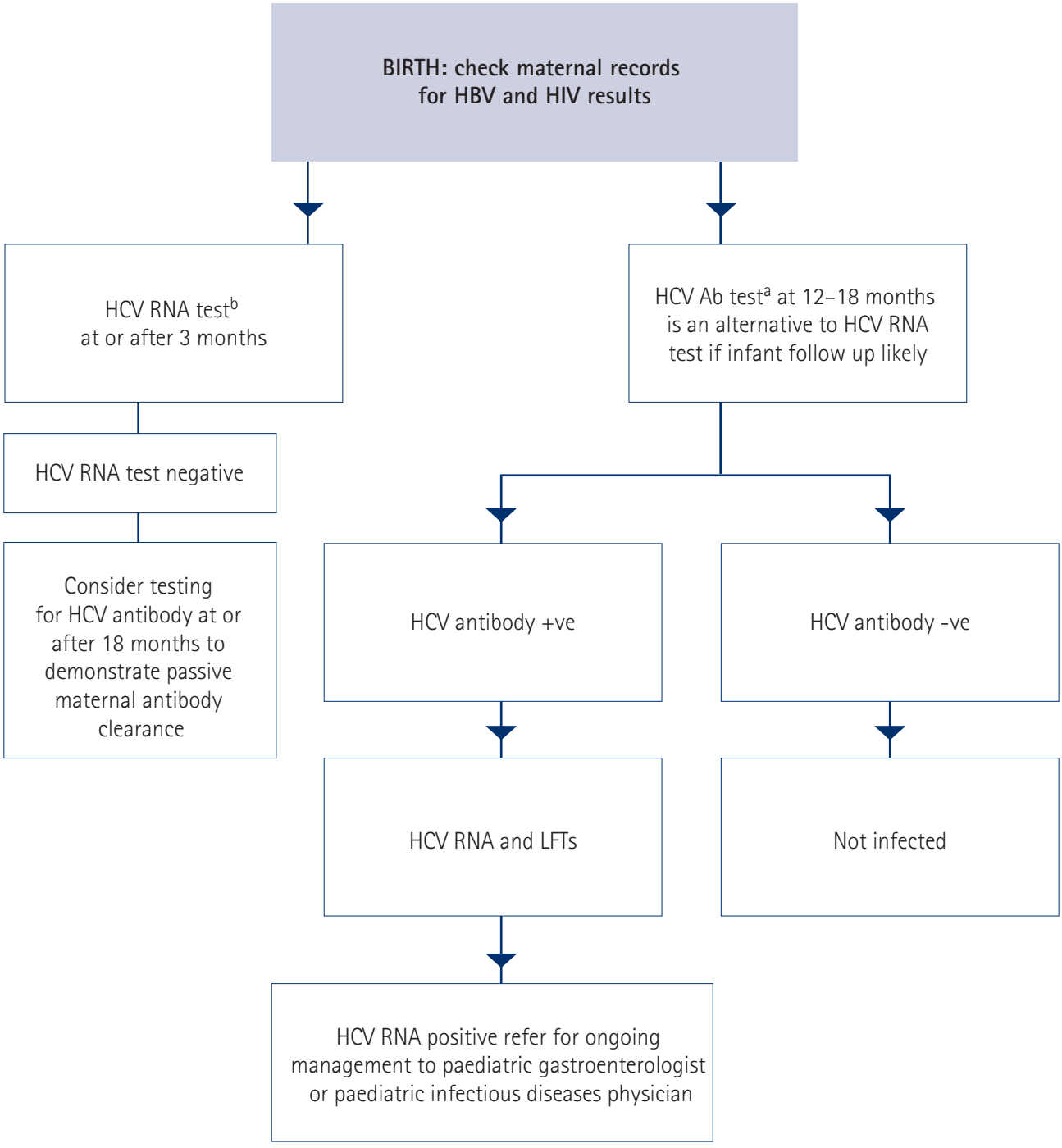


COMMENTS

a. Treatment during pregnancy is contraindicated. However HCV RNA positive women should be referred to a gastroenterologist or infectious diseases physician for consideration of treatment post partum.

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. If positive HCV antibody at 12 months repeat the test 3 months later or perform a HCV RNA 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.

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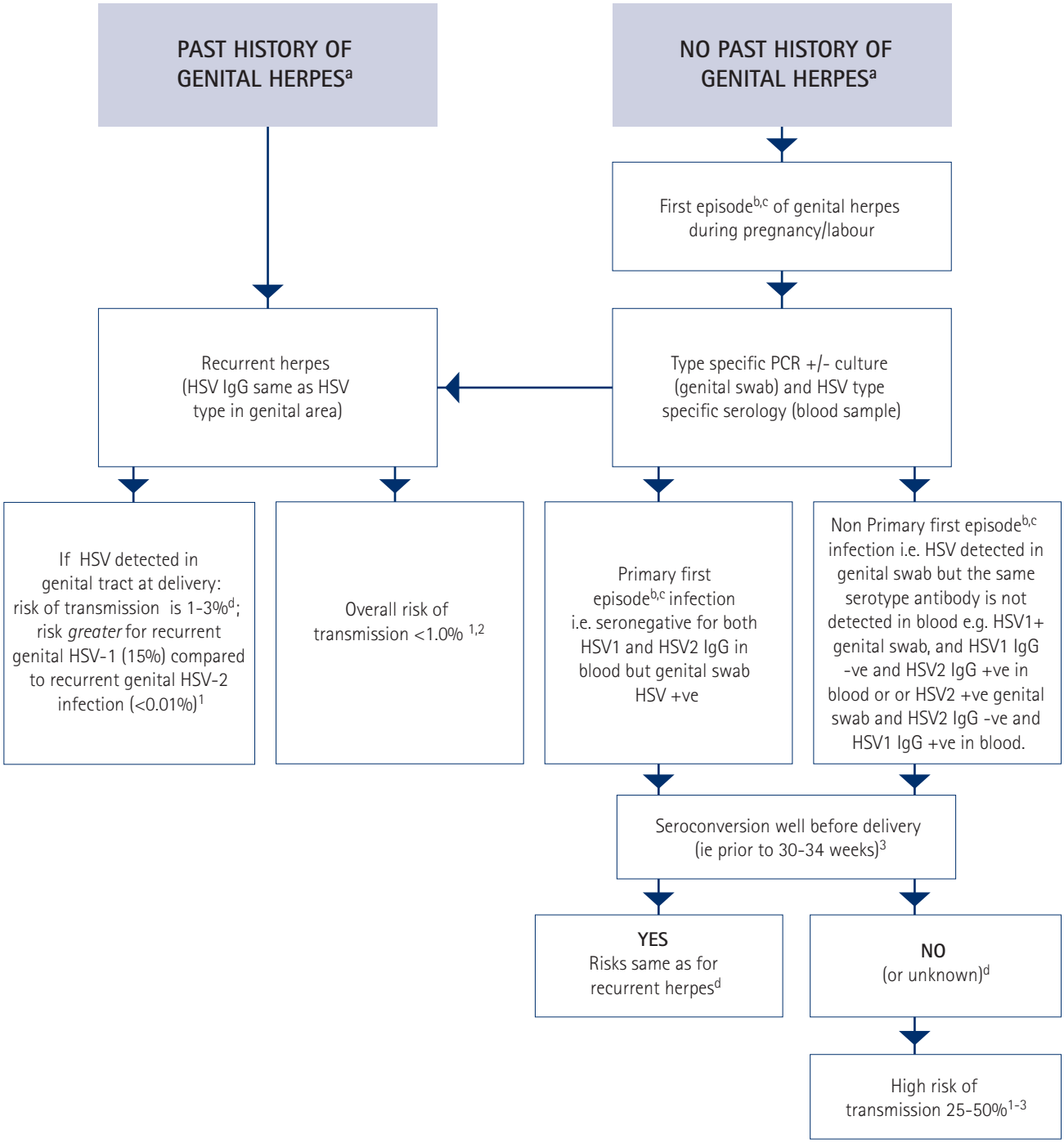
Herpes simplex virus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2014

HERPES SIMPLEX VIRUS – ALGORITHM 1

HSV IN PREGNANCY: RISK OF VERTICAL TRANSMISSION



COMMENTS

a. 85% of neonatal HSV infections are acquired perinatally. True intrauterine infection accounts for ≤ 5% of reported cases, usually to women with newly acquired infection. Spontaneous abortion, IUGR, preterm labour have also been reported. These complications are rare (<1%) for women with primary or recurrent disease[3].

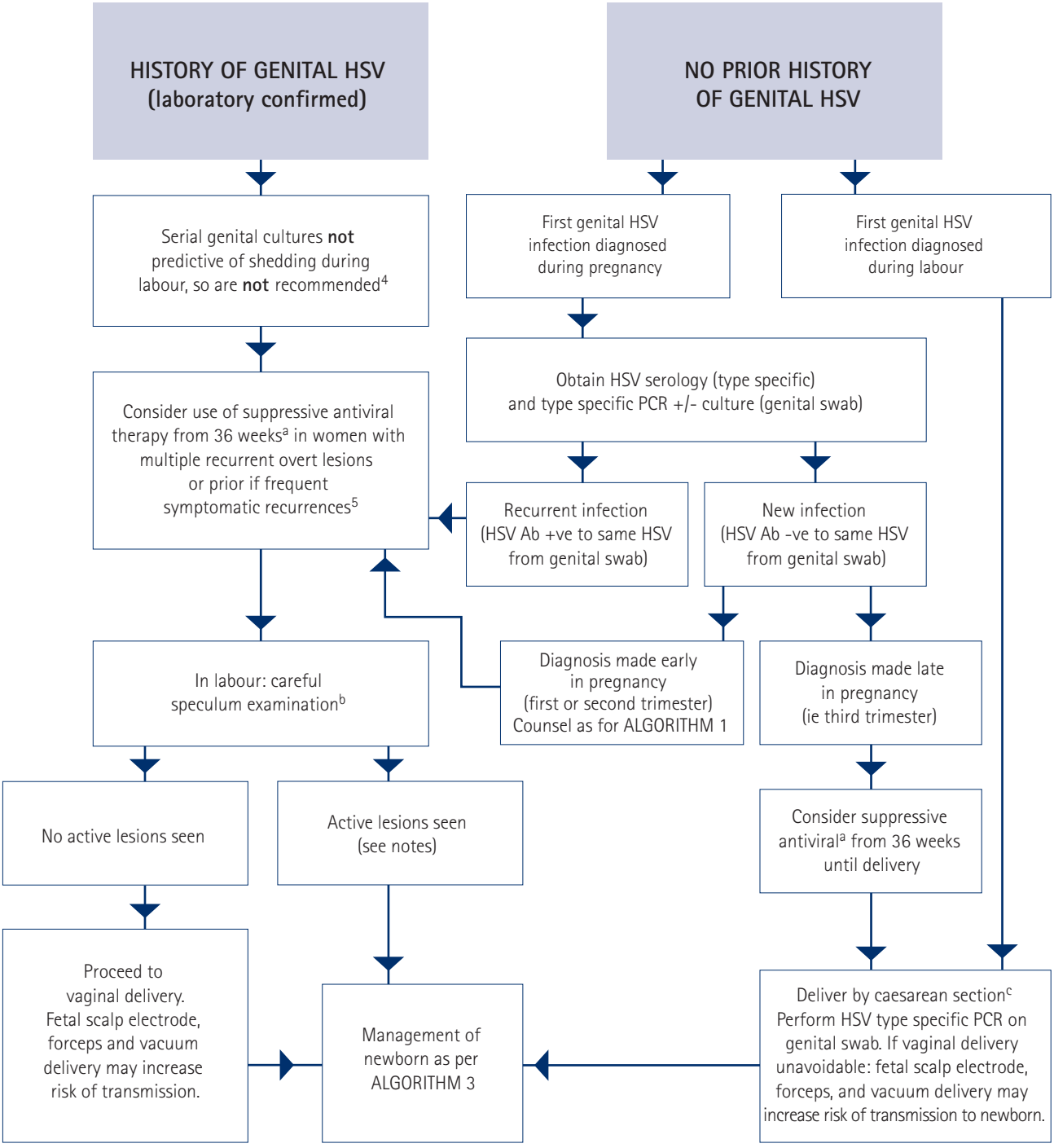
b. Most genital HSV infections (primary, non-primary or recurrent) are asymptomatic. ie most mothers of infants with neonatal HSV disease were previously unaware of their own infection.

c. Primary first episode refers to new acquisition of either HSV serotype without prior exposure (i.e. seronegative in blood to both HSV IgG 1 and 2). Non primary first episode infection refers to new acquisition of an HSV serotype, with evidence of exposure (i.e. HSV IgG +ve) to the other serotype.

d. If virus in genital tract:
   - use of scalp electrodes increases risk of transmission (OR 6.8)[1,3]
   - caesarean delivery reduces risk of transmission (OR 0.14)[1,3]
   - However, in clinical practice this is not often known at delivery.

HERPES SIMPLEX VIRUS – ALGORITHM 2

MANAGEMENT OF GENITAL HSV IN PREGNANCY



COMMENTS

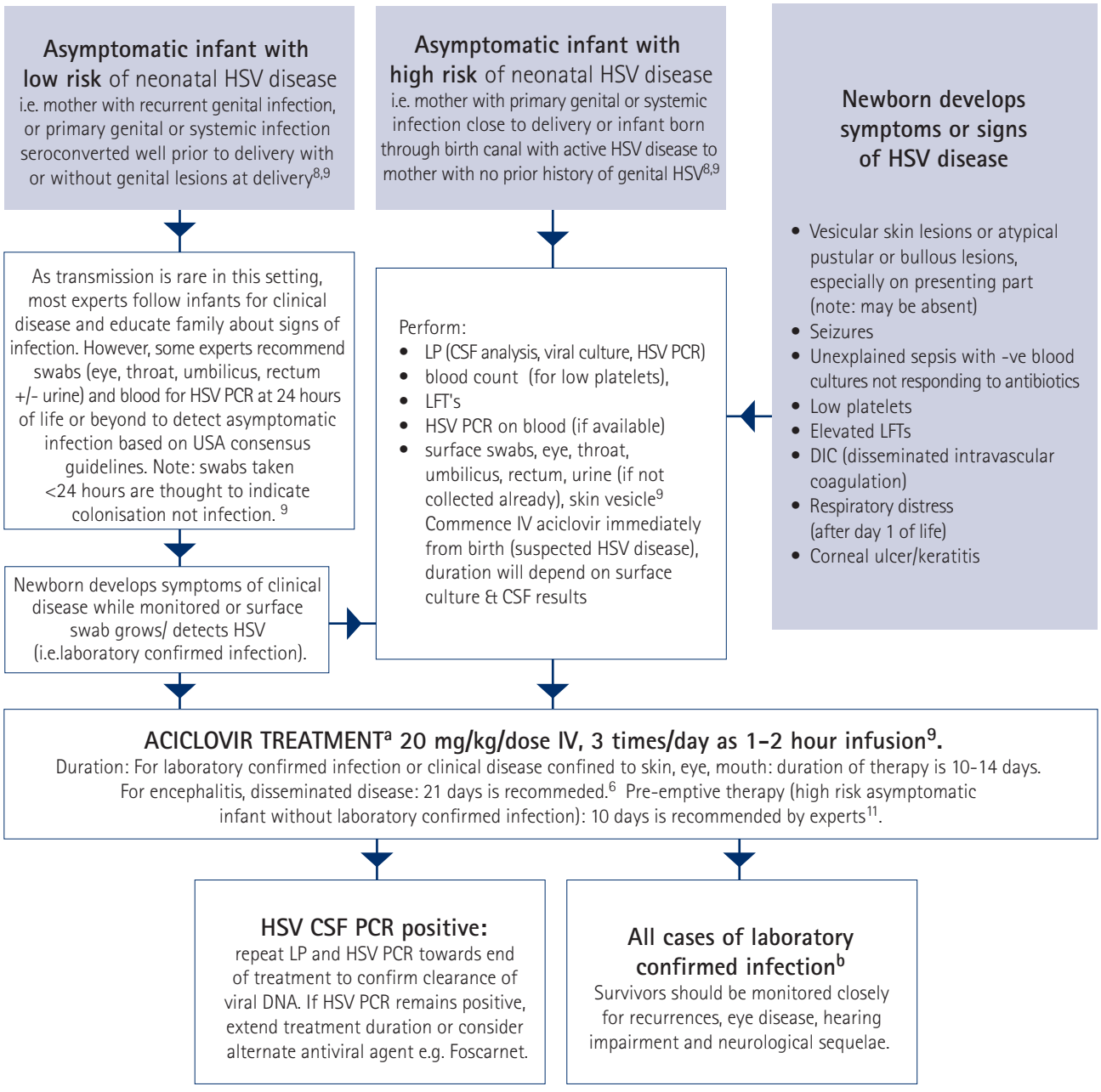
a. Suppressive oral aciclovir 400mg po tds or valaciclovir 500mg po bd reduces clinical recurrences, asymptomatic shedding, rate of caesarean section and virus in genital tract. Use must be balanced with risks of medication to newborn[5,6]. Clinical trials underpowered to evaluate efficacy of preventing transmission to the newborn[5,6] and neonatal disease has been reported after maternal suppression[7].

b. Careful speculum examination for active genital HSV should be performed on all women at delivery.

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. [1,3].

HERPES SIMPLEX VIRUS – ALGORITHM 3

HSV INFECTIONS IN PREGNANCY: NEONATAL MANAGEMENT



ACICLOVIR PROPHYLAXIS 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/dose, three times daily) for 6 months after completion of IV treatment shown to improve CNS outcomes (data mostly from HSV-2 CNS disease). [11]

Skin eye mouth or Disseminated infection without CNS involvement: Some experts also use 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, but not routinely recommended as not shown to alter neurological outcome.[8]

COMMENTS

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

b. There is little data to guide management of recurrences after neonatal HSV disease[8]. Most experts recommend CSF examination including HSV PCR should be performed and empiric IV aciclovir commenced for cutaneous recurrences after treatment ceases in early infancy (e.g. 3 months), for recurrences after previous neonatal encephalitis at any age, for representation with neurological signs +/- fever at any age.

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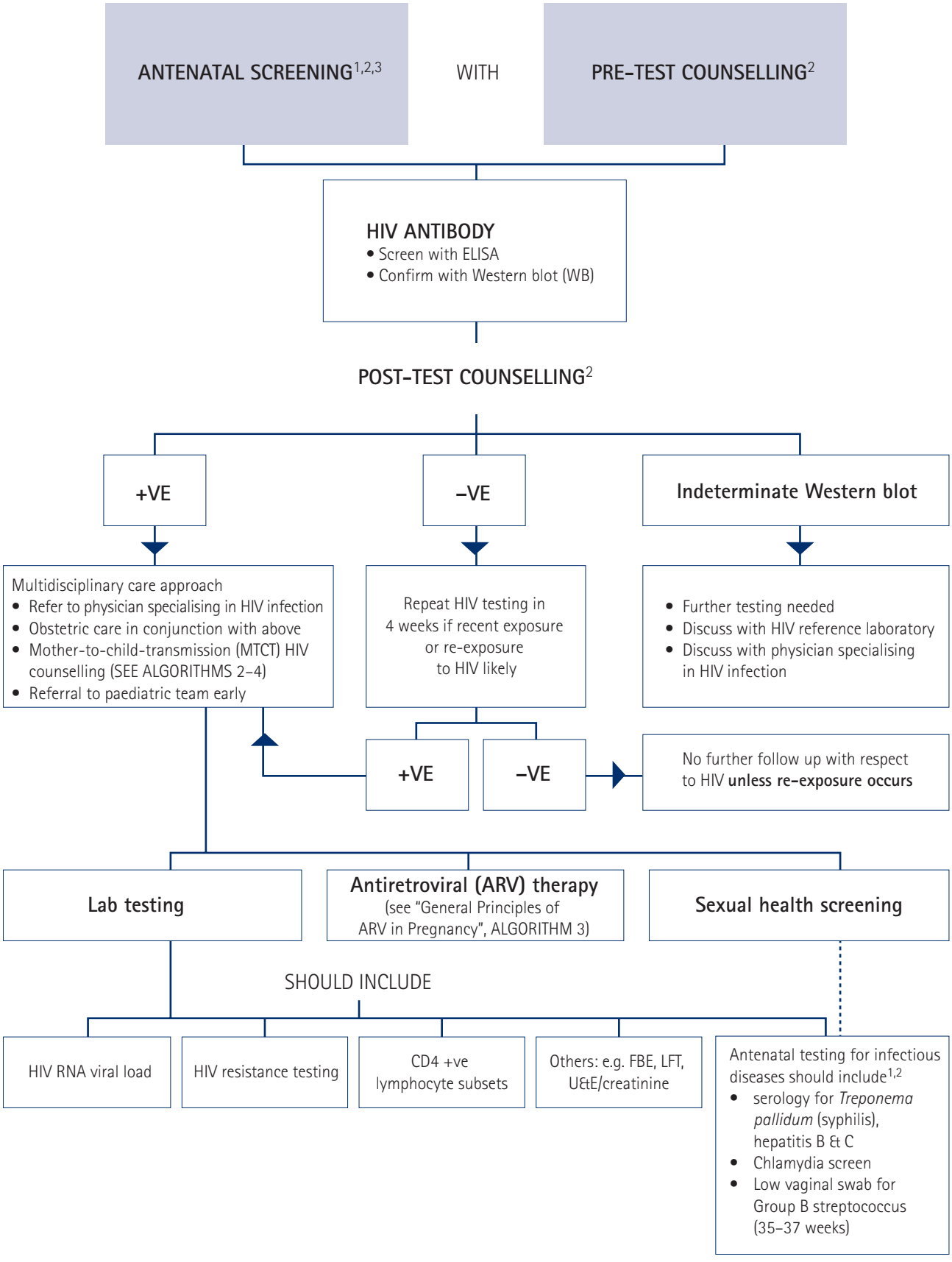
Human immunodeficiency virus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2014

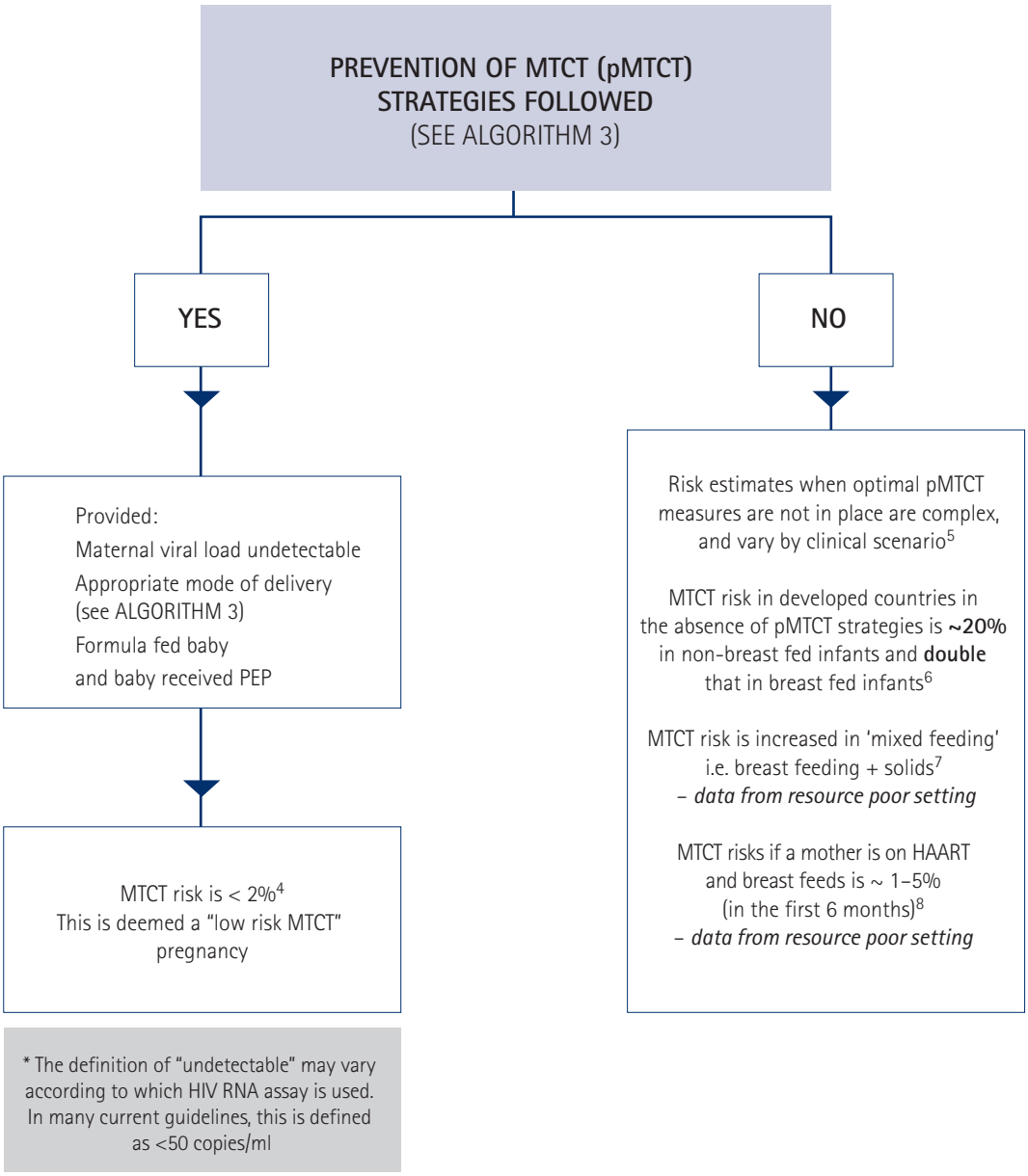
HIV – ALGORITHM 1

DIAGNOSIS OF HIV INFECTION IN PREGNANT WOMEN



HIV – ALGORITHM 2

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



COMMENTS

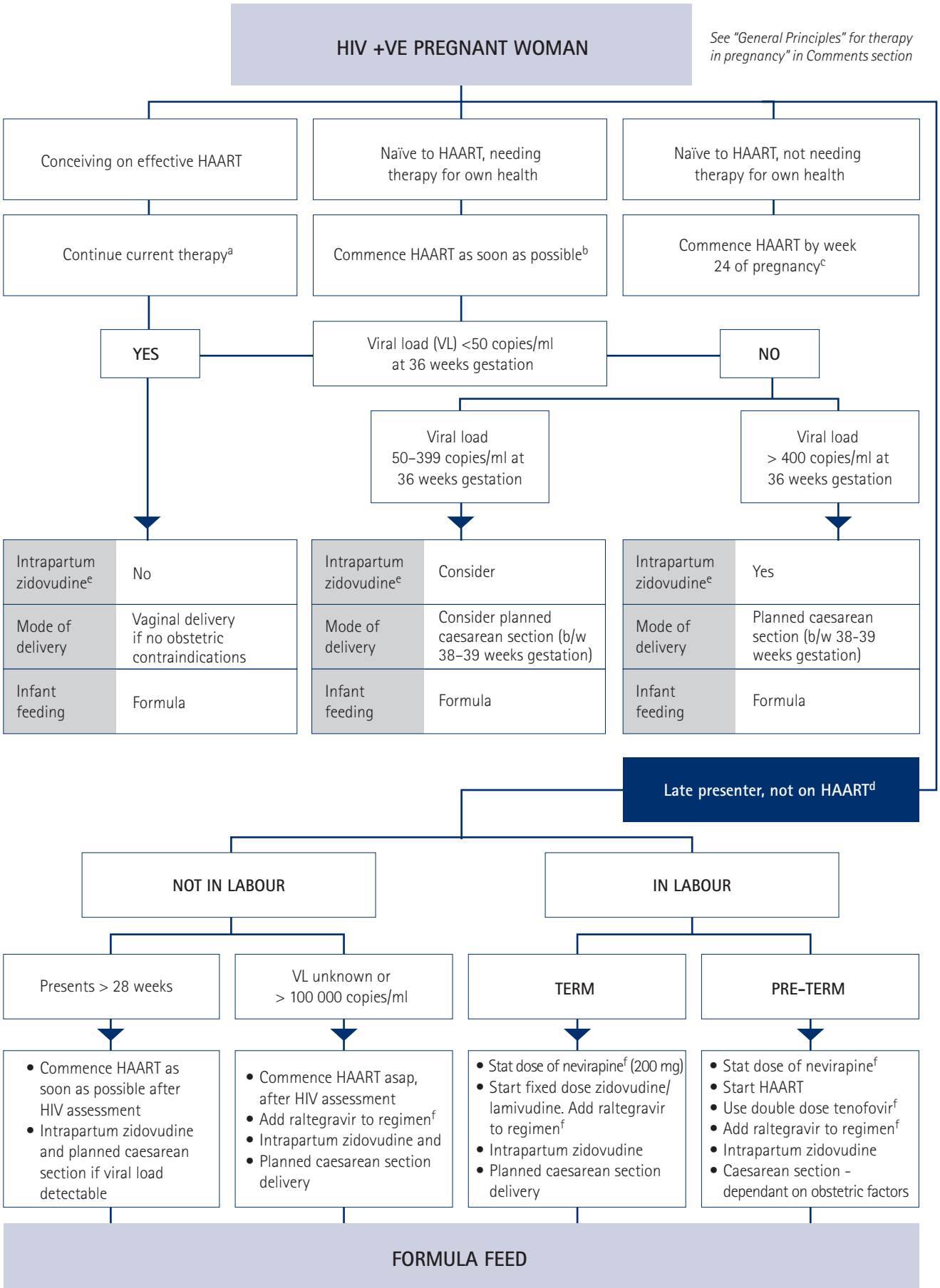
a. Perinatal counselling should include
   - MTCT risks
   - strategies to prevent transmission (SEE ALGORITHM 3)
   - management of baby at birth, including ARV prophylaxis (ALGORITHM 4)
   - testing schedule and clinical follow-up of baby (ALGORITHM 4).

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.

HIV – ALGORITHM 3

STRATEGIES TO MINIMISE MTCT HIV[9 - 13]



HIV – ALGORITHM 3

STRATEGIES TO MINIMISE MTCT HIV[9 - 13]

COMMENTS

a. Conceiving on effective HAART
   i. Continue regimen even if efavirenz is part of regimen
   ii. Stavudine (D4t) and DDI should not be prescribed in pregnancy

b. ARV naive, needing HAART for own therapy
   i. Commence HAART as soon as possible
   ii. Choice of regimens
      - Nucleoside backbone: zidovudine + lamivudine OR tenofovir + emtricitabine OR abacavir + lamivudine
      - Third agent: efavirenz or nevirapine (if CD4 cell count < 250 cells/uL) OR boosted PI

c. Naïve to HAART, not needing therapy for own health
   i. Commence ARV, preferably second trimester but by week 24
   ii. Nucleoside backbone: zidovudine + lamivudine OR tenofovir + emtricitabine OR abacavir + lamivudine
   iii. Third agent: boosted PI

   Whilst zidovudine monotherapy has been suggested in some cases as acceptable if VL < 10 000 copies/ml and CD4 > 350 cells/uL AND delivery is via planned caesarean section, this would not be the standard of care in Australia.

d. Late presenting woman, not on HAART, commence HAART without delay.

e. Intrapartum zidovudine: 2 mg/kg for the first hour, followed by continuous infusion, 1 mg/kg/hour.

f. These ARVs (nevirapine, raltegravir or double dose tenofovir) readily cross the placenta and are added in situations such as these to "load" the fetus pre-delivery. Note: data on the additional double dose of tenofovir is theoretical and not based on clinical outcome data.

HIV – ALGORITHM 4

MANAGEMENT OF INFANT AT RISK OF MTCT HIV [9,10]

CLINICAL ASSESSMENT AT BIRTH[a,b]

Commence antiretroviral (ARV) prophylaxis

CLINICAL

- Clinical examination, growth parameters & neurodevelopmental assessment
- Routine childhood vaccination as per Australian childhood immunisation schedule
- It is recommended that 'exposed non-infected children' have regular follow-up particularly during the first 5 years of life to determine any health or developmental issues

LABORATORY
(see Table 2)

- HIV PCR (DNA or RNA)[c]
- HIV antibody (only at ≥18 months of age – See Table 2)

ANTIRETROVIRAL PROPHYLAXIS[d]

Low risk MTCT*
(see definition below)
- single agent (AZT)
- start within 6–12 hours of birth
- zidovudine (AZT)
- 4 mg/kg/dose, 12 hourly
- for 4 weeks[14]
- PJP prophylaxis not needed[f]

High risk MTCT#
(see definition below)
- "Additional ARV" to AZT is recommended
- No consensus on the optimal regimen
- The preferred regimen is **AZT + 3TC + nevirapine**
- PJP prophylaxis [f]

See "Comments" for dosing schedule

Table 2: Suggested Testing Regimen

TIME OF TESTING	TEST	
	PCR – Proviral DNA or HIV RNA[c]	HIV Antibody
Week 1	+	No
Week 6	+	No
3 months	+	No
6 months	No	No
12 months	No *(clinical visit only)*	No
18 months		Yes *(to document clearance of maternal HIV antibodies and confirm infant's HIV-ve status)*

- Testing should occur at least 2 weeks and 2 months after antiretroviral prophylaxis is ceased, hence testing at 6 weeks and 3 months.
- Whilst testing at 6 and 12 months is no longer recommended, clinical visits here provide the opportunities for clinical assessment, routine childhood immunisations and maintenance of contact with family

***Low risk MTCT: Transmission risk estimated to be < 2%**
These include circumstances where optimal pMTCT strategies were in place in a bottle fed baby
- *And maternal viral load was undetectable*
- *or maternal HIV strain was zidovudine resistant but maternal viral load was undetectable at ≥ 36 weeks gestation*

#High risk MTCT: Transmission risk estimated to be > 2%
These include circumstances where
- *optimal pMTCT strategies were not in place*
- *Detectable maternal VL,*
- *Late maternal presentation with no or unknown VL or*
- *Mother found to be HIV +ve just after delivery (prophylaxis in this context is expected to be optimal if commenced within the first 3 days of birth)*

HIV – ALGORITHM 4

MANAGEMENT OF INFANT AT RISK OF MTCT HIV [9,10]

COMMENTS

a. There are no confirmed adverse events associated with in-utero/postnatal exposure to ARVs. No HIV embroyapathy syndrome has been described. The concern with mitochodrial toxicty after AZT +/- 3TC exposure *in-utero* remains to be confirmed.

b. Infected infants are unlikely to present with signs and symptoms of HIV at birth.

c. **Definitions**: "in-utero transmission" = +ve PCR result <48 hours of age. "peripartum transmission" = +ve PCR result >48 hours of age. HIV DNA PCR and HIV RNA PCR are highly specific and equivalent in sensitivity (~ 60% sensitivity at birth, 90% at 1 month and 100% at 3 and6 months) with high concordance.[14]

d. POSTNATAL ANTIRETRIVIRAL POST EXPOSURE PROPHYLAXIS (PEP) REGIMEN

A. If MTCT risk is low (< 2%)

- **Zidovudine monotherapy** is recommended if MTCT risk is low (<2%), even if the mother has a previous history of zidovudine resistance but has an 'undetectable' viral load. Prophylaxis should start as soon as possible after birth, (**within 6–12 hours of delivery**) for **4 weeks**[15]

Use

- **Zidovudine (AZT)**

  Zidovudine oral concentration 10 mg/ml

  - neonates born at ≥ 35 weeks gestation: 4mg/kg/dose orally, 12 hourly for 4 weeks
  - neonates born at 30–34 weeks gestation: 2 mg/kg orally, 12 hourly for 2 weeks, then 2 mg/kg, 8 hourly for 2 weeks
  - neonates born < 30 weeks gestation: 2 mg/kg orally, 12 hourly, for 4 weeks

  If neonates are unable to take oral zidovudine, give intravenously

  Zidovudine IV formulation: 10 mg/ml

  - Term neonate: 1.5 mg/kg/dose IV, 6 hourly
  - Premature: 1.5 mg/kg/dose IV, 12 hourly

B. If MTCT risk is high (> 2%):

ARVs in addition to zidovudine is indicated: MTCT transmission is considered significant (> 2%) e.g. if maternal VL is detectable at ≥ 36 weeks, or late maternal presentation and VL is unknown. **Lamivudine** and **nevirapine** is added to zidovudine, with a "tapering" regimen to cover the long half life of nevirapine[10]. Commence together with zidovudine as soon as possible after birth within 6–12 hours of delivery

In addition to **zidovudine**, use

- **Lamivudine (3TC)**, 3TC oral solution: concentration, 10 mg/ml
  2mg/kg/dose orally, 12 hourly for **4 weeks**

plus

- **Nevirapine (NVP)**

  Nevirapine oral suspension: concentration, 10mg/ml

  Nevirapine dosing:

  If mother has never taken nevirapine or was taking nevirapine for < 3 days

  - 2 mg/kg/dose orally, daily for **1 week**
  - Then 4 mg/kg/dose orally, daily for **1 week** in the second week, then stop

  If mother was taking nevirapine for the last 3 days or more

  - 4 mg/kg/dose, daily for **2 weeks**, then stop

Note: Lopinavir/ritonavir (Kaletra) is not used in early newborn PEP regimens as it is contraindicated in term newborns ≤14 days old or in premature babies till ≥14 days past their due date (reports of adrenal dysfunction).

e. Maternal zidovudine resistant strain: Monotherapy with zidovudine (postnatal) is still the recommended ARV of choice if MTCT risk is low (<2%) i.e. where maternal VL is undetectable and there are are no other risk factors contributing to increased MTCT risk.

f. *Pneumocystis jiroveci pneumonia* (PJP) prophylaxis: PJP prophylaxis with cotrimoxazole is recommended if MTCT risk is high (> 2%). Commence PJP prophylaxis when ARV PEP is discontinued at end of 4 weeks. Continue PJP prophylaxis until HIV infection is excluded. If HIV infected, PJP prophylaxis should be continued and managed as per treatment guidelines. Dosing: Co-trimoxazole 900 mg/m^2 once daily, Mon/Wed/Fri. Age <6 months: 120 mg once daily, Mon/Wed/Friday. Age 6-12 months: 240 mg once daily, Mon/Wed/Friday.

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Listeria

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2014

LISTERIA – ALGORITHM 1

DIAGNOSIS OF SUSPECTED MATERNAL LISTERIOSIS AND MANAGEMENT OF PROVEN MATERNAL INFECTION

- unwell febrile pregnant woman, observed most often in third trimester (includes 'flu-like' illness).
- ~ 1/3rd may be asymptomatic

ACUTE LISTERIOSIS

Laboratory investigations

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

- Blood culture
- Gram stain and cultures of genital tract

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

Positive for *Listeria monocytogenes*

Amoxycillin/Ampicillin for 14 days [1, 2, 3] (≥ 2 g, 4–6 hrly, IV) + **gentamicin for 14 days [1, 2, 3]

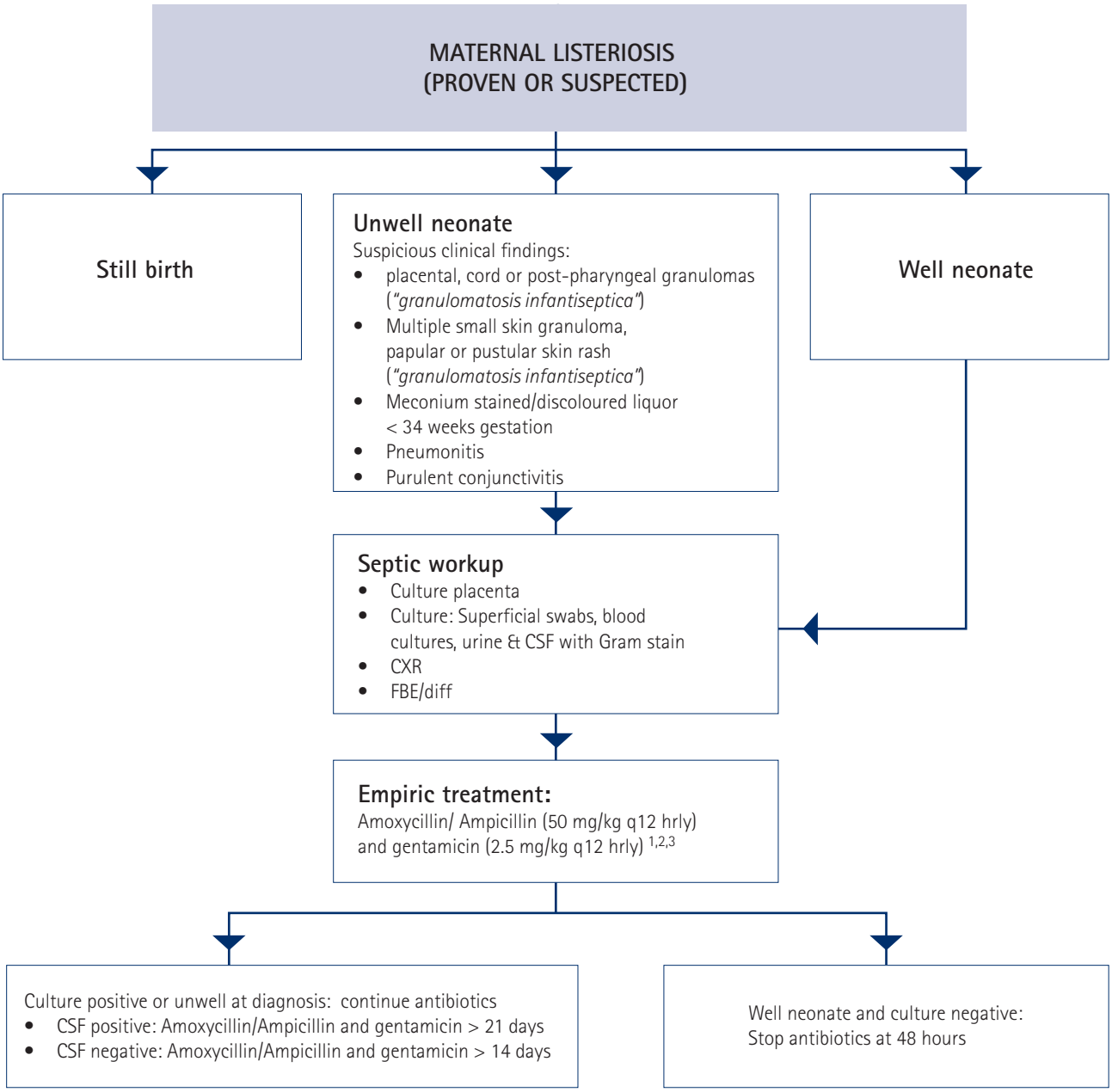
Urgent delivery depends on severity of maternal illness and gestation

COMMENTS

- Listeriosis is uncommon in Australia (0.3 cases per 100 000 population). However, listeriosis is significantly more common in pregnancy than in the non-pregnant population, and accounted for ~14% in one Australian report. [4]
- 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 a mortality of 40-50% for the fetus. [3,5,6]
- 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]
- Whilst the efficacy of this approach has not been verified, it is suggested that asymptomatic individuals at high risk of listeriosis who have ingested food implicated in an outbreak be given oral amoxicillin (2-3 g/day) or trimethoprim-sulphamethoxazole (if not in first trimester of pregnancy) for 7 days.[7]
- The incubation period of for invasive listeria infection has been estimated to range from 1–67 days, median 8 days, with ~ 6 weeks for pregnancy-associated cases.[8]
- 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 observations and case reports. No randomised controlled trials have been performed to establish optimal treatment regimens or to support efficacy of penicillin over ampicillin, but ampicillin or amoxicillin is generally considered the preferred agent.[1, 2, 3]
- Synergism for penicillin or ampicillin with gentamicin has only been reported in-vitro[3]. The risk for ototoxicity and fetal toxicity needs to be balanced with clinical risk. **Gentamicin is thus is generally recommended in combination with ampicilllin/amoxycillin in severe infections, including meningitis. Dosing is not standardised and should be in accordance with local guidelines. Dosing ranges cited include "maximum of 2.5 mg/kg/day"[1] to "maximum of 360 mg per day, as an infusion".[2]
- Erythromycin (4 g/day) or Trimethoprim/sulphamethoxazole (TMP/SMX, 200mg–32 mg of TMP per day) are suggested as alternatives in the penicillin allergic patient but TMP/SMX may be best avoided in early pregnancy because of anti-folate activity. [2]

LISTERIA – ALGORITHM 2

DIAGNOSIS AND MANAGEMENT OF INFANT AT RISK OF PERINATAL LISTERIOSIS



COMMENTS

- Preterm delivery is common. Mortality rates range from 3-60% in infected neonates born alive.
- Perinatal listeria 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 (7 days to 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%. [5,6]
- Surface cultures with Gram stain from placenta, meconium, rectal and external ear canal have all been found to have a high yield in isolating the organism. [5, 6]
- 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.[1, 2, 3]
- Alternative antibiotics: Trimethoprim/sulphamethoxazole reserved in the of event of lack of response to standard therapy; Rifampicin effective in vitro but inadequate clinical information available; erythromycin sensitive but bacteriostatic and crosses the placenta poorly.
- Linezolid and quinolones are not recommended in pregnancy and for newborns.
- There is no role for cephalosporins as listeria are resistant to this class of agents.

LISTERIA
APPENDIX AND REFERENCES

APPENDIX

Avoid high risk foods

These foods include:

- Unpasteurized 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 salads and coleslaws

AND

Use safe food handling practices

- Wash hands before preparing foods
- Thoroughly cook raw food from animal sources
- 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
- and salads in which raw vegetables may have previously been dipped
- Thoroughly wash raw fruit and vegetables
- 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

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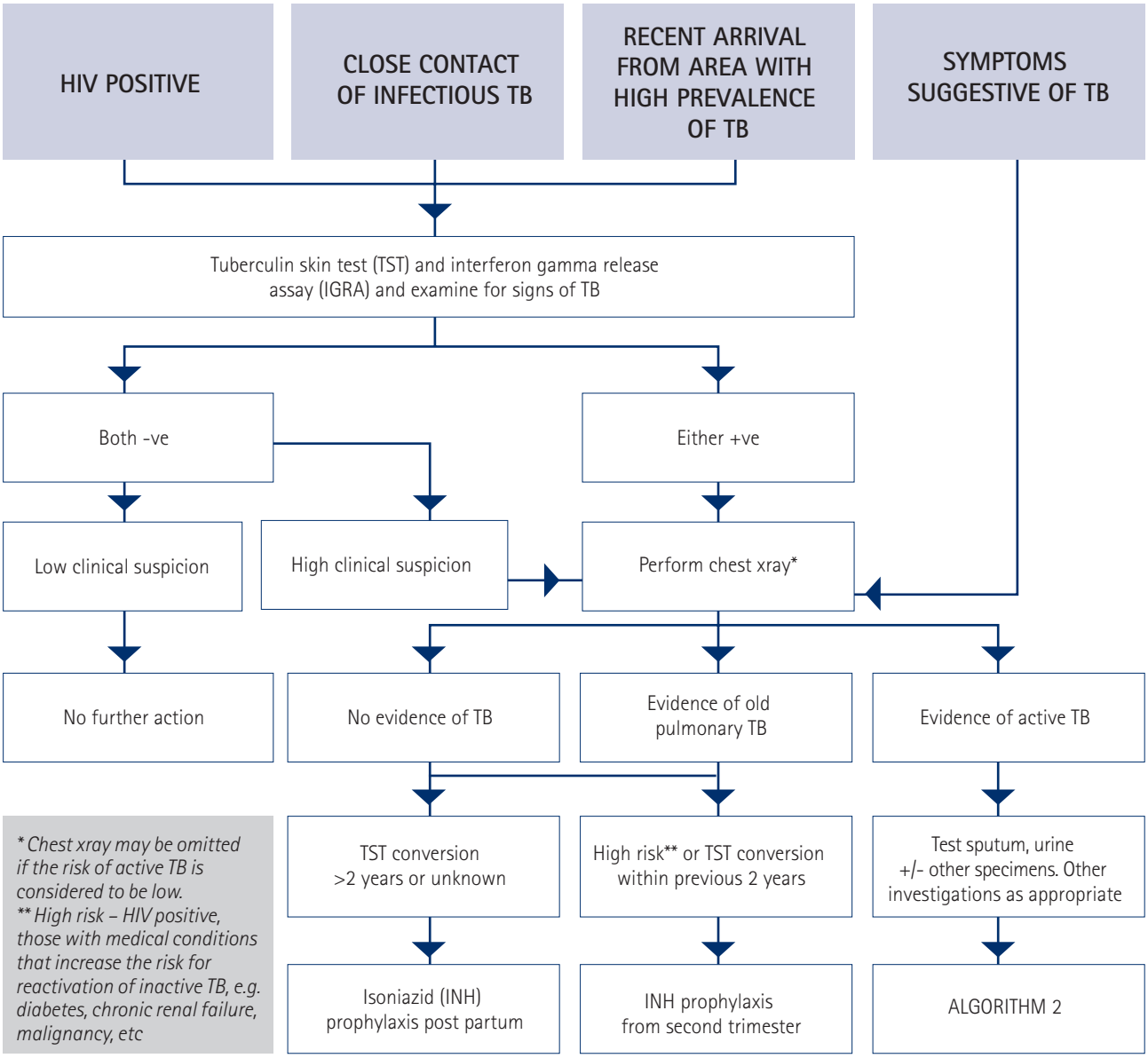
Mycobacterium tuberculosis

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2014

MYCOBACTERIUM TUBERCULOSIS – ALGORITHM 1

ANTENATAL DIAGNOSIS: MANAGEMENT OF PREGNANT WOMAN



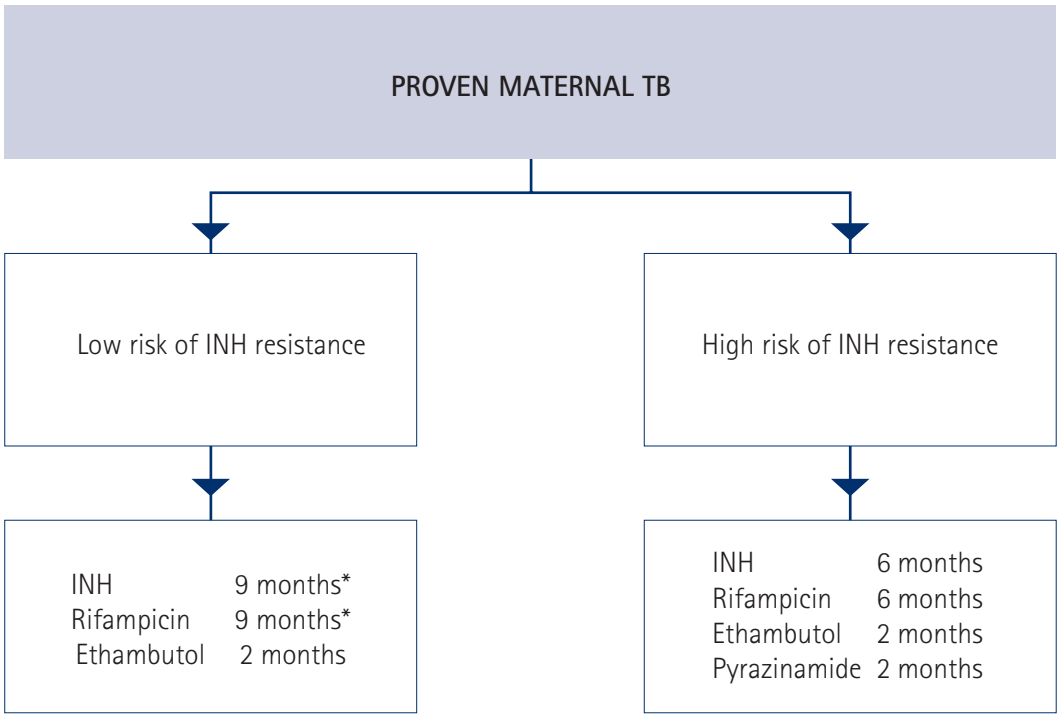
** Chest xray may be omitted if the risk of active TB is considered to be low.*
*** High risk – HIV positive, those with medical conditions that increase the risk for reactivation of inactive TB, e.g. diabetes, chronic renal failure, malignancy, etc*

COMMENTS

- The development, clinical presentation and progression of TB are not altered by pregnancy.
- Pregnancy is not thought to increase the risk of inactive TB becoming active.
- 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.
- Routine screening for TB in pregnancy is not standard practice.
- Screening with a Tuberculin skin test (TST) or T cell interferon gamma release assay (IGRA) should be 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 need to be fully investigated.
- The performance of IGRA for detecting LTBI has been evaluated in pregnant women and compared with TST. These tests 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.
- TST has limited specificity and sensitivity, particularly in HIV-infected individuals.
- IGRA appears to better detect LTBI after recent TB exposure than does the TST.
- TST testing of contacts is usually performed by local Health authorities, and may need to be repeated at 12 weeks after break of contact.
- TST: intradermal injection of 0.1 ml of a 50 tuberculin unit/ml solution of purified protein derivative (PPD), with induration measured at 48-72 hours.
- Chest xray should be performed with appropriate abdominal shielding.
- INH is safe in pregnancy.
- Pyridoxine should be given with INH to pregnant and breast-feeding women (50 mg/day), and to their breast-fed infants (10 mg/day) whether or not the infant is taking INH.
- TST interpretation: See page 49.

MYCOBACTERIUM TUBERCULOSIS – ALGORITHM 2

MANAGEMENT OF PROVEN MATERNAL TB

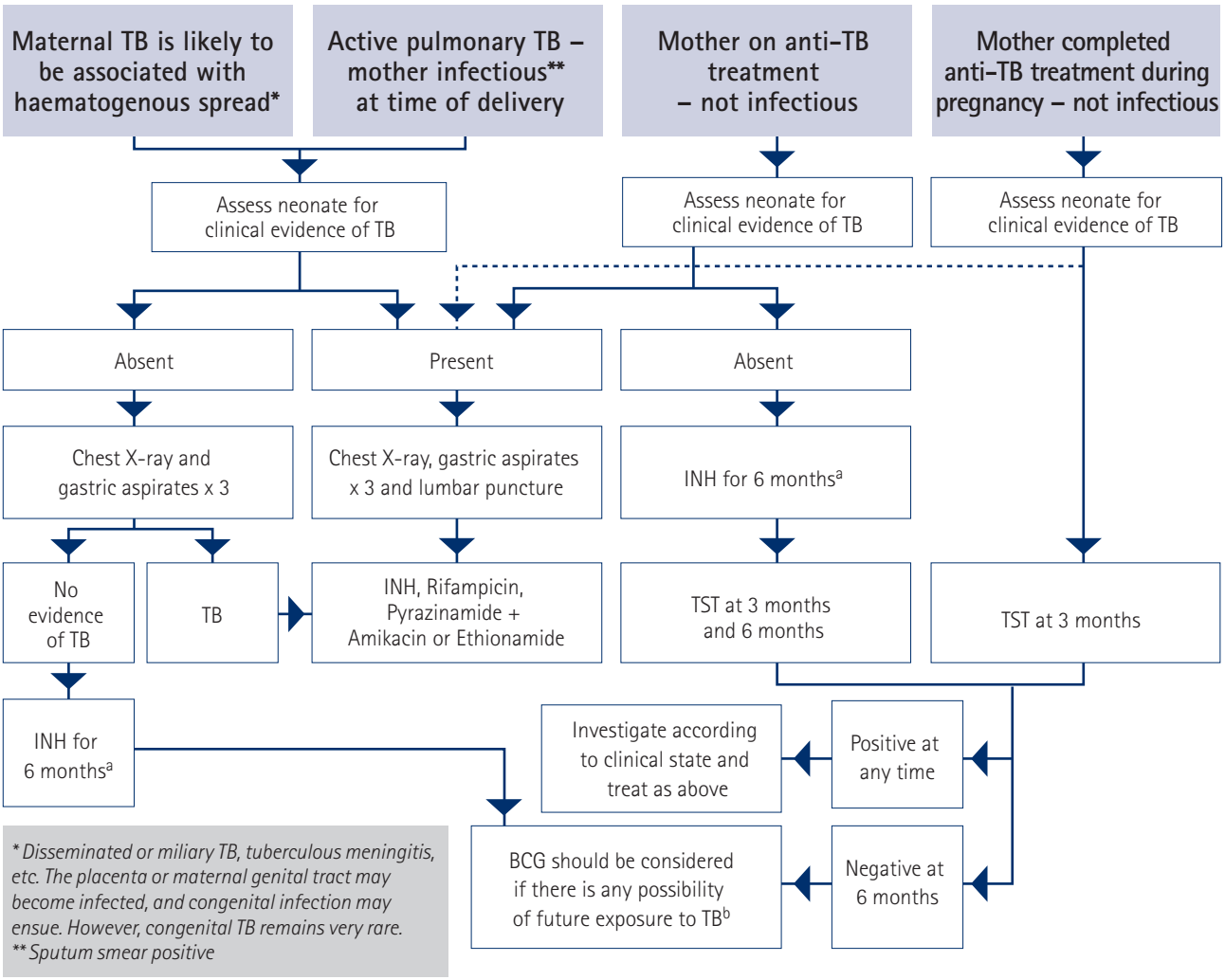


COMMENTS

- 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.
- High risk of INH resistance should generally be assumed, particularly for HIV +ve women, recent arrivals from an area of high prevalence, and those who have had previous anti-TB treatment.
- Duration of therapy with each drug may vary according to the resistance pattern of the isolate, and according to the form of TB (e.g. longer for TB meningitis).
- The duration of treatment with INH and rifampicin is longer for cases when Pyrazinamide is not given in the first 2 months*.
- Directly observed therapy (DOT) is ideal practice, but may not be feasible for all patients with TB, application varies across Australia.
- All of the anti-TB drugs cross the placenta and reach a low concentration in fetal tissues. However, INH, Rifampicin and Ethambutol are all safe in pregnancy. Compared with other first line anti-TB agents, there are less safety data for Pyrazinamide. However, there is no clear evidence that it is teratogenic and it is recommended by the World Health Organisation for all pregnant women with TB, during all trimesters of pregnancy. Other authorities recommend it in certain scenarios such as when multi-drug resistance is suspected, when the pregnant woman is HIV infected, or for treatment of TB meningitis, especially when INH resistance is a possibility. Streptomycin is contraindicated in pregnancy.
- **INH** – 300 mg po daily (give with pyridoxine 50 mg daily – note increased dose in pregnant and breast-feeding women).
- **Rifampicin** – 450 mg po daily (< 50 kg), 600 mg po daily (≥ 50 kg).
- **Ethambutol** – 15 mg/kg po daily.
- **Pyrazinamide** – 25-40 mg/kg (max 2g) po 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



** Disseminated or miliary TB, tuberculous meningitis, etc. The placenta or maternal genital tract may become infected, and congenital infection may ensue. However, congenital TB remains very rare.*
*** Sputum smear positive*

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 is sick enough to require hospitalisation for TB.
- Other family members and close contacts should be assessed for TB infection or disease. If a close contact is infectious, separation is preferable, but, if impossible, INH prophylaxis should be given to the neonate until the contact has been culture-negative for 3 months.
- Respiratory distress, hepatosplenomegaly, fever, lymphadenopathy and poor feeding are the most common presenting features of perinatal 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.
- TST conversion may be delayed for up to 6 months; thus INH prophylaxis must be continued until this time.[a]
- TST interpretation: please see page 49.
- IGRA performance in children is less well understood than that in adults. The frequencies of indeterminate IGRA results in children vary greatly among studies (range: 0–17%) and between different IGRA formats.
- IGRA cannot be recommended routinely for children <5 years of age or for immunocompromised children of any age because of a lack of published data.
- BCG should be considered for Aboriginal neonates, infants born to migrant parents and those travelling to high TB incidence settings.[b]

DRUG TREATMENT

- The decision regarding number and choice of drugs for management of neonates and infants with TB is difficult, and warrants specialist advice.
- INH 10 mg/kg po daily for 6 months. Pyridoxine 10 mg po daily must be added for breast-fed infants.
- Rifampicin 15 mg/kg po daily for 6 months.
- Pyrazinamide 35 mg/kg po daily until drug susceptibility results are available.
- Amikacin 15 mg/kg iv daily until drug susceptibility results are available.
- Ethionamide or prothionamide 15-20 mg/kg daily until drug susceptibility results are available. May be difficult to obtain.
- Ethambutol 20 mg/kg po daily may be used in place of amikacin or ethionamide, but should be reserved for special cases. It may induce optic neuritis, which is difficult to identify in infants.
- Streptomycin is no longer recommended.
- These drugs are excreted in breast milk. If a breast-feeding mother and neonate are both on anti-TB therapy, there is a small risk of toxic levels in the neonate. This can be minimised if the mother takes her medications immediately after a breast feed.

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GUIDE TO INTERPRETATION OF THE TST

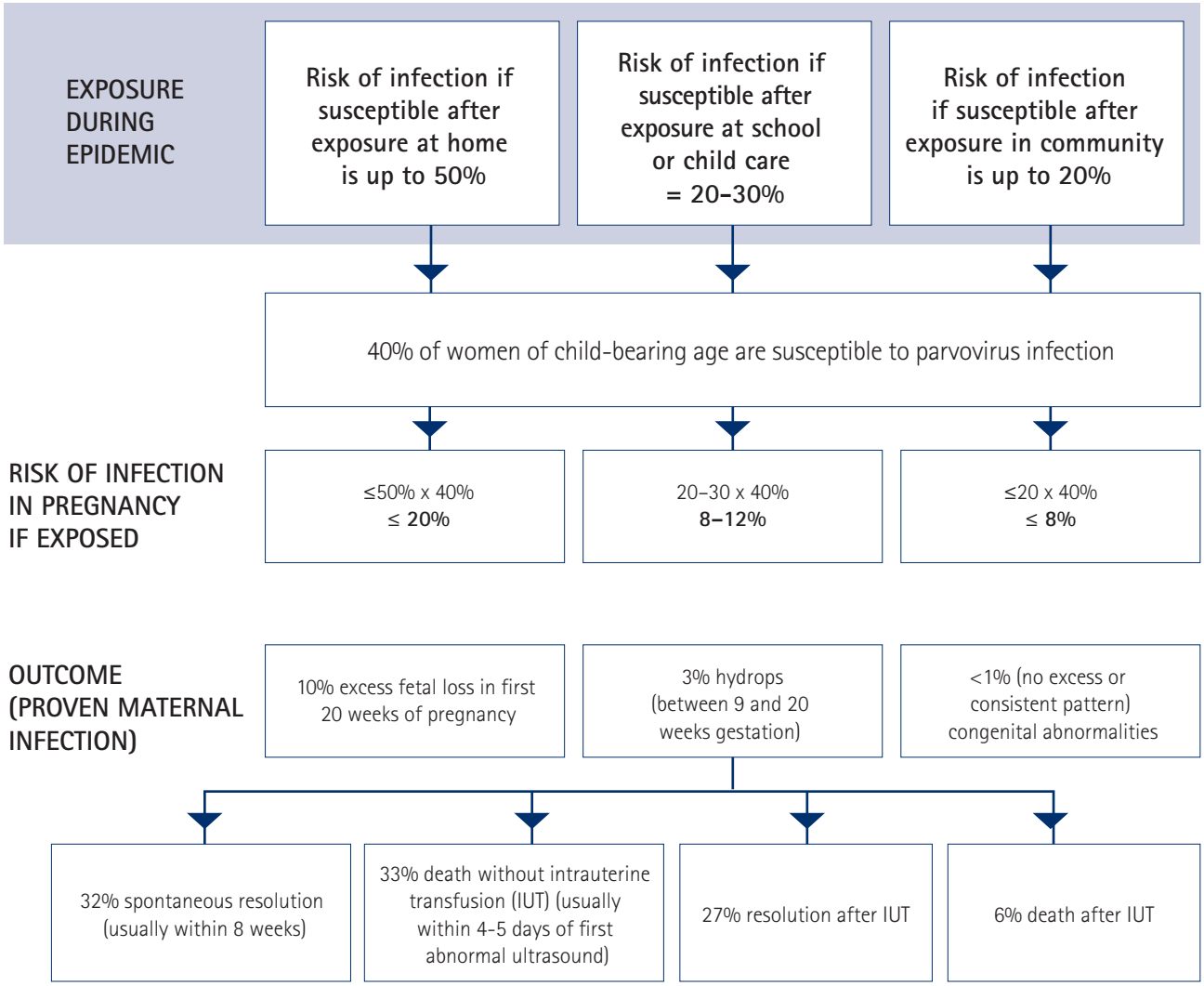
	LOW RISK	MODERATE RISK	HIGH RISK
	No risk factors	• Ethnic origin from high prevalence population • Locally identified high risk populations • Adult HIV patient with CD4 count > 500/mL • Children aged 1-5 years	• Household contacts of infectious cases • HIV-infected or other immuno-suppression (including 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**

Parvovirus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2014

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)

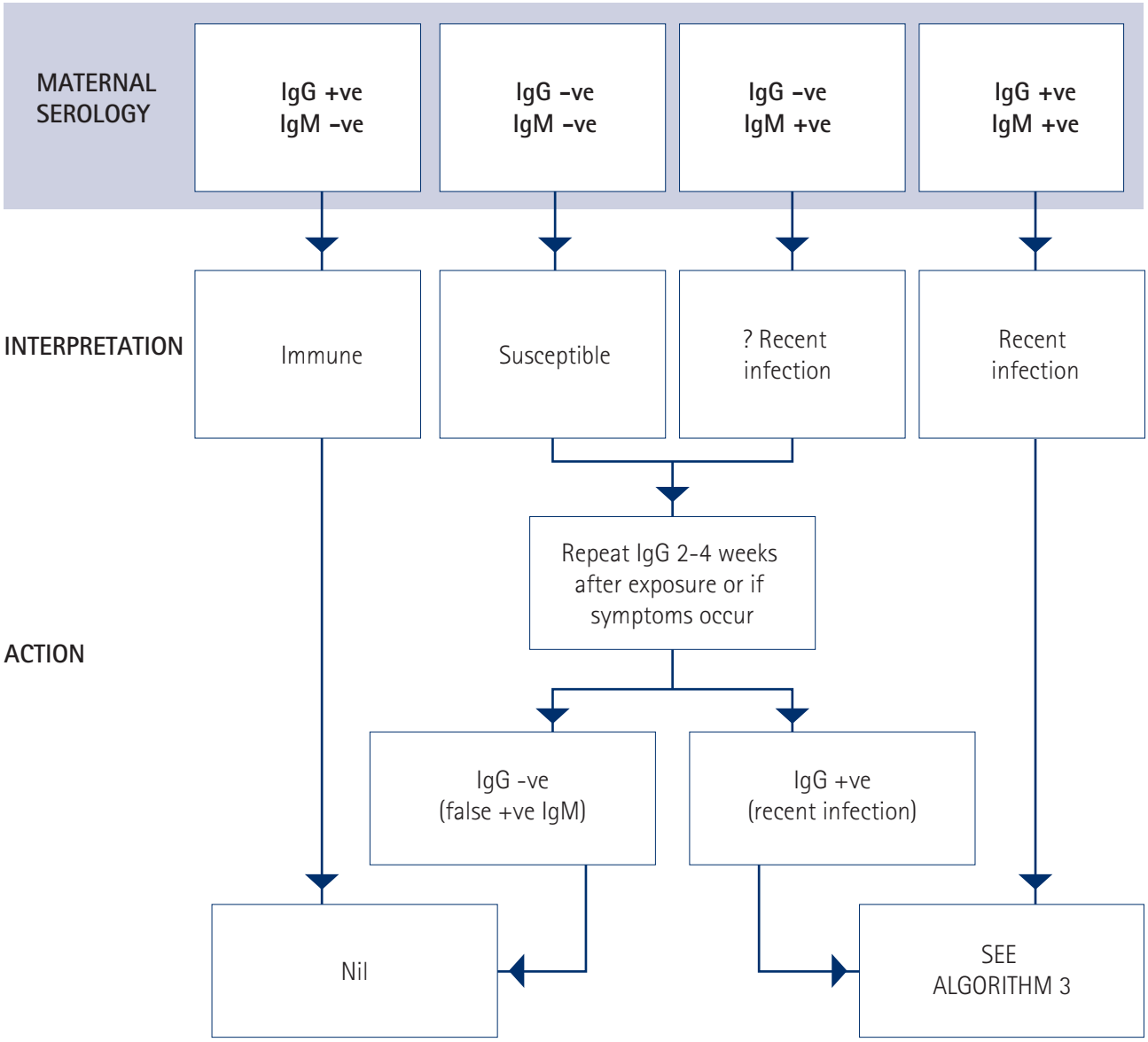
Pregnant women who are exposed should be informed of risks, and offered serological testing.

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%).

PARVOVIRUS – ALGORITHM 2

ANTENATAL DIAGNOSIS & MANAGEMENT



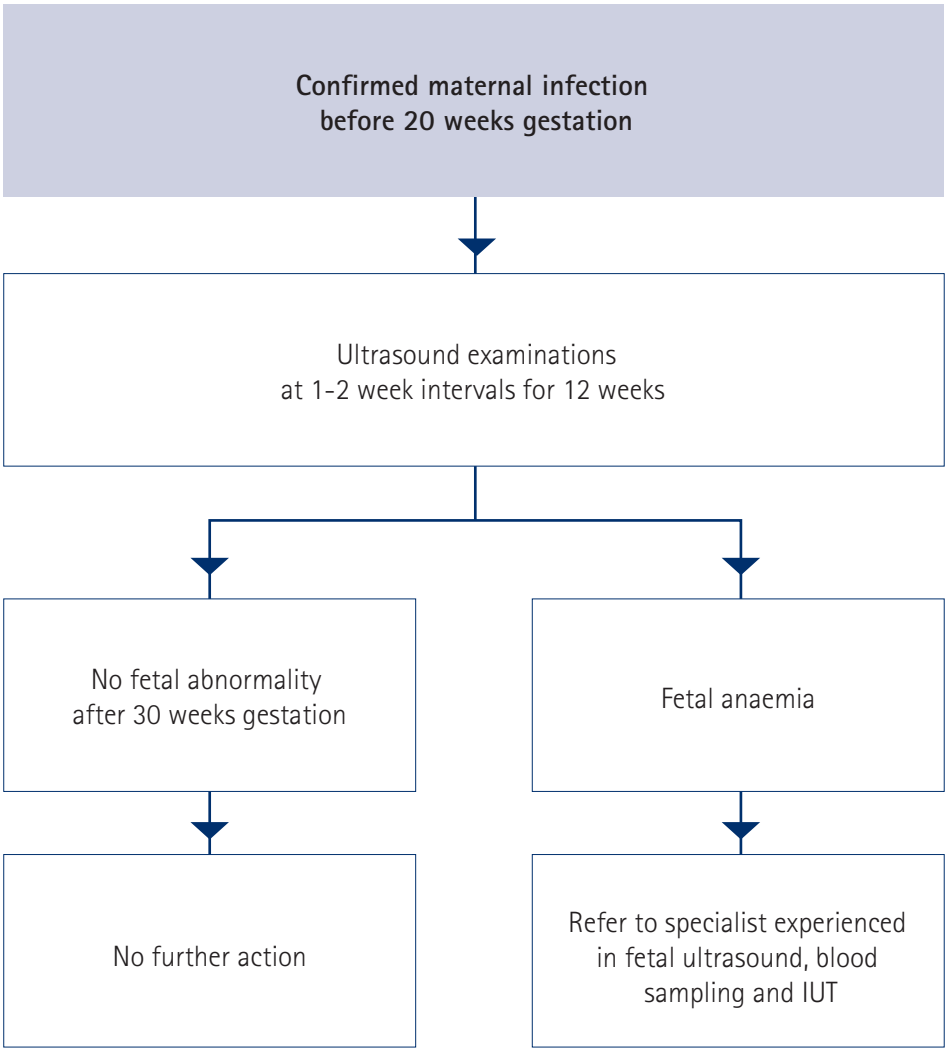
COMMENTS

- 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.
- Termination is not indicated because of low risk of fetal 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. Quantitative PCR is available in some centres.
- Pregnancy should be monitored by repeated 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 and provides 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.

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Rubella

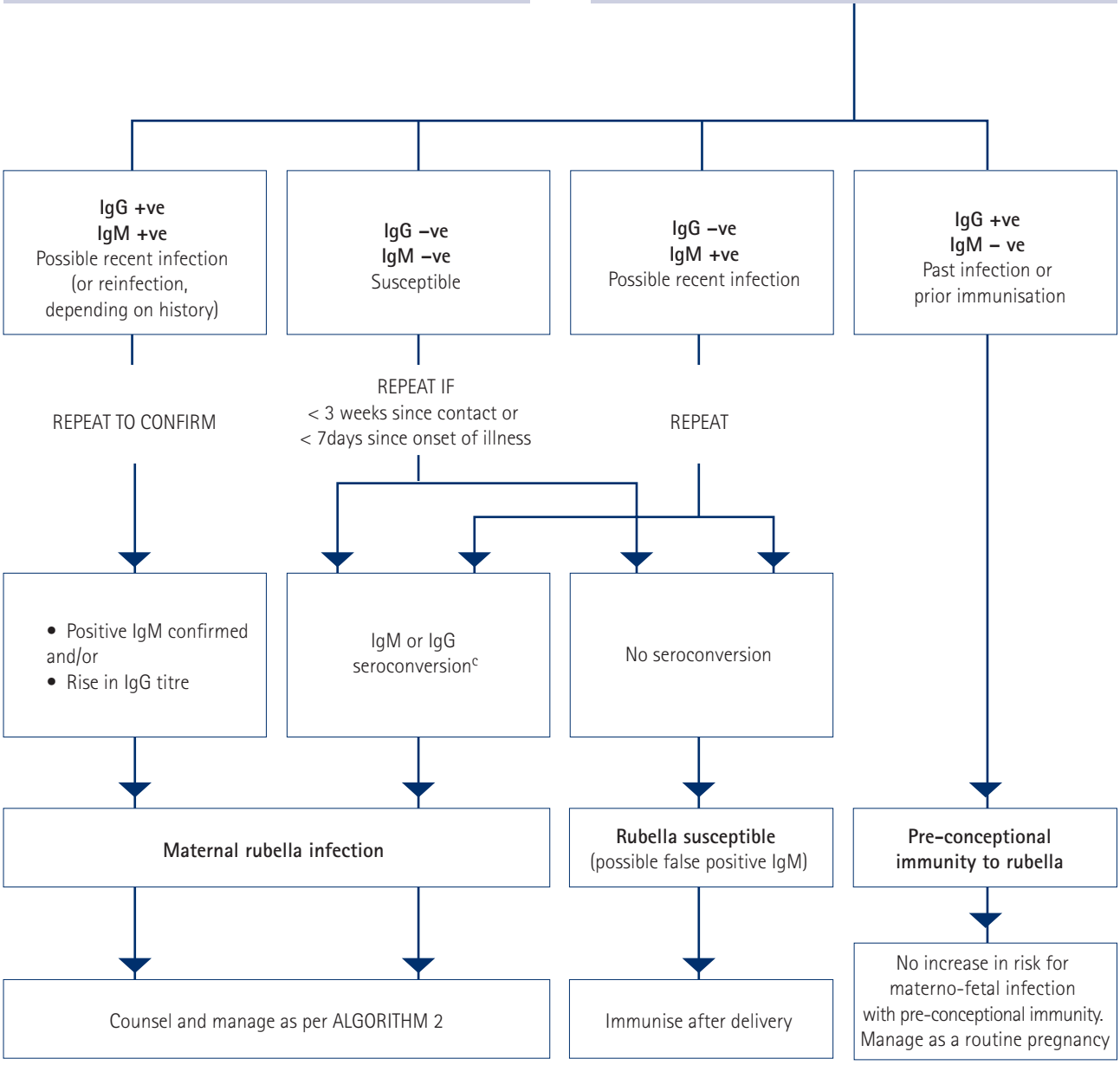
AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2014

RUBELLA – ALGORITHM 1

DIAGNOSIS OF SUSPECTED MATERNAL RUBELLA INFECTION

a) Routine antenatal screening (IgG only)[a] [1,2,3]
If IgG –ve, immunise after delivery
If IgG +ve; if >10 IU/mL; minimal risk of reinfection
If <15 IU/mL; consider reimmunisation after delivery

b) Rubella testing (IgG/IgM)[b] because of
(i) contact with rubella
(ii) rubella-like illness (fever, erythema, arthralgia)

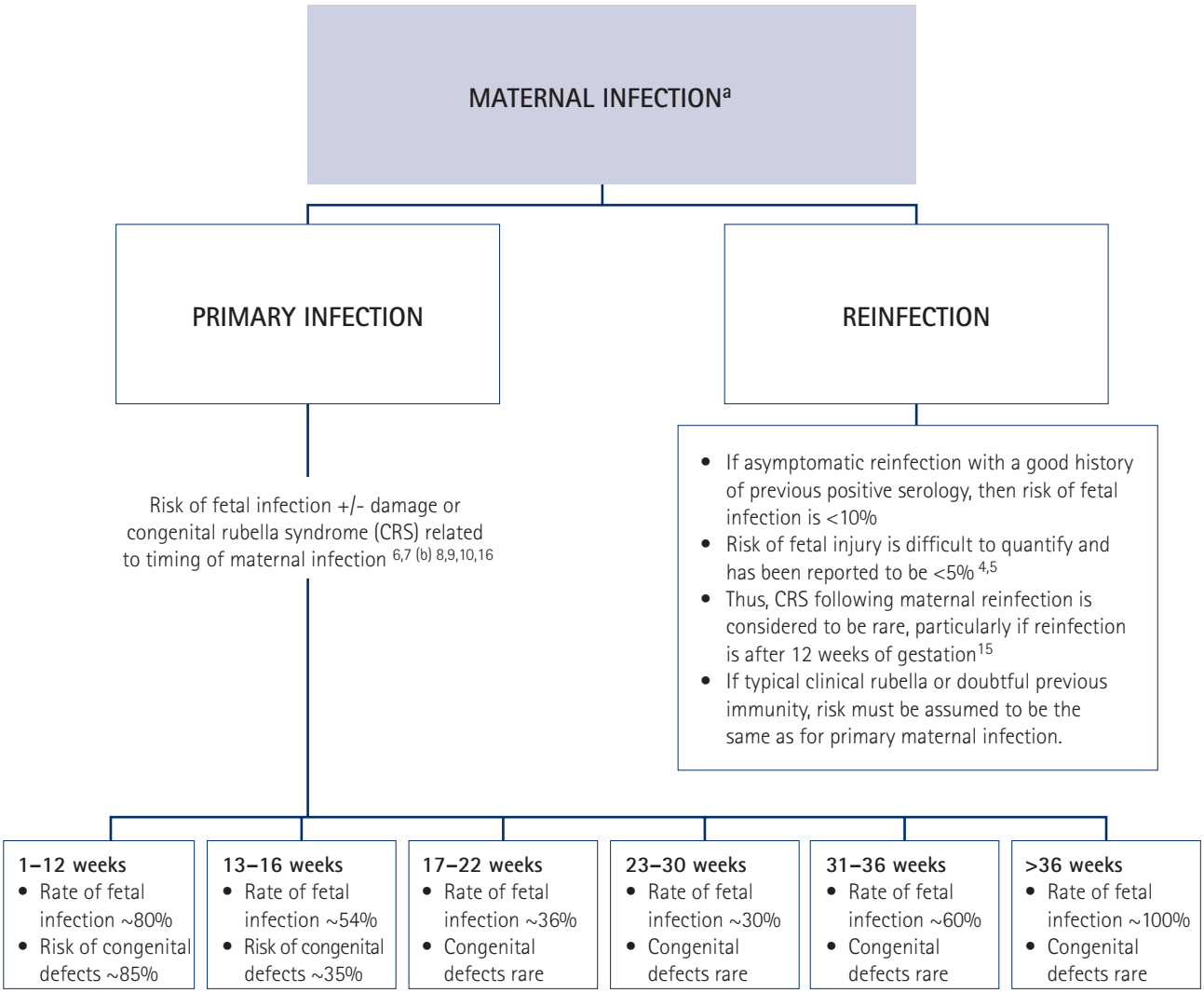


COMMENTS

a. Note: Different laboratories use various cut-offs for reporting low IgG levels ranging from 7 to as high as 50 IU/mL. Levels corresponding to protection from reinfection are imprecise, but only a small proportion of women are affected by reinfection [1,2]
b. Reinfection can occur without detectable IgM. Previously stored serum, if available, should be retrieved and tested in parallel with current serum, for evidence of pre-existing antibodies or seroconversion.
c. Seroconversion should be checked by testing the sera in parallel.

RUBELLA – ALGORITHM 2

MANAGEMENT OF PROVEN MATERNAL RUBELLA INFECTION



- Consider termination of pregnancy if maternal infection in first trimester.
- If maternal infection occurred in second trimester, consider fetal testing.
- Maternal infection after 20 weeks is rarely associated with CRS

Prenatal fetal diagnosis/testing

- Rubella PCR, rubella culture and fetal IgM can be performed following chorionic villus sampling (CVS) or amniocentesis. 10,11,12 c
- Prenatal testing is recommended at least 6 weeks after known maternal infection is and best performed after the 20th week of gestation 13

However

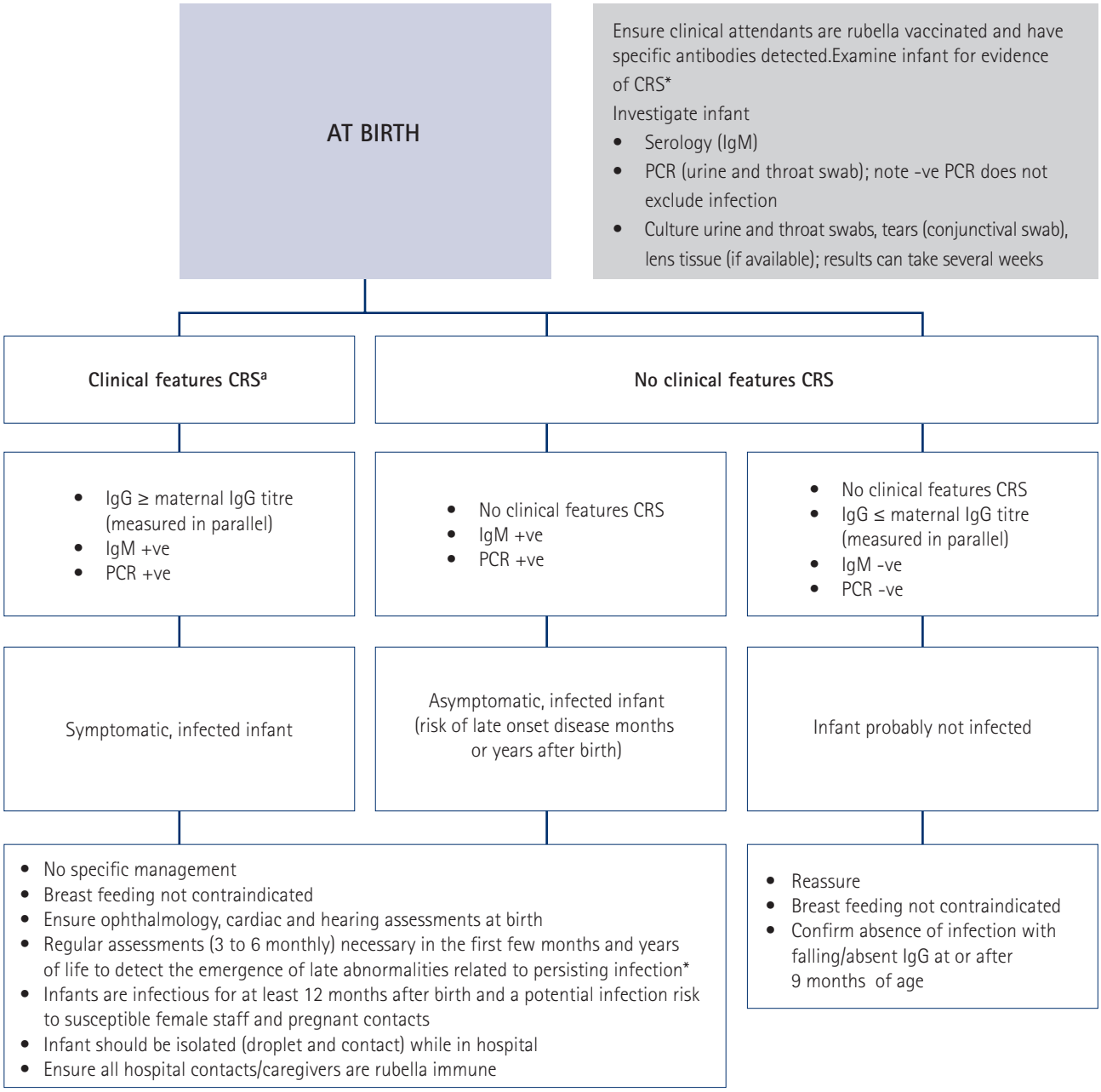
- CVS is associated with risk of contamination with maternal tissue giving false +ve PCR.
- PCR is not widely available and sensitivity is generally not well validated. However, a positive result will be helpful[13] (assuming that contamination can be excluded).[12]
- False negative fetal IgM is common until late in pregnancy. 11,14

COMMENTS

a. No specific management of mother (rubella specific immunoglobulin is not effective as post-exposure prophylaxis and normal human immunoglobulin not indicated).
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.

RUBELLA – ALGORITHM 3

MANAGEMENT AND FOLLOW UP OF THE INFANT AT RISK OF INFECTION



COMMENTS

a. **Features of CRS[15, 16]**

At birth or early manifestations

- Deafness (sensory neural hearing loss, 60–75%), central nervous system dysfunction (10–25%, mental retardation, developmental delay, microcephaly), cardiovascular defects (10–20%, patent ductus, pulmonary artery stenosis, pulmonary stenosis), ophthalmological abnormalities (10–25%, cataracts, micropthalmos, retinopathy, glaucoma, strabismus, cloudy cornea), Others: growth retardation, haematological abnormalities, GI tract abnormalities, pneumonitis & osteitis.

Late manifestations

- Deafness (sensory neural 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

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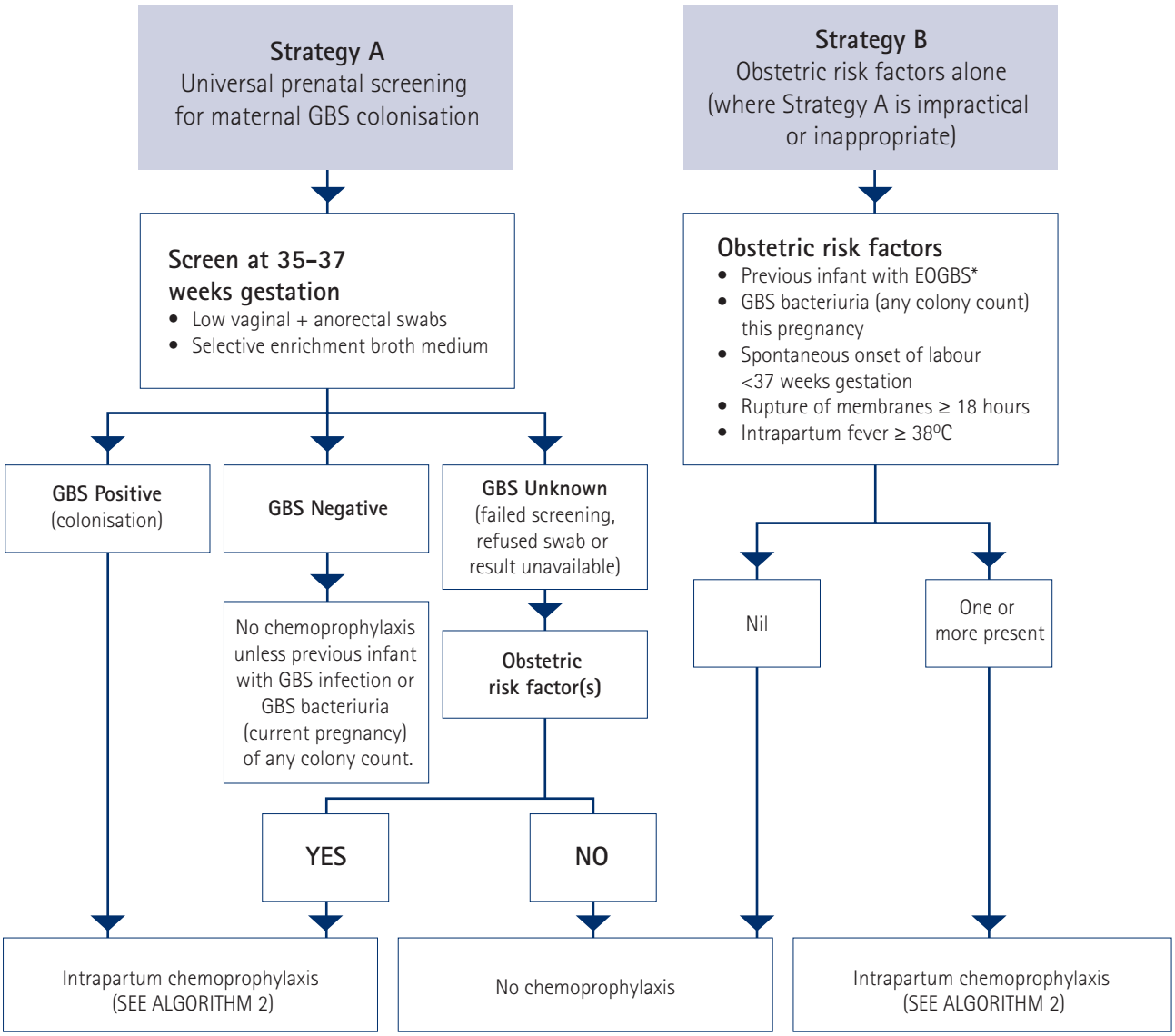
Streptococcus, group B

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2014

STREPTOCOCCUS, GROUP B – ALGORITHM 1

MANAGEMENT OF PREGNANCY WITH RESPECT TO GROUP B STREPTOCOCCAL (GBS) INFECTION

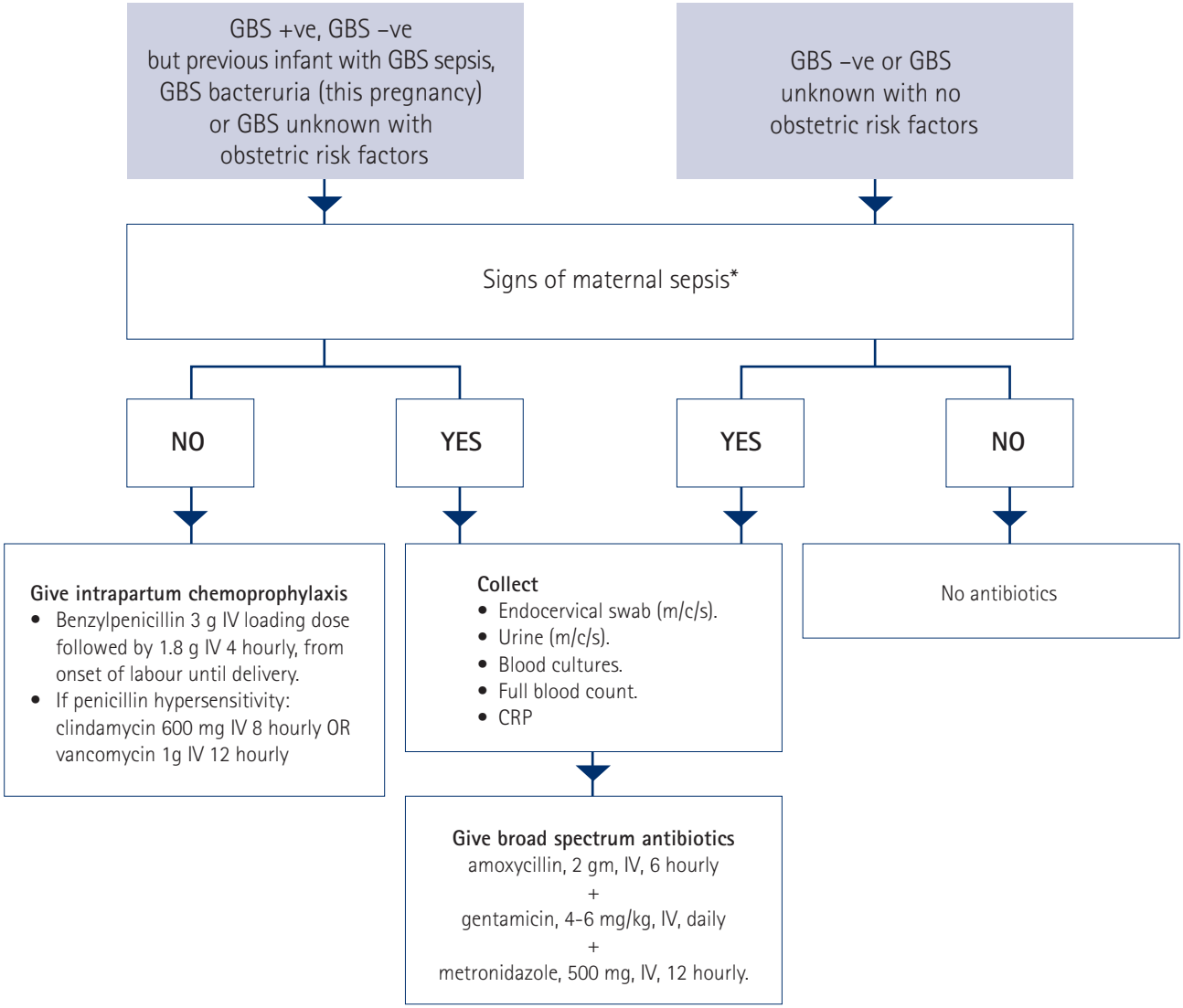


COMMENTS

- 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]
- Intrapartum chemoprophylaxis is highly effective in reducing neonatal colonisation with GBS and preventing EOGBS.[3, 4]
- In a large retrospective cohort study, a stronger protective effect (more cases of EOGBS prevented) was seen for microbiological screening for GBS colonisation (culture based), as compared to the obstetric risk based prevention strategy (RR 0.46; 95% CI 0.36-0.6).[5] A recent Australian study supports this.[1]
- In New Zealand, the obstetric risk-based strategy is generally recommended.
- 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).[1,5,6]
- 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.[7]
- Intrapartum antibiotic prophylaxis is associated with both delayed and milder presentation of late onset GBS disease.[7]
- Selective enrichment broth is more sensitive than standard solid media. Examples include Todd-Hewitt broth supplemented with either gentamicin and nalidixic acid or with colistin and nalidixic acid.[4]
- Chromogenic agars can facilitate detection of beta-haemolytic GBS, but the majority will not detect nonhaemolytic strains.
- 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.

STREPTOCOCCUS, GROUP B – ALGORITHM 2

INTRAPARTUM ANTIBIOTIC PROPHYLAXIS FOR PREVENTION OF EARLY ONSET NEONATAL GBS SEPSIS



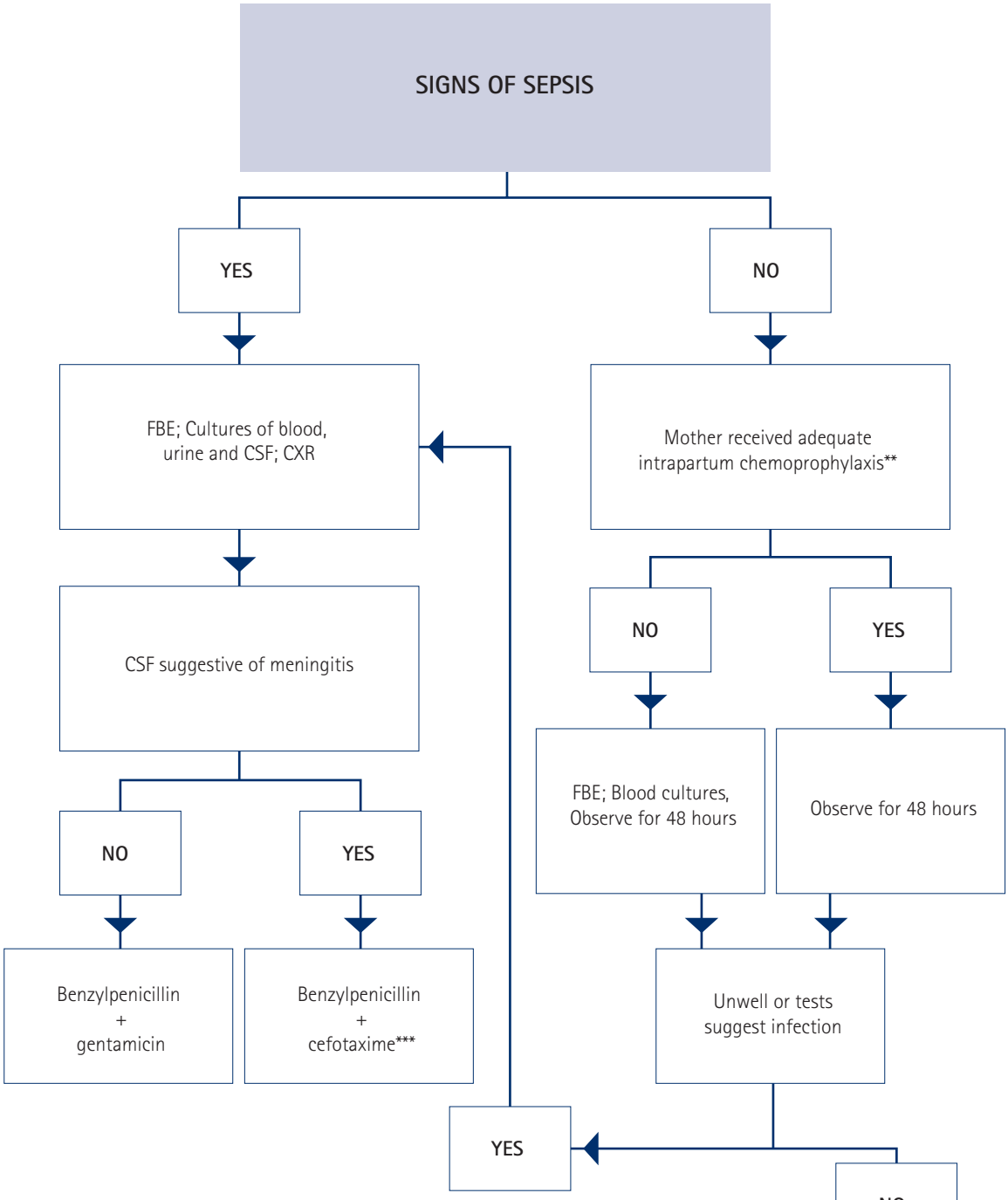
COMMENTS

- 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, 7]
- 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 a cephalosporin should receive cephazolin 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).

STREPTOCOCCUS, GROUP B – ALGORITHM 3

MANAGEMENT OF INFANT AT RISK OF GBS SEPSIS*



* 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]

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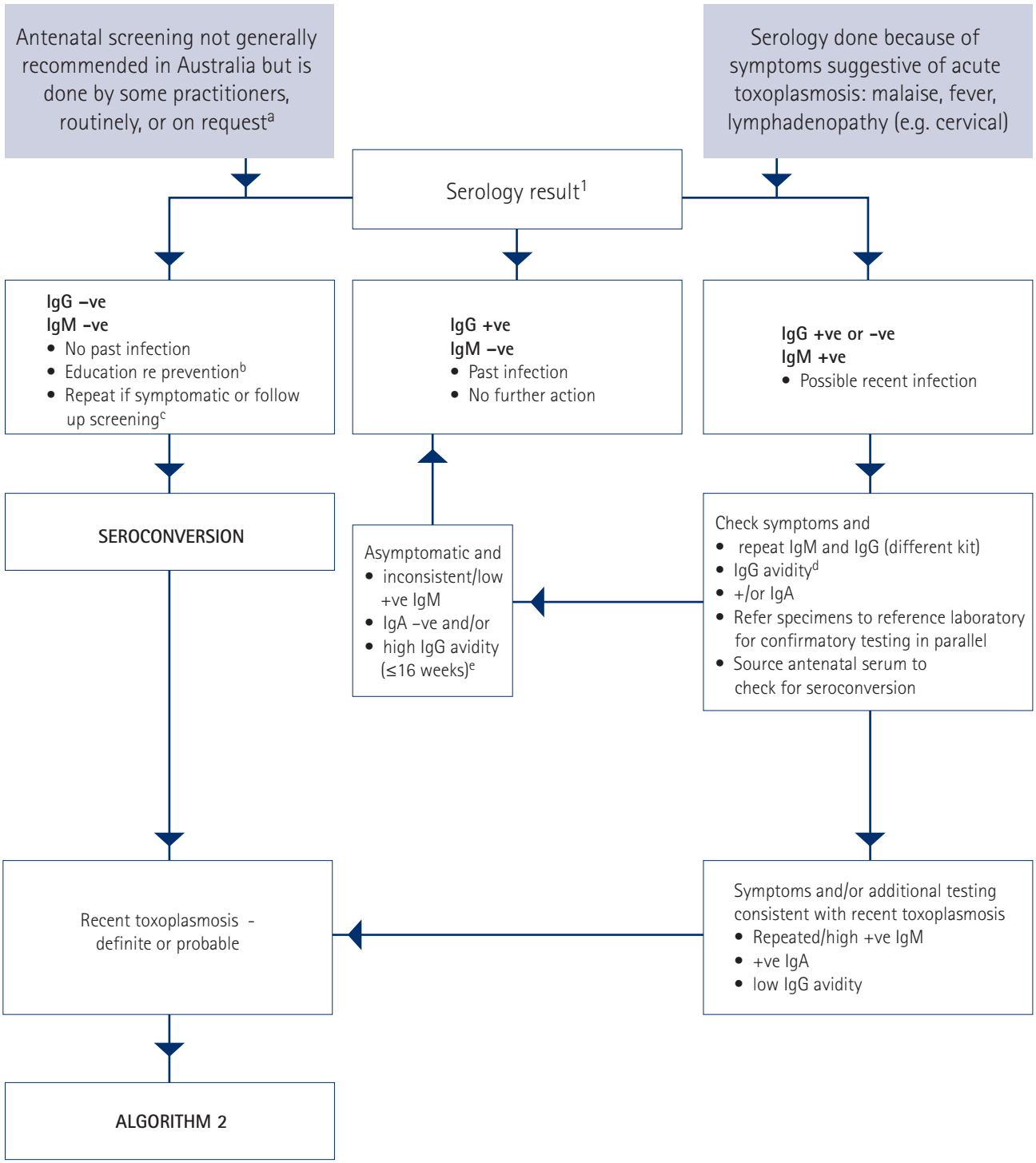
Toxoplasma gondii

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2014

TOXOPLASMA GONDII (T. GONDII) – ALGORITHM 1

ANTENATAL EVALUATION

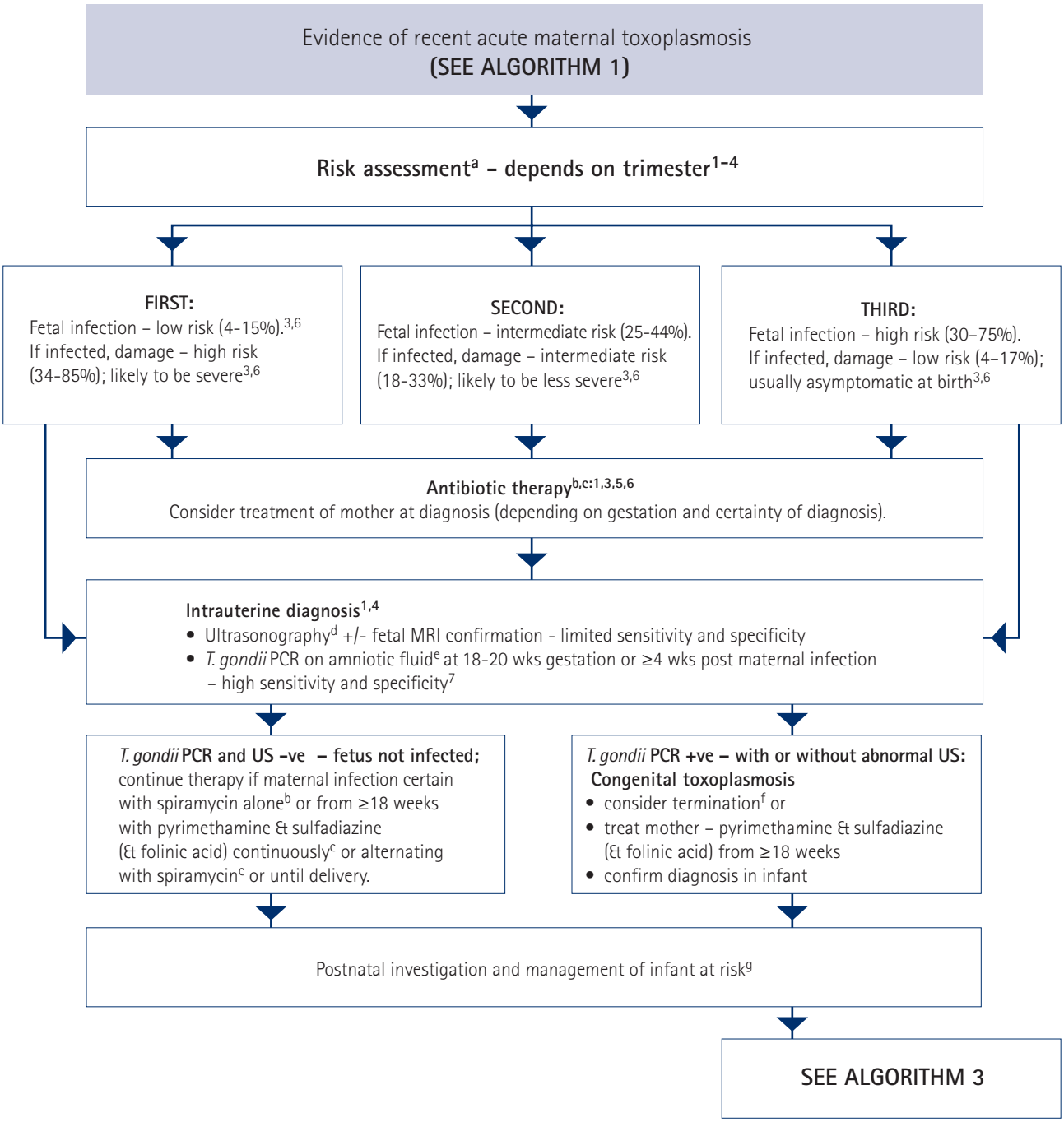


COMMENTS

a. Pros & cons of antenatal screening 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; IgA, 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 (T. GONDII) – ALGORITHM 2

INVESTIGATION AND MANAGEMENT OF MATERNAL TOXOPLASMOSIS

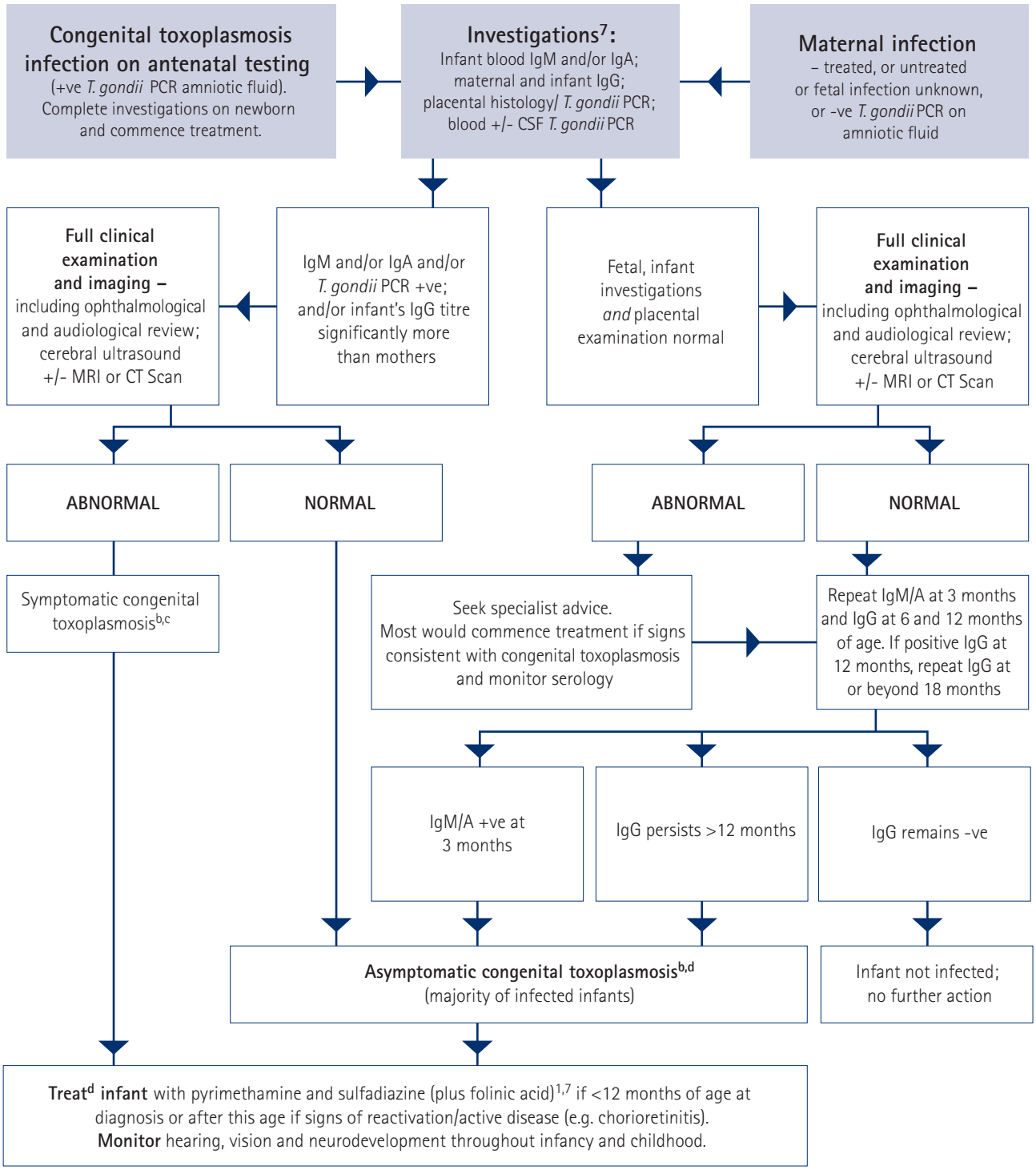


COMMENTS

a. Estimated risks also vary according to the methods of diagnosis, duration of follow-up and treatment.
b. ≤ 18 weeks: Consider spiramycin[c] to prevent vertical transmission until intrauterine diagnosis. Spiramycin not routinely available in Australia, but can be imported on request. Does not readily cross placenta and therefore does not treat infected fetus. Efficacy not been confirmed in randomised controlled trials. Some experts continue drug +/- other drugs until term if *T.gondii* PCR negative on aminiotic fluid.[1,4-6,7]
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 not confirmed in randomised controlled trials[1,4-6,7] Pyrimethamine and sulphadiazine: potentially toxic in first trimester.
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[1,4,8]: 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 (T. 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)
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 h for 2 days followed by 1 mg/kg per day for 6 months followed by the same dose, three-times a week to complete 12 months; sulfadiazine: 50 mg/kg every 12 h; 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]

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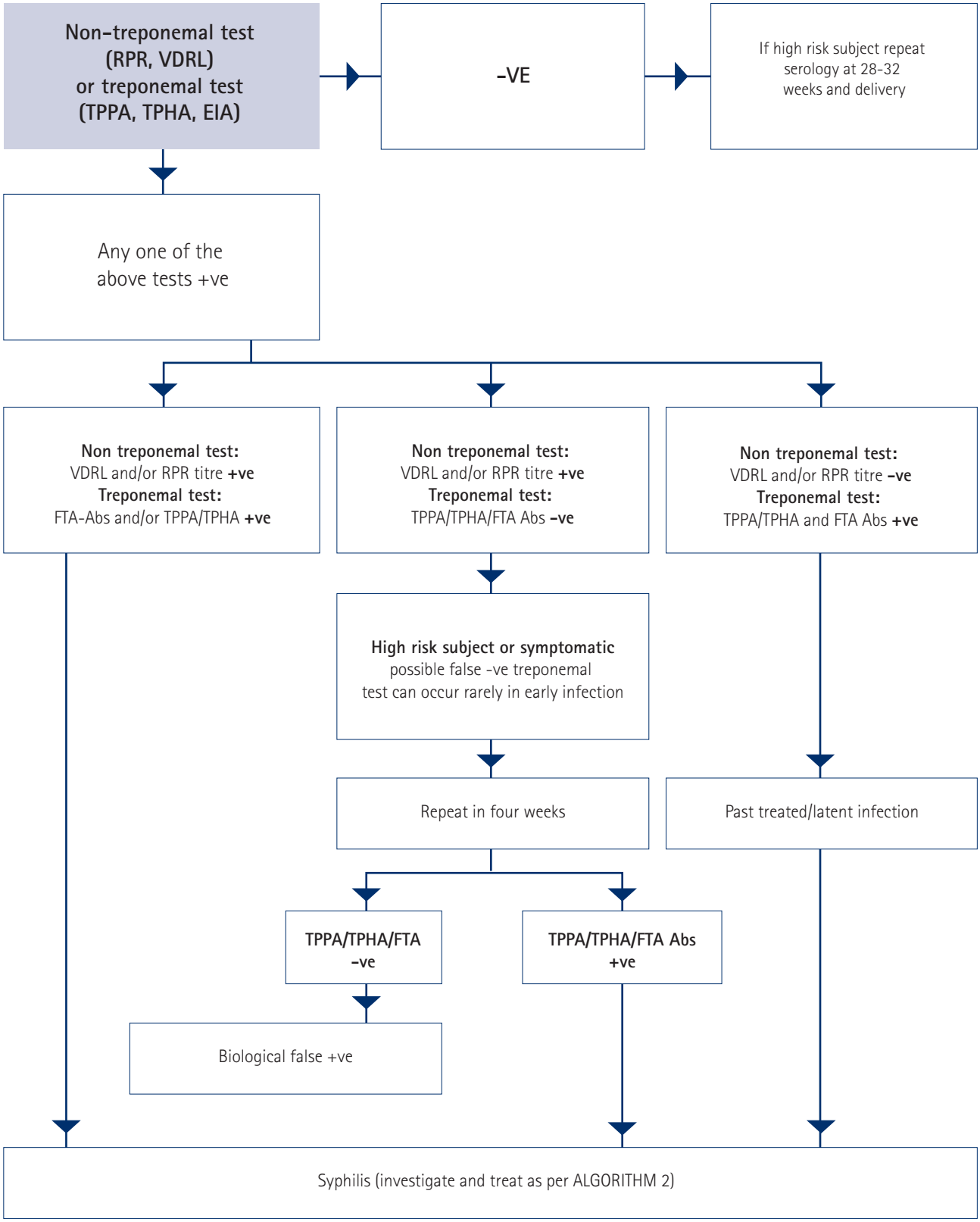
Treponema pallidum (Syphilis)

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2014

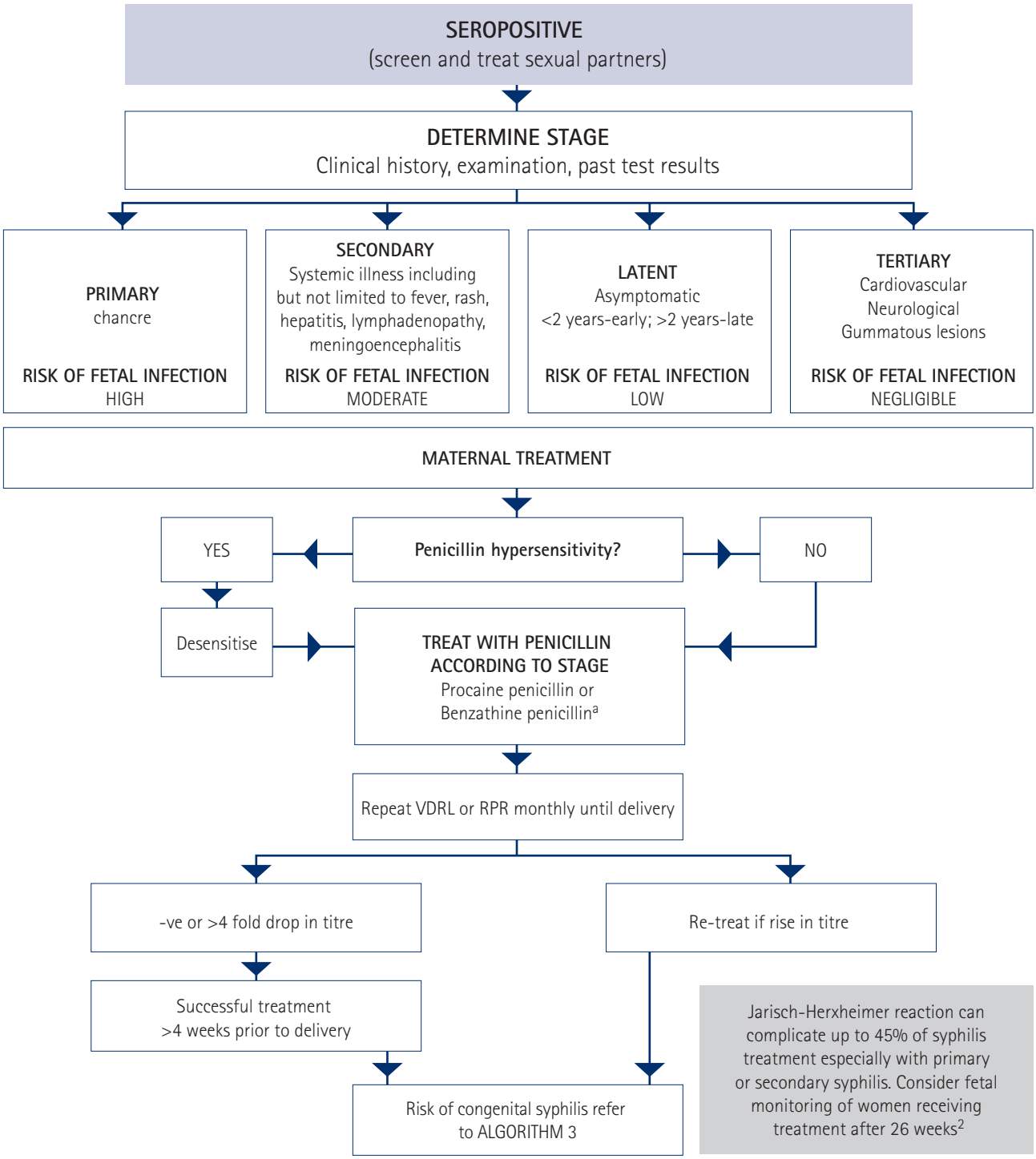
TREPONEMA PALLIDUM (SYPHILIS) – ALGORITHM 1

ANTENATAL SCREENING FOR SYPHILIS



TREPONEMA PALLIDUM (SYPHILIS) – ALGORITHM 2

INVESTIGATION AND TREATMENT OF MATERNAL SYPHILIS



COMMENTS

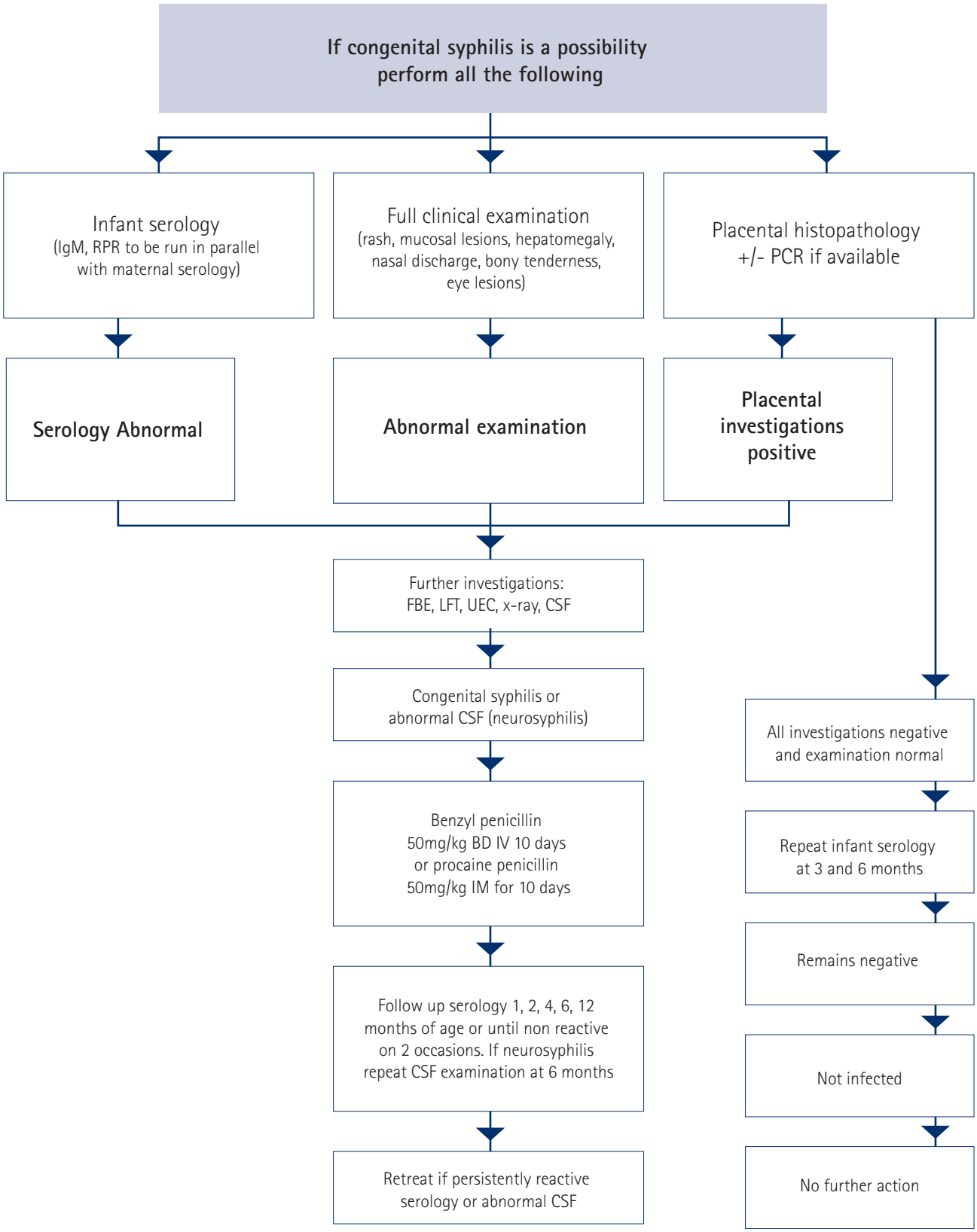
a. Early syphilis (primary, secondary or early latent syphilis) treatment:
- Benzathine penicillin 1.8g (= 2.4 million units) IM, as a single dose OR
- Procaine penicillin 1.5g IM, daily for 10 days

Late syphilis (>2 years or unknown duration) treatment:
- Benzathine penicillin 1.8g (= 2.4 million units) IM, once weekly for 3 weeks OR
- Procaine penicillin 1.5g 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 pencillin 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 penicillin with other antibiotics in the setting of pregnancy[1].

TREPONEMA PALLIDUM (SYPHILIS) – ALGORITHM 3

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



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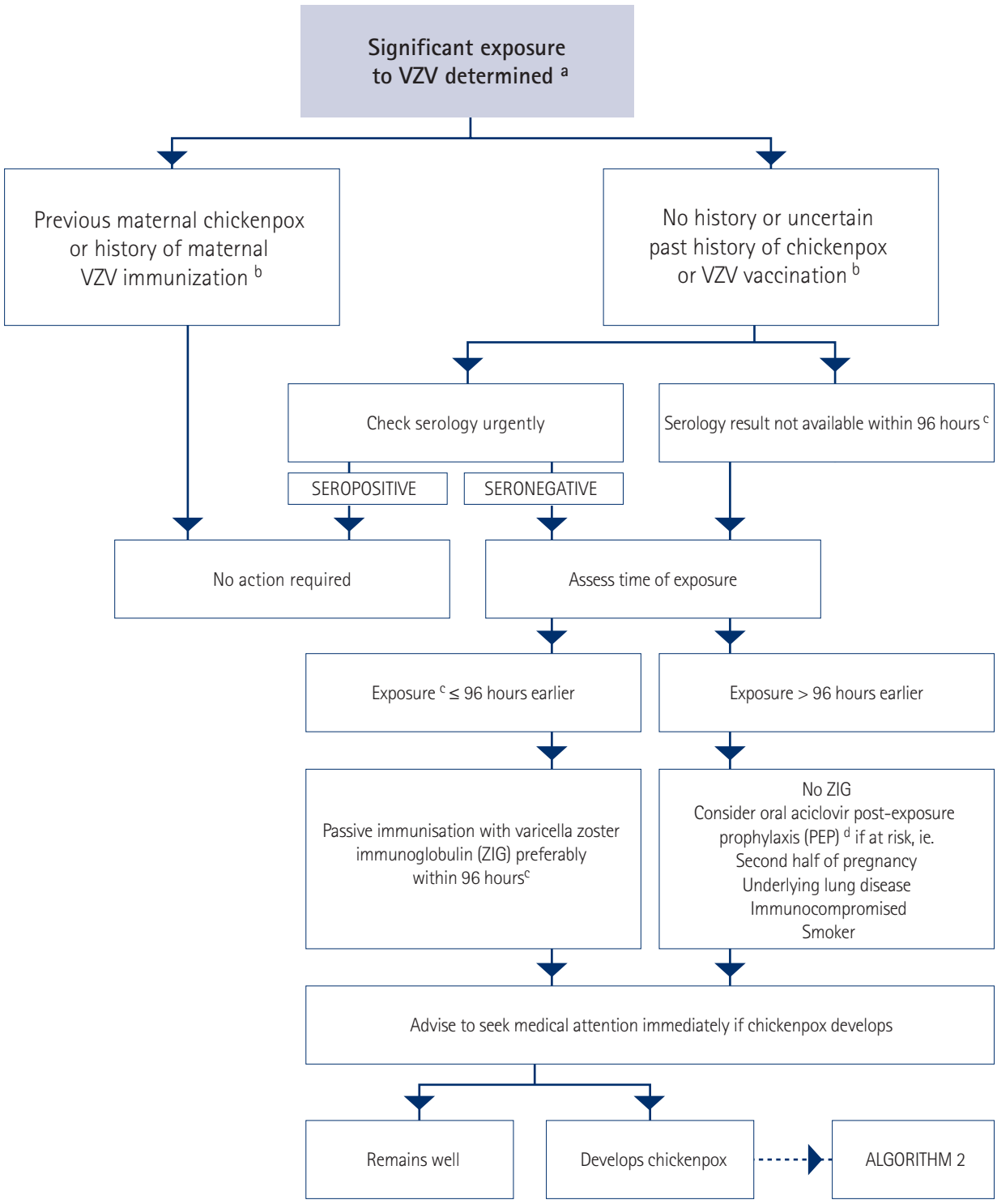
Varicella zoster virus

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2014

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 lesion crusted.

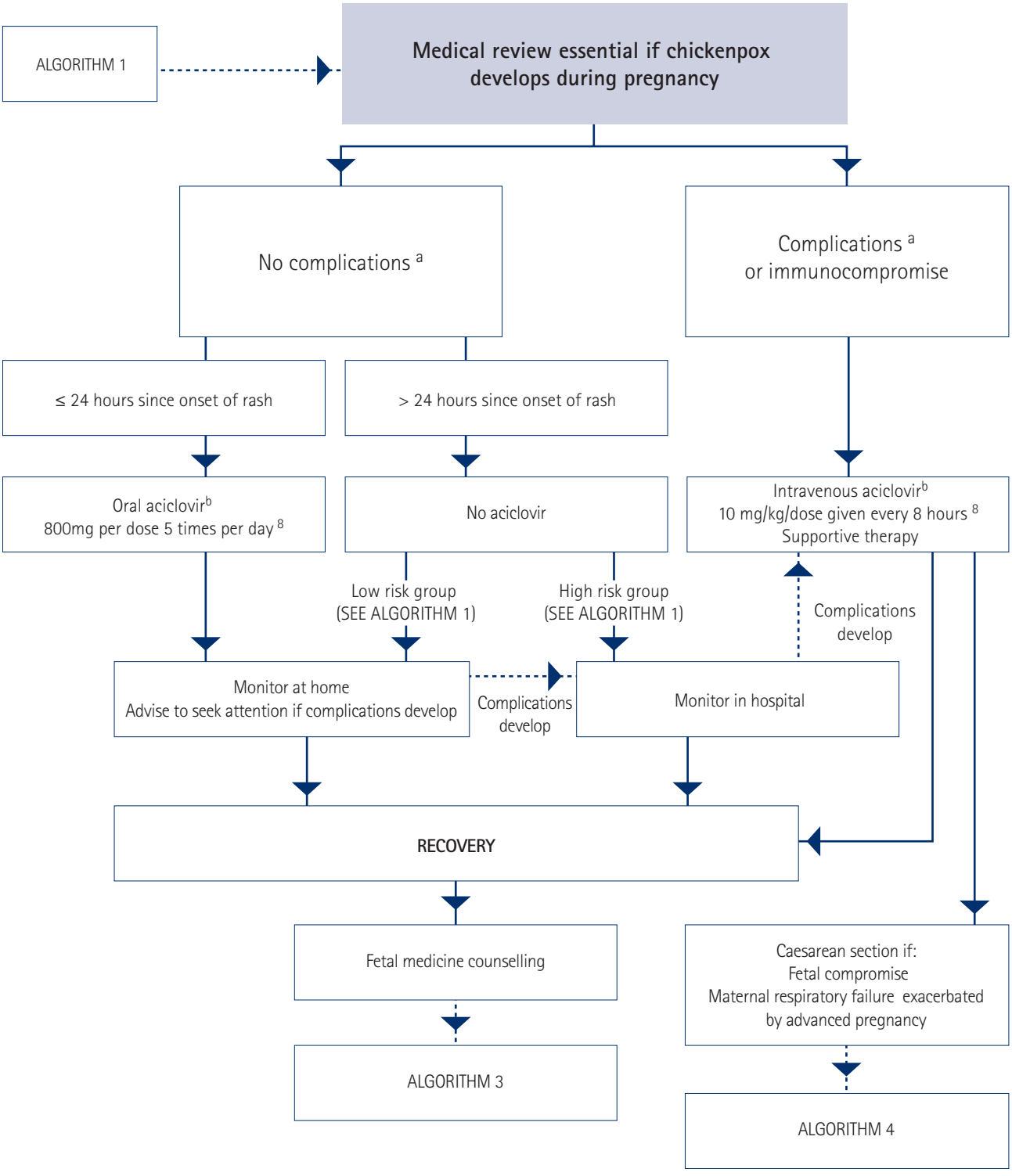
b. VZV vaccine not recommended during pregnancy. However, inadvertent administration of VZV vaccine to pregnant women has not been shown to be associated with congenital varicella. [3]

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 (SEE ALGORITHM 2). [1,4]

d. Efficacy of aciclovir PEP in pregnancy not tested in controlled trials. 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



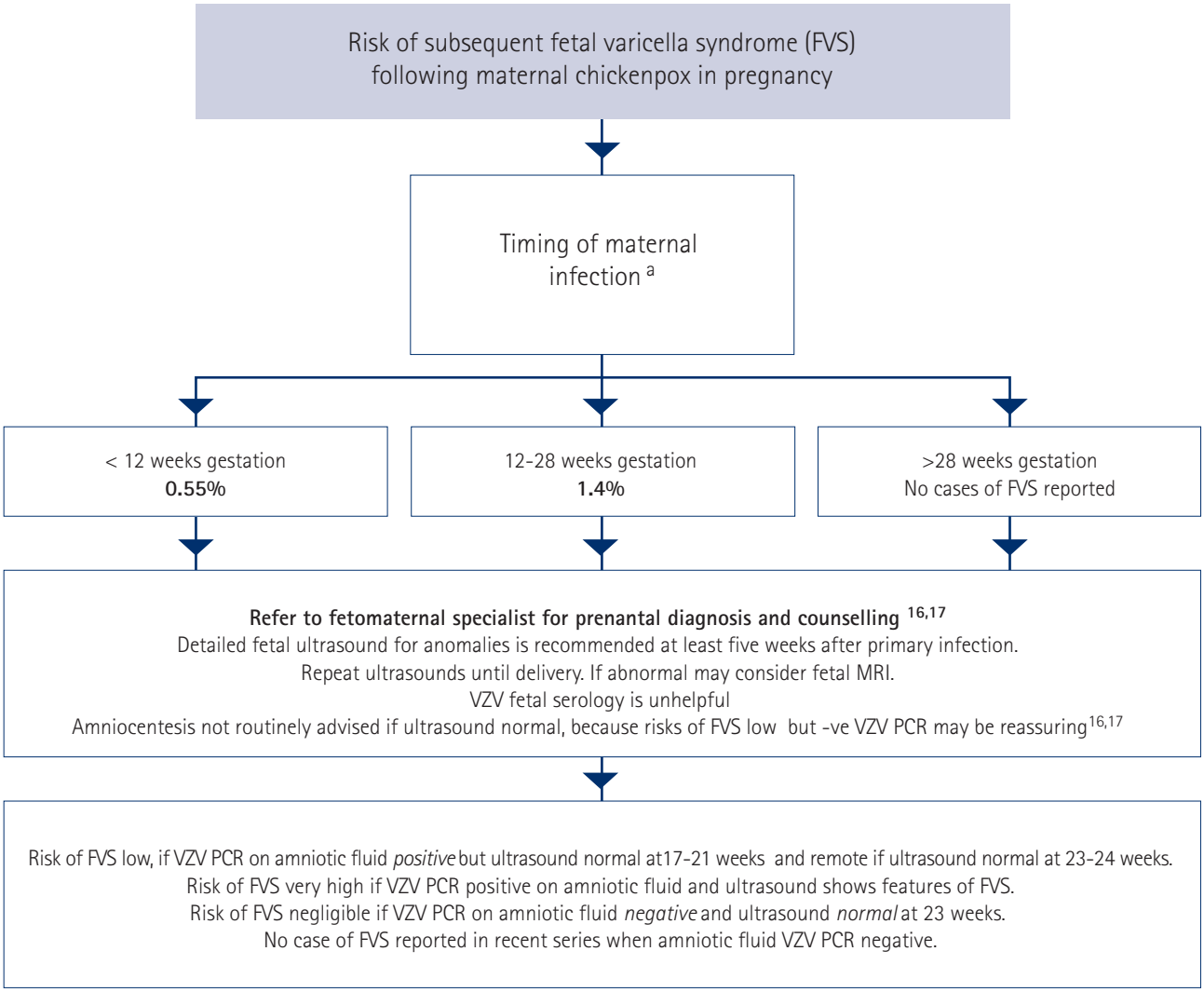
COMMENTS

a. Complications [4]:
- Respiratory symptoms
- Haemorrhagic rash or bleeding
- New pocks 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 pro-drug valaciclovir safe. Insufficient data to support use of famciclovir in pregnancy.

VARICELLA ZOSTER VIRUS – ALGORITHM 3

FETAL MEDICINE COUNSELLING FOLLOWING CHICKENPOX IN PREGNANCY



Varicella Syndrome manifestations

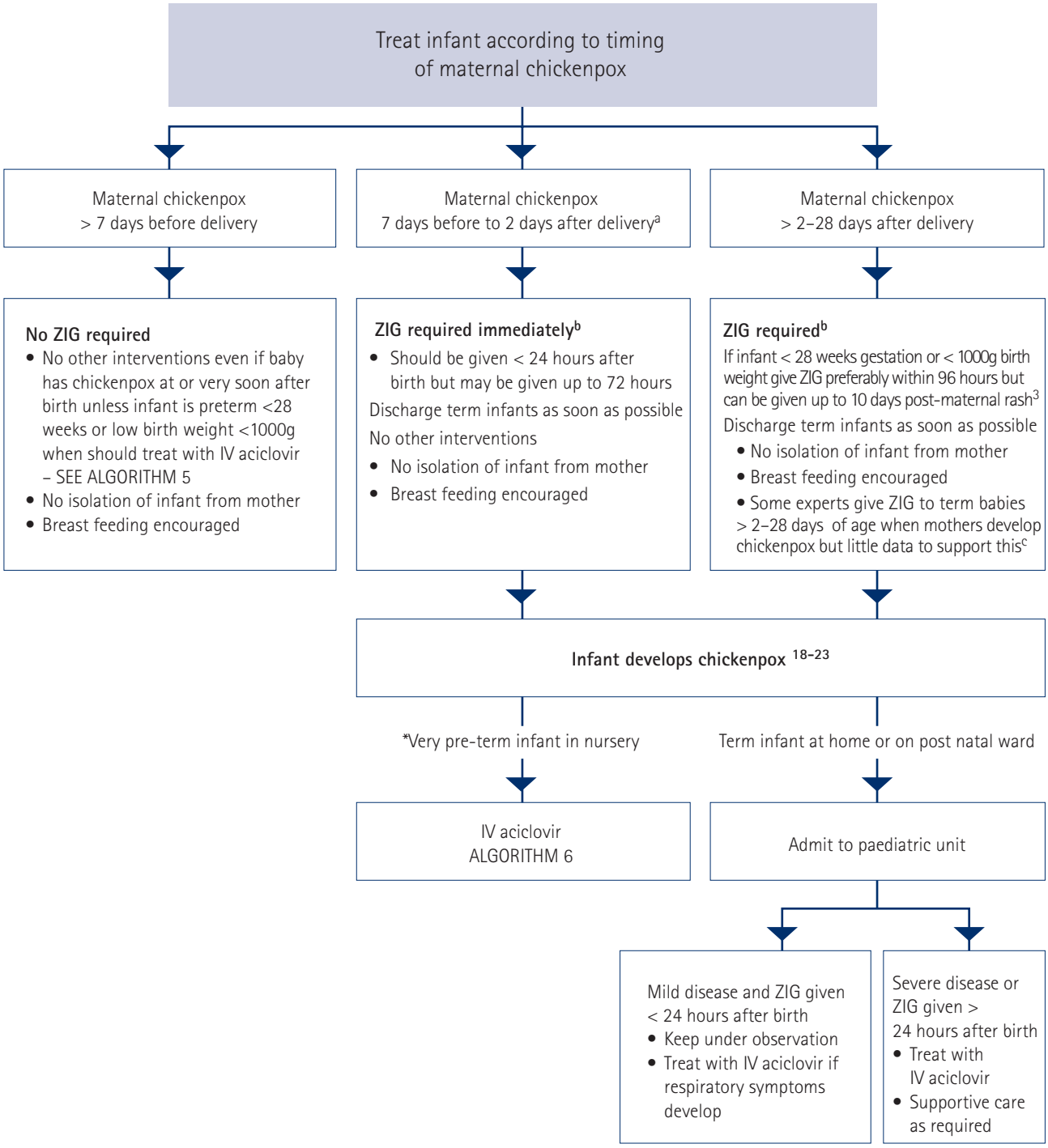
Abnormalities	Frequency
Skin scars	78%
Eye abnormalities	60%
Limb abnormalities	68%
Prematurity, low birth weight	50%
Cortical atrophy, mental retardation	46%
Poor sphincter control	32%
Early death	29%

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

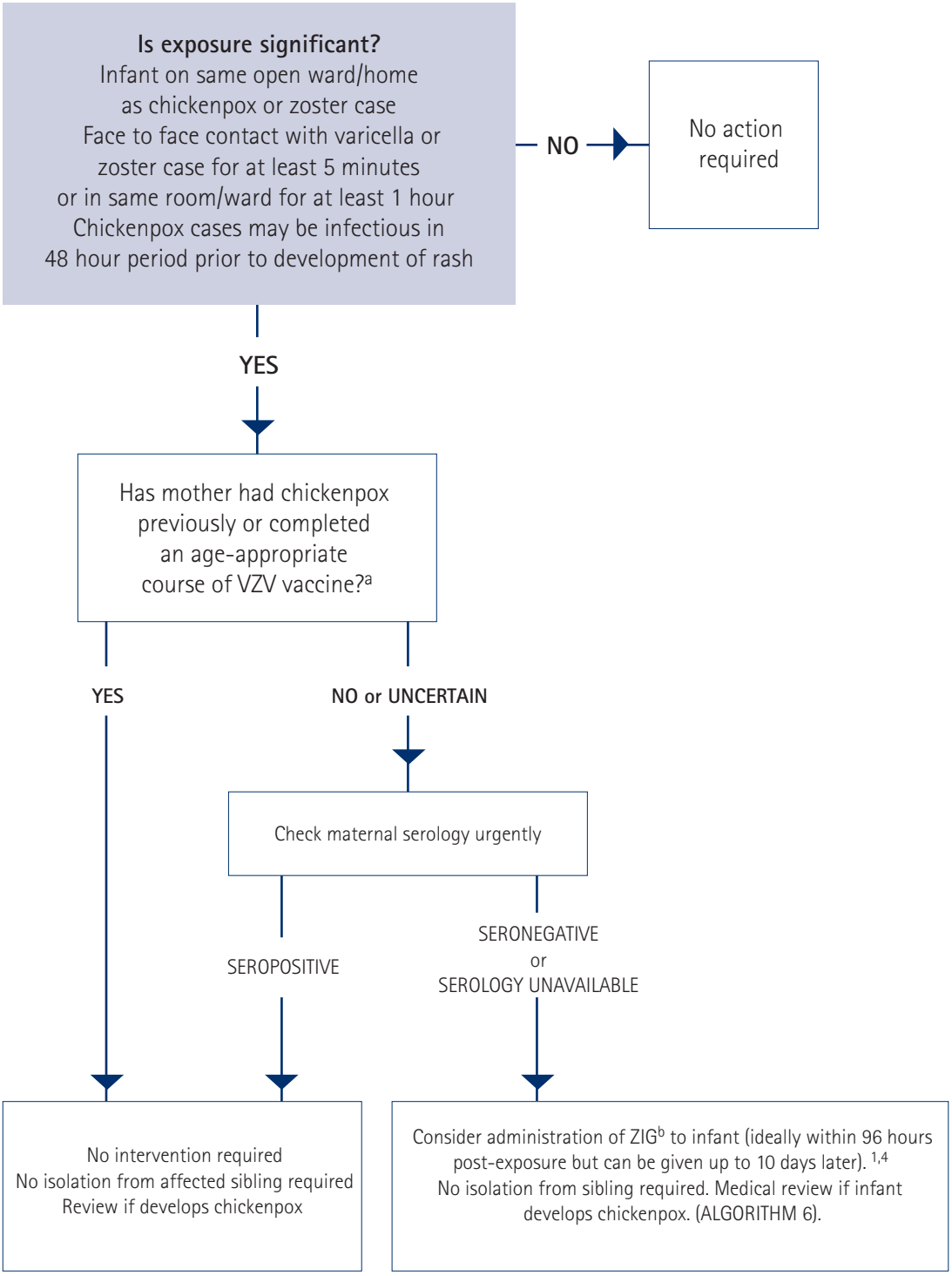


COMMENTS

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 Ab /2 ml. Recommended dose: 2 ml (200 units) for 0-10 kg, 4 ml for 11-30 kg and 6 ml .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



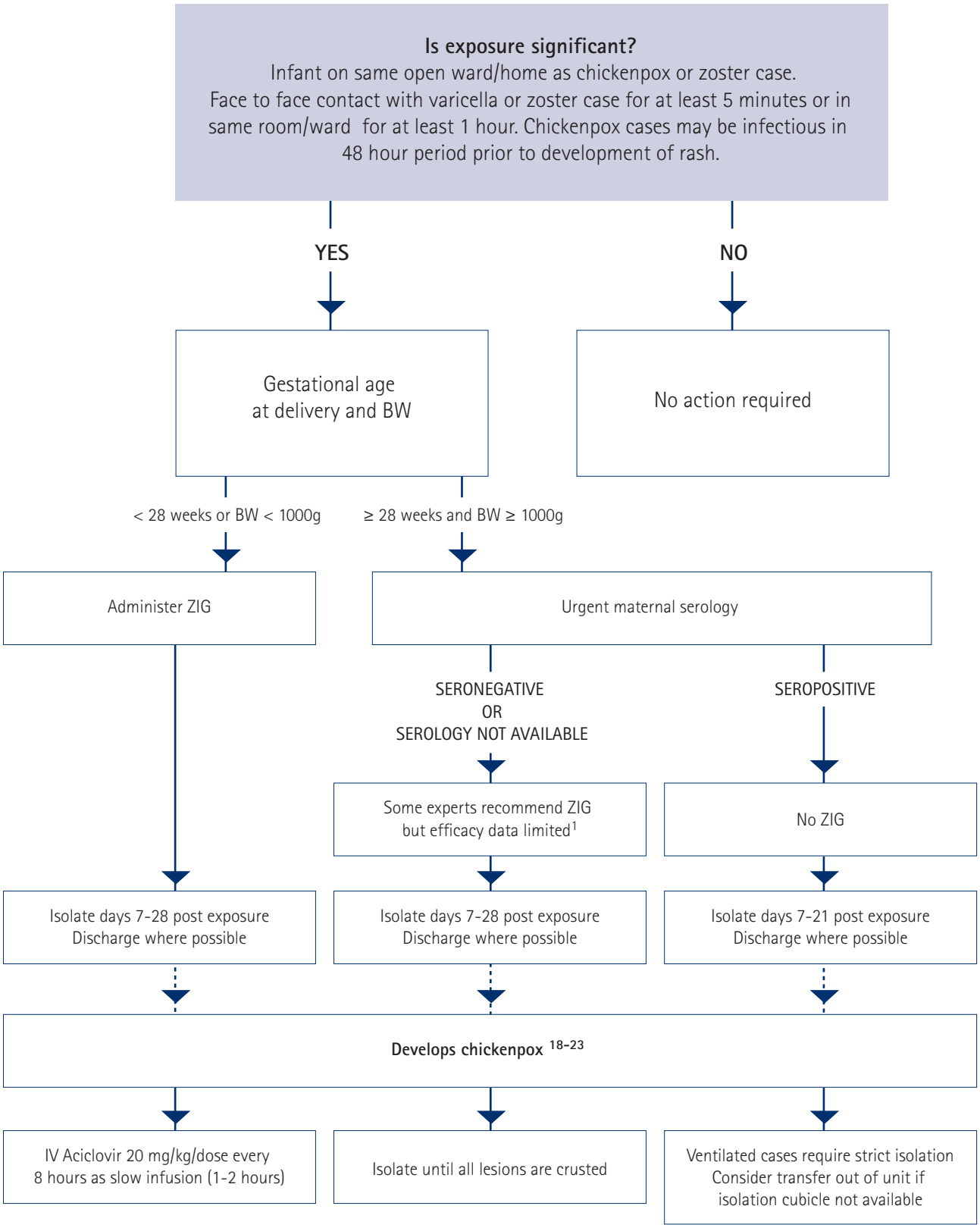
COMMENTS

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



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Management of Perinatal Infections