Management of Perinatal Infections

Cytomegalovirus
Enterovirus
Hepatitis B
Hepatitis C
Herpes Simplex Virus
Human Immunodeficiency Virus
Listeria
Mycobacterium Tuberculosis
Parvovirus
Rubella
Streptococcus - Group B
Toxoplasma
Treponema Pallidum (Syphilis)
Varicella Zoster Virus

Edited by Dr Pamela Palasanthiran, Dr Mike Starr, and Dr Cheryl Jones

Introduction by Prof Lyn Gilbert

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2002

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Some updates and/or emendations have been included for selected algorithms under the heading "Emendations". The comments are not comprehensive and are meant as added information pending a new edition of this publication.
The Editors

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FOREWORD

This comprehensive set of contemporary algorithms on the management of perinatal infections has been written by a team of Australian and New Zealand paediatric infectious disease experts who are all members of the Australasian Society of Infectious Diseases (ASID).

The impetus behind this project was the recognition that simple guidelines are needed for general practitioners, obstetricians and paediatricians to address common issues once an infectious agent complicates a pregnancy. Questions such as 'Do I really have this infection?' 'Can it be treated during my pregnancy?' 'Will I pass it on to my baby?' and 'What will happen if I do?' frequently arise. Thus, the algorithms follow 4 themes (where possible): antenatal diagnosis of the infectious agent, antenatal management, perinatal transmission risks, intervention strategies if available, and management of the newborn. It is stressed that these algorithms are evidence-based where possible but in many cases, represent consensus recommendations and are intended only as a set of guidelines.

We acknowledge the contributions of Drs. Sonia Grover and Ted Weaver who reviewed the final versions of these algorithms and provided invaluable feedback on behalf of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) and members of ASID who provided comments and feedback on early drafts. We also wish to thank ASID and in particular the ASID council for funding for this project.

Above all, we acknowledge the authors for the invaluable time they have contributed to this project, on top of their primary work commitments. We also thank Professor Lyn Gilbert for her encouragement and unfailing guidance. Their combined support has been a significant force behind this achievement

We hope these algorithms will be as useful to you as they have been for us.

Pamela Palasanthiran
Mike Starr
Cheryl Jones
March 2002

INTRODUCTION

An infection during pregnancy that could damage the fetus or infant is much less common than suspicion or fear of infection. Vague, nonspecific symptoms – malaise, aches and pains, headache, tiredness, nausea – are the hallmarks of many vertically transmissible maternal infections but they are also common during pregnancy or in any busy, stressful life. In pregnant women they can't be dismissed as trivial as they may be in others. Laboratory tests may provide the answer but can be hard to interpret. On the other hand, vertically transmissible infections are often asymptomatic. Routine antenatal screening is recommended for some on the basis of criteria including:

- Incidence of maternal infection, transmission to the fetus and damage if infection occurs.
- Availability of a reliable screening test
- Availability of a safe effective intervention to prevent fetal/infant infection and reduce damage.

Sometimes asymptomatic women are screened for infections other than those recommended. An unexpectedly positive result then creates a problem that must be managed. It can be difficult to determine the predictive value of a positive test, in the absence of symptoms. The result may not indicate current or recent infection, but this may become apparent only after additional serological testing and/or examination of amniotic fluid. Meanwhile, it will have caused anxiety to the patient and her family. Her medical adviser will be worried, not only for the wellbeing of the patient and her fetus, but also about the potential for litigation if things go wrong. If the results remain uncertain – as they often do – the patient may choose to terminate her pregnancy because she cannot tolerate even a small risk of having an abnormal infant. On the other hand, even an inappropriate screening test will sometimes detect a significant infection and the potential to intervene and prevent an unfortunate outcome.

Negotiating this minefield of psychological, medicolegal, ethical and medical dilemmas is difficult enough for the specialist with a particular interest in infections in pregnancy. But for the average GP or obstetrician, for whom they are rare complications, it can be nerve-wracking. These algorithms outline recommended antenatal screening tests, how to manage symptomatic infection or a positive screening test and the range of tests available to assist in risk assessment.

There are a few common themes:

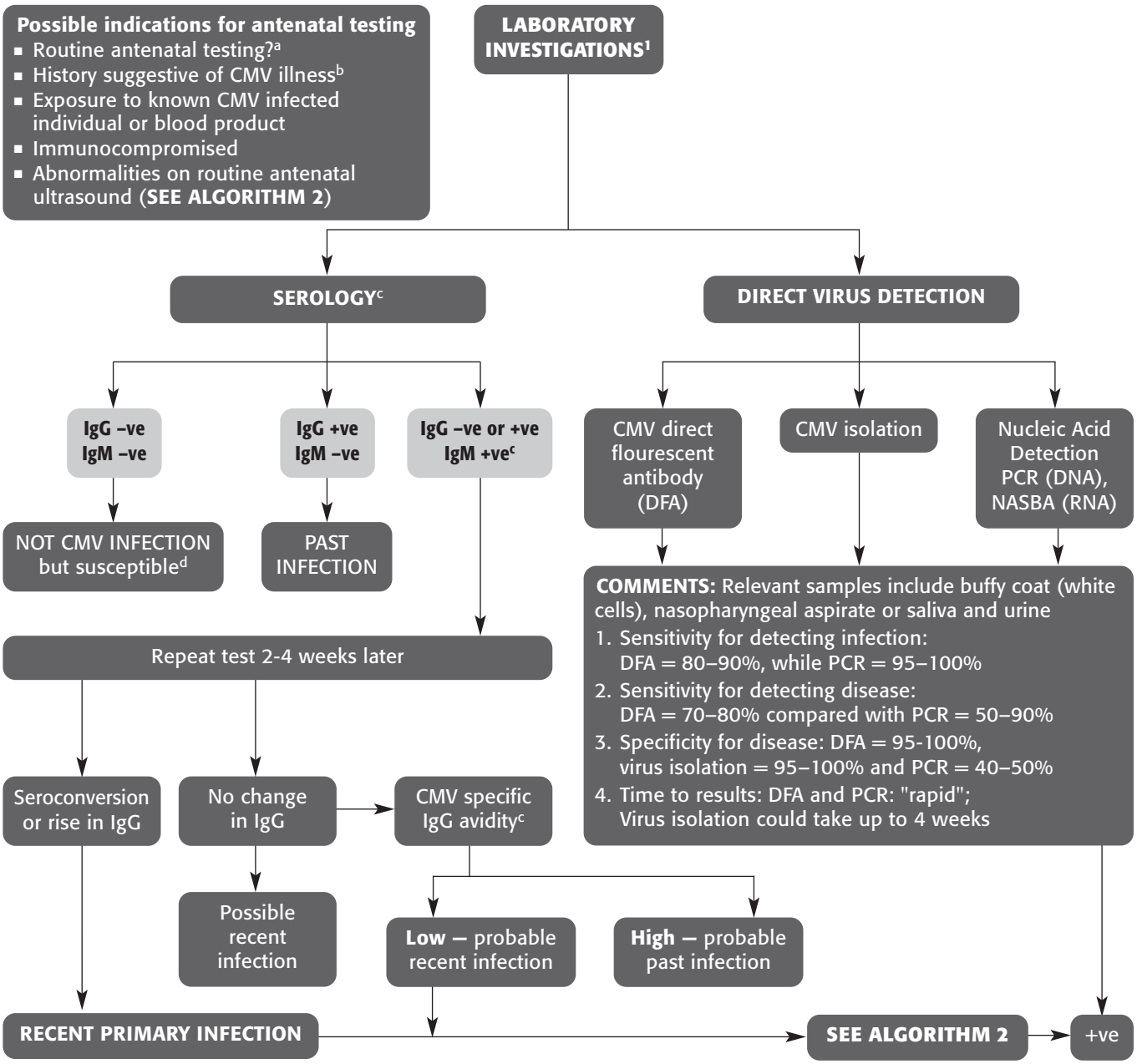
- Significant decisions about management of a suspected infection during pregnancy should never be based on the result of single test. The test should always be repeated, preferably by a different method and on another specimen of serum. False positive IgM results are not uncommon and, even in the best laboratories, sera occasionally get mixed up.
- Laboratories are advised to keep serum, sent for routine antenatal screening, for at least 12 months. If the possibility of infection arises later it can be retrieved and tested in parallel with a later specimen, to show or exclude seroconversion, which is much better evidence of recent infection than IgM.
- If only a single serum is available or the results do not change in serial samples, measuring IgG avidity (a measure of maturity of the IgG response, which develops over a period of several months) can help. A high avidity can exclude recent infection, even in the presence of persisting IgM. The reverse is not necessarily true - low avidity does not always imply recent infection.

This publication represents a consensus among specialists in perinatal infection. Its completion is a major achievement for the editors, Pamela Palasanthiran, Mike Starr and Cheryl Jones. It has been endorsed by the Australasian Society for Infectious Diseases and the Royal College of Obstetricians and Gynaecologists of Australia and New Zealand. We hope it will not discourage nonspecialists from referring pregnant women with suspected infection during pregnancy, but that it will help to guide the initial assessment and investigation of the patient, and prevent unnecessary anxiety or hasty decisions.

Lyn Gilbert
Centre for Infectious Diseases and Microbiology
Institute of Clinical Pathology and Medical Research
Westmead Hospital
March 2002

ALGORITHM 1

Diagnosis of Suspected Maternal CMV Infection



NOTES

a As CMV is the leading cause of congenital infections (0.3 – 2% of live births), antenatal testing remains a consideration, especially in counselling issues for primary maternal CMV infections. If done, there should be appropriate management plans.
   —All pregnant women should be advised about simple infection control precautions to reduce transmission risk eg handwashing after nappy changes and contact with respiratory tract secretions, especially with children <2 years of age attending day care
   —Some groups identified at higher risk of primary CMV as determined by annual seroconversion rates
      I. Day care workers 11% per annum
      II. Parents with child in day care 20–30% per annum
      In comparison, healthcare workers seroconvert at a rate comparable to the general population ie 2–3% per annum

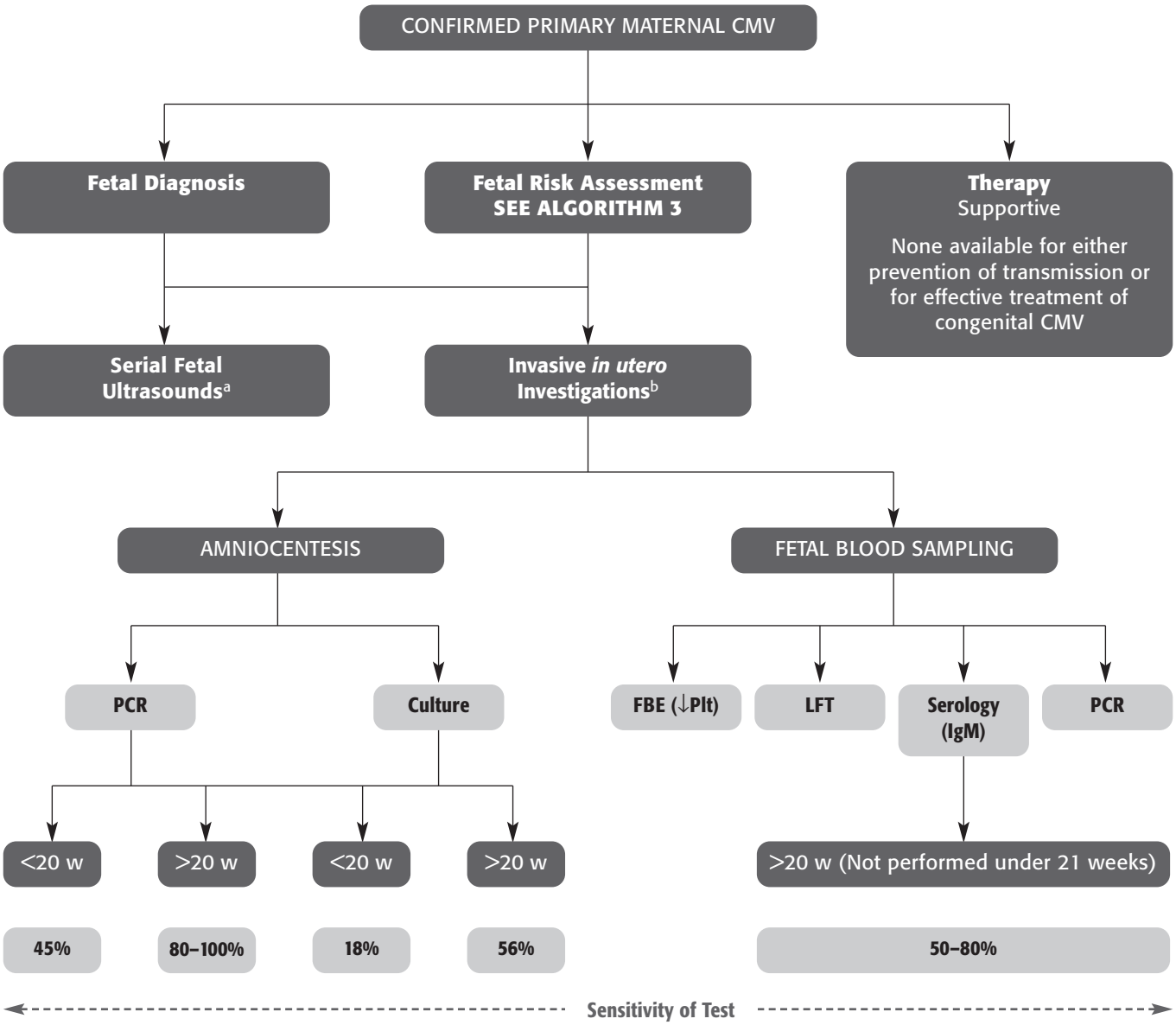
b Most primary CMV infections are asymptomatic. Suspect primary CMV disease in a viral illness associated with atypical lymphocytosis which is "Monospot" negative (also seen in primary toxoplasmosis) or with clinical syndromes associated with CMV disease

c Overall, IgM is ~75% sensitive by ELISA
   —Commercially available assays: IgM results may lack specificity (~75% specificity). More sensitive assays can detect IgM in 5% for up to 2 years
   —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, pregnancy or autoimmune disorders
   —CMV IgG avidity assay is reported to be a reliable indicator of primary infection. Low avidity = probable recent infection, with progression to high avidity with time[2]

d If still concerned or if serology taken within 2 weeks of clinical illness, repeat in 2 weeks

ALGORITHM 2

Management of Primary Maternal CMV Infection



NOTES

a. Features associated with symptomatic congenital CMV infection include:

microcephaly	hydrocephalus (ventricular dilation)
ascites	intrauterine growth retardation (IUGR)
hydrops fetalis	pleural or pericardial effusions
oligo or polyhydramnios	intracranial calcification
hepatomegaly	abdominal calcification
pseudomeconium ileus	

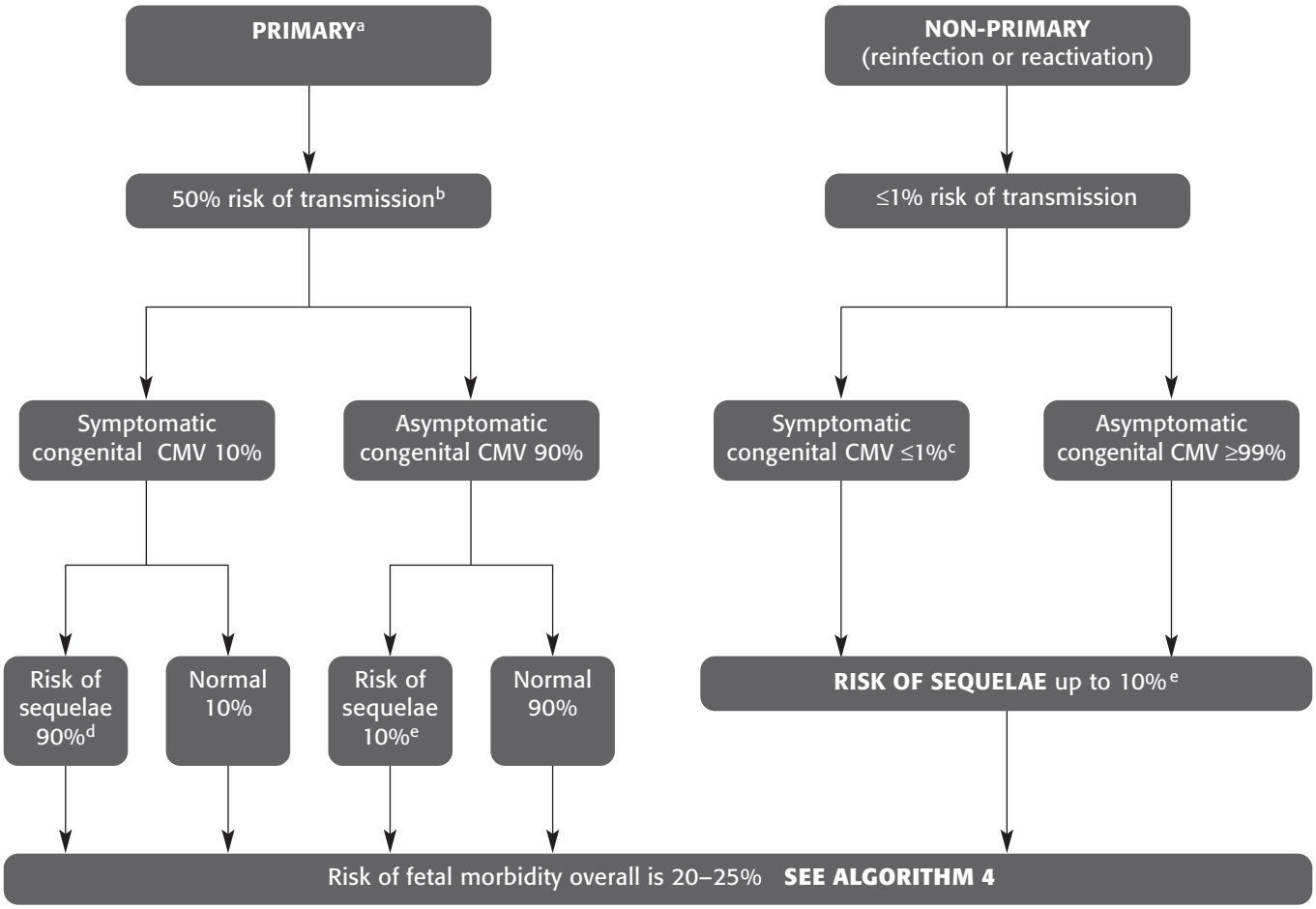
Caution advised in interpretation of findings as presence of signs not always predictive of degree of fetal damage. The sensitivity of fetal ultrasound is hard to evaluate from the literature. Overall, ? 30–50% sensitive.

b. Invasive in utero investigations[3–5]

- Techniques available but all lack sensitivity. Experience with fetal blood sampling is limited.
- Diagnosis is best achieved by a combination of fetal ultrasound + amniocentesis (for PCR) +/- fetal serology
- Diagnosis by amniocentesis testing (PCR & culture) and fetal IgM is about 45% sensitive overall if taken < 20 weeks and 80–100% sensitive if taken > 20 weeks gestation. Specificity approaches 100%
- Sensitivity is increased by waiting ≥ 6 weeks after maternal infection
- Positive results do NOT predict any degree of fetal damage
- Quantitative PCR and/or culture may identify infected fetuses at risk of symptomatic disease (direct relationship between high load and risk)[6]
- Further data required before active recommendation. Positive results: pregnancy — termination is an option by informed choice.

ALGORITHM 3

Congenital CMV: Fetal Risk Assessment



NOTES

a. Australian epidemiology: The incidence of primary CMV infection in pregnancy in Australia is estimated to be 6/1000 pregnancies. The incidence of congenital CMV is estimated to be 0.3 to 0.6%[7]

b. The risk of transmission is distributed equally between the 3 trimesters. However,
   - Risk of severe adverse neurological outcome more likely in 1º infection in first half of pregnancy. Features of fetus affected in early infancy include small for gestational age (SGA), microcephaly and intracranial calcifications
   - A fetus affected late in pregnancy is more likely to have acute visceral disease (hepatitis, pneumonia, purpura and severe thrombocytopenia)

c. Infection of CMV-seropositive women with a different CMV strain can lead to intrauterine transmission and symptomatic congenital infection.[8]

d. Main concerns of symptomatic congenital CMV infection are:
   1. A mortality rate of between 10–30%
   2. Neurological sequelae of microcephaly (35–50%), seizures (10%), chorioretinitis (10–20%), mental retardation (≤70%)
   3. Sensory neural hearing loss (SNHL, 25–50%)[9]

Unilateral	30%)		
Bilateral	70%)	Progressive	57% (over 2 to 6 years?)
Stable	43%)		

e. Main concerns of asymptomatic congenital CMV are
   1. Sensory neural hearing loss (5%)

Unilateral	64%)		
Bilateral	36%)	Progressive	36% (over 2 to 6 years?)
Stable	64%)		

   If hearing is preserved at age 12 months, intellectual development is unlikely to be affected[10]
   2. Chorioretinitis (2%)[11]

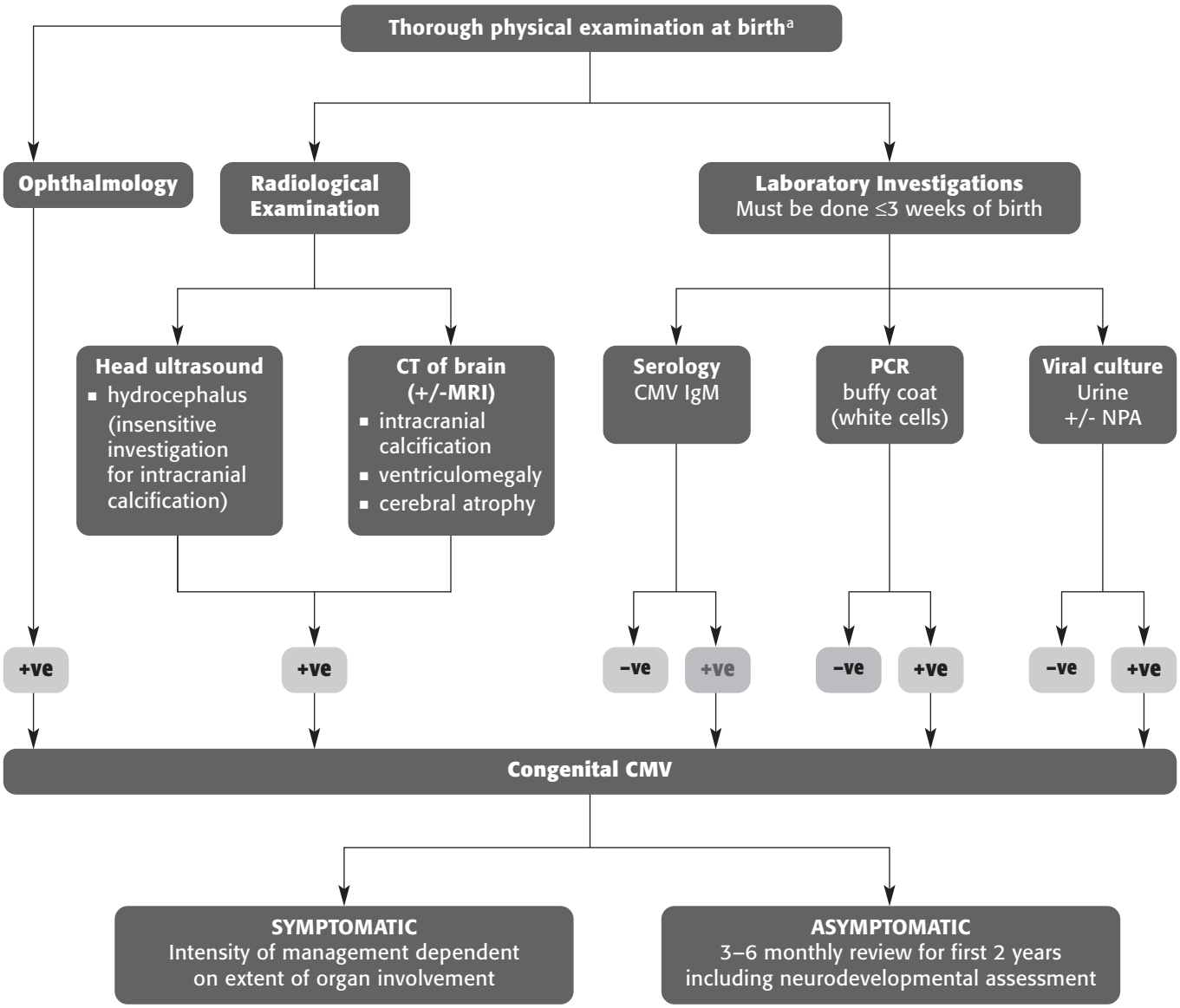
Emendation 2006

Algorithm 3: Congenital CMV: Fetal risk assessment

Prior maternal CMV immunity (i.e. seropositivity) results in an approximate 70% reduction in the risk of congenital CMV infection.[E1] However, it has now been demonstrated that the risk of congenital CMV infection after primary maternal CMV infection remains elevated for up to four years post-seroconversion, with the highest risk being in the first two years post seroconversion. The overall risk is 12.7% post seroconversion, that decreases to the baseline 1% risk by about 4 years post seroconversion.[E2] The time of seroconversion is usually unknown, however, this information may be helpful when counselling a women of a child with congenital CMV infection about the time of a subsequent pregnancy

ALGORITHM 4

Management of the Newborn at Risk of Congenital CMV



NOTES

a. Features of (typical) symptomatic congenital CMV
   1. Neurological: (see text box, Algorithm 3)
   2. Non-neurological: SGA (50%), petechiae/purpura (50–75%), hepatosplenomegaly (40–60%), neonatal jaundice (40–65%), pneumonia (<1%), dental abnormalities (30%), inguinal hernias (males), infant mortality (10–30%).
   3. Laboratory abnormalities: hemolytic anemia (10-50%), platelets ≤ 75,000/mm (50%), direct hyperbilirubinemia ≥ 3 mg/dL (35–70%), AST > 100 IU/L (25–80%), CSF protein >120 mg/dL (45–50%)
   4. Risk of serious bacterial infection (5%)

NOTES

1. Other baseline tests at birth: FBE & differential and LFT
2. Hearing tests: due to improved prognosis for speech development if hearing abnormality detected early, suggest testing before 6 months, then annually for the first 2 years of life, then close review till age 6 years if no problems detected
3. All CMV-infected infants should have fundoscopy for retinal lesions and visual assessment by ophthalmologist at diagnosis. If abnormalities detected, annual review recommended. Otherwise, monitor vision during infancy with formal review if abnormalities detected.
4. Treatment options: nil. Ganciclovir (IV) for retarding the progress of hearing loss in CNS disease associated with congenital CMV has been studied, but follow-up data yet to confirm efficacy[12]
5. Congenitally infected babies are high CMV shedders. Pregnant health care workers should be aware of this and infection control practices e.g., hand-washing emphasised.

Emendation 2006

Algorithm 4: Management of the newborn

A randomised, controlled trial on intravenous ganciclovir therapy (for 6 weeks) in newborns with symptomatic congenital CMV and CNS disease showed normal or improved hearing at 6 months (results did not reach significance) and no hearing deterioration at 1 year (highly significant). However, the high loss to follow-up (~ 60%) makes the clinical significance of the data difficult to interpret and 63% had significant neutropenia. Therefore, the potential side effects and social cost of 6 weeks of intravenous ganciclovir therapy in an individual child must be weighed against a possible, but yet unproven long term gain with this treatment.[E3] There is currently no indication for systemic antiviral therapy for infants without clinical signs of CMV infection at birth (i.e. asymptomatic infection).

ALGORITHM 1

Antenatal Diagnosis of Maternal Enteroviral Infections

If concerns raised about whether pregnant woman has an enteroviral infection, are there features consistent with enterovirus infection?

No

Observe mother and infant after birth

SYMPTOMS OF ENTEROVIRAL DISEASE INCLUDE*:

Asymptomatic
Fever
GIT symptoms eg diarrhoea
Encephalitis
Flaccid paralysis
Herpangina
Hand-foot and mouth syndrome
Lymphonodular pharyngitis
Exanthem
Epidemic conjunctivitis
Myositis
Guillain-Barre syndrome
Mononucleosis-like syndrome
Pleurodynia
Acute haemorrhagic conjunctivitis
Myocardidits

Yes

If there are clinical concerns, the diagnosis can be made via serology, viral culture (nasopharynx or throat swab & faeces) and/or PCR

DIAGNOSIS

Serology – very insensitive, very specific
Viral culture – varying sensitivity and specificity
PCR – variable sensitivity

INTERPRETATION OF RESULTS

Serology:
If the results are positive indicates infection; if the results are negative infection is not excluded due to poor sensitivity.

Viral Culture:
Sensitivity varies depending on the sample. Culture has high specificity but due to prolonged shedding in faeces a viral culture may be a "false positive" and not indicate a current enteroviral infection.

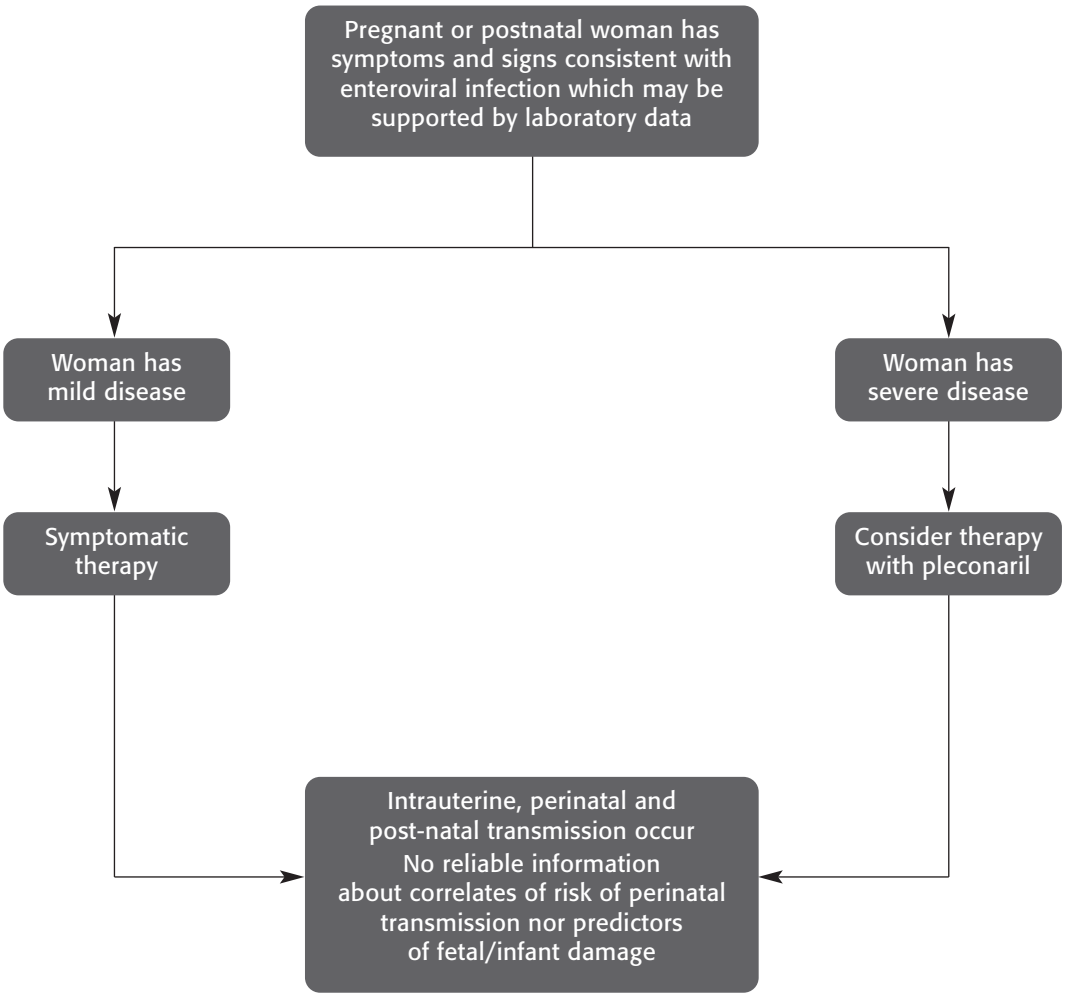
PCR:
Sensitivity and specificity are good.

*** peak incidence in the Spring/Summer months in non-tropical or temperate regions of Australia**

NOTES
Enteroviral infections generally cause insignificant illness, and perinatal transmission of enteroviruses leading to significant symptomatic disease in infants is rare. The literature on this is not comprehensive. Hence, these algorithms are based largely on anecdotal evidence and represent broad guidelines.
To date, there are no data on indicators of perinatal transmission risks nor predictors of fetal or infant damage.

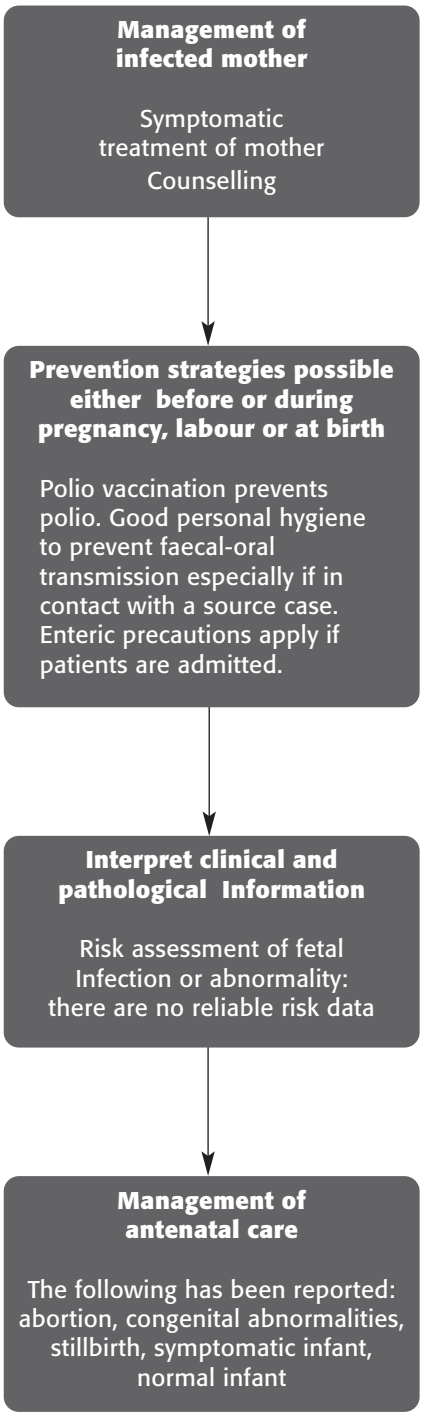
ALGORITHM 2

Management of Proven Maternal Infection



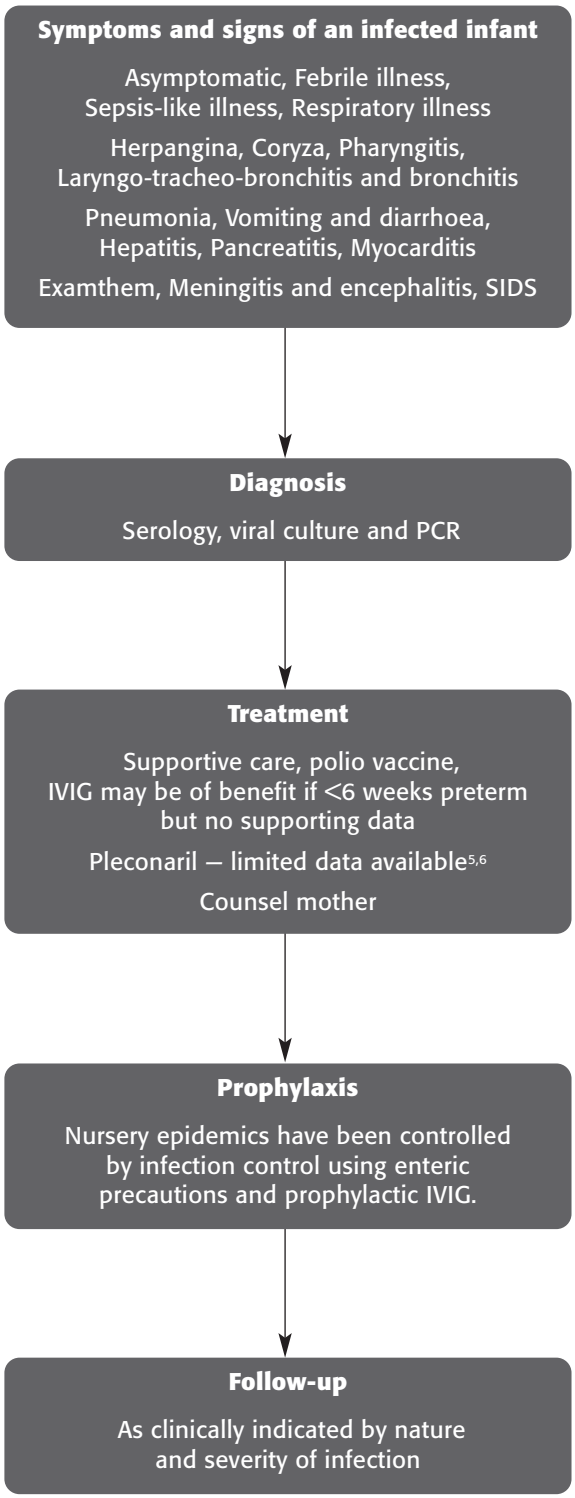
ALGORITHM 3

Antenatal Management and Prevention Strategies



ALGORITHM 4

Diagnosis, Management and Follow-up of 'At-Risk' Infants



NOTES

Improved survival in small case series of severe neonatal Ev sepsis. Data group was too small to determine if outcome was significant. No activity against Ev 71.[5]

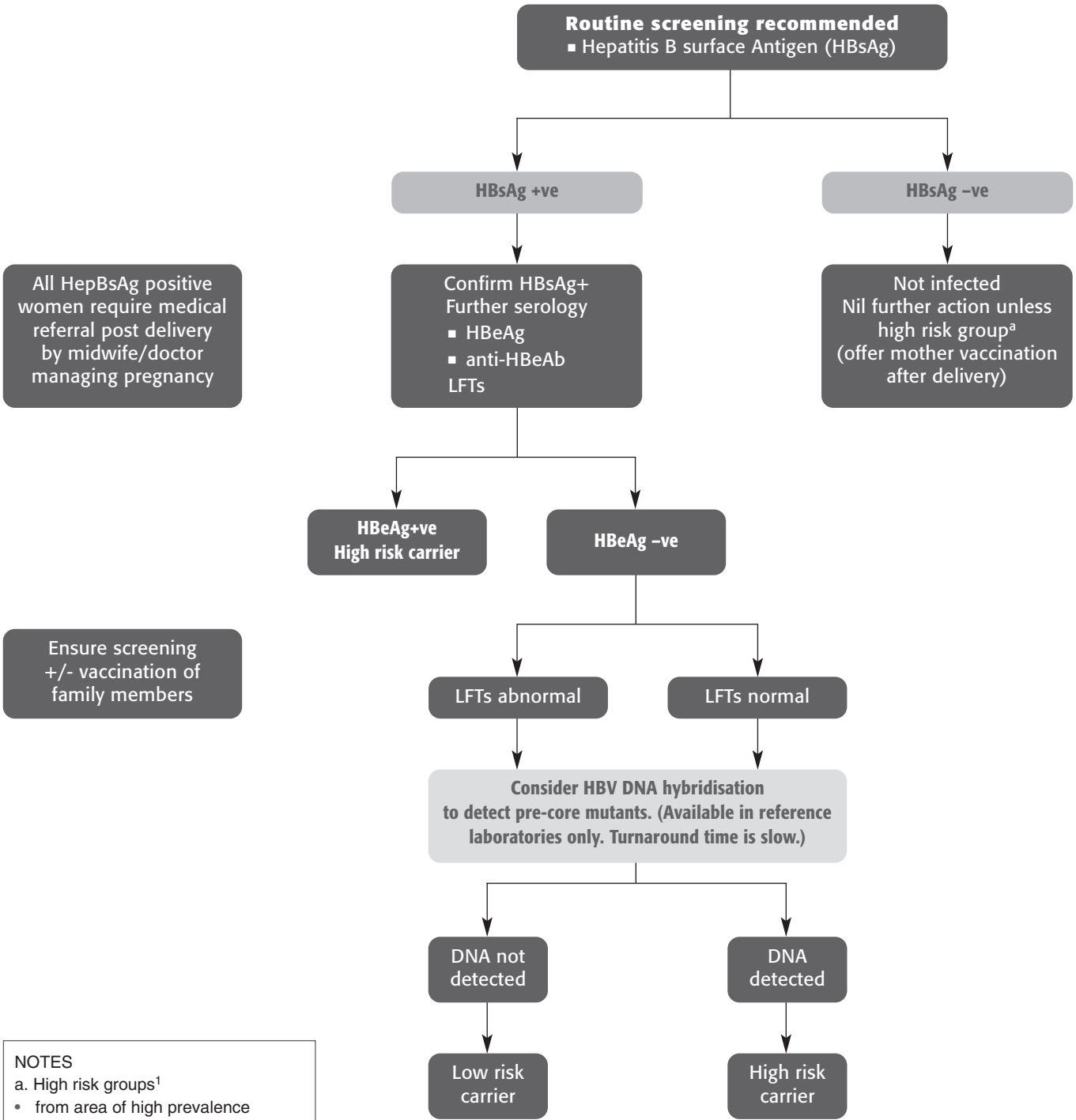
Recommended neonatal dose is 5mg/kg given orally every 8 hours. Bioavailability in neonates is satisfactory.[6]

Emendation 2006

Enterovirus- Algorithm 4: A double blind placebo-controlled trial of oral *Pleconaril* in 21 infants with enteroviral meningitis demonstrated plasma levels sufficient for in vitro inhibition of enterovirus replication.[E4] However, oral *Pleconoril* has since been withdrawn from the market.

ALGORITHM 1

Antenatal Diagnosis of Hepatitis B



NOTES

a. High risk groups[1]

- from area of high prevalence
- household contact HB carrier
- multiple sexual partners
- IV drug use
- tattoos/body piercing

ALGORITHM 2

Management of Hepatitis B in Pregnancy

Acute Hepatitis B

Trimester 1 and 2
- perinatal transmission risk ~10%[2]

Late Pregnancy
- perinatal transmission risk ~75%[2]

Refer for supportive medical management

No demonstrated role for antenatal HBIG in reducing subsequent perinatal transmission

Lamivudine (3TC) and α-IFN contra-indicated in pregnancy

Delivery:
- no data regarding mode of delivery in acute hepatitis
- Caesarean section lowers risk of perinatal transmission in chronically infected HepBeAg positive mothers[3]

Baby:
- HBIG and HB vaccine at birth
- further HB vaccine at 2,4 & 12 months (multivalent vaccines after first dose)[5]
- arrange follow-up serology at 12 months **(SEE ALGORITHM 4)**

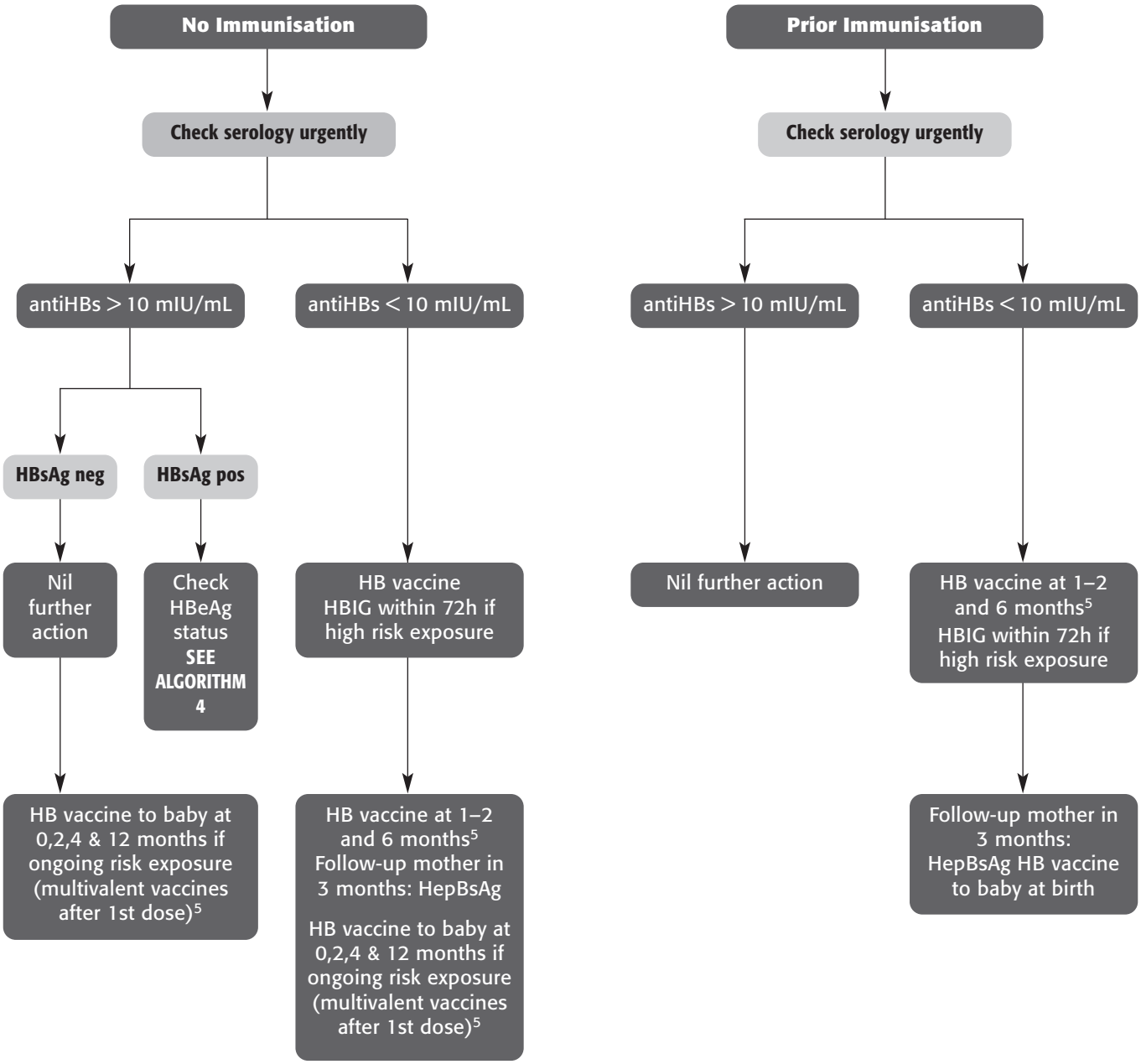
Chronic Hepatitis B infection (HepBsAg+)

SEE ALGORITHM 1

NOTE
Current prospective data does not support an increased risk of vertical transmission of Hep B after amniocentesis.[4]

ALGORITHM 3

Hepatitis B: Exposure During Pregnancy



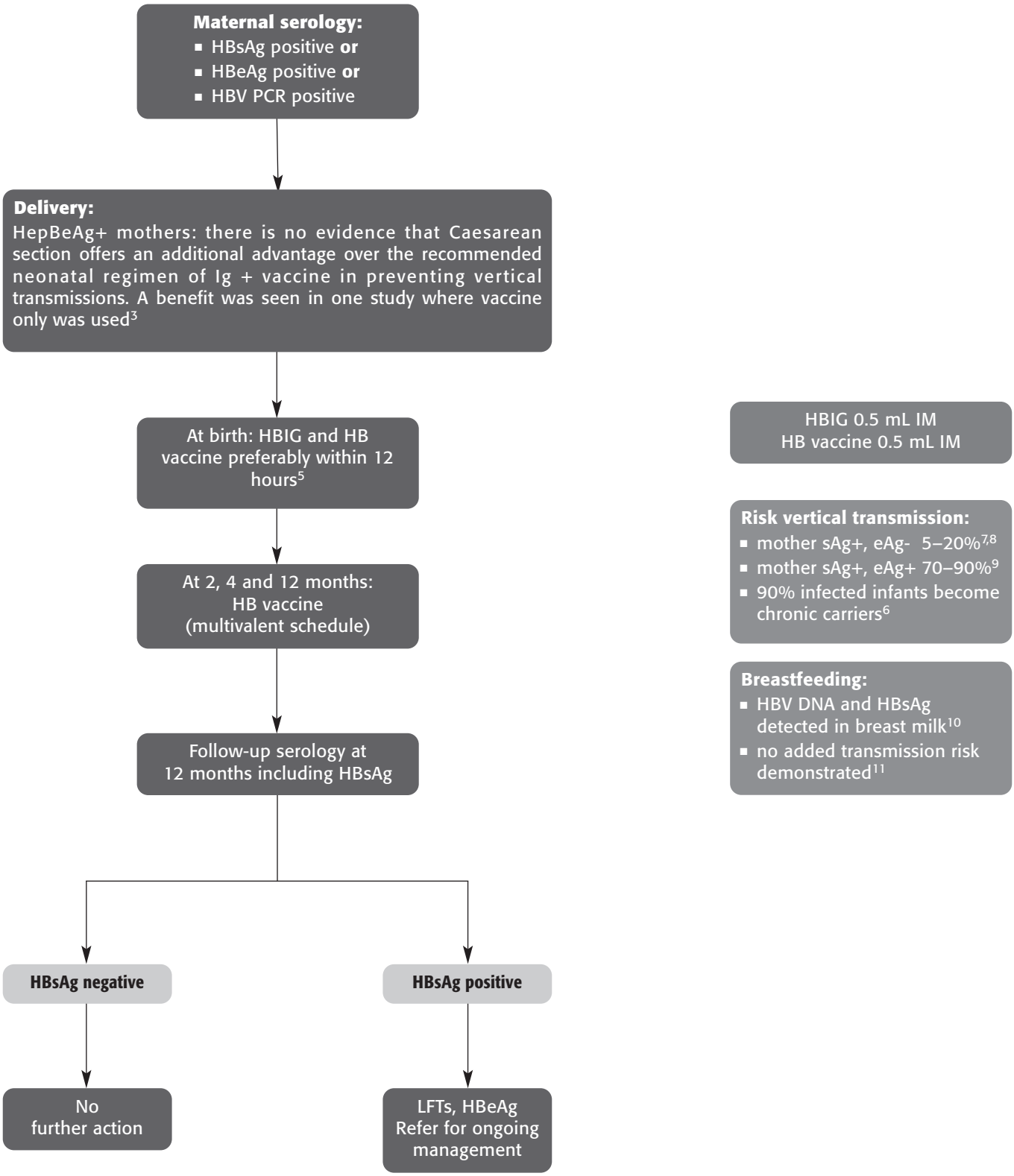
NOTES

Maternal risk of infection by mode of exposure:

- needlestick: if donor eAg+ high risk 20-40%[6]
- sexual contact
- mucosal exposure

ALGORITHM 4

Management of Infants of Mothers with Hepatitis B



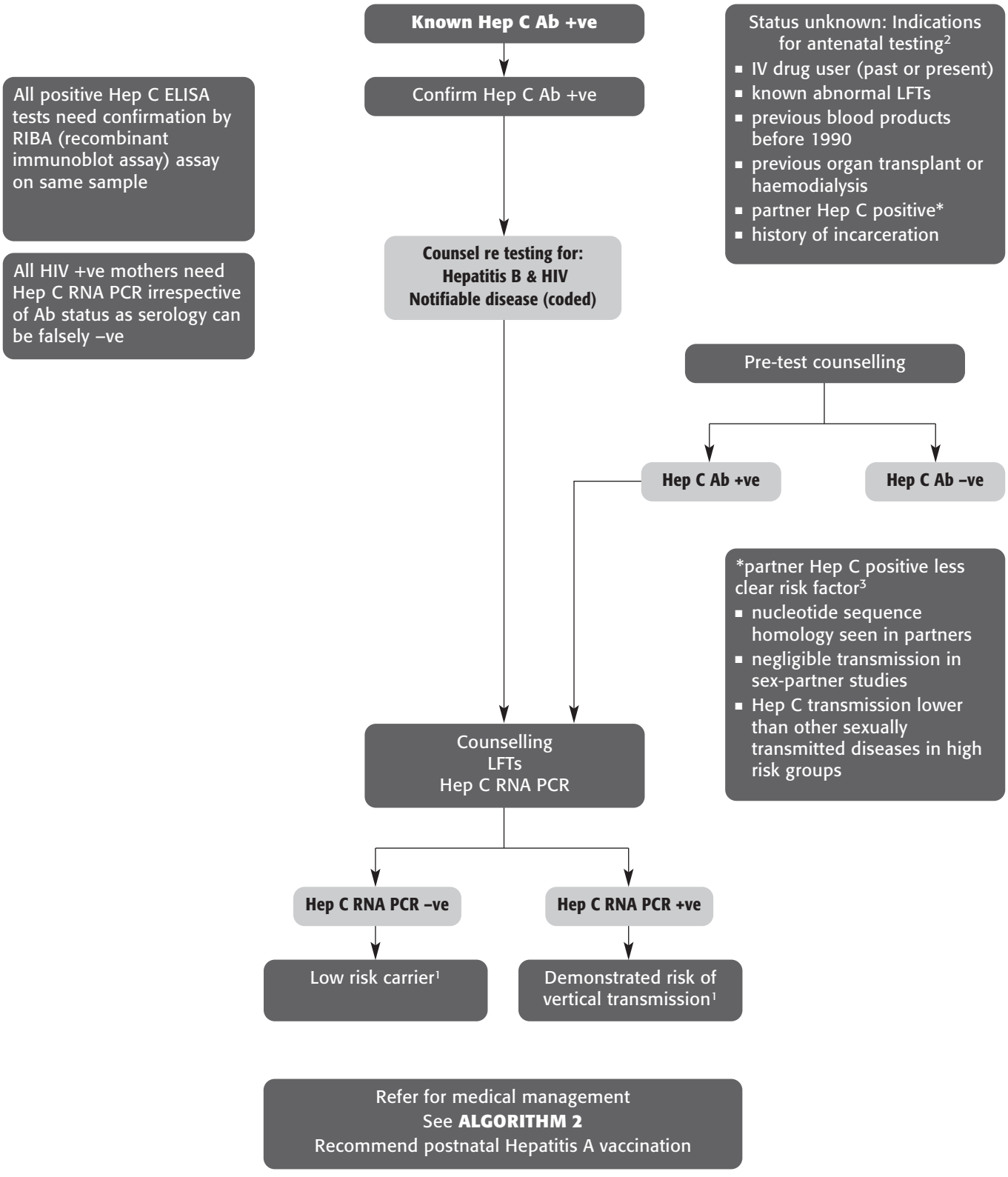
Emendation 2006

HEPATITIS B

- Management of a mother exposed to HB during pregnancy (see Algorithm 3). If maternal antiHBs titre < 10mIU/ml, give mother HBIG (400 IU, IM) as soon as possible but within 72 hours of exposure. Also, give the mother HB vaccine within 7 days of exposure and at 1 and 6 months post initial dose.[E5]
- Management of an infant born to a HB carrier mother (see Algorithms 2 & 4): e.g. mother with acute HBV in pregnancy or is HB antigen or PCR +ve. Give HBIG (100 IU, IM) to the infant preferably within 12 hours of delivery (efficacy markedly reduced if administration delayed beyond 48 hours after birth). Monovalent HB vaccine should be given at the same time (other limb) if possible, but do not delay beyond 7 days of life. Complete schedule with 3 more doses at 2, 4 and 6 or 12 months (timing dependent on combination vaccine used). [E5]
- Revised recommendation for primary HB vaccine schedule for babies (Algorithm 3): when the risk of perinatal HBV transmission is low, the routine Australian schedule is recommended i.e. birth (monovalent HB vaccine), then combination vaccines at 2, 4 and 6 or 12 months (timing dependent on combination vaccine used). [E5]

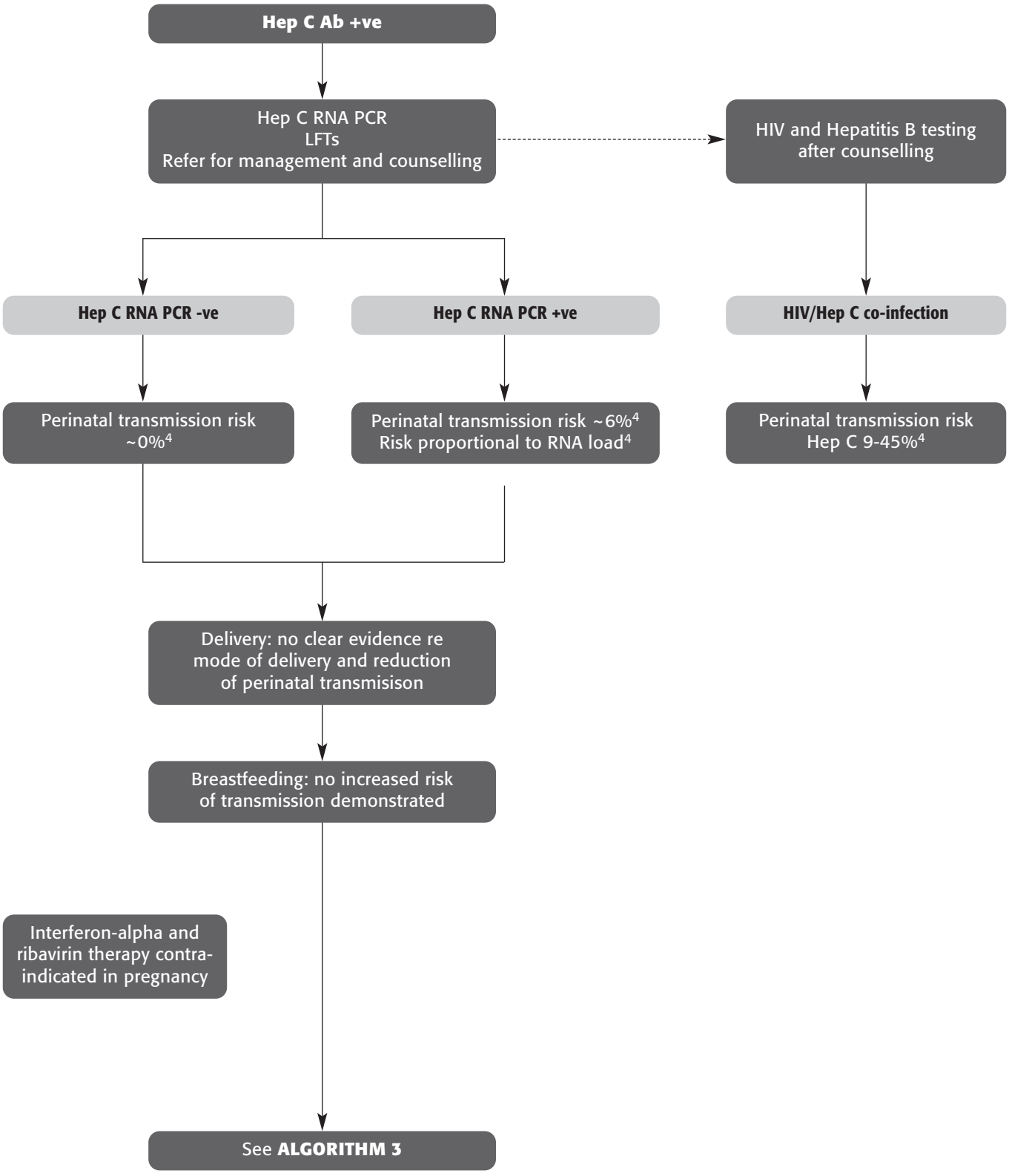
ALGORITHM 1

Antenatal Diagnosis of Hepatitis C



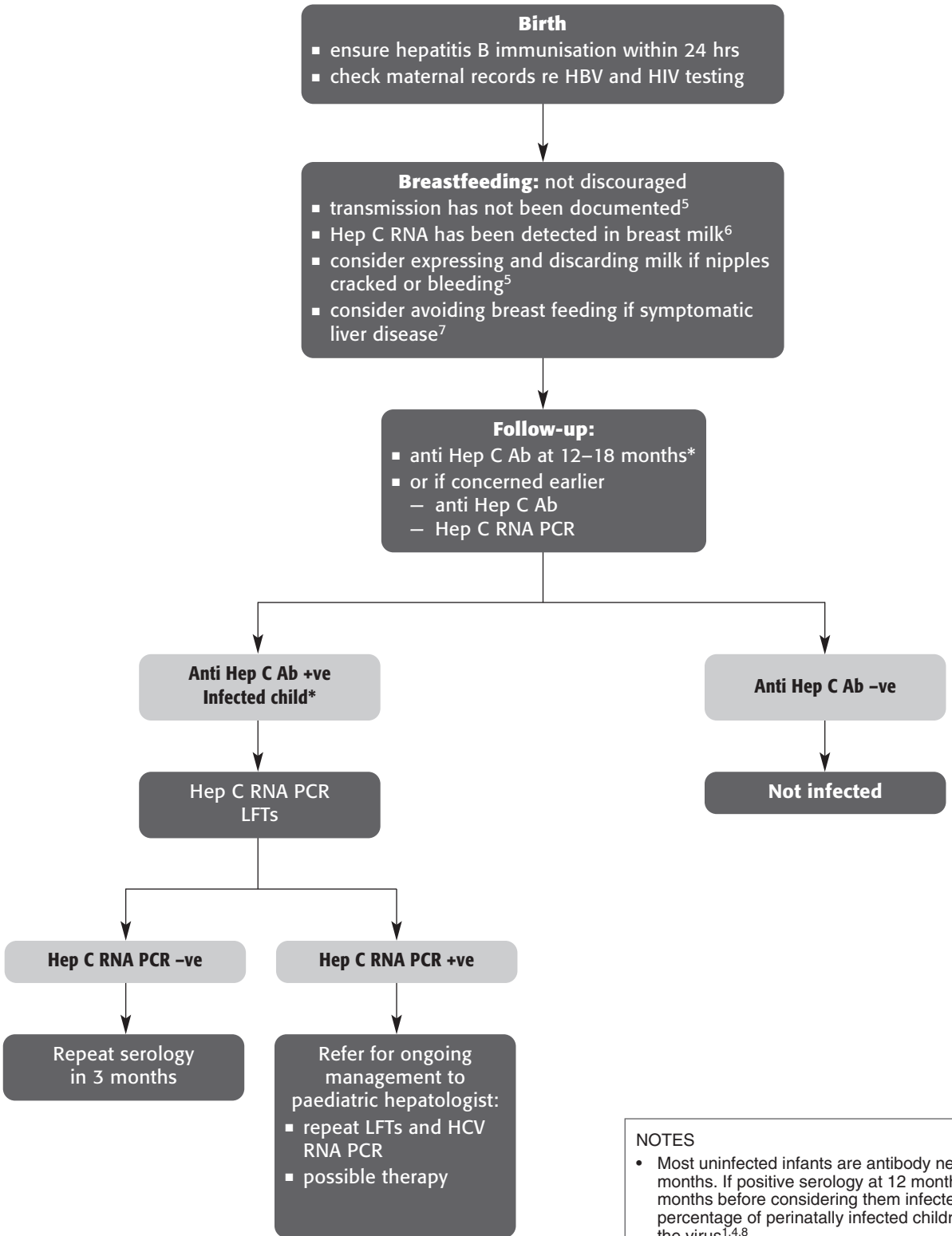
ALGORITHM 2

Management of Hepatitis C in Pregnancy



ALGORITHM 3

Management and Follow-up of Infants of Hepatitis C Infected Mothers



NOTES

- Most uninfected infants are antibody negative by 12 months. If positive serology at 12 months, retest in 3 months before considering them infected. A small percentage of perinatally infected children may 'clear' the virus[1,4,8]

Emendation 2006

HEPATITIS C

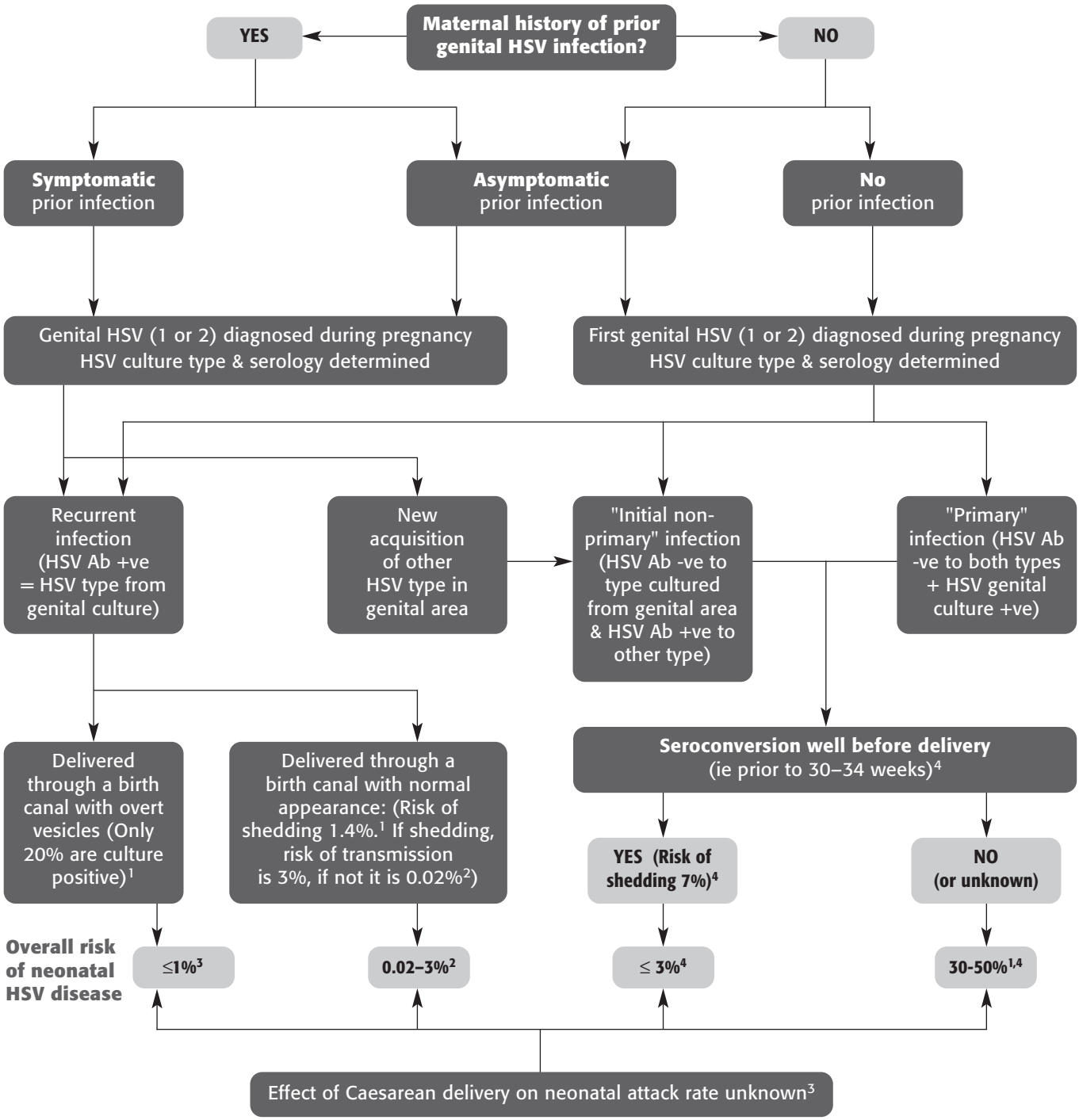
Algorithm 3 : Follow-up of infants of hepatitis C infected mothers [E6]

The general recommendation for testing a well child with perinatal HCV exposure is to test the child for HCV antibodies at ≥18 months of age as transplacental maternal HCV antibodies should clear by then.

When follow up cannot be guaranteed however, testing by HCV RNA PCR (include LFT) should be performed earlier, but **not** at less that one month of age as the sensitivity of HCV RNA PCR is 22 % at < 1 month of age. A single positive PCR result after 1 month of age gives a post-test probability of infection of 73% for a child born to an HIV–ve/HCV+ve woman, and 90% for a child born to an HIV+ve/HCV+ve woman.[E7] A positive or negative PCR result should be confirmed on a separate occasion.[E8] Negative PCR results but positive anti HCV antibody in a child < 18 months of age usually suggests that the child is not infected.[8] However, HCV antibody (with accompanying liver function tests) should be retested at or beyond 18 months of age to confirm this, as occasionally it represents infection of the child in the absence of HCV viremia. [E6, E 8]

ALGORITHM 1

Herpes Simplex Virus Infections in Pregnancy: Risk Assessment of Neonatal Disease

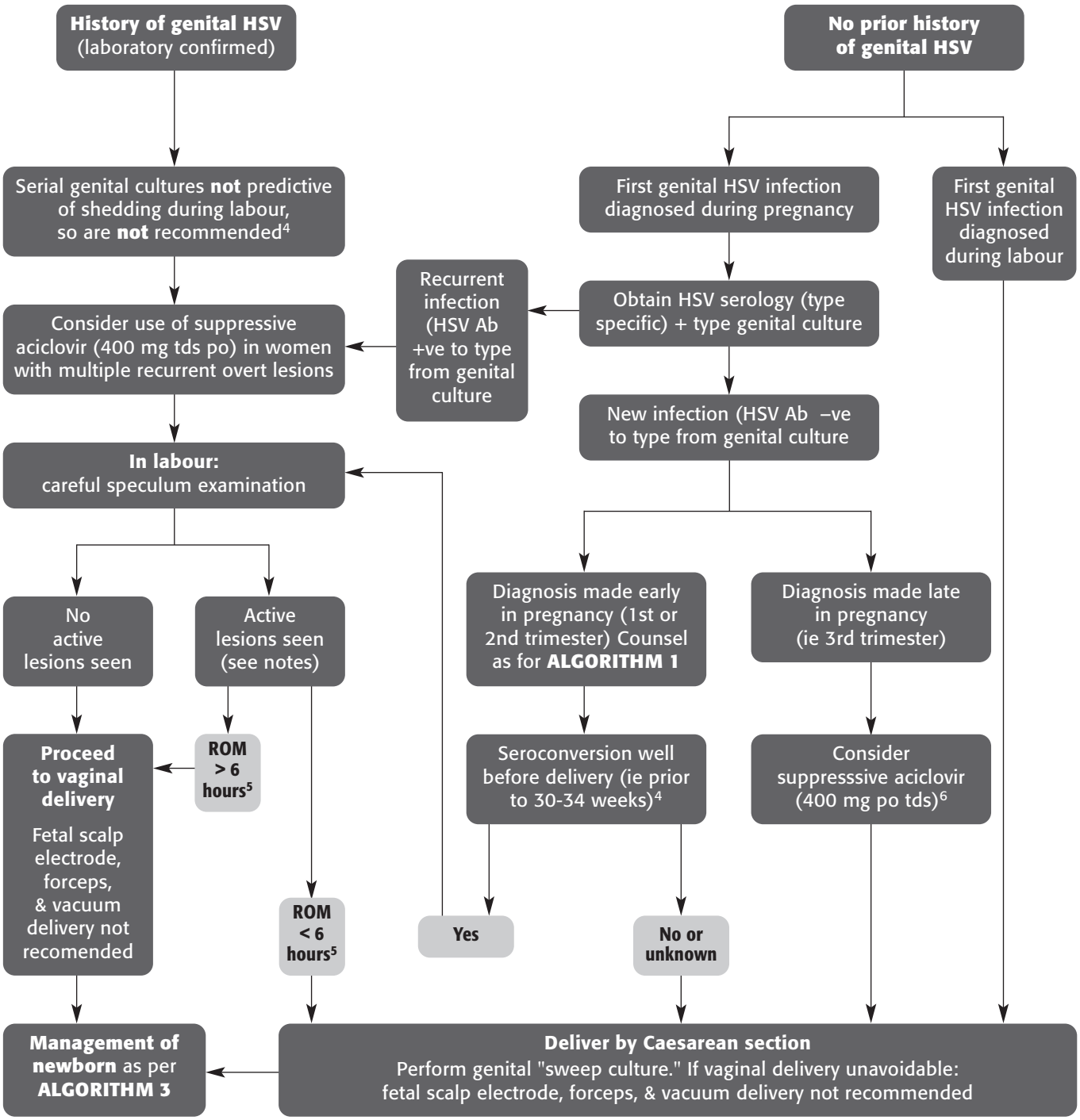


NOTES

- 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.
- HSV-1 genital infection is being increasingly recognised- but is less likely to recur than genital HSV-2.
- 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.[4]

ALGORITHM 2

Maternal Management of Genital Herpes Simplex Virus Infections in Pregnancy



NOTES

- Insufficient data are available on the effect of suppressive aciclovir on transmission to the newborn for either active recurrent or primary genital maternal disease.
- Careful speculum examination for active genital HSV should be performed on all women at delivery.
- ROM>6 hours has been observed in one small study to increase risk of neonatal infection.[5] However the efficacy of Caesarean delivery in preventing neonatal HSV infections is unknown, and this practice has been recently challenged in two large studies in which infected infants were born in the presence of intact membranes.[3]

Emendation 2006:

HERPES SIMPLEX VIRUS

- Algorithm 1 and 2: HSV in pregnancy: risk assessment/management of neonatal disease
  Caesarean section reduces risk of HSV transmission in **women shedding HSV** at the time of birth, particularly in women with first time infections who are HSV type specific antibody negative. [E9]

ALGORITHM 3

Herpes Simplex Virus Infections in Pregnancy: Neonatal Management

Low risk
of neonatal HSV disease
ie mother with recurrent infection, or primary infection seroconverted well prior to delivery

Collect surface swabs at 24 hours of life – eye, throat, umbilicus, rectum, urine
Follow for signs of infection

Positive surface swab or sick newborn

Perform lumbar puncture (CSF analysis, viral culture, PCR for HSV DNA), blood count (for low platelets), LFTs, & HSV PCR on blood (if available)
Commence IV aciclovir immediately, duration will depend on surface culture & CSF results

High risk of neonatal HSV disease
ie mother with primary infection close to delivery or infant born through birth canal with active HSV disease to mother with no prior history of genital HSV

Perform:
- surface swabs at birth (onset of clinical signs) – eye, throat, umbilicus, rectum, urine
- blood count (for low platelets),
- LFTs
- HSV PCR on blood (if available)
- Commence IV aciclovir immediately from birth
- If clinical signs of HSV disease develop, perform LP (CSF analysis, viral culture, HSC PCR), CNS imaging and repeat blood count, LFTs.

Infant with clinical signs of neonatal HSV disease (regardless of maternal history)

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

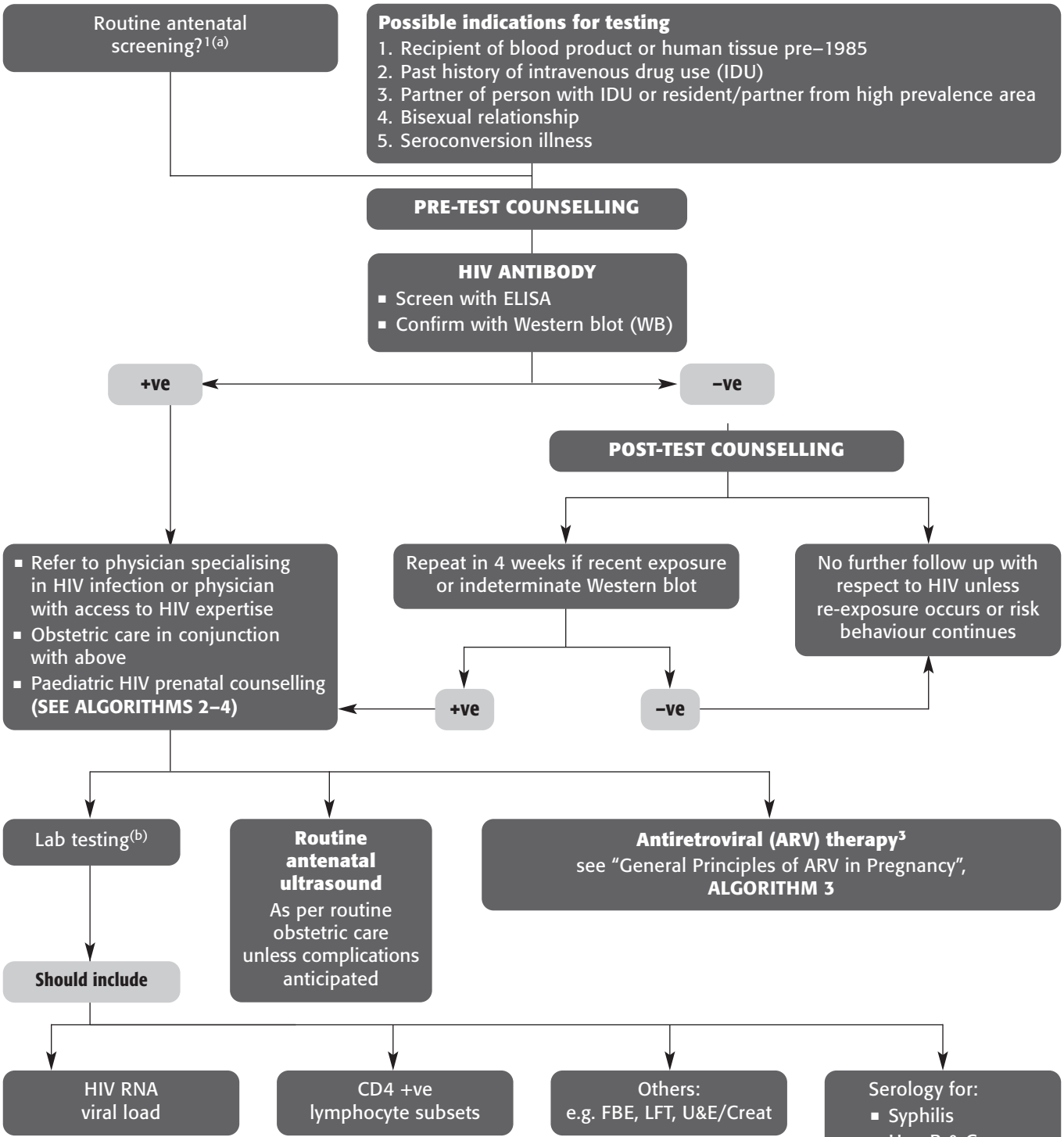
ACICLOVIR THERAPY
Oral therapy **should not** be used for empiric or therapeutic treatment of HSV in the neonate.
The current recommended dose is 20 mg/kg/dose IV, 3 times/day as 1–2 hour infusion. For disease confined to skin, eye, mouth: duration of therapy is 14 days. For encephalitis, disseminated disease: 21 days is recommended.[7]

Follow up:
- Survivors should be monitored closely for recurrences, eye disease, CNS sequelae. LP should always be performed on all infants with suspected HSV relapse to exclude CNS involvement.
- A phase I/II trial of oral aciclovir to prevent adverse neurological outcome in infants with frequent cutaneous recurrences after HSV-2 skin, eye, mouth disease demonstrated neutropenia in 50%, development of aciclovir-resistant virus in 4% and reduction of cutaneous recurrences (CNS outcome was not studied).[8] Until results of larger, ongoing phase III trial available, suppressive therapy cannot be routinely recommended.

NOTES
The incidence of neonatal HSV disease in Australia is approximately 3.0 per 100,000 live births.[9]

ALGORITHM 1

Diagnosis of HIV Infection in Pregnant Women



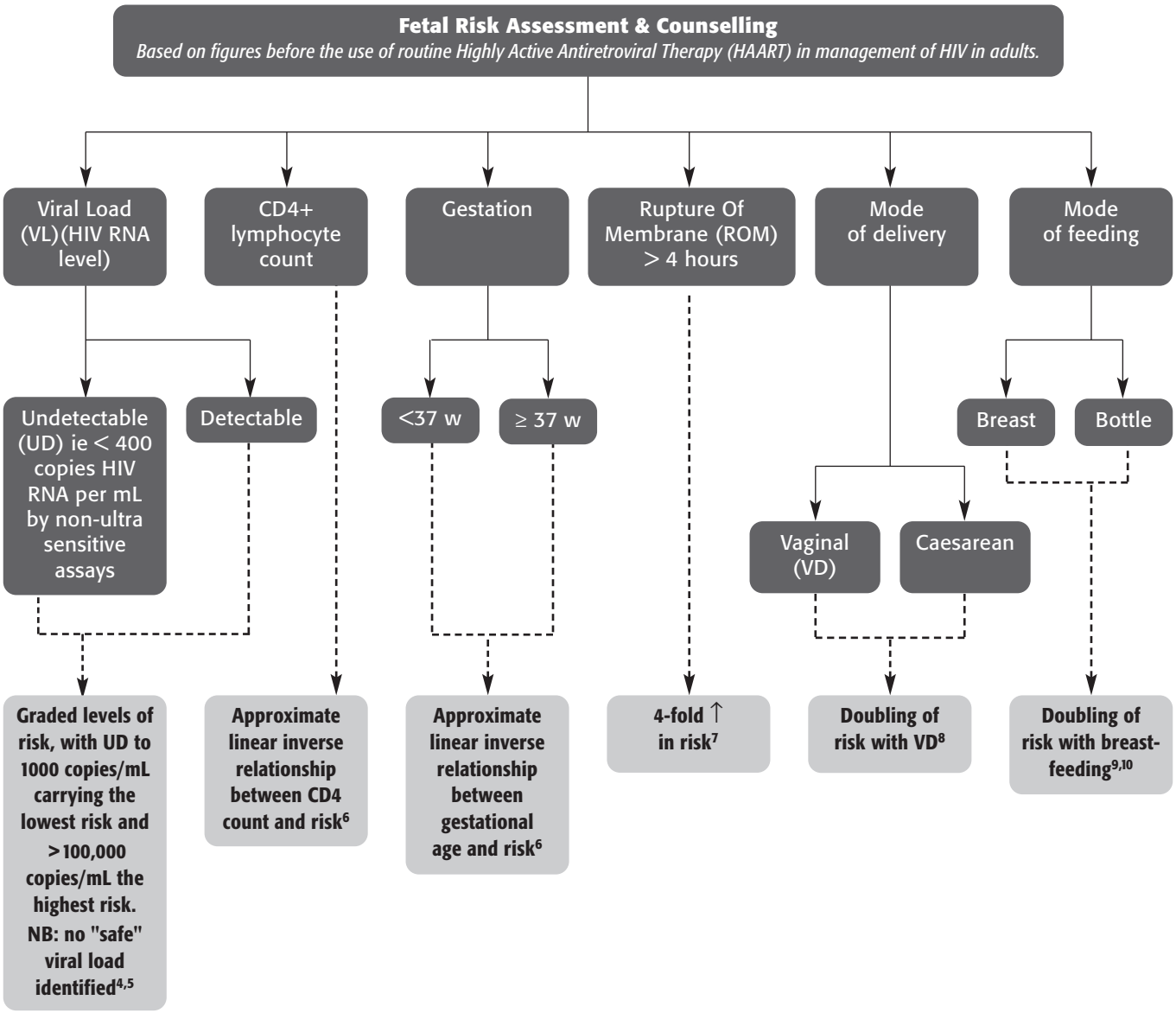
NOTES

a. As effective strategies to prevent perinatal HIV transmission exist, knowing the HIV status in pregnant women may be warranted. Half of HIV +ve pregnant women are unaware of their HIV status and two-thirds have no risk factors.[2]

b. Consideration should be given to resistance testing and/or viral subtyping if HIV acquired outside of Australia.

ALGORITHM 2

Assessment of Risk Factors in Perinatal Transmission of HIV

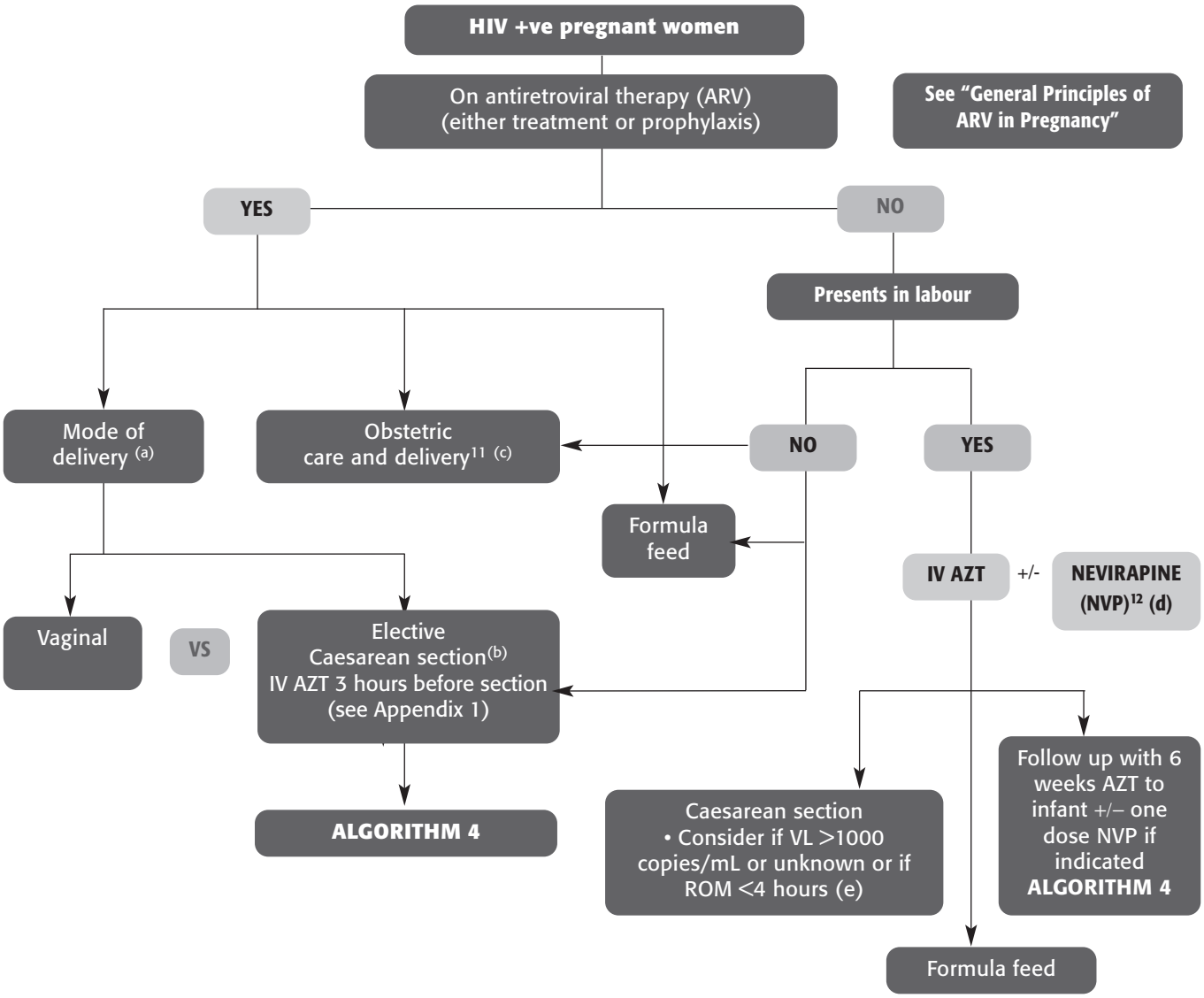


COMMENTS

- Other relative risk factors include the first born twin and the presence of co-infections (eg sexually transmitted diseases and chorioamnionitis).
- Antenatal tests as per routine obstetric follow-up. Also, see ALGORITHM 1.
- Apart from risk assessment, counselling should include
  - strategies to prevent transmission (see ALGORITHM 3)
  - management of baby at birth, including ARV and prophylaxis
  - testing of baby
  - care plan before delivery
  - care plan for future with respect to a family that has HIV "infected" and HIV "affected" members.

ALGORITHM 3

Strategies to Minimise the Perinatal Transmission (PNT) of HIV



COMMENTS

See Table 1 for estimated PNT risks by selected strategic options.

a If a pregnant woman is already on HAART, the added benefit of caesarean section may be marginal particularly if viral load is undetectable. The combined risk estimates for vertical transmission for women already on an AZT containing regimen is 1 – 12% (mean 5.7%) with HIV RNA level near delivery of 1000 – 10, 000 copies/ml and 9 – 29% (mean 12.6%) if HIV RNA levels are > 10, 000 copies/ml. Based on this, the American College of Obstetricians recommend elective caesarean section as an added strategy if VL > 1000 copies/ml. http://hivatis.org/guidelines

b If labour commences before planned caesarean section and membranes are ruptured for < 4hours, semi-urgent elective caesarean section should be considered (especially if not on ARV prophylaxis and viral load detectable). (see comment e)

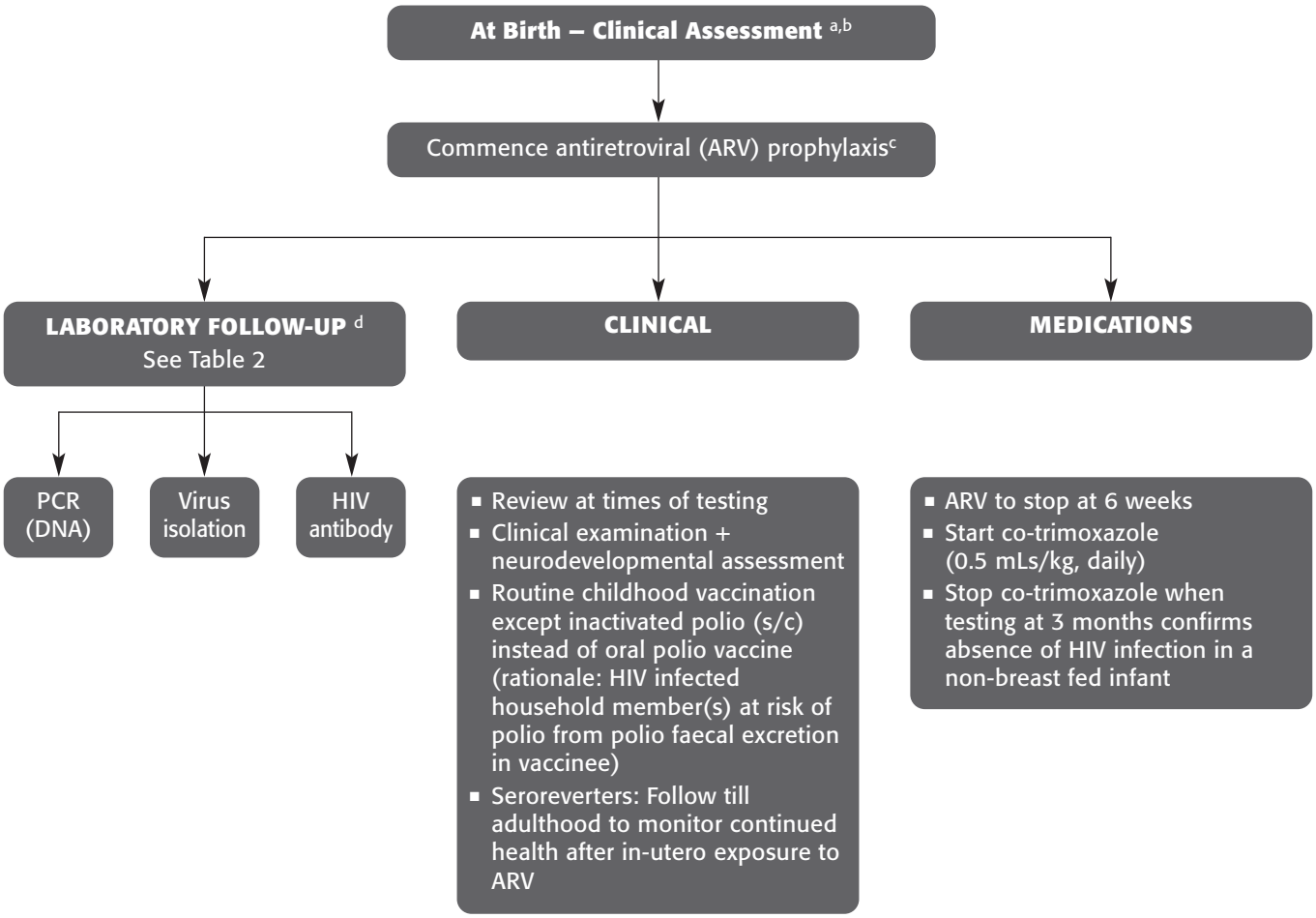
c Includes avoidance of invasive procedures e.g. fetal scalp electrodes, episiotomy. If resuscitation needed, gentle oral suction of baby only (if possible). Wash baby down as soon as possible after birth.

d HIVNET 012: Single dose NVP, 200 mg, to mother intrapartum, and follow up with single dose to infant (2mg/kg) within 3 days of birth. Caution: Preliminary data report NVP resistance in some mothers and infected infants after a single dose in HIV NET 012 study. Significance not currently known.[14] The role of additional NVP prophylaxis when a woman is already on an established ARV regimen is unknown and currently not recommended.[15]

e The value of caesarean section in reducing HIV PNT after a short duration of ROM has not been established. However as a continuum of PNT risk following ROM exists, some would perform caesarean section to shorten labour and hence duration of ROM.

ALGORITHM 4

Management of Infant at Risk of Perinatal HIV



COMMENTS

a No HIV embroyapathy syndrome has been described.

b A third of perinatal HIV transmission occurs in utero and $^{2}/_{3}$ during the peripartum period. Hence, infected infants are less likely to present with signs and symptoms of HIV at birth. Definitions: "in utero transmission" = +ve PCR result < 7 days of age. "peripartum transmission" = +ve PCR result ≥ 7 days of age.

c Postnatal ARV Regimen: AZT is recommended, regardless of the mother's therapy. Zidovudine (AZT syrup,10 mg/mL), 4mg/kg/dose B.D. – to start within 8 hours of delivery, given for 6 weeks. The benefit of adding 3TC to AZT postpartum for 6 weeks if mothers have been on combination of antiretrovirals during pregnancy is unclear. If added, dose of 3TC solution (strength, 10 mg/mL) is 2 mg/kg/dose B.D. – to start within 8 hours of delivery, for 6 weeks. If nevirapine is indicated, 2 mg/kg, single dose, to be given within 3 days of birth. No confirmed short/medium term adverse events associated with in-utero/postnatal exposure to AZT. Concern with mitochodrial toxicity after AZT +/- 3TC exposure in-utero remains to be confirmed.

d Any positive virological test (PCR or virus culture) must be confirmed on a separate sample due to the potential for false +ve results.

—PCR has equivalent sensitivity of detection as virus isolation but is available sooner (takes ~1 week) than viral culture (4–6 weeks). Close to 100% sensitivity of detection at 3 months in non-breast fed infants.

—Traditionally, seroreversion i.e. disappearance of passive (maternal) antibodies is documented before declaring a child uninfected. Antibody testing after 6 months may be useful to document declining maternal antibodies titres in uninfected babies.[16]

TABLE 1

Perinatal Transmission (PNT) Risk Estimates by Selected Intervention Strategies

	ANTIRETROVIRALS					
	Mother *Pregnancy*	Mother *Intrapartum*	Baby	Delivery	Feeding	PNT Risk
Baseline[a]	0	0	0	Vaginal	Formula	20%
Dunn, 1992[9]	0	0	0	Vaginal	Breast	40%
Nduati, 2000[10] (Uganda)[b]	0	0	0	Vaginal	Breast	~36%
The International Perinatal HIV Group, 1999[8]	0	0	0	Caesarean	Formula	10%
Connor, 1994[13] (Full course AZT, 076 Study)	+	+	+	Vaginal	Formula	8%
The International Perinatal HIV Group, 1999[8]	+	+	+	Caesarean	Formula	2%
Shaffer, 1999[17] (Short course AZT, Thai study)	+	+	0	Vaginal	Formula	10%
Wade, 1998[18]	0	0	+	Vaginal	Formula	10%
Wade, 1998[18]	0	+	0	Vaginal	Formula	20%
Guay, 1999[12] (HIV NET 012, Uganda)	0	NVP	NVP	Vaginal	Formula	~10%

Key: Shaded rows represent risks when no intervention strategies are in place. 0 = no ARV prophylaxis, + = ARV given. Unless stated, the antiretroviral referred to is AZT. NVP = nevirapine

a Prior to the introduction of recommended intervention strategies, a child born to an "asymptomatic" HIV infected woman with CD4+ counts > 200c/mm^3 who did not breast feed had ~20% of being infected perinatally (in developed countries). For the purpose of these algorithms, this figure is referred to as the "baseline" and increases or decreases in risk are referable to this baseline.

b The approximate doubling of risk in breast fed babies over formula fed babies in this randomised clinical trial was seen over a range of breast feeding duration (6 weeks to 2 years), with 75% infected in the first 6 months of breastfeeding.

GENERAL PRINCIPLES OF ARV IN PREGNANCY

1. ARV regimens are either treatment schedules or regimens for preventing perinatal transmission ("prophylaxis"). Women are now generally on HAART at time of pregnancy.
2. Pregnancy should not preclude use of optimal therapeutic regimen.[3] If initiating therapy, consideration could be given to waiting till the second trimester. A possible association of pre-term delivery with combination therapy has been found but not confirmed. http://hivatis.org/guidelines
3. Efavirenz and hydroxurea (teratogenesis, animal studies) are not recommended in pregnancy. Caution has been raised with d4T + ddI in combinations with protease inhibitors in pregnancy (fatal lactic acidosis. Pharmaceutical company drug alert, January 2001)
4. The three part ZDV prophylactic regimen (Protocol 076) is considered best practice, and is recommended for all pregnant women with HIV infection regardless of RNA viral load.[13] (Appendix 1) Thus, ZDV should be included as a component of antenatal regimen where possible. If ZDV is not included antenatally, intrapartum and newborn ZDV are still recommended. However, if d4T is part of antenatal ARV regimen, intrapartum ZDV is not recommended because of potential drug interaction.

TABLE 2

Suggested Testing Regimen

	TESTS			
Time	T Cell Subsets	PCR	Virus Isolation	HIV Antibody
(Day 1)		+	(+)	–
Week 1	+	+	+	–
Week 6	+	+	+	–
3 months		+	(+)	–
6 months		+	(+)	(+)
12 months		–	–	+
18 months (if still seropositve at 12 mo)		–	–	+

Texts in parenthesis denote optional time or type of test.

APPENDIX 1: PACTG 076 ZIDOVUDINE REGIMEN[13]

Time of ZDV Administration	Regimen
Antepartum	Oral administration of 100 mg ZDV 5 times daily*, initiated at 14-34 weeks gestation and continued throughout the pregnancy.
Intrapartum	During labour, intravenous administration of ZDV in a one-hour initial dose of 2 mg/kg body weight, followed by a continuous infusion of 1 mg/kg body weight/hour until delivery.
Postpartum	Oral administration of ZDV to the newborn (ZDV syrup at 2 mg/kg body weight per dose every six hours) for the first six weeks of life, beginning at 8 -12 hours after birth.** (Note: intravenous dosage for infants who cannot tolerate oral intake is 1.5 mg/kg body weight intravenously every six hours).

* Oral ZDV administered as 200 mg three times daily is an acceptable alternative regimen

** 4 mg/kg per dose, twice daily is an acceptable alternative regimen

Emendation 2006:

HUMAN IMMUNODEFICIENCY VIRUS

- Nevirapine toxicity in women: The risk of hepatic toxicity is increased in women particularly if CD4 counts are > 250 c/ml, usually in the first 6 weeks of starting therapy. Pregnancy may be an added risk factor. Thus, caution is warranted and close monitoring recommended if this agent is included in therapeutic/prophylactic HAART regimens started during the antenatal period. E10

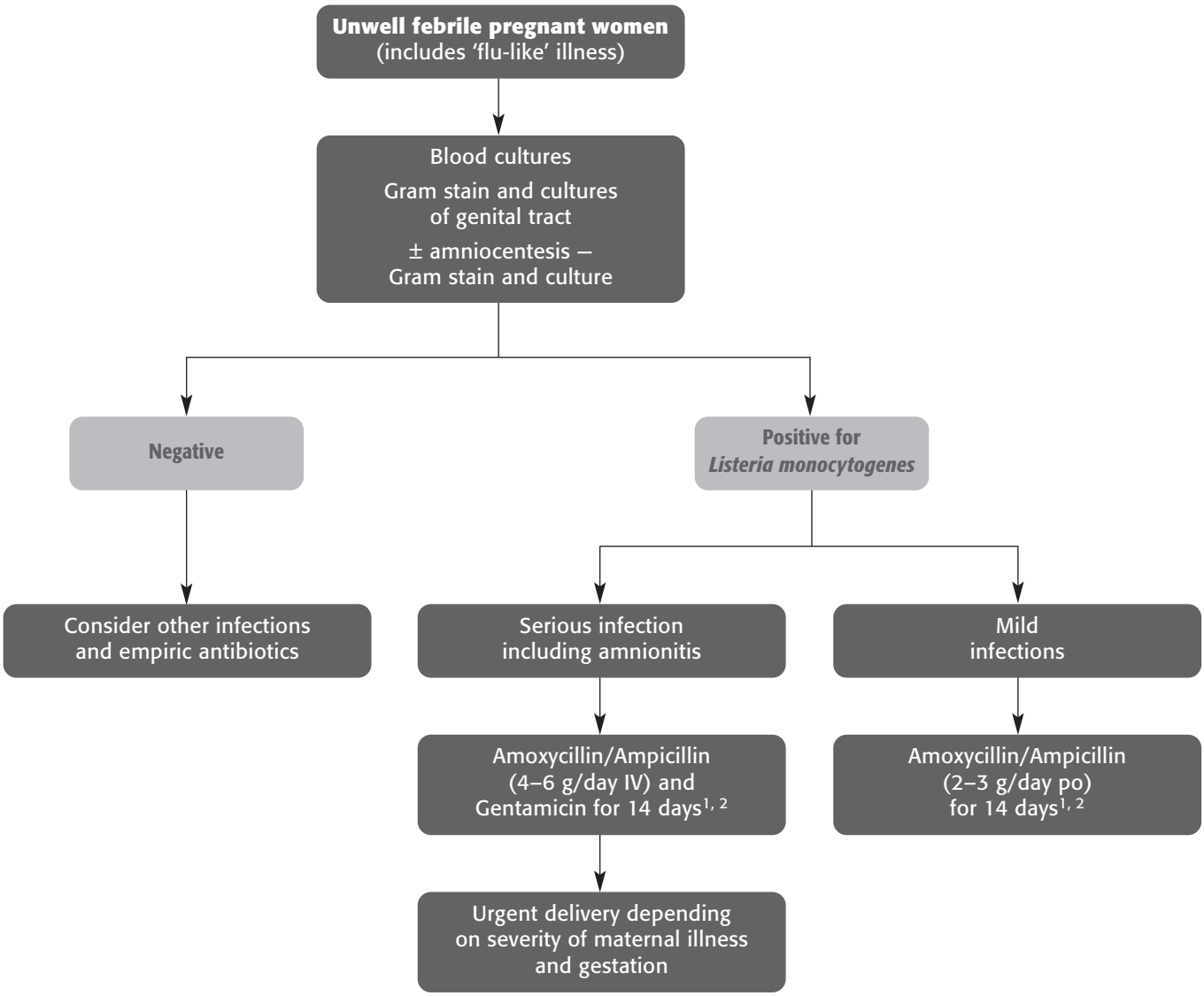
- Erratum, Table 1: In the Guay 1999 study (HIV NET 012), infants were breast fed (not formula fed)

- Revised suggested postnatal testing times and review
    - *HIV PCR at 1, 6, 12 weeks and at 6 months. Virus isolation and T-cell subsets are no longer routinely done in this setting.
    - If all PCRs remain negative, then clinical review only is recommended at 12 months. HIV antibody at 18 months to document sero-reversion builds further confidence in the diagnosis of "non-infection" in the infant.

      Nb: * As the proviral DNA PCR is currently not commercially available (2006), HIV RNA PCR is used.

ALGORITHMS 1 & 2

Diagnosis of Suspected Listeriosis and Management of Proven Maternal Infection

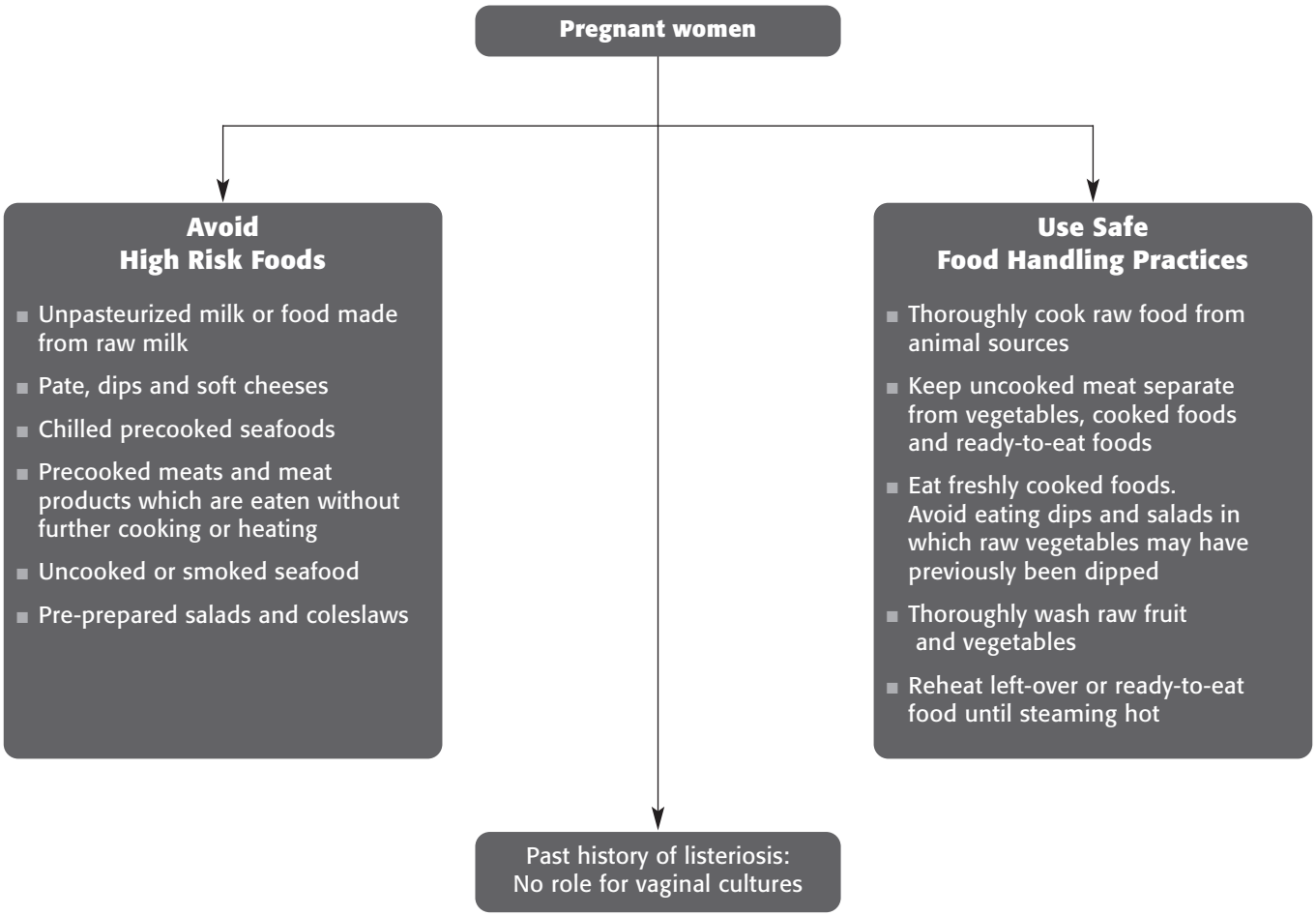


NOTES

- Maternal listeriosis in 2nd/3rd trimester results in a mortality of 40–50% for the fetus
- Serology is not a useful tool for diagnosing listeria[3]
- Early treatment of maternal infection can improve perinatal outcome
- The recommended treatment regimens above are based on observations and case reports. No randomized controlled trials have been performed to establish optimal treatment regimens or to support efficacy of penicillin over ampicillin, but ampicillin or amoxycillin is generally considered the preferred agent.[1–3]
- Synergism exists for penicillin or ampicillin with gentamicin.[3]
- Trimethoprim/sulphamethoxazole is suggested as an alternative in the penicillin allergic patient.

ALGORITHM 3

Antenatal Prevention Strategies for Perinatal Transmission of Listeria



NOTES

* Intrapartum antibiotic therapy is not recommended for mothers with a past history of perinatal listeriosis. No data to suggest reculture during subsequent pregnancy has any value

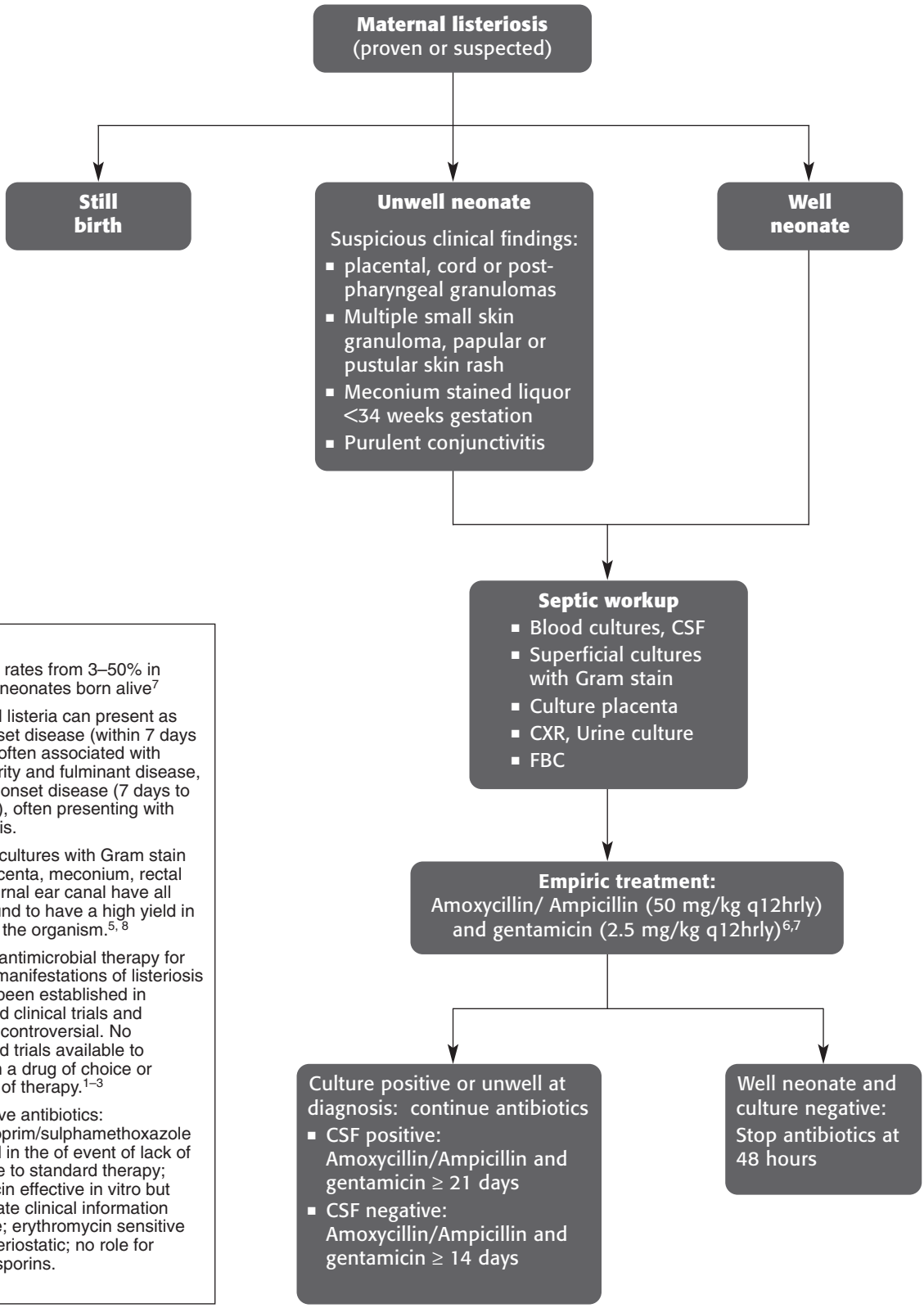
* Asymptomatic vaginal carriage of L. monocytogenes is rare. Faecal carriage of L. monocytogenes is found in 0.6–16% of the population at any one time.[4] The significance of faecal excretion in perinatal infection is uncertain.

* If listeria found on vaginal/rectal culture, it may be appropriate to try to eradicate the organism before delivery with oral amoxycillin or erythromycin (250 mg q6hrly for 10 days). While this approach may seem reasonable it has not been definitively studied.[5]

* Local Public Health Department publications, with detailed advice, are available.

ALGORITHM 4

Diagnosis and Management of Infant at Risk of Perinatal Listeriosis

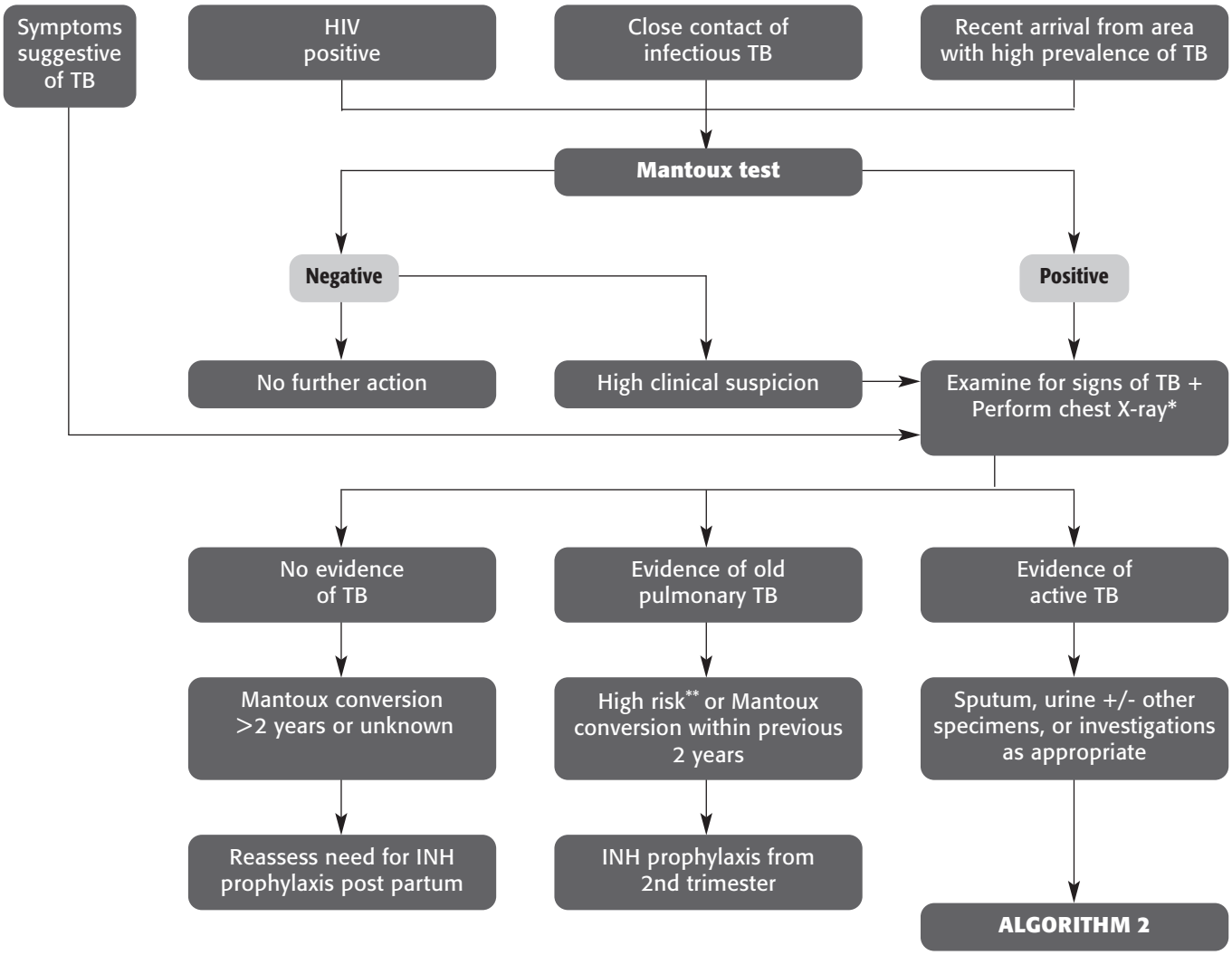


NOTES

- Mortality rates from 3–50% in infected neonates born alive[7]
- Perinatal listeria can present as early-onset disease (within 7 days of birth) often associated with prematurity and fulminant disease, and late onset disease (7 days to 6 weeks), often presenting with meningitis.
- 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.[5,8]
- 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.[1–3]
- 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; no role for cephalosporins.

ALGORITHM 1

Antenatal Diagnosis



* Chest X-ray 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, eg diabetes, chronic renal failure, malignancy.

NOTES

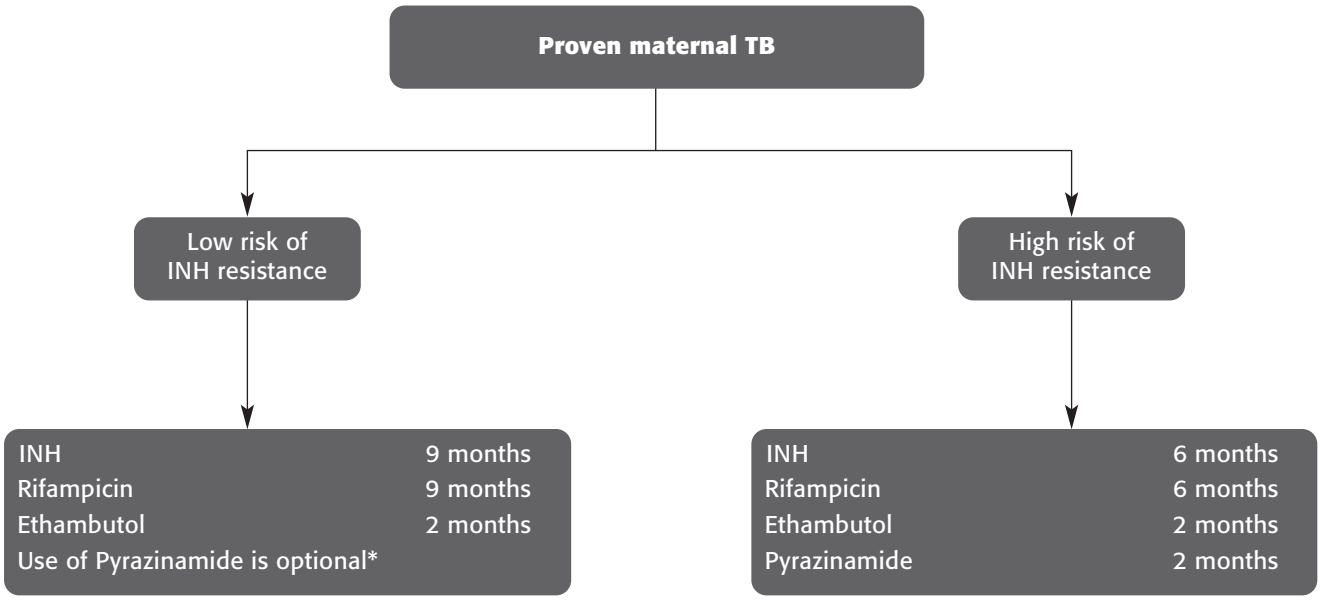
- The development, clinical presentation and progression of TB are not altered by pregnancy.[1,2]
- Although data are conflicting, pregnancy is not thought to increase the risk of inactive TB becoming active.
- The symptoms of extrapulmonary TB are frequently non-specific, and may be attributed to physiological changes of pregnancy.
- Areas with high prevalence of TB include South East Asia, Pacific Islands, Africa, Eastern Europe, Latin America.
- Mantoux testing of contacts is usually performed by local Health authorities, and may need to be repeated at 12 weeks after break of contact.
- Mantoux skin testing: intradermal injection of 0.1 mL of a 100 international unit/mL solution of purified protein derivative (PPD), with induration measured at 48-72 hours.
- The Mantoux test is not affected by pregnancy.
- Chest X-ray should be performed with appropriate abdominal shielding.
- Isoniazid (INH) "prophylaxis" is not true prophylaxis, and is often referred to as "treatment of latent TB infection". Usual duration is 6 months.
- INH is safe in pregnancy.[3]
- 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.[4,5]

Interpretation of Mantoux skin test positivity [Source: American Thoracic Society, 1999]

- ≥ 5 mm diameter in people with HIV infection, in people in close contact with someone with infectious TB, or in people with a chest X-ray suggestive of previous TB;
- ≥ 10 mm diameter in recent arrivals (< 5 years) from high prevalence areas, in injecting drug users, residents/employees of prisons, homeless shelters, residential facilities for AIDS patients, high risk patients** or in children < 4 years old;
- ≥ 15 mm diameter in those ≥ 4 years old with no risk factors for TB, and in children who have had BCG.

ALGORITHM 2

Initial Management of Suspected Maternal TB

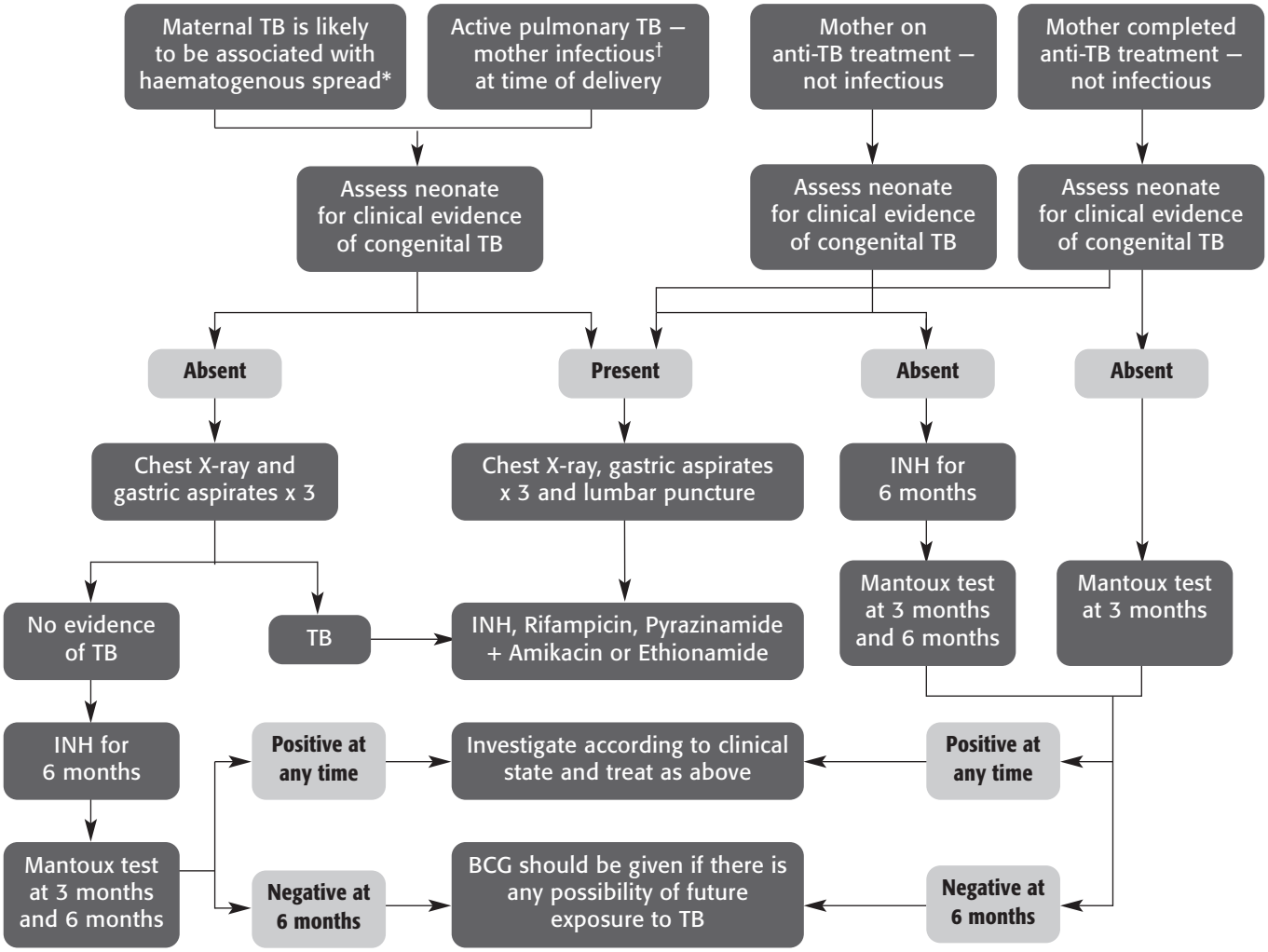


NOTES

- 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.[1,2]
- High risk of INH resistance should generally be assumed, particularly for HIV-positive 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 (the states vary on the application of DOT).
- All of the anti-TB drugs cross the placenta and reach a low concentration in fetal tissues.[3] However, INH, Rifampicin and Ethambutol are all safe in pregnancy. Little is known about the effects of Pyrazinamide in pregnancy, but it has been used without adverse effects. Many internationally recognised TB organisations recommend its routine use in pregnancy.[6] Streptomycin is contraindicated in pregnancy.[6]
- 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.[7]
- INH — 300 mg po daily (give with Pyridoxine 50 mg daily – note increased dose in pregnant and breastfeeding women).
- Rifampicin — 450 mg po daily (< 50 kg)
600 mg po daily (≥ 50 kg).
- Ethambutol — 15 mg/kg po daily.
- Pyrazinamide — 1.5 g po daily (< 50 kg)
2 g po daily (≥ 50 kg).

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.[7,8]

† Sputum smear positive

NOTES

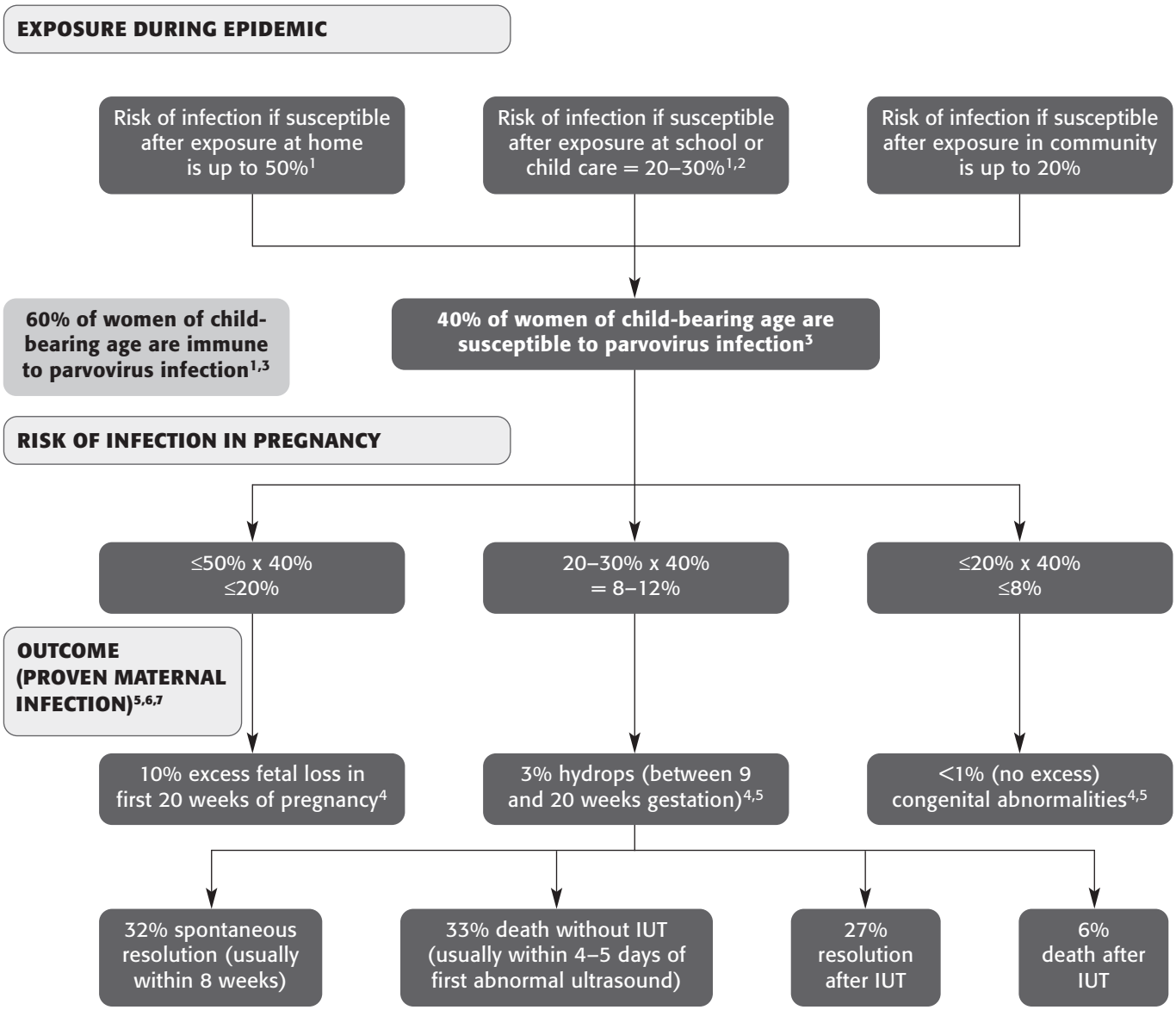
- Most cases of neonatal TB occur as a result of airborne spread after delivery. However, separation of mother and neonate is only necessary if the mother is sick enough to require hospitalisation for TB.[5]
- Other family members and close contacts should be assessed for TB infection or disease. If a close contact is infectious, separation is preferable, but, if impossible, INH prophylaxis should be given 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 congenital TB.[8,9]
- If congenital infection is suspected, the placenta should be examined and microscopy, culture and histology performed.
- The Mantoux test is likely to be negative for the first few weeks of life, even if the neonate has TB.[3,4,10]
- Mantoux conversion may be delayed for up to 6 months; thus INH prophylaxis must be continued until this time.

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 5-15 mg/kg po daily for 6 months (Pyridoxine 10 mg po daily must be added for breastfed infants).
- Rifampicin 10–20 mg/kg po daily for 6 months.
- Pyrazinamide 15–30 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 15 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 15–20 mg/kg im daily may also be used in place of Amikacin or Ethionamide, but injection is painful and it is difficult to obtain.
- These drugs are excreted in breast milk. If a breastfeeding 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.

ALGORITHM 1

Parvovirus B19 Infections During Pregnancy: Risk Assessment



NOTES

- It is not practicable to prevent exposure at home. Exclusion from work of pregnant school teachers or child care workers is not recommended during a parvovirus epidemic (nor is exclusion of infected children).
- Susceptible pregnant HCW should not care for patients with known complicated parvovirus infection (eg aplastic crisis) or chronic parvovirus infection (eg in an immunocompromised host).
- Routine antenatal screening is not indicated.
- There is a 50% risk of transmission from an infected mother to her fetus.[8]
- Fetal loss = 15%, compared with 5% overall (ie excess loss = 10%).[4]
- Onset of hydrops 2-17 weeks (average 5 weeks) after maternal infection.
- Congenital abnormalities — anecdotal reports only (less than rate of major malformations in newborns of 2%).[4,5]
- IUT = intrauterine transfusion.

OVERALL RISKS

	Any pregnant woman exposed to parovovirus	Pregnant woman with proven recent infection
Excess fetal loss in first 20 weeks	0.4–1% (1 in 100–1 in 250)	5% (1 in 20)
Death from hydrops or its treatment	0.05–0.1% (1 in 850–1 in 2000)	0.6% (1 in 170)

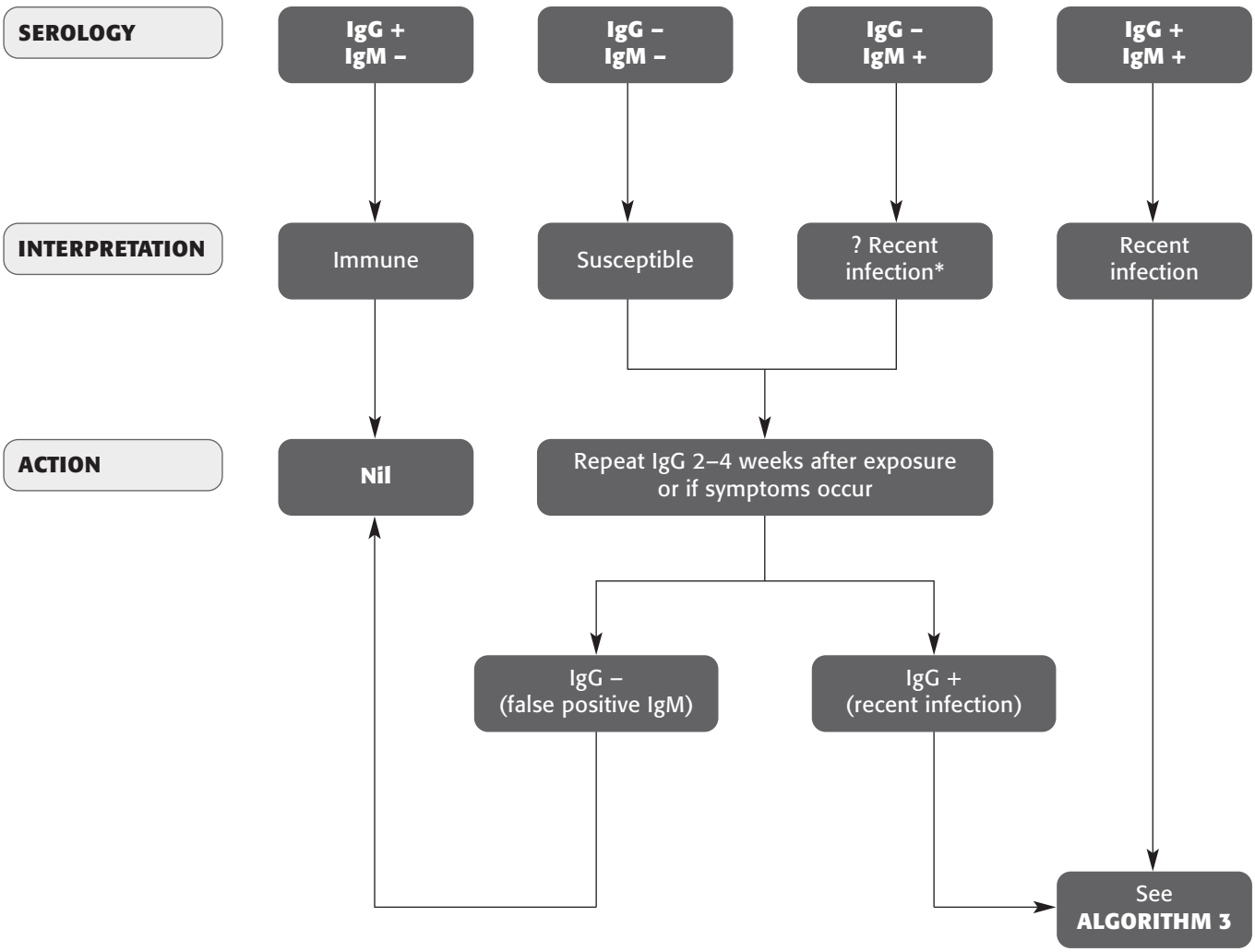
Pregnant women who are exposed should be informed of risks, and offered serological testing.

ALGORITHM 2

Parvovirus B19 Infections During Pregnancy: Antenatal Diagnosis and Management

DIAGNOSIS OF INFECTION FOLLOWING CONTACT OR ILLNESS WITH RASH DURING PREGNANCY[9,10]

(Check rubella serology – symptoms are similar and cross-reactions can occur)



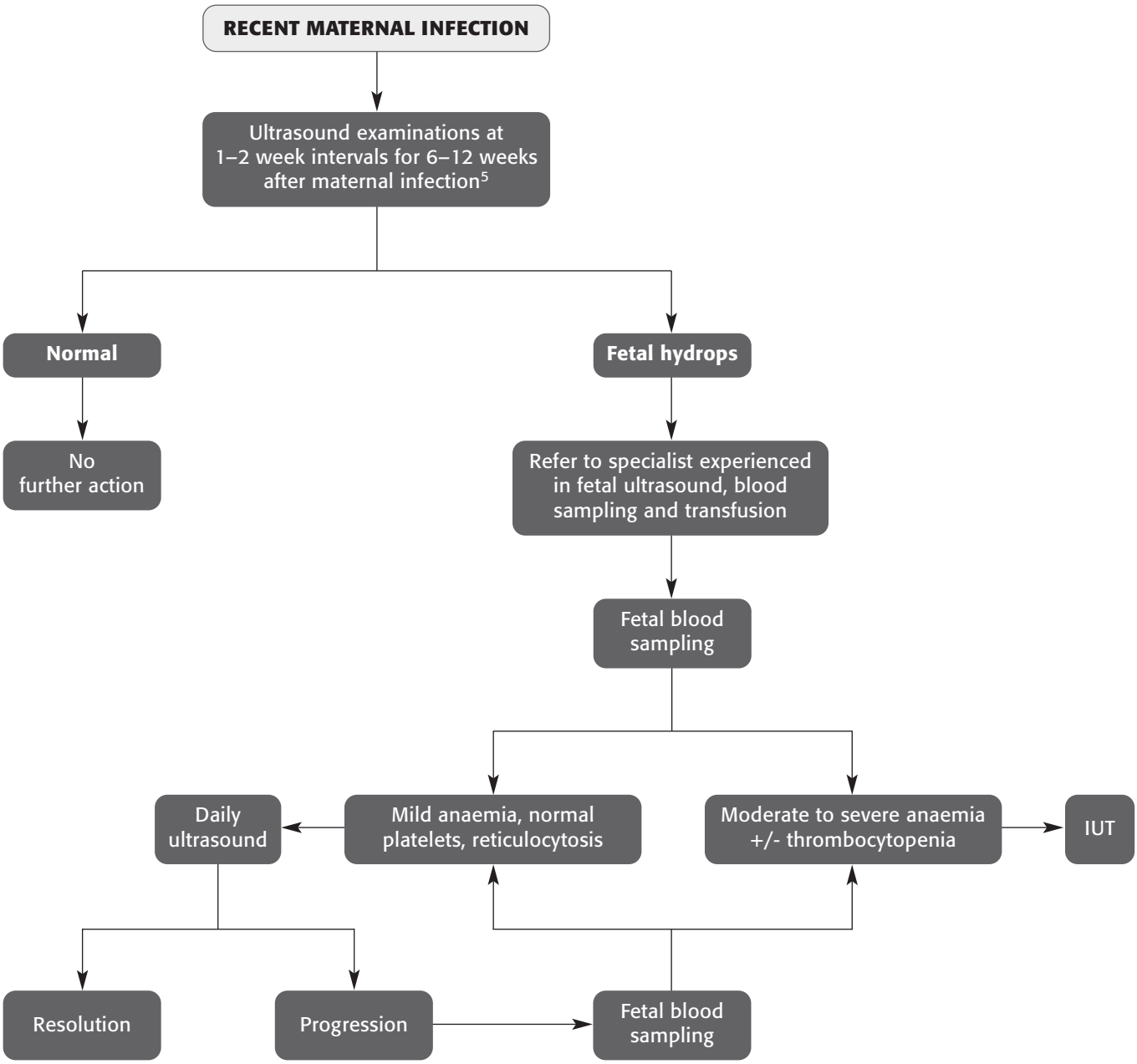
NOTES

- IgM is detectable within 1–3 weeks of exposure and usually remains detectable for 2–3 months.
- IgM reference standard: mu-capture radioimmunoassay (MACRIA).
- 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)[9]
  Note: absence of IgM does not exclude recent infection

* Symptoms include non-specific illness, rash, and/or arthralgia/arthritis).

ALGORITHM 3

Parvovirus B19 Infections During Pregnancy: Management of Proven Maternal Infection

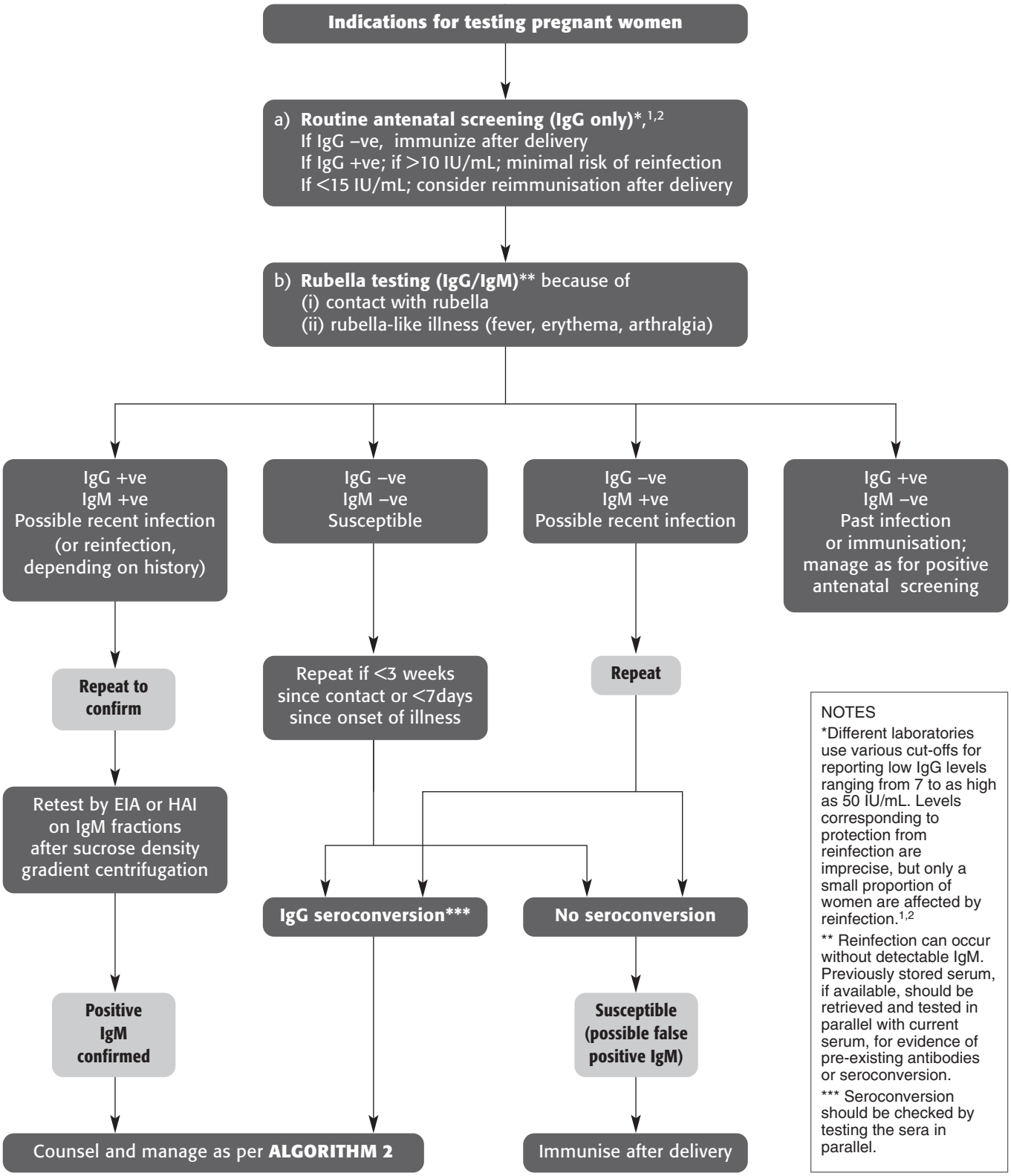


NOTES

- 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.
- a-fetoprotein levels are not helpful – previous reports that increased levels predict poor outcome have not been confirmed.[5]
- Pregnancy should be monitored by repeated ultrasound examination to detect hydrops fetalis.
- A fetus with mild hydrops may be profoundly anaemic.
- Fetal blood sampling – measure haemoglobin, platelets and reticulocyte count.
- No specific investigation is indicated in normal infants.
- Infants in whom hydrops has occurred and resolved should be monitored for evidence of anaemia.

ALGORITHM 1

Diagnosis of Suspected Maternal Rubella Infection



NOTES

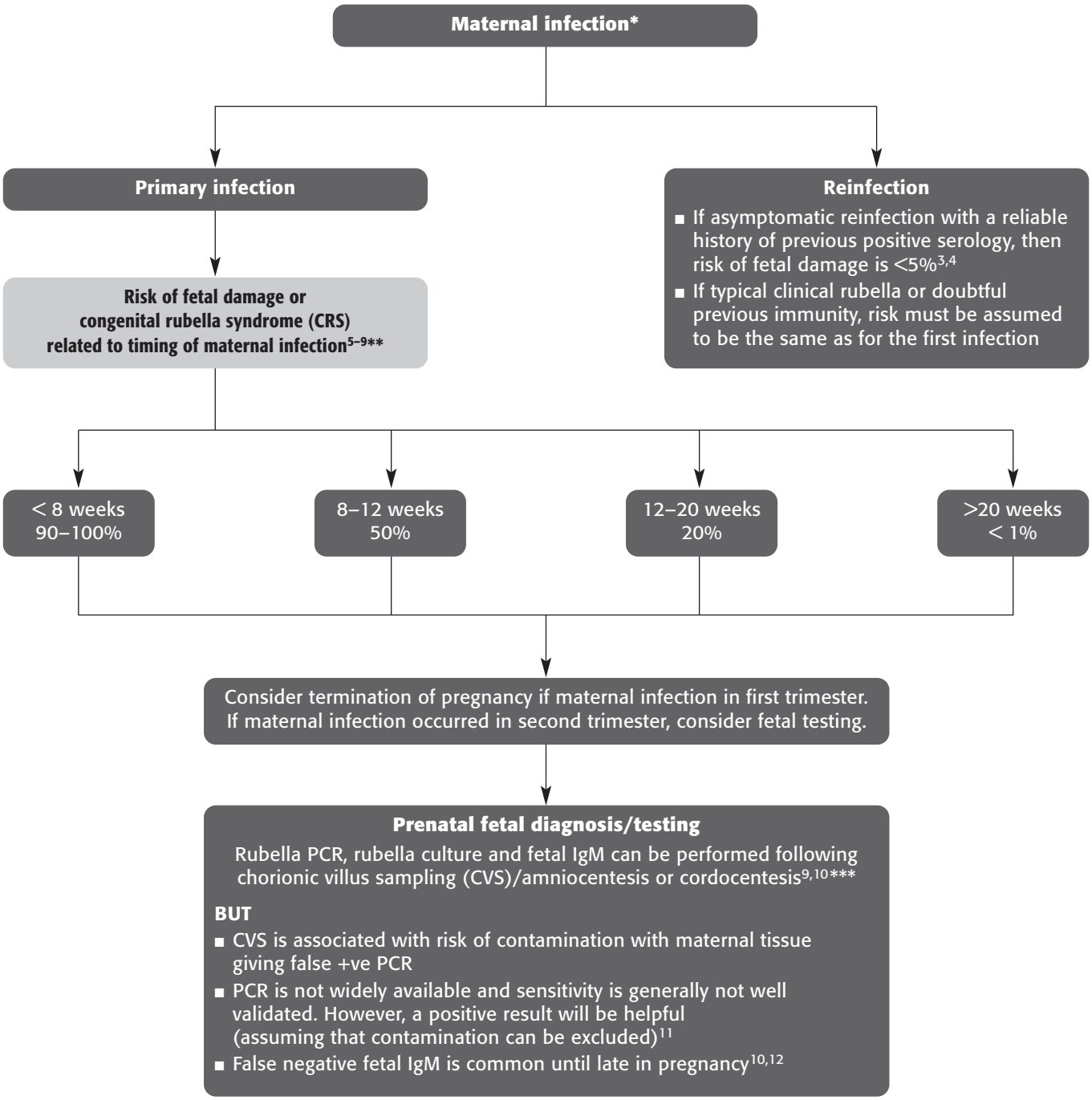
*Different laboratories use various cut-offs for reporting low IgG levels ranging from 7 to as high as 50 IU/mL. Levels corresponding to protection from reinfection are imprecise, but only a small proportion of women are affected by reinfection.[1,2]

** 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.

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

ALGORITHM 2

Management of Proven Maternal Rubella Infection



NOTES

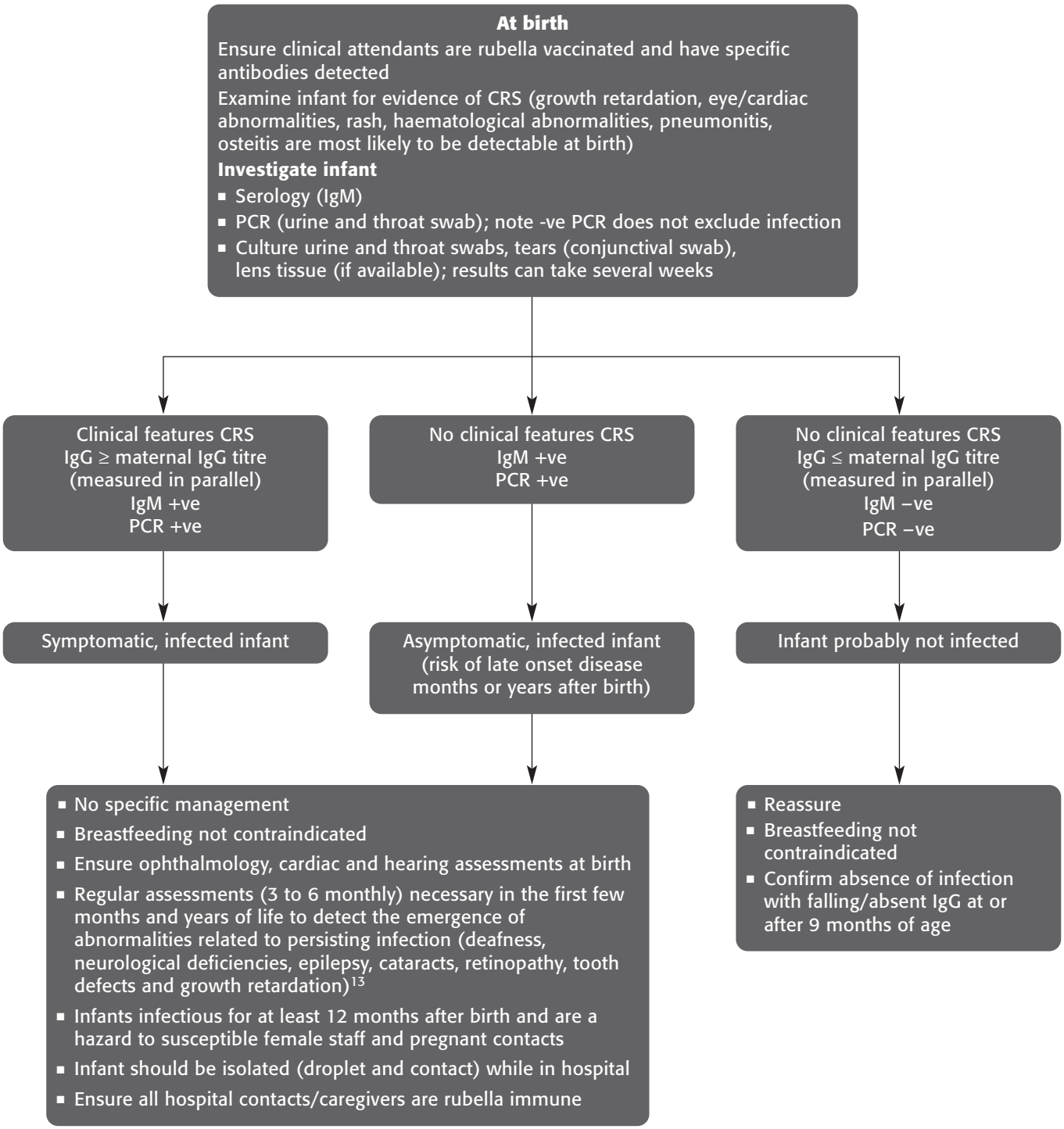
* No specific management of mother (rubella specific immunoglobulin not available and normal human immunoglobulin NOT indicated).

** Transmission risks and details of incidence and type abnormalities can be found in textbooks[8,9]

*** Contact your local Public Health Virology Laboratory for information about the availability of rubella culture or PCR

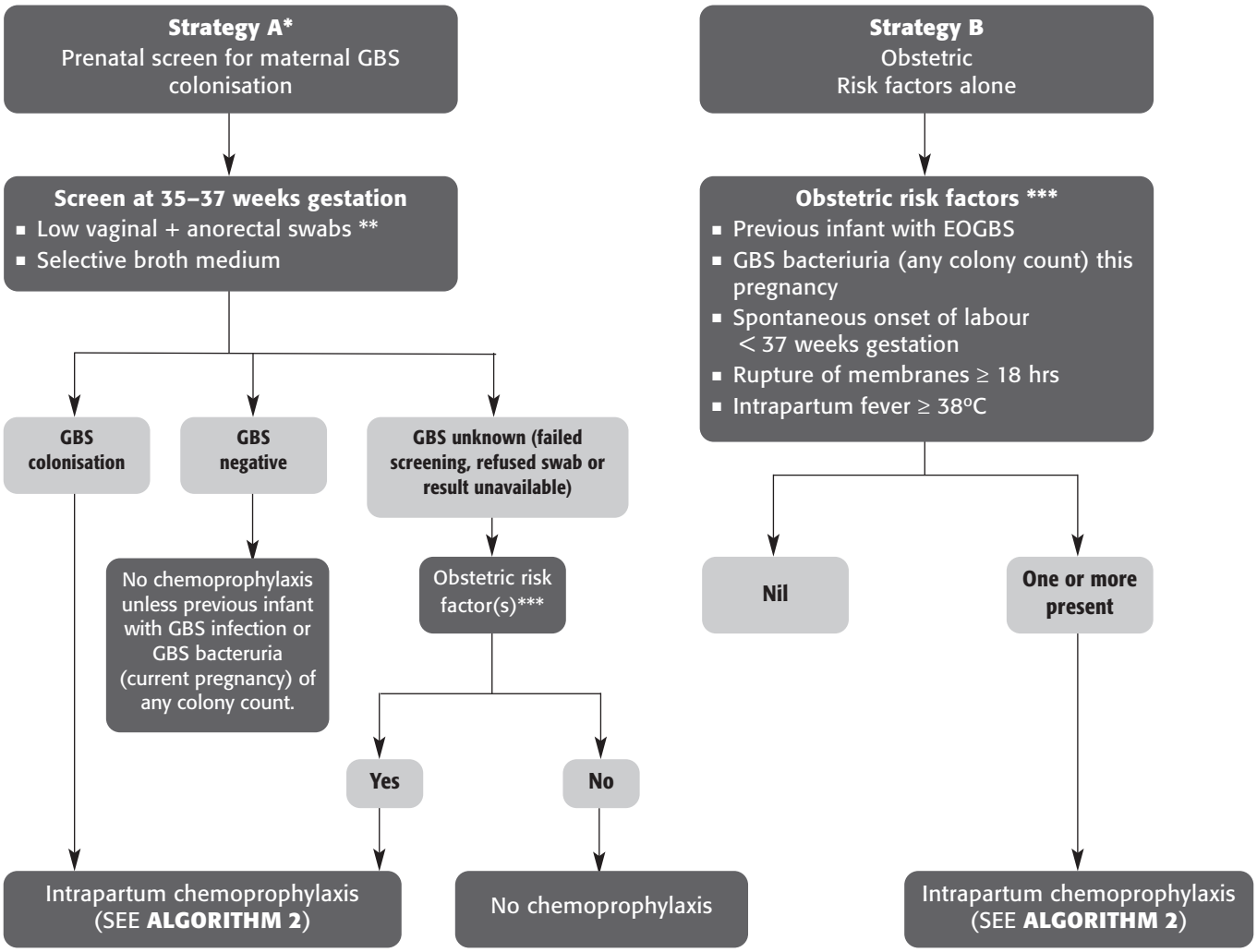
ALGORITHM 3

Management and Follow Up of the Infant at Risk of Infection



ALGORITHM 1

Management of Pregnancy with Respect to Group B Streptococcal (GBS) Infection

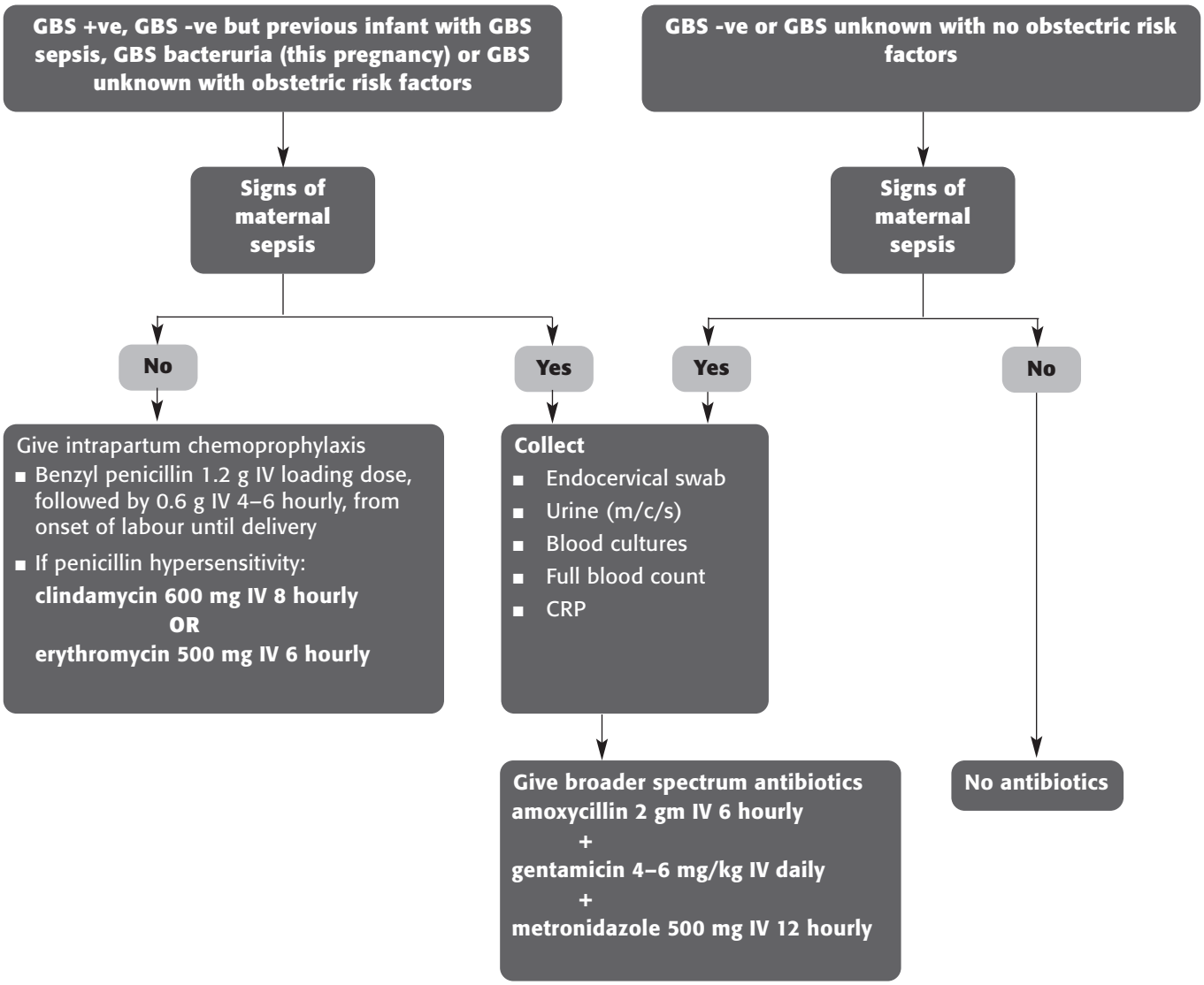


NOTES

- Colonisation of the genital tract with GBS occurs in approximately 20% of women. Early onset GBS disease (EOGBS, within the first week of life) occurs at a rate of 1–2 per 1000 live births, although this is declining.[1]
- Intrapartum chemoprophylaxis is highly effective in reducing neonatal colonisation with GBS and preventing EOGBS.[1,2,3]
- * A recent Centers for Disease Control & Prevention (CDC) study in >600,000 live births found the "Screening" approach >50% more effective than the "Risk Factor" approach in preventing GBS disease.[4] The application of this in Australia remains to be determined.
- Prenatal screening (<35w) to detect GBS does not reliably predict carriage at delivery. The later in pregnancy 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 vaginal swab.[6] A single swab may be used, provided the vagina is swabbed prior to the anorectal area. Samples may be obtained by the patient.
- Maternal carriage of GBS does not predict premature rupture of membranes or preterm delivery.[7]
- Selective broth media are more sensitive than standard solid media. Examples include NPC broth (Todd-Hewitt broth supplemented with colistin, nalidixic acid and crystal violet) and semi-solid new Granada medium.[8]
- *** The obstetric factors listed are associated with increased risk for EOGBS.[2,9] However, 25-30% of cases are not associated with maternal risk factors.[2]
- 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.

ALGORITHM 2

Intrapartum Antibiotic Prophylaxis for Prevention of Early Onset Neonatal GBS Sepsis

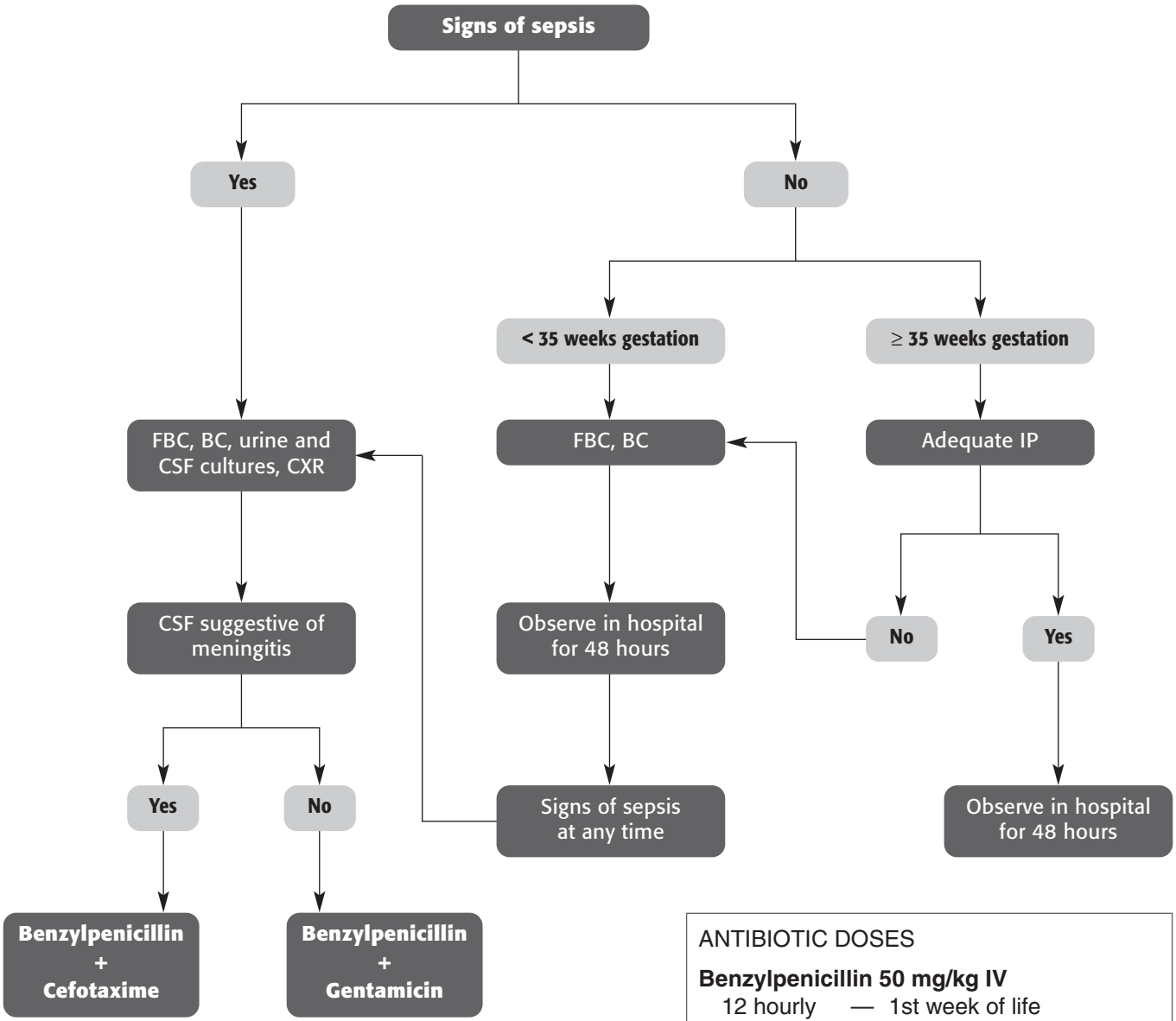


NOTES

- 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 are active in vitro against GBS, but their efficacy in prevention of EOGBS has not been evaluated. Clindamycin resistance has been reported in 3.4% of invasive GBS isolates, and erythromycin resistance in 7.4% (USA). Nonetheless, they are recommended by most experts as alternatives for women who have hypersensitivity to penicillin.[6]
- Pathogens responsible for chorioamnionitis include GBS, anaerobic cocci, and enteric Gram-negative bacilli (often polymicrobial).

ALGORITHM 3

Management of Infant Born to Mother Who Received Intrapartum Prophylaxis



NOTES

- The relative risk of EOGBS is significantly greater in preterm neonates than in babies born at term
- Duration of intrapartum prophylaxis (IP) is inversely proportional to the percentage of babies colonised with GBS
- Adequate IP is defined as ≥2 doses of antibiotics given before delivery
- FBC = full blood count; BC = blood culture; CSF = cerebrospinal fluid; CXR = chest X-ray
- Urine must be obtained by suprapubic aspiration or urethral catheter
- IP = intrapartum (antibiotic) prophylaxis
- Caftriaxone should be avoided in neonates.

ANTIBIOTIC DOSES

Benzylpenicillin 50 mg/kg IV

12 hourly — 1st week of life
6 hourly — over 1 week of age

Cefotaxime 50 mg/kg IV

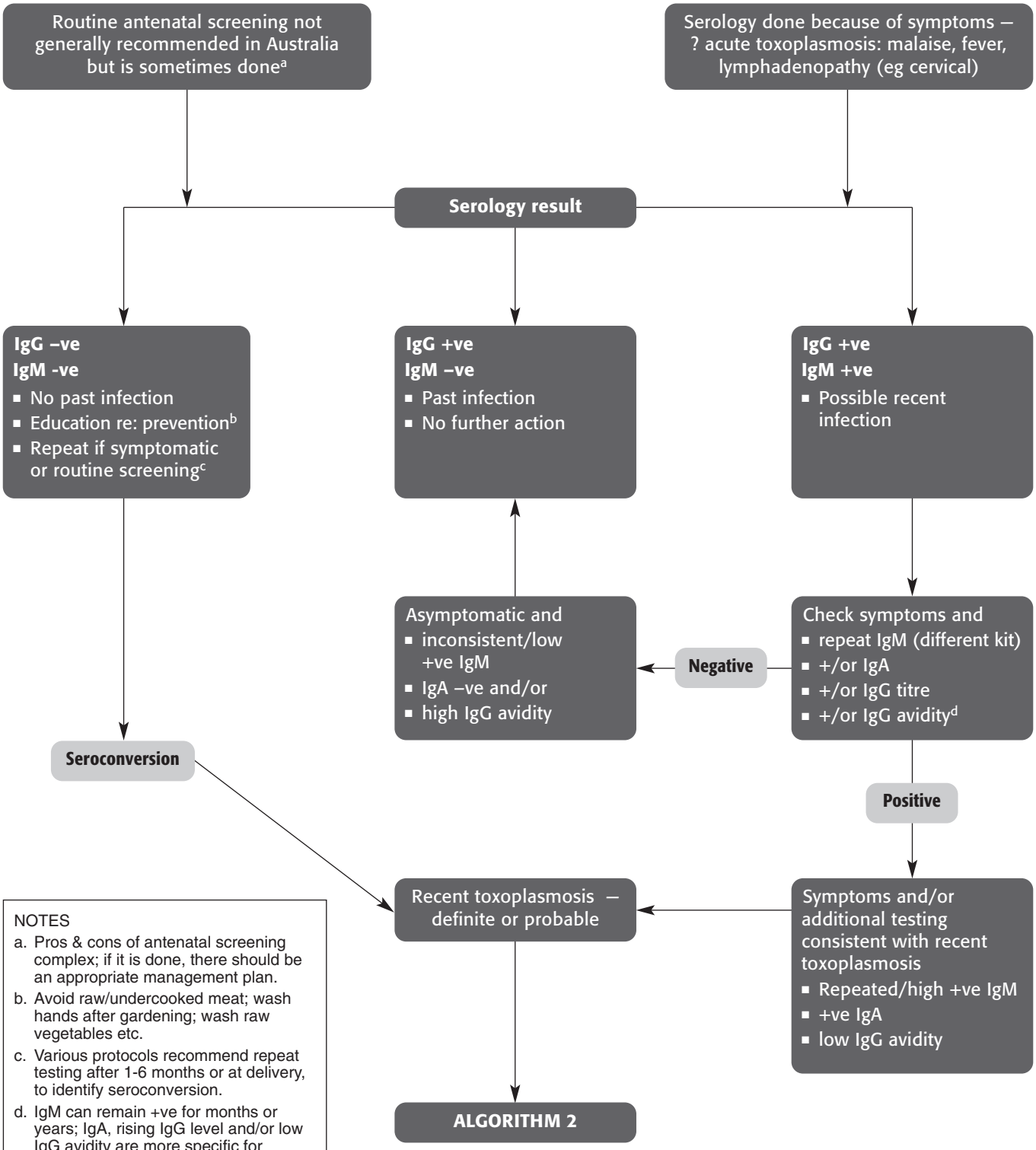
12 hourly — preterm
8 hourly — 1st week of life (term)
6 hourly — over 1 week of age

Gentamicin single daily dose

2.5 mg/kg — < 30 weeks gestation
3.5 mg/kg — 30–35 weeks gestation
5 mg/kg — 1st week of life (term)
7.5 mg/kg — 1 week–10 years of age

ALGORITHM 1

Antenatal Evaluation

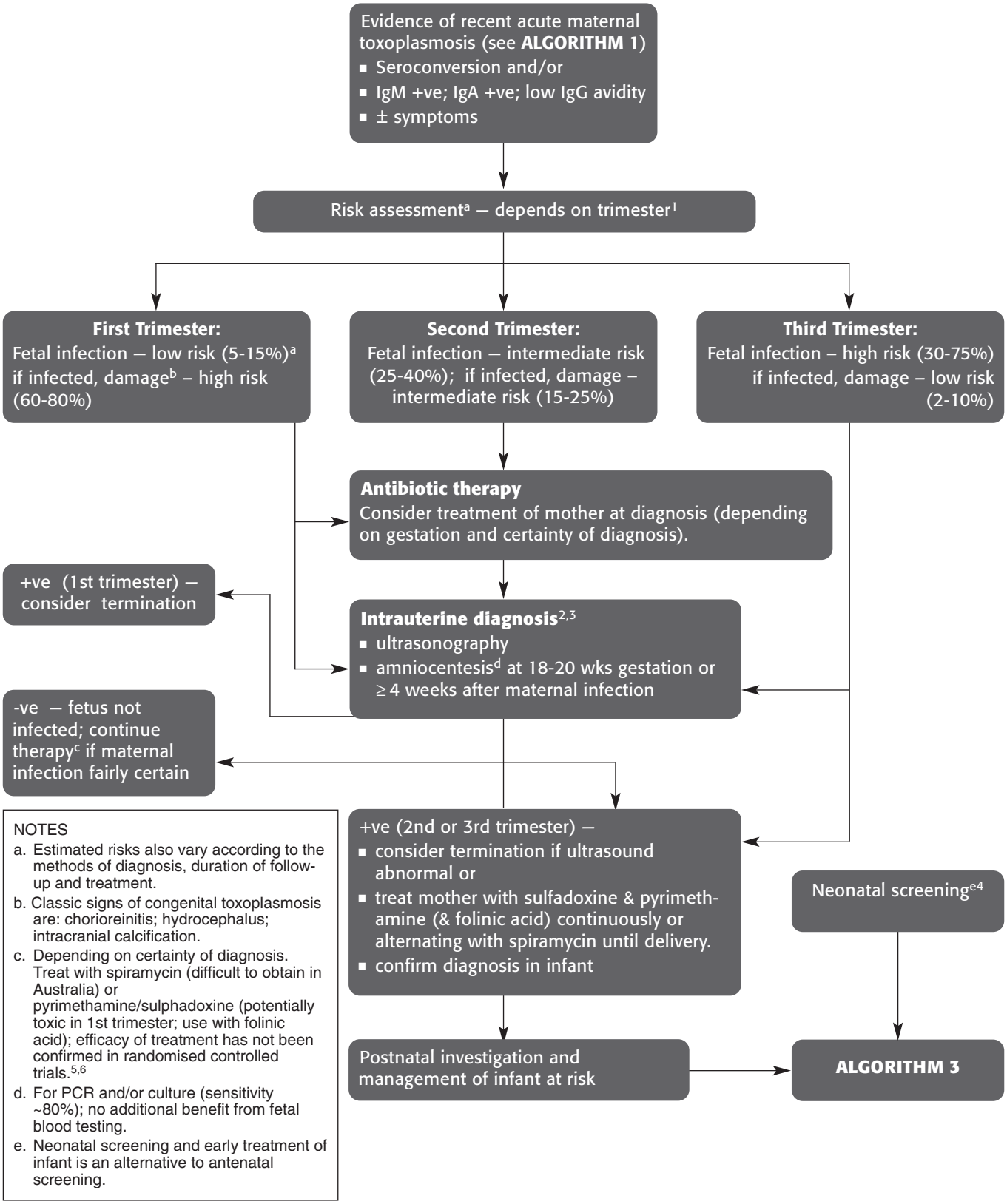


NOTES

a. Pros & cons of antenatal screening complex; if it is done, there should be an appropriate management plan.
b. Avoid raw/undercooked meat; wash hands after gardening; wash raw vegetables etc.
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)

ALGORITHM 2

Investigation and Management of Maternal Toxoplasmosis

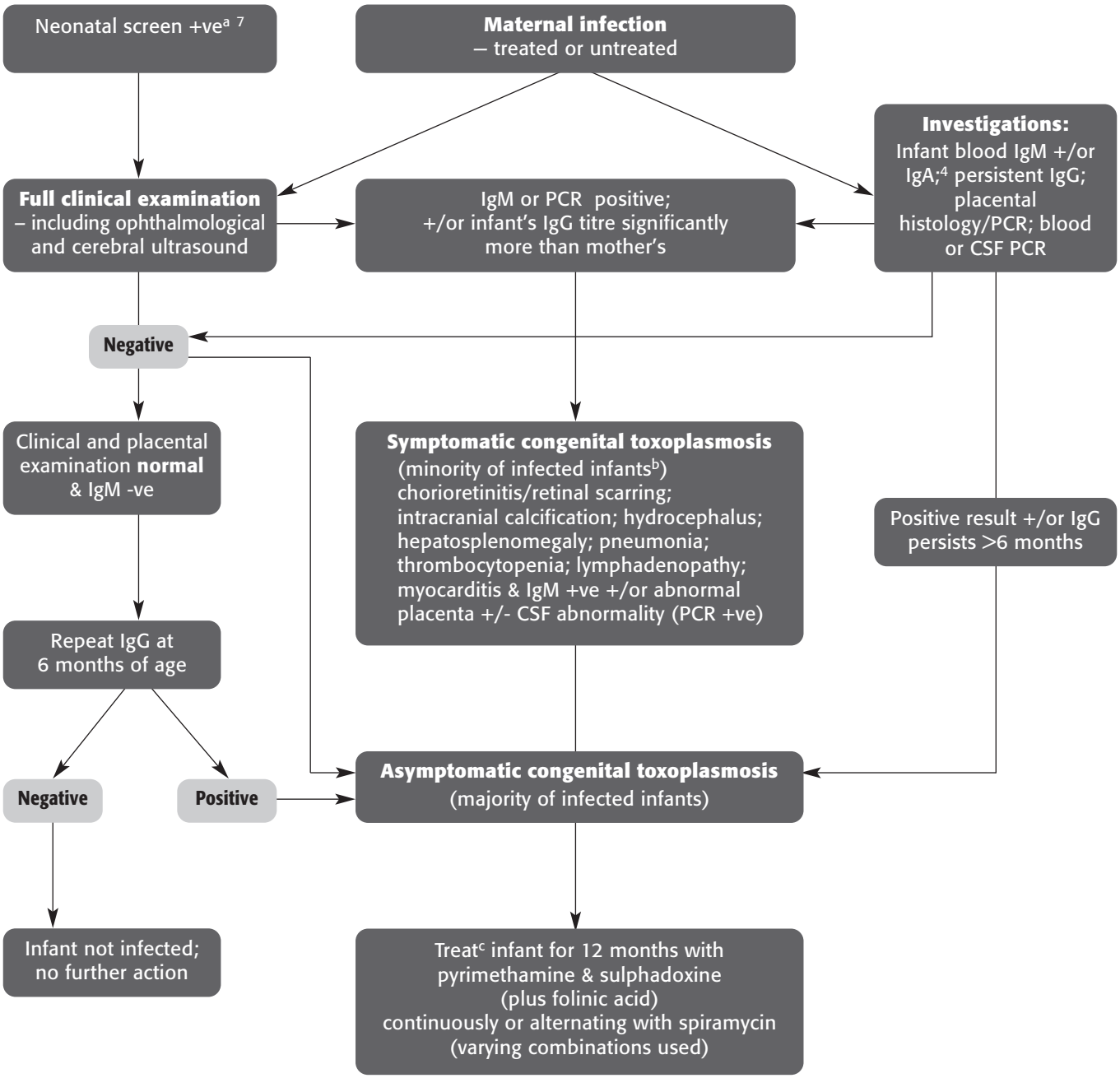


NOTES

a. Estimated risks also vary according to the methods of diagnosis, duration of follow-up and treatment.
b. Classic signs of congenital toxoplasmosis are: chorioreinitis; hydrocephalus; intracranial calcification.
c. Depending on certainty of diagnosis. Treat with spiramycin (difficult to obtain in Australia) or pyrimethamine/sulphadoxine (potentially toxic in 1st trimester; use with folinic acid); efficacy of treatment has not been confirmed in randomised controlled trials.[5,6]
d. For PCR and/or culture (sensitivity ~80%); no additional benefit from fetal blood testing.
e. Neonatal screening and early treatment of infant is an alternative to antenatal screening.

ALGORITHM 3

Investigation and Management of Infant at Risk of Toxoplasmosis



NOTES

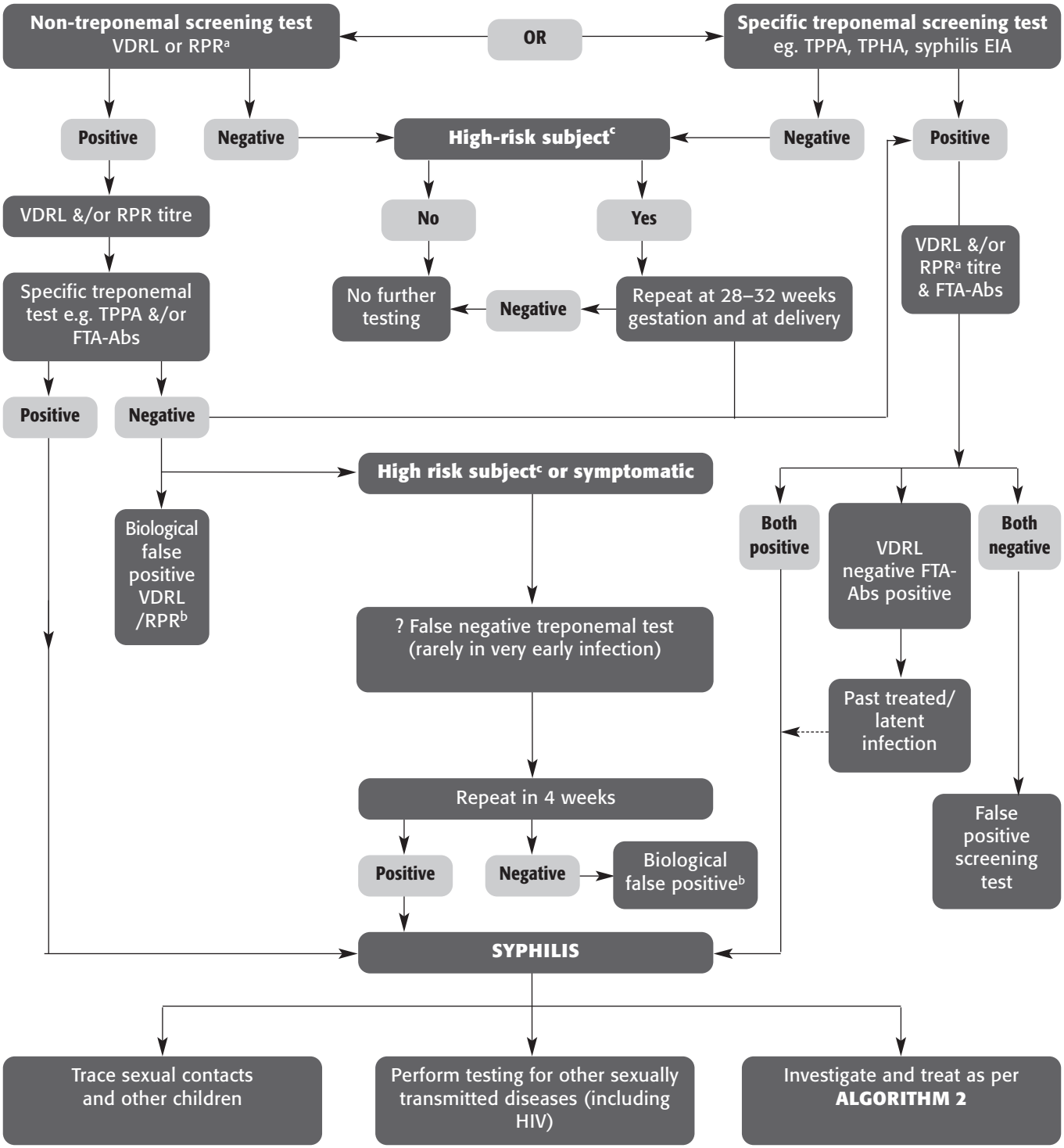
a. Neonatal screening not often done, but is an alternative to antenatal screening to detect infected infants for treatment.[7]

b. Proportion of infants infected and severity depends on when maternal infection occurred and if/how treated.

c. High incidence of longterm sequelae (eg chorioretinitis) in untreated infants even if asymptomatic at birth — can be reduced by treatment.

ALGORITHM 1

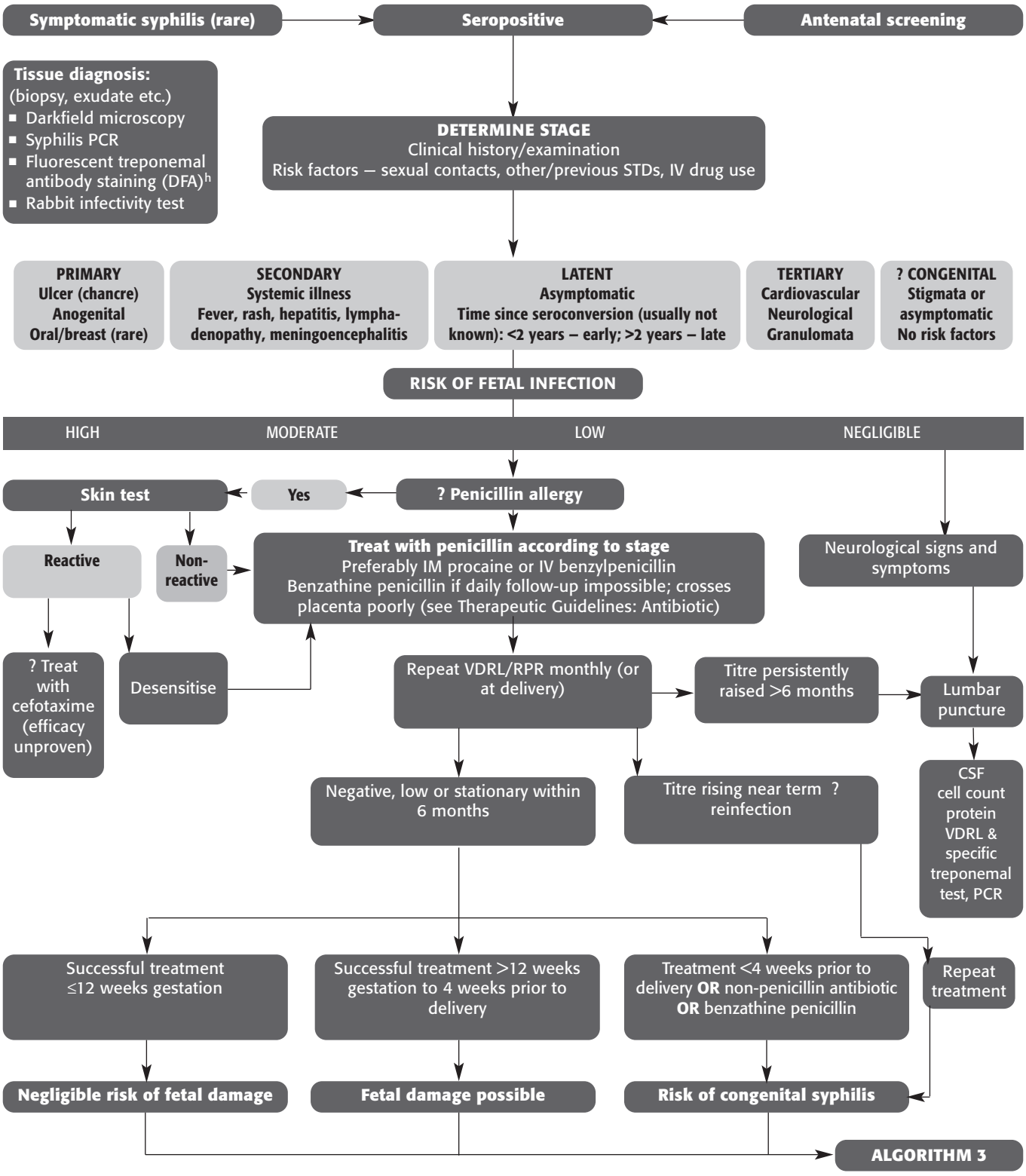
Routine Antenatal Screening for Syphilis



NOTE:
Lettered superscripts refer to notes (see page 44). For reading list, see page 54.

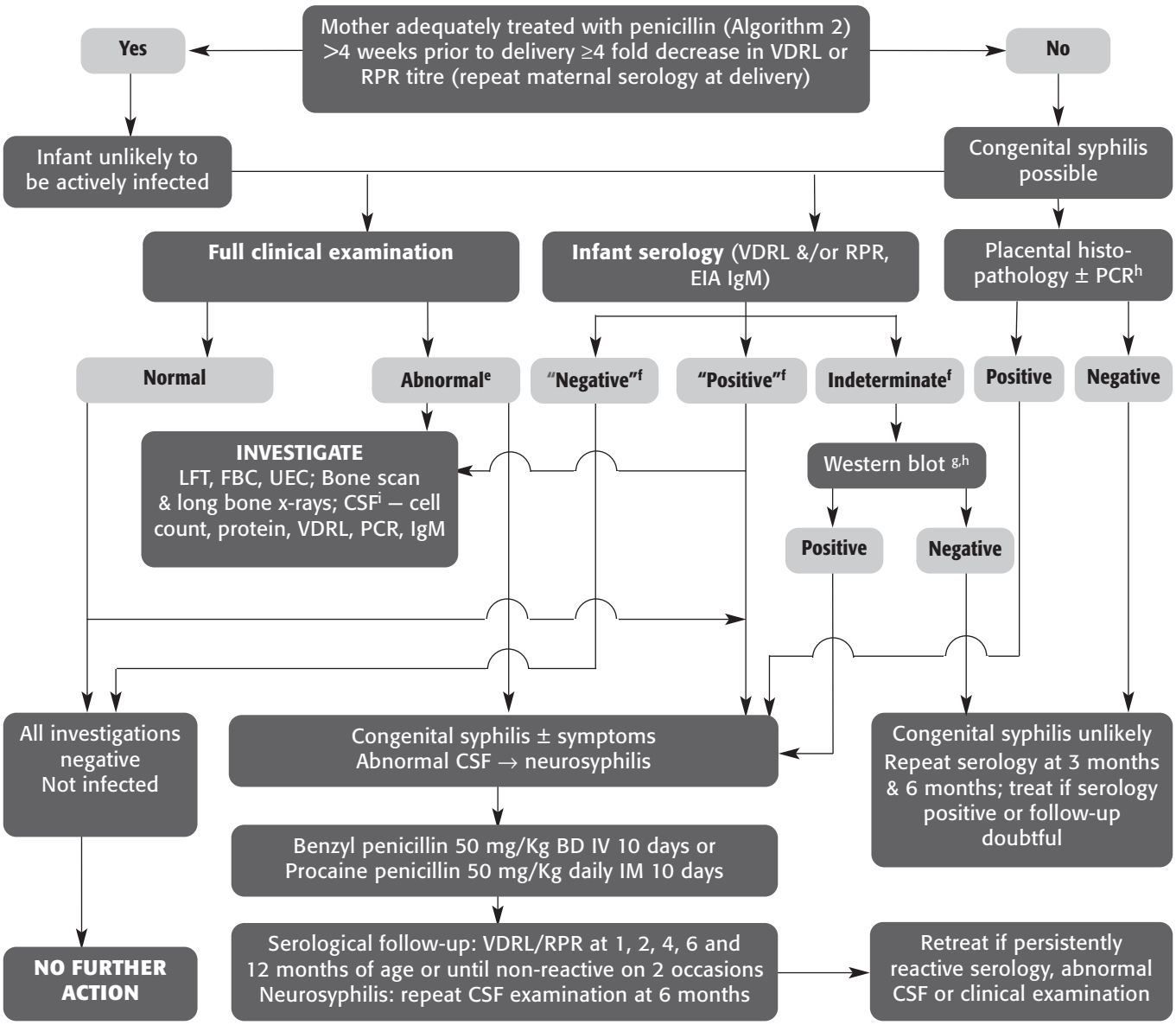
ALGORITHM 2

Investigation and Treatment of Maternal Syphilis



ALGORITHM 3

Investigation and Management of a Neonate[j] Born to a Mother with Syphilis

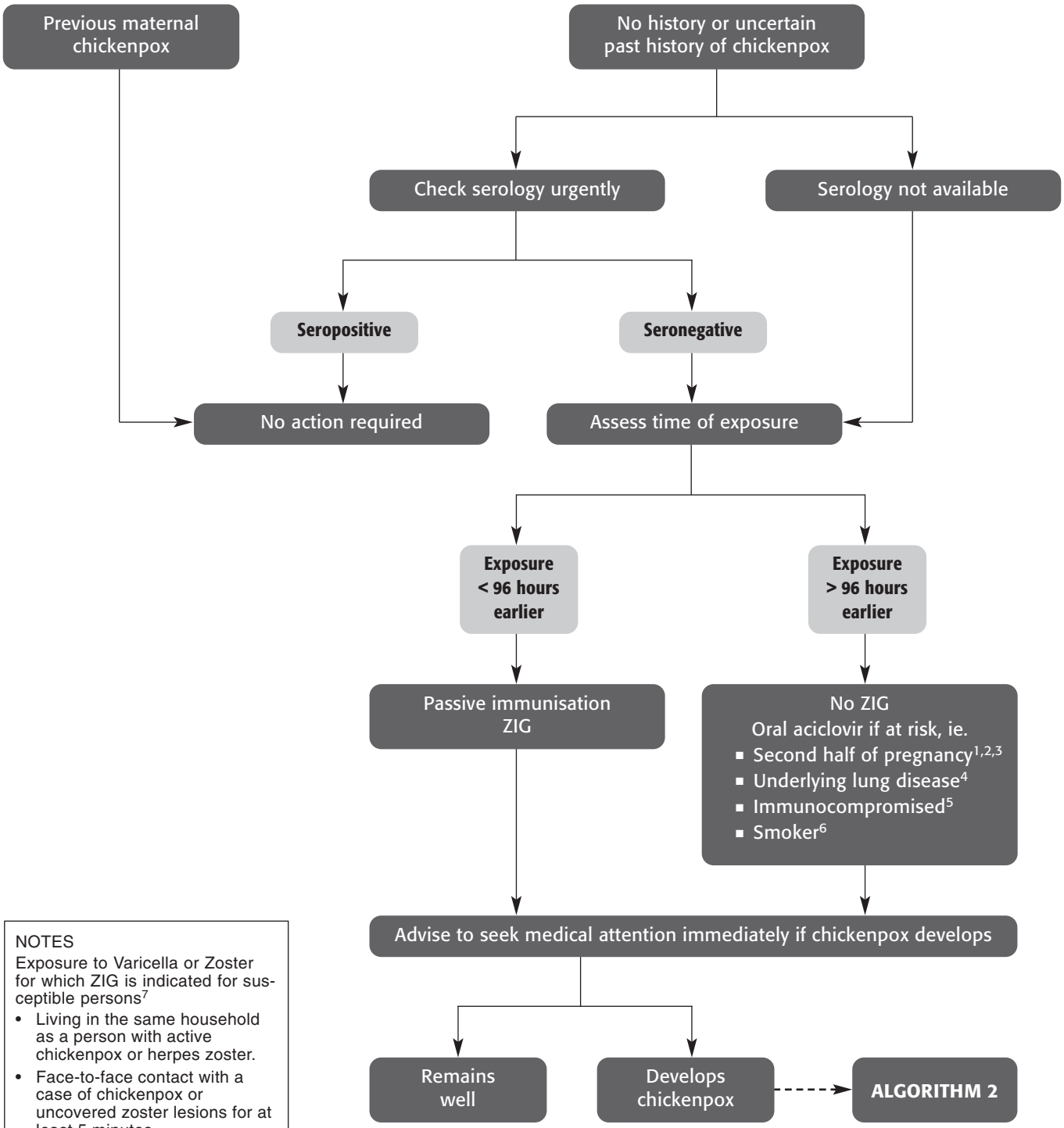


NOTES

a. VDRL has largely been replaced by RPR (except for CSF examination). RPR titre is generally higher than VDRL and titres cannot be directly compared.
b. Biological false positive VDRL/RPR results occur in people with intercurrent viral and other infections, autoimmune diseases and in pregnancy.
c. High risk groups: young age, single, low socioeconomic status, poor education, poor antenatal care, substance abuse, prostitution.
d. Untreated maternal infection in the first trimester is more likely to produce fetal damage.
e. Clinical abnormalities suggestive of congenital syphilis include rash (maculopapular or vesicular), mucosal lesions, nasal discharge, hepatomegaly, bony tenderness and eye lesions. If serology is "negative" investigate for other causes.
f. Infant serology "negative" if VDRL/RPR titre at least four times less than the mother's and EIA IgM negative; "positive" if VDRL/RPR titre at least four times greater than the mother's and/or EIA IgM positive; indeterminate if otherwise.
g. Western blot "positive" if infant serum reacts with additional bands compared with mother's serum.
h. Western immunoblotting for syphilis antibodies, syphilis PCR and placental darkfield microscopy, PCR and fluorescent antitreponemal antibody staining are available as additional confirmatory tests in reference laboratories.
i. If CSF examination is not possible then give full 10 day penicillin course and, if possible, perform lumbar puncture at six months to exclude persistent neurosyphilis.
j. Infants whose mothers develop secondary or early latent syphilis within 1 year of delivery should be tested and treated if they have positive serology.
k. The clinical presentation of 'late' congenital syphilis (keratitis, deafness, Hutchinson's teeth etc.) may be delayed for several years and regular assessment may be warranted.
l. Serology should be performed on neonatal serum rather than cord blood because of the risk of contamination with maternal blood.

ALGORITHM 1

Exposure to Varicella Zoster Virus During Pregnancy



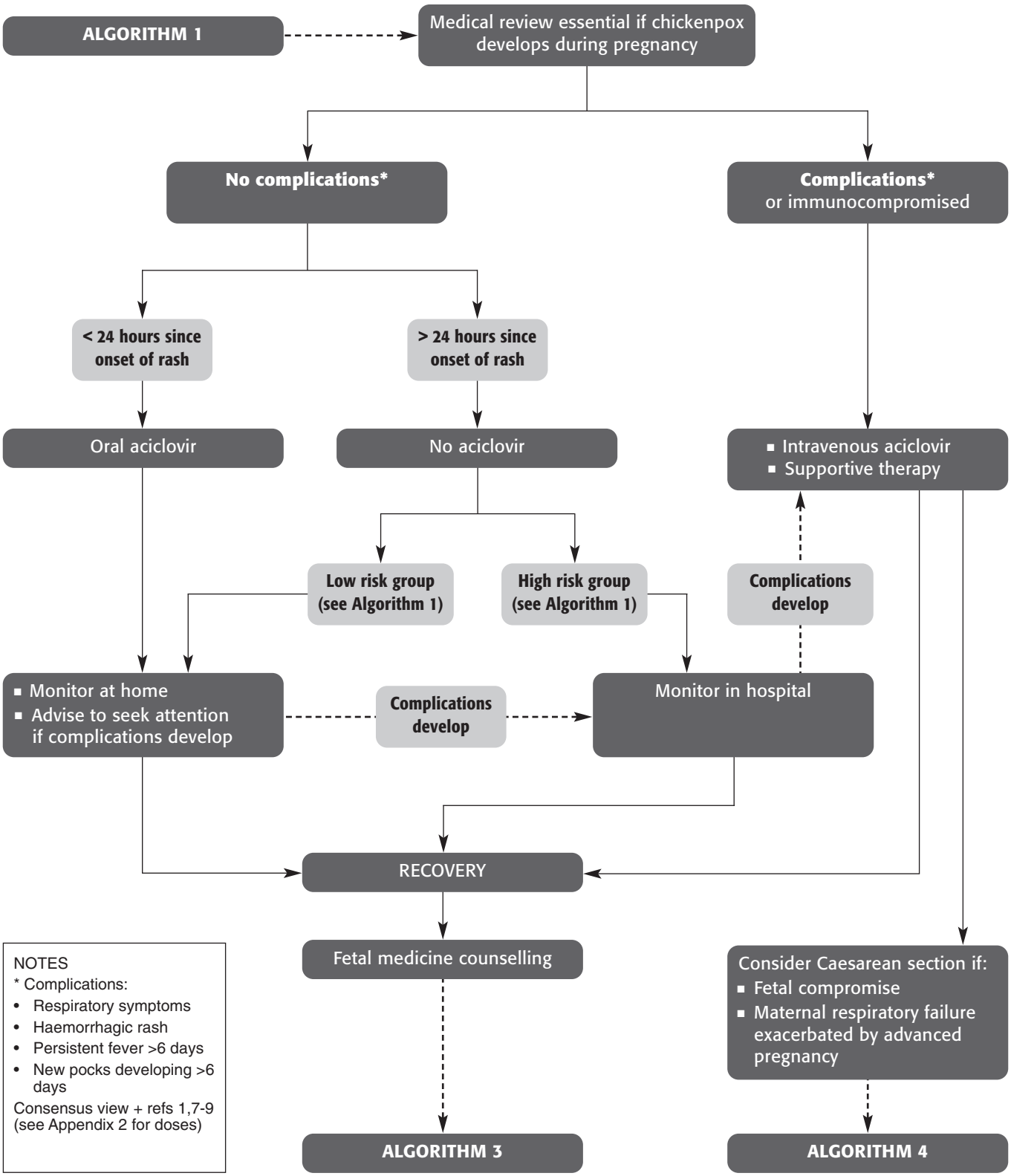
NOTES

Exposure to Varicella or Zoster for which ZIG is indicated for susceptible persons[7]

- Living in the same household as a person with active chickenpox or herpes zoster.
- Face-to-face contact with a case of chickenpox or uncovered zoster lesions for at least 5 minutes.

ALGORITHM 2

Management of Varicella Zoster in Pregnancy

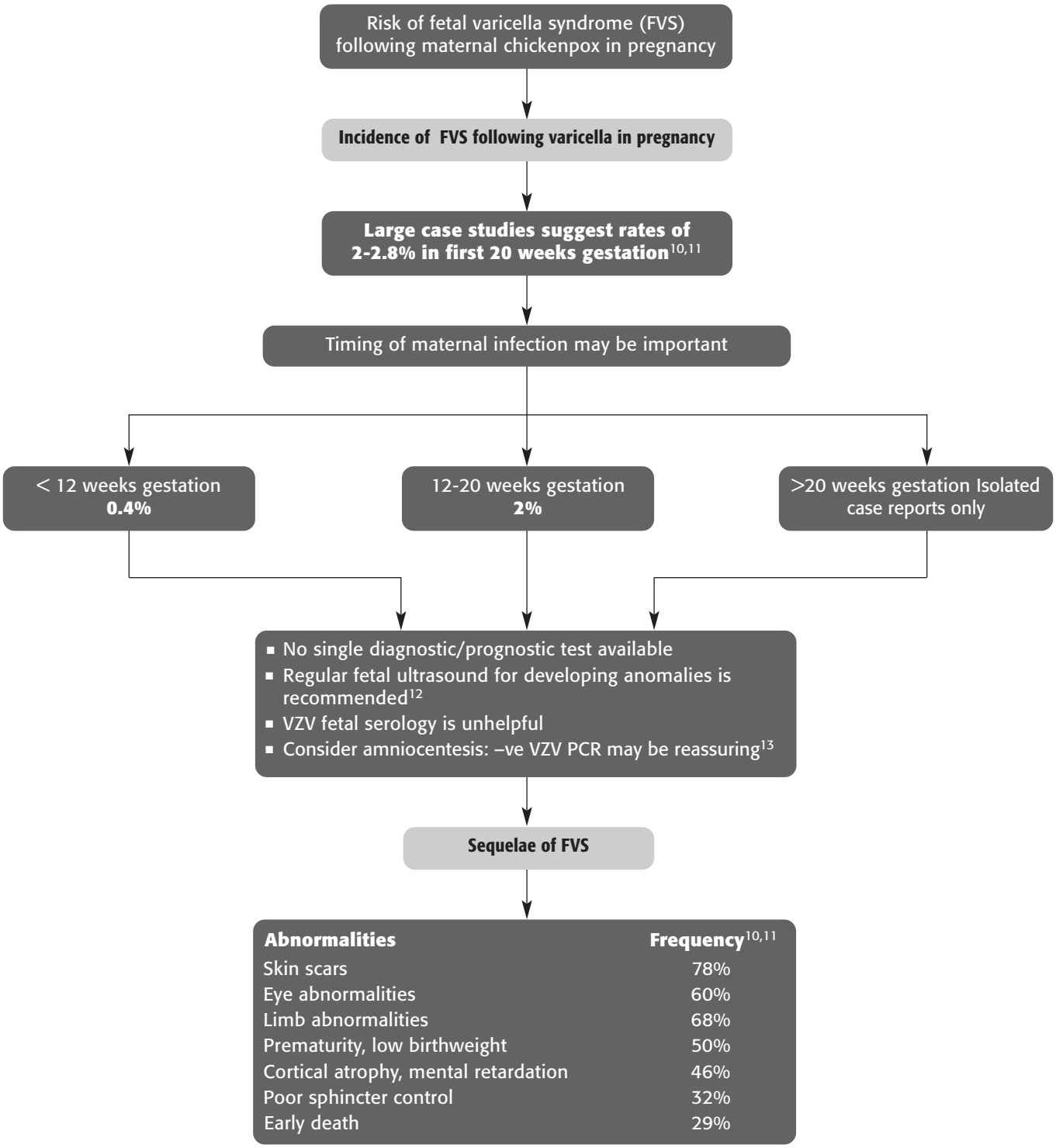


NOTES
* Complications:
- Respiratory symptoms
- Haemorrhagic rash
- Persistent fever >6 days
- New pocks developing >6 days

Consensus view + refs 1,7-9 (see Appendix 2 for doses)

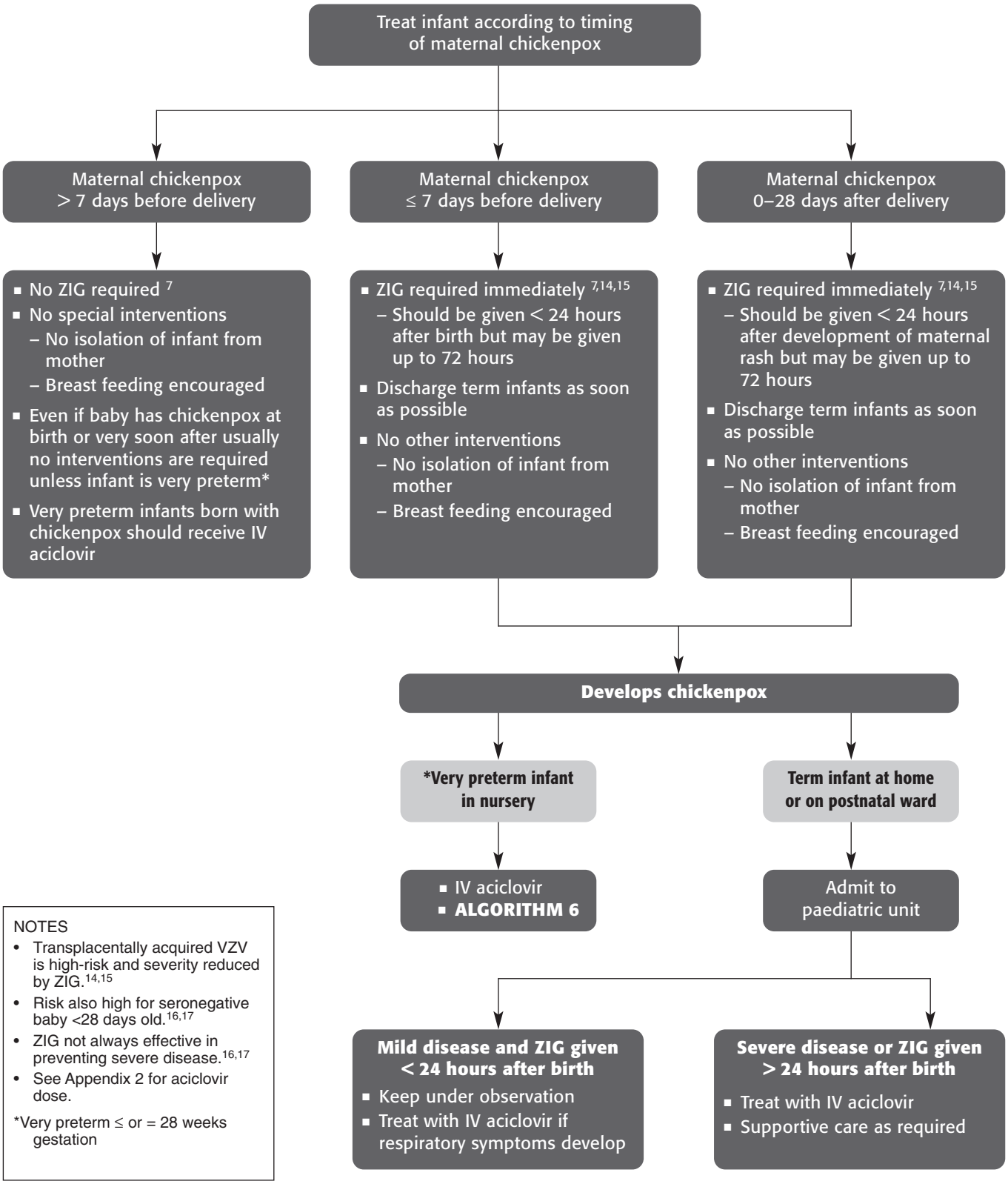
ALGORITHM 3

Fetal Medicine Counselling Following Varicella Zoster in Pregnancy



ALGORITHM 4

Management of Infants from Mothers with Perinatal Varicella Zoster



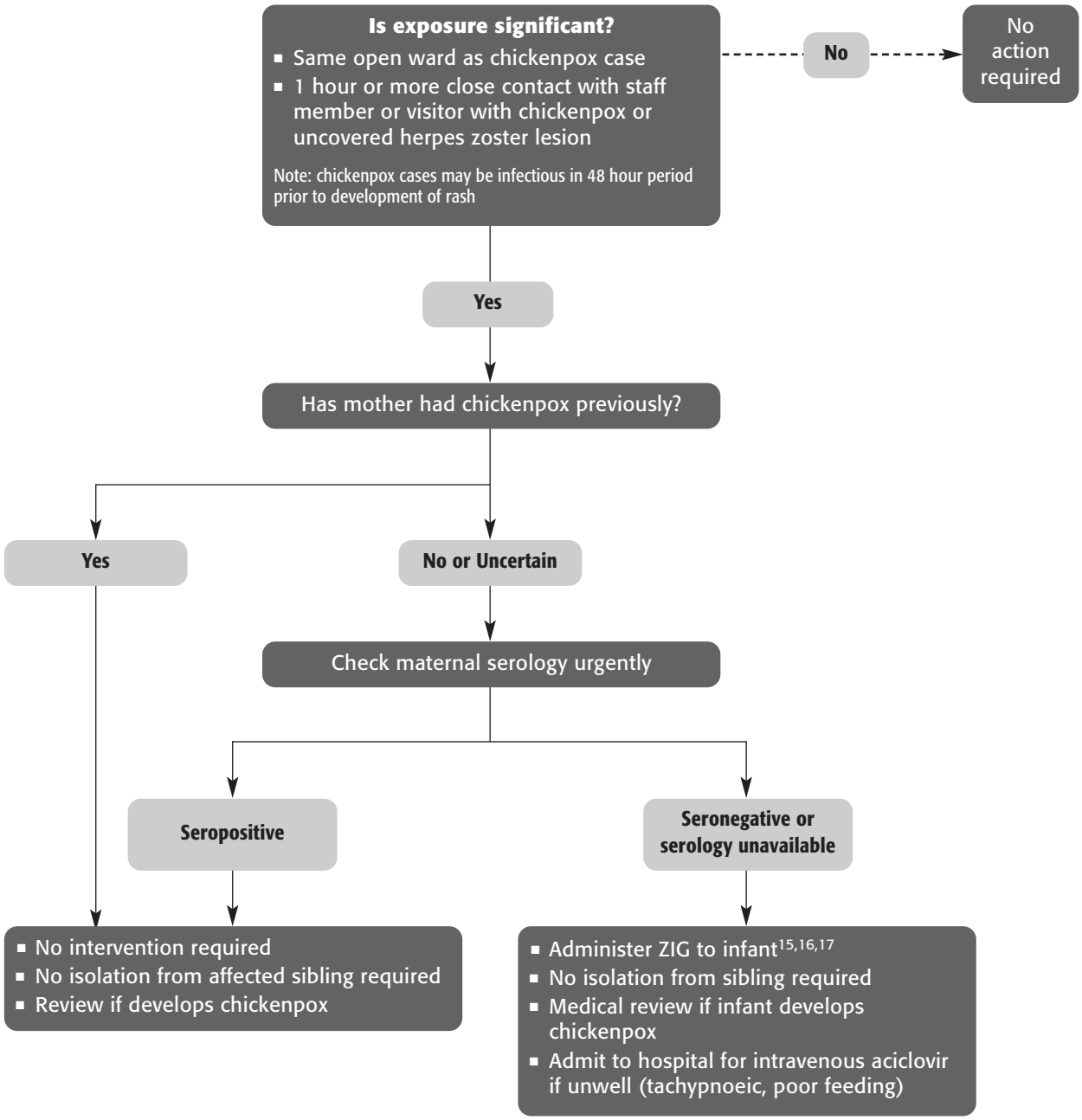
NOTES

- Transplacentally acquired VZV is high-risk and severity reduced by ZIG.[14,15]
- Risk also high for seronegative baby <28 days old.[16,17]
- ZIG not always effective in preventing severe disease.[16,17]
- See Appendix 2 for aciclovir dose.

*Very preterm ≤ or = 28 weeks gestation

ALGORITHM 5

Management of Term Neonates Exposed to Varicella Zoster in the Postnatal Wards or at Home

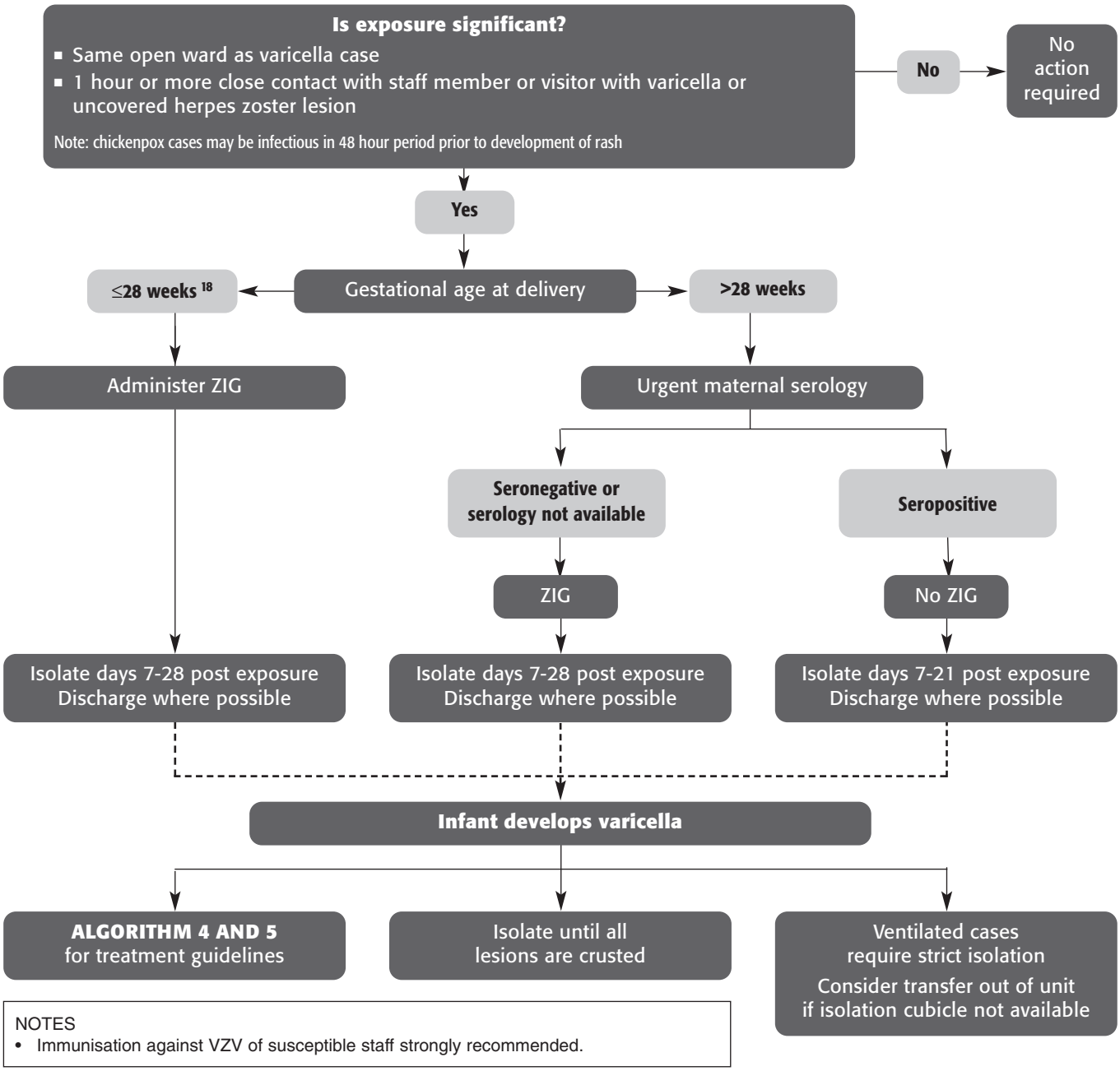


NOTES
Exposure to Varicella or Zoster considered to be significant within the neonatal unit or postnatal ward.

- Patient sharing the same open ward as case of chickenpox or zoster.
- Face-to-face contact with a case of chickenpox or uncovered zoster lesions for at least 5 minutes.
- Contact for 1 hour or more with case (either staff or patient) with chickenpox lesions or who developed lesions ≤ 24 hours later.

ALGORITHM 6

Treatment and Isolation of Infants Exposed to Varicella Within the Neonatal Unit



NOTES
- Immunisation against VZV of susceptible staff strongly recommended.

APPENDIX 1

Varicella zoster immune globulin

High titre varicella zoster immune globulin (ZIG) is available from the Red Cross Blood Transfusion Service in Australia on a restricted basis for the prevention of varicella in high risk subjects. Each vial contains 2 ml (16% solution of gammaglobulin fraction of human plasma from donors with high titre of varicella antibodies + thiomersal 0.01% w/v). The recommended dose is 2 ml for children 0-5 years, 4 ml for children 6-12 years and 6 ml for adults.[7]
Administration is by intramuscular injection with few adverse effects other than local discomfort reported. This can be lessened if the ZIG is at room temperature when administered. ZIG should never be given intravenously.[7]

APPENDIX 2

Aciclovir

Aciclovir appears to be a safe and relatively well tolerated drug although it may impair renal function if given to patients who are not adequately hydrated.[9] It is not licensed for use in pregnancy but appears to be safe[9] and its use is indicated in the high risk situations outlined.
The recommended intravenous dose for treating VZV infection in adults and infants is 10-20 mg/kg every 8 hours.
The oral dose for adults is 800 mg five times daily. The use of oral acyclovir in the neonate is not recommended.

Cytomegalovirus

References

1 Rawlinson WD. Broadsheet. Number 50: Diagnosis of human cytomegalovirus infection and disease. Pathology 1999; 31(2): 109–15.

2. Lazzarotto T, Spezzacatena P, Pradelli P et al. Avidity of immunoglobulin G directed against human cytomegalovirus during primary and secondary infections in immunocompetent and immunocompromised subjects. Clin. Diagn. Lab. Immunol. 1997; 4: 469–73.

3. Donner C, Liesnard C, Brancart F et al. Accuracy of amniotic fluid testing before 21 weeks' gestation in prenatal diagnosis of congenital cytomegalovirus infection. Prenat.Diagn. 1994; 14: 1055–9.

4. Lipitz S, Yagel S, Shalev E et al. Prenatal diagnosis of fetal primary cytomegalovirus infection. Obstet. Gynecol. 1997; 89: 763–7.

5. Gouarin S, Palmer P, Cointe D, et al. Congenital HCMV infection: a collaborative and comparative study of virus detection in amniotic fluid by culture and by PCR. J Clin Virol. 2001; 2: 47-55.

6. Lazzarotto T, Varani S, Guerra B et al. Prenatal indicators of congenital cytomegalovirus infection. J. Pediatr. 2000; 137:905.

7. Hayes K. Cytomegalovirus: The challenge of a common virus infection. Med. J. Aust. 1985; 142: 174–6.

8. Boppana SB, Rivera LB, Fowler KB, Mach M, Britt WJ. Intrauterine transmission of cytomegalovirus to infants of women with preconceptional immunity. N Engl J Med. 2001; 344: 1366-71.

9. Noyola DE, Demmler GJ, Nelson CT, et al. Early predictors of neurodevelopmental outcome in symptomatic congenital cytomegalovirus infection. J Pediatr 2001; 138: 325-31.

10. Fowler KB, McCollister FP, Dahle AJ et al. Progressive and fluctuating sensorineural hearing loss in children with asymptomatic congenital cytomegalovirus infection. J. Pediatr. 1997; 130(4): 624–30.

11. Ivarsson SA, Lernmark B, Svanberg L. Ten-year clinical, developmental, and intellectual follow-up of children with congenital cytomegalovirus infection without neurologic symptoms at one year of age. Pediatrics 1997; 99: 800–3.

12. Whitley RJ, Cloud G, Gruber W et al. Ganciclovir treatment of symptomatic congenital cytomegalovirus infection: results of a phase II study. National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. J. Infect. Dis. 1997; 175(5): 1080–6.

Acknowledgements

A/Professor William Rawlinson (SEALS Pathology, Virology, Prince of Wales Hospital, Randwick), and Dr Peter Robertson (SEALS Pathology, Serology, Prince of Wales Hospital, Randwick) for comments on diagnosis.

Enterovirus

Further Reading

1. Robath, HA. Antiviral therapy for enteroviral infections. Ped. Infect. Dis. J. 1999; 18: 632–3

2. Sawyer MH. Enteroviral Infections. Ped. Infect. Dis. J. 1999; 18: 1033–40

3. Kearns GL et al. Pleconaril Pharmacokinetics in Neonates Ped. Infect. Dis. J. 2000; 19: 833–8

4. Cherry JD. Enteroviruses. In: Infectious Diseases of the Newborn Infant. 4th Edn, 404–46. Remington JS, Klein JO, Eds, WB Saunders & Co., Philadelphia, 1995.

5. Rotbart HA, Webster D. Treatment of potentially life-threatening enterovirus infections with pleconaril. Clin Infect Dis 2001; 32: 228-35

6. Kearns GL, Bradley JS, Jacobs RF et al. Single dose pharmacokinetics of pleconaril in neonates. Pediatr Infect Dis J 2000; 19: 833-9.

Hepatitis B Virus

References

1. Juszczyk J. Clinical course and consequences of hepatitis B infection. Vaccine 2000; 18 Suppl 1: S23–S25

2. Schweitzer IL, Dunn AE, Peters RL et al. Viral hepatitis B in neonates and infants. Am. J. Med. 1973; 55: 762–71

3. Lee SD, Lo KJ, Tsai YT et al. Role of Caesarean section in prevention of mother-infant transmission of hepatitis B virus. Lancet 1988; 2: 833–4

4. Towers CV, Asrat T, Rumney P. The Presence of hepatitis B surface antigen and deoxyribonucleic acid in amniotic flueid and cord blood. Am J Obset. Gyencol. 2001; 184: 1514-8.

5. The Australian Immunisation Handbook, 7th Edn, NH&MRC, Canberra, p. 130

6. Sepkowitz KA. In: Principles and Practice of Infectious Diseases. 5th Edn, Mandell, Dougles & Bennett, Eds, Churchill Livingstone, Philadelphia, p. 3040

7. Theppisai U, Thanuntaseth C, Chiewsilp P et al. A comparison between the efficacy of passive-active and active immunization for prevention of perinatal transmission of hepatitis B virus. J. Med. Assoc. Thai. 1987; 70: 459–62.

8. Xu ZY, Francis DP, Liu CB et al. Prevention of hepatitis B virus carriage of infants using HBV vaccine in Shanghai. Preliminary report of a randomized double-blind placebo-controlled trial. Chin. Med. J. Engl. 1985; 98: 623–6

9. http://www.who.int/vaccines-diseases/diseases/hepatitis_b.htm

10. Boxall EH, Flewett TH, Dane DS et al. Letter: Hepatitis-B surface antigen in breast milk. Lancet 1974; 2: 1007–8

11. Report of the Committee on Infectious Diseases, 25th ed. Elk Grove, Ill, American Academy of Pediatrics, p. 300

Acknowledgements

Dr Joe Sasadeusz at Walter and Eliza Hall Institute, University of Melbourne and Dr David McIntosh at Wyeth Vaccines, Maidenhead, UK

Hepatitis C Virus

References

1. Dore GJ, Kaldor JM, McCaughan GW. Systematic review of role of polymerase chain reaction in defining infectiousness among people infected with hepatitis C virus [see comments]. BMJ. 1997; 315: 333–7

2. Dore GJ, Pritchard-Jones J, Fisher D et al.
Who's at risk? Risk factors for HCV infection in Australia. Aust. Fam. Physician 1999; 28: S8–S13

3. Dienstag JL. Sexual and perinatal transmission of hepatitis C. Hepatology 1997; 26: 66S–70S

4. Spencer JD, Latt N, Beeby PJ et al. Transmission of hepatitis C virus to infants of human immunodeficiency virus-negative intravenous drug-using mothers: rate of infection and assessment of risk factors for transmission. J. Viral. Hepat. 1997; 4: 395–409.

5. Report of the Committee on Infectious Diseases, 25th edn. Elk Grove, Ill, American Academy of Pediatrics, p. 304

6. Polywka S, Schroter M, Feucht HH et al. Low risk of vertical transmission of hepatitis C virus by breast milk. Clin. Infect. Dis. 1999; 29: 1327–9

7. Kumar RM, Shahul S. Role of breast-feeding in transmission of hepatitis C virus to infants of HCV-infected mothers. J. Hepatol. 1998; 29: 191–7

8. Garland SM, Tabrizi S, Robinson P et al. Hepatitis C — role of perinatal transmission. Aust. NZ J. Obstet. Gynaecol. 1998; 38: 424–7

Acknowledgements

Dr Joe Sasadeusz at Walter and Eliza Hall Institute, University of Melbourne and Dr David McIntosh at Wyeth Vaccines, Maidenhead, UK

Herpes Simplex Virus

References

1. 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. N Engl. J. Med. 1986; 315: 796–800
2. Brown ZA, Benedetti J, Ashley R et al. Neonatal herpes simplex virus infection in relation to asymptomatic maternal infection at the time of labour. N. Engl. J. Med. 1991; 324: 1247–52
3. Randolph AG, Washington E, Prober CG. Cesarian delivery for women presenting with genital herpes lesions. JAMA, 1993; 270: 77–82
4. Brown ZA, Selke A, Zeh J et al. The acquisition of herpes simplex virus during pregnancy. N. Engl. J. Med 1997; 337: 509–15.
5. Nahmias AJ, Josey WE, Naib ZM et al. Perinatal risk associated with maternal genital herpes simplex virus infection. Am. J. Obstet. Gynecol. 1997; 110: 825-–37.
6. Scott LL, Hollier LM, McIntire D et al. Acyclovir suppression to prevent clinical recurrences at delivery after first episode genital herpes in pregnancy: an open-label trial. Infect Dis obstet Gynecol 2001; 9 (2): 75-80.
7. 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. Pediatrics. 2001; 108: 230-8.
8. Kimberlin D, Powell D, Gruber W et al. Administration of oral acyclovir suppressive therapy after neonatal herpes simplex virus disease limited to the skin, eyes, and mouth: results of a phase I/II trial. Pediatr. Infect. Dis. J. 1996; 15: 247–54
9. Jones CA, Isaacs D, McIntyre P, Minutillo C, Cunningham A. Neonatal herpes simplex virus infection. Seventh Annual Report, Australian Paediatric Surveillance Unit 1999; 32-3.

Acknowledgements

Associate Professor Suzanne Garland

Human Immunodeficiency Virus

References

Information pertaining to HIV antiretroviral management including maternal and perinatal issues is constantly under review. Updates can be accessed on http://hivatis.org. Information was last accessed on February 2002.

1. Ziegler JB. Antenatal screening for HIV in Australia: time to revise policies? Med J Aust 1999;171:201-3.
2. Macdonald A, Cruickshank M, Ziegler JB, Elliot E, Kaldor J. Perinatal exposure to HIV in Australia, 1982-1994. Med J Australia 1997;166:77-80.
3. Carpenter CC, Cooper DA, Fischl MA, Gatell JM, Gazzard BG, Hammer SM et al. Antiretroviral therapy in adults: updated recommendations of the International AIDS Society-USA Panel. JAMA 2000 Jan 2000;283:381-90.
4. Dickover RE, Garraty EM, Herman SA, Myung-Shin S, Plaeger S, Boyer PJ et al. Identification of levels of maternal HIV-1 RNA associated with risk of perinatal transmission Identification of levels of maternal HIV-1 RNA associated with risk of perinatal transmission. Effect of maternal zidovudine treatment on viral load. JAMA 1996;275(8):599-605.
5. Garcia PM, Kalish LA, Pitt J, Minkoff H, Quinn TC, Burchett SK et al. Maternal levels of plasma human immunodeficiency virus type 1 RNA and the risk of perinatal transmission. Women and Infants Transmission Study Group. N Engl J Med 1999;341:394-402.
6. Newell ML, Dunn DT, Peckham CS, Semprini AE, Pardi G. Vertical transmission of HIV-1: maternal immune status and obstetric factors. The European Collaborative Study. AIDS 1996;10(14):1675-81.
7. Landesman SH, Kalish LA, Burns DN, Minkoff H, Fox HE, Zorrilla C et al. Obstetrical factors and the transmission of human immunodeficiency virus type 1 from mother to child. The Women and Infants Transmission Study [see comments]. New England Journal of Medicine 1996;334(25):1617-23.
8. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1 - a meta-analysis of 15 prospective cohort studies. The International Perinatal HIV Group. N Engl J Med 1999;340:977-87.
9. Dunn DT, Newell ML, Ades AE, Peckham CS. Risk of human immunodeficiency virus type 1 transmission through breastfeeding. Lancet 1992;340(8819):585-8.
10. 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 Mar 1;283(9):1167-74. 2000;283:1167-74.
11. Mandelbrot L, Mayaux MJ, Bongain A, Berrebi A, Moudoub-Jeanpetit Y, Benifla JL et al. Obstetric factors and mother-to-child transmission of human immunodeficiency virus type 1: the French perinatal cohorts. SEROGEST French Pediatric HIV Infection Study Group. American Journal of Obstetrics & Gynecology 1996;175(3 Pt 1):661-7.
12. Guay LA, Musoke P, Fleming T, Bagenda D, Allen M, Nakabiito C et al. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. Lancet 1999;354:795-802.
13. Connor EM, Sperling RS. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine (AZT) treatment. N Engl J Med 1994; 331:1173-1180.
14. Jackson JB, Becker-Pergola G, Guay LA, Musoke P, Mracna M, Fowler MG et al. Identification of the K103N resistance mutation in Ugandan women receiving nevirapine to prevent HIV-1 vertical transmission. AIDS 2000;14(11):F111-F115.
15. Dorenbaum, A. Report of results of PACTG 316: An international Phase III trial of standard antiretroviral (ARV) prophylaxis plus nevirapine (NVP) for prevention of perinatal HIV transmission. 8th Conference on Retroviruses and Opportunistic Infections, Chicago . 2001. (Abstract LB7).
16. Palasanthiran P, Robertson P, Ziegler JB, Graham GG. Decay of transplacental human immunodeficiency virus type 1 antibodies in neonates and infants. J.Infect.Dis. 1994;170(6):1593-6.
17. Shaffer N, Chuachoowong R, Mock PA, Bhadrakom C, Siriwasin W, Young NL et al. Short-course zidovudine for perinatal HIV-1 transmission in Bangkok, Thailand: a randomised controlled trial. Bangkok Collaborative Perinatal HIV Transmission Study Group. Lancet 1999;353:773-80.
18. Wade NA, Birkhead GS, Warren BL, Charbonneau TT, French PT, Wang L et al. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. N Engl J Med 1998;339:1409-14.

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Listeria

References

1. Gellin BG, Broome CV. Listeriosis. JAMA 1989; 261: 1313–20
2. Lorber B. Listeriosis. Clin. Infect. Dis. 1997; 24: 1-11
3. Hof H, Nichterlein T, Kretschmar M. Management of listeriosis. Clin. Microbiol. Rev. 1997; 10: 345–57
4. Enocksson E, Wretlind B, Sterner G et al. Listeriosis during pregnancy and in neonates. Scand. J. Infect. Dis. 1990; 71(Suppl): 89–94

5. Farmer K, Kreth HW. Listeriosis. Pediatric Therapy 3rd Edn. Eichenwald & Stroder, Eds, Mosby 1993; 749–51
6. Farmer K. Listeriosis. In: Current therapy in Pediatric Infectious Diseases. 2nd Edn, Nelson, Ed., Decker 1988; 210–12
7. Bortulussi R, Schlech WF. Listeriosis. In: Infectious Diseases of the Fetus and Newborn. Remington JS, Klein JO, Eds, 4th Edn, WB Saunders Co., Philadelphia. 1055–73
8. Boucher M, Yonekura ML. Perinatal listeriosis (early-onset): Correlation of antenatal manifestations and neonatal outcome. Obstet. Gynecol. 1986; 68: 593–7

Mycobacterium Tuberculosis

Further Reading & Sources

1. Hamadeh M, Glassroth J. Tuberculosis and pregnancy. Chest 1992; 101: 1114–20
2. Miller K, Miller, J. Tuberculosis in pregnancy: Interactions, diagnosis, and management. Clin. Obstet. Gynecol. 1996; 39: 1204–2
3. Brost B, Newman R. The maternal and fetal effects of tuberculosis therapy. Obstet. Gynecol. Clin. North Am. 1997; 24: 659–73
4. American Academy of Pediatrics Committee on Infectious Diseases: Chemotherapy for tuberculosis in infants and children. Pediatrics 1992; 89: 161–5
5. Starke J. Tuberculosis. An old disease but a new threat to the mother, fetus, and neonate. Clin. Perinatol. 1997; 24: 107–27
6. Chemotherapy and management of tuberculosis in the United Kingdom: Recommendations 1998. Joint Tuberculosis Committee of the British Thoracic Society. Thorax 1998;.53: 536–48
7. Riley L. Pneumonia and tuberculosis in pregnancy. Infect. Dis. Clin. North Am. 1997; 11: 119–33
8. Cantwell MF, Shehab ZM, Costello AM, et al. Brief Report: congenital tuberculosis. N Engl J Med. 1994; 330: 1051-4
9. Abughali N, Van der Kuyp F, Annable W et al. Congenital tuberculosis. Pediatr. Infect. Dis. J. 1994; 13: 738–41
10. Voss L. Position paper: Management of tuberculosis in children. J. Paediatr. Child Health 2000; 36: 530–6

Parvovirus

References

1. Harger JH, Adler SP, Koch WC et al. Prospective evaluation of 618 pregnant women exposed to parvovirus B19: risks and symptoms. Obstet. Gynecol. 1998; 91: 413–20
2. Gillespie SM, Cartter ML, Asch S et al. Occupational risk of human parvovirus B19 infection for school and day-care personnel during an outbreak of erythema infectiosum. JAMA 1990; 263: 2061–5
3. Kelly HA, Siebert D, Hammond R et al. The age-specific prevalence of human parvovirus immunity in Victoria, Australia compared with other parts of the world. Epidemiol. Infect. 2000; 124: 449–57
4. Miller E, Fairley CK, Cohen BJ et al. Immediate and long term outcome of human parvovirus B19 infection in pregnancy. Brit. J. Obstet. Gynaecol. 1998; 105: 174–8
5. Schild RL, Bald R, Plath H et al. Intrauterine management of fetal parvovirus B19 infection. Ultrasound Obstet. Gynecol. 1999; 13: 161–6
6. Fairley CK, Smoleniec JS, Caul OE et al. Observational study of effect of intrauterine transfusions on outcome of fetal hydrops after parvovirus B19 infection. Lancet 1995; 346: 1335–7
7. Rodis JF, Borgida AF, Wilson M et al. Management of parvovirus infection in pregnancy and outcomes of hydrops: A survey of members of the Society of Perinatal Obstetricians. Am. J. Obstet. Gynecol. 1998; 179: 985–8
8. Koch WC, Harger JH, Barnstein B et al.. Serologic and virologic evidence for frequent intrauterine transmission of human parvovirus B19 with a primary maternal infection during pregnancy. Pediatr. Infect. Dis. J. 1998; 17: 489–94
9. Cohen BJ, Bates CM. Evaluation of 4 commercial test kits for parvovirus B19-specific IgM. J. Virol. Methods 1995; 55: 112–5
10. Torok TJ, Wang QY, Gary GWJ et al. Prenatal diagnosis of intrauterine infection with parvovirus B19 by the polymerase chain reaction technique. Clin. Infect. Dis. 1992; 14: 149–55

Rubella

References

1. Gilbert GL, Field P. What do rubella antibody tests mean? Inoculum 1997; 6(3): 1–3
2. Sintchenko V, Field PR, Gilbert GL. Rubella antibody in antenatal clinic patients. Aust. NZ J. Med. 1999; 29: 284
3. Morgan-Capner P, Hodgson J, Hambling, MH et al. Detection of rubella-specific IgM in subclinical rubella reinfection in pregnancy. Lancet 1985; 1: 244–6
4. Cradock-Watson JE, Ridehalgh MKS, Anderson MJ et al.. Outcome of asymptomatic infection with rubella virus during pregnancy. J. Hyg. 1981; 87: 147–54
5. Miller E, Craddock-Watson JE, Pollock TM.. Consequences of confirmed maternal rubella at successive states of pregnancy. Lancet 1982; ii: 781–4
6. Enders G, Nickerl-Pacher U, Miller E et al. Outcome of confirmed periconceptional maternal rubella. Lancet 1988; i: 144–57
7. Peckham C. Clinical and laboratory study of children exposed in utero to maternal rubella. Arch Dis Child 1972; 47: 571–7
8. Infectious disease in pregnancy and the newborn infant. Gilbert, GL, Chur, Harvard Academic Publishers, Switzerland, New York, USA. 1990
9. Infectious Disease of the Fetus and Newborn, 5th Edn, Remington J, WB Saunders, 2000
10. Daffos F, Forestier F, Grangeot-Kerros L et al. Prenatal diagnosis of congenital rubella. Lancet 1984: 2: 1–3
11. Revello MG, Baldanti F, Sarasini A et al. Prenatal diagnosis of rubella virus infection by direct detection and semiquantitation of viral RNA in clinical samples by reverse transcription. J. Clin. Microbiol. 1997; 35(3): 708–13
12. Enders G, Jonatha W. Prenatal diagnosis of intrauterine rubella. Infection; 1987; 15: 162–4
13. Menser MA, Forrest JM. Rubella- high incidence of defects in children considered normal at birth. Med. J. Aust. 1974; 1: 123–6

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Streptococcus, Group B

References and Sources

1. Prevention of perinatal group B streptococcal disease: a public health perspective. Centers for Disease Control and Prevention. MMWR Morb Mortal Wkly Rep 1996; 45(RR-7): 1-24
2. Boyer KM, Gotoff SP. Prevention of early-onset neonatal group B streptococcal disease with selective intrapartum chemoprophylaxis. N. Engl. J. Med. 1986; 314(26): 166–59
3. Schrag SJ, Zywicki S, Farley MM et al. Group B streptococcal disease in the era of intrapartum antibiotic prophylaxis. N. Engl. J. Med. 2000; 342: 15–20
4. Centers for Disease Control and Prevention. 2002. Prevention of perinatal group B streptococcal disease: Revised guidelines from the Centers for Disease Control and Prevention. MMWR Recommendations and Reports: In press.

5. Yancey MK, Schuchat A, Brown LK et al. The accuracy of late antenatal screening cultures in predicting genital group B streptococcal colonization at delivery. Obstet. Gynecol. 1996; 88: 811–5.
6. Boyer KM, Gadzala CA, Kelly PD et al. Selective intrapartum chemoprophylaxis of neonatal group B streptococcal early-onset disease. II. Predictive value of prenatal cultures. J. Infect. Dis. 1983; 148: 802–9
7. Garland SM, Kelly N, Ugoni AM. Is antenatal group B streptococcal carriage a predictor of adverse obstetric outcome? Infect. Dis. Obstet. Gynecol. 2000; 8: 138–42
8. Rosa-Fraile M, Rodriguez-Granger J, Cueto-Lopez M et al. Use of Granada medium to detect group B streptococcal colonization in pregnant women. J. Clin. Microbiol. 1999; 37: 2674–77
9. Schuchat A, Deaver-Robinson K, Plikaytis BD et al. Multistate case-control study of maternal risk factors for neonatal group B streptococcal disease. The Active Surveillance Study Group. Pediatr. Infect. Dis. J. 1994; 13: 623–9
10. Boyer KM, Gadzala CA, Kelly PD, et al. Selective intrapartum chemoprophylaxis of neonatal group B streptococcal early-onset disease. III. Interruption of mother-to-infant transmission. J Infect Dis. 1983; 148: 810-6

Toxoplasma

References

1. Dunn D, Wallon M, Peyron F et al. Mother-to-child transmission of toxoplasmosis: Risk estimates for clinical counselling. Lancet 1999; 353: 1829–33
2. Foulon W, Pinon JM, Stray-Pedersen B et al. Prenatal diagnosis of congenital toxoplasmosis: a multicenter evaluation of different diagnostic parameters. Am. J. Obstet. Gynecol. 1999b; 181: 843–7
3. Robert-Gangneux F, Gavinet MF, Ancelle T et al. Value of prenatal diagnosis and early postnatal diagnosis of congenital toxoplasmosis: retrospective study of 110 cases. J. Clin. Microbiol. 1999; 37: 2893–8
4. Naessens A, Jenum PA, Pollak A et al. Diagnosis of congenital toxoplasmosis in the neonatal period: A multicenter evaluation. J. Pediatr. 1999;135: 714–9
5. Foulon W, Villena I, Stray-Pedersen B et al. Treatment of toxoplasmosis during pregnancy: A multicenter study of impact on fetal transmission and children's sequelae at age 1 year. Am. J. Obstet. Gynecol. 1999a; 180: 4105
6. Wallon M, Liou C, Garner P et al. Congenital toxoplasmosis: systematic review of evidence of efficacy of treatment in pregnancy. BMJ 1999; 318: 1511–4
7. Petersen E, Eaton RB. Control of congenital infection with Toxoplasma gondii by neonatal screening based on detection of specific immunoglobulin M antibodies eluted from phenylketonuria filter-paper blood-spot samples. Acta Paediatr. Suppl. 1999; 88: 36–9

Treponema Pallidum (Syphilis)

Further Reading

Centers for Disease Control and Prevention. 1998 Guidelines for treatment of sexually transmitted diseases. MMWR 1998; 47(No. RR-1): 284–9

Hollier LM, Cox SM. Syphilis. Semin. Perinatol. 1998; 22: 323–31

Humphrey MD, Bradford DL. Congenital syphilis: Still a reality in 1996. Med. J. Aust. 1996; 165: 382–5

Larsen SA, Steiner BM, Rudolph AH. Laboratory diagnosis and interpretation of tests for syphilis. Clin. Microbiol. Rev. 1995; 8; 1–21

Romanowski B, Sutherland R, Fick et al. Serologic response to treatment of infectious syphilis. Ann. Intern. Med. 1991; 114: 1005–9

Sanches PJ. Syphilis and Pregnancy in Sexually Transmitted Diseases and Adverse Outcomes of Pregnancy. ASM Press, Washington 1999; 125–50

Sanchez PJ, Wendel GD, Grimprel E et al. Evaluation of molecular methodologies and rabbit infectivity testing for the diagnosis of congenital syphilis and neonatal central nervous system invasion by Treponema pallidum. J. Infect. Dis. 1993; 167: 148–57

Sheffield JS, Wendel GD. Syphilis in pregnancy. Clin. Obstet. Gynecol. 1999; 42: 97-1–06

Stoll BJ, Francis KL, Larsen S et al. Clinical and serological evaluation of neonates for congenital yphilis: a continuing diagnostic dilemma. J. Infect. Dis. 1993; 167: 1093–9

Therapeutic Guidelines: Antibiotic. Therapeutic Guidelines Ltd, Melbourne, 11th Edn 2000: 73-4.

Varicella Zoster Virus

References

1. Gilbert GL. Chickenpox during pregnancy. BMJ 1993; 306: 1079-80
2. Preblud SR, Cochi SL, Orenstein WA. Varicella zoster infection in pregnancy. N. Engl. J. Med. 1986; 315: 1416–7
3. Nathwani D, Maclean A, Conway S, Carrington D. Varicella infectiouns in pregnancy and the newborn. J Infect 1998; 36 (supp 1): 59-71.
4. Haake DA, Zakowski PC, Haake DL et al. Early treatment with acyclovir for varicella pneumonia in otherwise healthy adults. Rev. Infect. Dis. 1990; 12: 788–97
5. Rice P, Simmons K, Carr R et al. Near fatal chickenpox during prednisolone treatment. Br. Med. J. 1994; 309: 1069-–70
6. Grayson ML, Newton-John H. Smoking and varicella pneumonia. .J Infect. 1988; 16: 31–2
7. The Australian Immunisation handbook. 7th Edn. Canberra, Australian Government Publishing Service, 2000
8. Lin TY, Huang YC, Ning HC et al. Oral aciclovir prophylaxis after intimate contact. Pediatr. Infect. Dis. J. 1997; 16: 116–25
9. Andrews EB, Yankasksas BC, Cordero JF et al. Aciclovir in pregnancy registry: 6 years experience. The aciclovir in pregnancy registry advisory committee. Obstet. Gynecol. 1991; 78: 111–26
10. 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
11. Jones KL, Johnson KA, Chambers CD. Offspring of women infected with varicella during pregnancy: a prospective study. Teratology 1994; 49: 29–32
12. Pretorius DH, Hayward I, Jones KL et al. Sonographic evaluation of pregnancies with maternal varicella infection. J. Ultrasound Med. 1992; 11: 459–63
13. Mouly F, Mirlesse V, Meritet J et al. 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
14. Miller E, Cradock-Watson JE et al. Outcome of newborn babies given anti varicella zoster immunoglobulin after peronatal maternal infection with varicella zoster virus. Lancet 1989; ii: 371–3
15. Hanngren K, Grandien M, Granstrom G. Effect of zoster immunoglobulin for varicella prophylaxis in the newborn. Scand. J. Infect Dis. 1985; 17: 34–37
16. Rubin L. Disseminated varicella in the neonate and implications for immunoprophylaxis in neonates exposed to varicella. Pediatr. Infect. Dis. J. 1986; 56: 100–2
17. 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
18. Conway SP, Dear PRF, Smith I. Immunoglobulin profile of the preterm baby. Arch. Dis. Child 1985; 60: 208–12

Emendations: References

E1. Fowler KB, Stagno S, Pass RF. Maternal immunity and prevention of congenital cytomegalovirus infection. *JAMA.*. 2003;*289:1008-11*

E2. Fowler KB, Stagno S, Pass RF. Interval between births and risk of congenital cytomegalovirus infection. *Clinical Infectious Diseases.* 2004;*38:1035-7*

E3. Kimberlin DW, Lin CY, Sanchez PJ, Demmler GJ, Dankner W, Shelton M et al. Effect of ganciclovir therapy on hearing in symptomatic congenital cytomegalovirus disease involving the central nervous system: a randomized, controlled trial. *Journal of Pediatrics.* 2003;*143:16-25*

E4. Abzug MJ, Cloud G, Bradley J, Sanchez PJ, Romero J, Powell D et al. Double blind placebo-controlled trial of pleconaril in infants with enterovirus meningitis. *Pediatric Infectious Disease Journal.* 2003;*22:335-41*

E5. Chapter 3.9 Hepatitis B. *The Australian Immunisation Handbook*. 8th edition, 2003.

E6. Hardikar W, Elliott EJ, Jones CA. The silent infection: should we be testing for perinatal hepatitis C and, if so, how? *Med.J.Aust.* 2006;184: 54-5

E7. Dunn DT, Gibb DM, Healy M, Goodall RL, Butler K, Cafferkey M et al. Timing and interpretation of tests for diagnosing perinatally acquired hepatitis C virus infection. *Pediatric Infectious Disease Journal.* 2001;20:715-6

E8. Polywka S, Pembrey L, Tovo PA, Newell ML. Accuracy of HCV-RNA PCR tests for diagnosis or exclusion of vertically acquired HCV infection. *J.Med.Virol.* 2006;78:305-10

E9. 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.* 2003;*289:203-9*

E10. Lyons F, Hopkins S, Kelleher B, McGeary A, Sheehan G, Geoghegan J et al. Maternal hepatotoxicity with nevirapine as part of combination antiretroviral therapy in pregnancy. *HIV.Medicine.* 2006;**7**:255-60

An infection during pregnancy that could damage the fetus or infant is much less common than suspicion or fear of infection. Vague, nonspecific symptoms – malaise, aches and pains, headache, tiredness, nausea - are the hallmarks of many vertically transmissible maternal infections but they are also common during pregnancy or in any busy, stressful life. In pregnant women they can't be dismissed as trivial as they may be in others.

This publication represents a consensus among specialists in perinatal infection. It has been endorsed by the Australasian Society for Infectious Diseases and the Royal College of Obstetricians and Gynaecologists of Australia and New Zealand. We hope it will not discourage nonspecialists from referring pregnant women with suspected infection during pregnancy, but that it will help to guide the initial assessment and investigation of the patient, and prevent unnecessary anxiety or hasty decisions.

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