WOMEN AND NEWBORN HEALTH SERVICE
King Edward Memorial Hospital

CLINICAL GUIDELINES
OBSTETRICS & MIDWIFERY

ANTEPARTUM CARE

INFECTIONS IN PREGNANCY

SYPHILIS IN PREGNANCY AND THE NEWBORN—DIAGNOSIS AND TREATMENT

Keywords: Syphilis, chancre, syphilis in pregnancy, Jarisch-Herxheimer reaction, antenatal syphilis screening

AIM

• To detect syphilis in pregnant women and offer treatment prior to delivery of the baby.
• To detect syphilis in the newborn and to treat before complications develop.

OVERVIEW

Syphilis is a potentially fatal, sexually transmitted infection that is caused by the spirochaete bacterium Treponema pallidum. It can be transmitted from a pregnant woman to her unborn baby. Pregnancies affected by syphilis may result in abortion, perinatal death, prematurity, low birth weight or the deformities of congenital syphilis. Although previously rare in developed countries, the incidence of syphilis is now increasing and rates in Western Australia are amongst the highest in Australia.

TRANSMISSION

Syphilis is primarily transmitted horizontally from person to person through direct contact with a syphilis sore also known as a chancre. Chancres occur mainly on the external genitals, vagina, anus, or in the rectum. They can also be on the mouth or lips and in the mouth. Transmission of the organism occurs during vaginal, anal or oral sex. Vertical transmission occurs in pregnant women with the disease who can pass it to the babies they carry.

SYMPTOMS

Primary stage
Incubation period – 10 to 90 days (average 21 days).
A single chancre or multiple chancres. The chancre is a firm, round, small and painless lesion. It appears where the syphilis bacterium entered the body. It lasts 2 to 6 weeks (range 1-12 weeks) and heals without treatment. If treatment is inadequate or absent, the infection progresses to the secondary stage.

Secondary stage
2-8 weeks after appearance of the chancre (30-150 days after exposure).
Skin rash – rough, red or reddish brown spots both on the hands and the bottoms of feet. It may also occur with a different appearance and on other sites of the body. Fever, swollen lymph glands, sore throat, patchy hair loss, headaches, weight loss, muscle aches and fatigue.
The signs and symptoms will resolve with or without treatment, but without treatment, the infection will progress to the latent and late stages of the disease.
This stage also lasts about 2 – 6 weeks.

Latent stage
Early latent syphilis is when clinical manifestations of syphilis are no longer apparent and lasts for up to ~4 yrs. Relapse may occur and the patient is “infectious.”
Late latent syphilis follows with infectivity being reduced only to vertical transmission or via transfused contaminated blood.
**Tertiary stage**

5-35 years after exposure affecting about 40% of those with untreated latent infection. Damage to internal organs, including the brain, eyes, heart, blood vessels, liver, bones and joints. Signs and symptoms include difficulty coordinating muscle movements, paralysis, numbness, gradual blindness and dementia. This damage may be serious enough to cause death.

**SYMPHILIS IN PREGNANCY AND THE NEWBORN**

The syphilis bacterium can infect the baby of a woman during her pregnancy. Depending on how long a pregnant woman has been infected, she may have a high risk of having a stillbirth or giving birth to a baby who dies shortly after birth. The risk of vertical transmission of syphilis from an infected, untreated mother decreases as maternal disease progresses. Thus transmission ranges from 70-100% in primary syphilis, 40% for early latent syphilis, 10% for late latent disease and is rare for tertiary syphilis. Transmission usually occurs between the 16th and 28th week of gestation but may be as early as 9 weeks.

Pregnancies affected by syphilis will result in miscarriage, still birth or perinatal death in approximately 35-40%. Prematurity or low birth weight occur in about 20-30% and another 20% have stigmata of congenital syphilis – two thirds of these developing symptoms by 3-8 weeks and almost all by 3 months.

Early manifestations of **congenital syphilis** resemble those of secondary syphilis listed above. Persistent rhinitis (snuffles) is often the earliest presenting symptom occurring in up to 40% of newborns with congenital syphilis. This is soon followed by a diffuse maculopapular (but sometimes vesicular and bullous) desquamative rash particularly prominent on the hands, soles, back, buttocks and thighs. After 2-3 months the perioral and perianal areas can be affected by condylomata lata: raised moist nodules or plaques that are highly infective. Other early manifestations include a necrotising funisitis (infection of the umbilical cord) which is virtually pathognomonic; hepatosplenomegaly which may be associated with jaundice, anaemia and thrombocytopenia; and non-tender generalised lymphadenopathy. Periostitis and osteochondritis (causing a pseudoparalysis) may be detected radiographically especially in the long bones.

Late manifestations usually occurring after 2 years, include bony and tooth deformities such as saddle nose, frontal bossing, sabre shins, and one or more of Hutchinson's triad: peg shaped central incisors (Hutchison's teeth); interstitial keratitis; and nerve deafness. Juvenile paresis may also occur.

**ANTENATAL SYMPPHILIS SCREENING**

All women should have syphilis serology carried out in the first trimester or first antenatal visit. Women at risk of acquiring syphilis should have a further test in the third trimester (34 wks) or if not done, at delivery. An initial negative test does not exclude infection as it can take 10-45 days after infection for serology to be positive.

There are two types of serology test performed together on maternal blood (not cord blood due to possible risk of maternal mixing):

**Treponemal tests** (TPPA, EIA IgG & IgM, FTA-Abs)
Reported as either reactive or non-reactive. Once reactive, they remain reactive for life even if adequate treatment has been given. They indicate previous exposure to syphilis and do not reflect disease activity.

**Non-treponemal tests** (RPR, VDRL)
Reported as a titre (1:2, 1:4 …etc). They have a moderate false positive rate and need to be confirmed with the treponemal test. They usually revert to non-reactive after treatment but frequently revert to non-reactive with time even without treatment. They are useful in determining disease activity and response to therapy. For example a four-fold increase in titre (2-dilution rise) over a previous result (1:2 increasing to 1:8) indicates new infection; a four-fold fall in titre (2-dilution fall) after treatment (1:32 decreasing to 1:8) indicates an adequate response to treatment.

(See appendix 1 for possible variations of the above tests and the corresponding interpretations).
ASSESSMENT AND MANAGEMENT OF POSITIVE SYPHILIS SEROLOGY

For all mothers with any positive syphilis serology, (assuming false positives have been considered and excluded – see Appendix 1), it is critical to establish what stage of syphilis the mother has (i.e. when infection occurred) and whether effective treatment has already been given. If effective treatment has been given it is important to exclude re-infection.

This usually requires three steps:

1. Past and present history of syphilis including treatment and potential for re-infection.

   Often it will be necessary to contact the public health unit in the patient’s current and/or past area of residence where diagnosis and treatment history is recorded in specialised databases:

   Communicable Disease Control Directorate (Perth): 9388 4999
   Kimberley Population Health Unit (Broome): 9194 1646
   Pilbara Population Health Unit (South Hedland): 9172 8306
   Geraldton Population Health Unit: 9956 1958
   Kalgoorlie-Boulder Population Health Unit (Boulder): 9080 8200
   Wheatbelt Population Health Unit (Northam): 9622 4320
   South West Population Health Unit (Bunbury): 9781 2350

2. Clinical examination for stigmata of the different stages of syphilis.

3. Past serology results.

   These are easily obtained by phoning the serology lab at Pathwest Nedlands on 9346 2966 which is the centralised recording site for syphilis serology. They have computer records from 1995 onwards and card records prior to 1995.

TREATMENT OF THE MOTHER ACCORDING TO STAGE OF SYPHILIS

- **Early syphilis** (primary, secondary or latent syphilis of less than 2 yrs duration).

  Benzathine penicillin 1.8g (2.4 million units) IM as single dose.*


  Sexual contacts in the last 3 months should also have the same treatment regardless of serology.

- **Late latent syphilis** (latent syphilis of more than 2 yrs or indeterminate duration in the absence of tertiary syphilis).

  Benzathine penicillin 1.8g (2.4 million units) IM once weekly for 3 weeks (ie 3 doses).*

- **Tertiary syphilis**.

  Benzylpenicillin 1.8g IV q4h (10.8g/d) for 15 days.
  Concomitant prednisolone 20mg bd for 3 doses to reduce Jarisch-Herxheimer reaction (see below)

  - Screening for other sexually transmitted diseases (ie chlamydia, gonorrhoea, HIV, HBV, HCV) should also be performed.
  - Sex partners from the last 3 months (if primary infection) and last 2 years (in the case of secondary and early latent syphilis) should also be assessed and treated. Patients with late latent and tertiary syphilis are not infectious to sexual partners.
  - Follow-up evaluation — RPR titres should be checked at 6 and 12 months following treatment. Titres should decrease four-fold by six months post therapy and become nonreactive by 12 to
24 months. Titres that show a four-fold rise or do not decrease appropriately suggest either treatment failure or re-infection (see Appendix 3). The treatment regimen should be repeated in these cases and LP considered.

* While existing guidelines suggest procaine penicillin as an alternative, we feel due to poor tolerability of prolonged courses (10-15 days) of IM injections, that there is no role for this form of penicillin.

**Jarisch-Herxheimer Reaction**

This reaction is a common occurrence in the treatment of early syphilis in adults (including pregnant women in up to 45%) and consists of fever, chills, malaise, hypotension and tachycardia. It begins within 2 hrs of treatment, peaks at 8 hrs and disappears in 24-36 hrs. Management is supportive care. It may precipitate uterine contractions, preterm labour, and/or non-reassuring foetal heart rate tracings in pregnant women treated in the second half of pregnancy. Women should be counselled to report symptoms of labour or decreased foetal activity; evaluation and treatment are according to usual obstetric standards.

**TREATMENT OF THE BABY ACCORDING TO RISK OF CONGENITAL SYPHILIS**

No Risk infant: 1. All maternal syphilis tests are negative.
2. Mothers who have had adequately treated syphilis documented **before** pregnancy and who have not been re-infected.

No lab investigations required.
No treatment or follow-up (unless there is some suspicion of re-infection late in pregnancy).

Low risk infant: Mother treated adequately for syphilis during current pregnancy (completed course of penicillin more than 30 days prior to birth with serological response).

Full examination of newborn.
Syphilis serology performed on mother (RPR, TPPA) and child (RPR, TPPA, EIA IgM):

- Examination normal; RPR < 4 times maternal RPR or negative; IgM negative:
  - **IM benzathine penicillin 37.5mg/kg (50 000units/kg) single dose.**
  - Follow-up serology (RPR, TPPA, EIA) and review at 6 mths (see appendix 3).
  - Notify Health Department on Notifiable Infectious Diseases form.

- Stigmata of congenital syphilis; RPR ≥ 4 times maternal RPR; IgM positive:
  - reclassify as high risk.

High risk infant: 1. Child reclassified from low risk to high risk or
2. Mother seropositive during pregnancy and any of the following:
   - Clinical features of congenital syphilis.
   - Maternal treatment inadequate (incomplete or non-penicillin agent).
   - Birth occurred within 30days of completing maternal treatment.
   - Maternal re-infection likely eg partner not treated.

Full examination of newborn.
Syphilis serology performed on mother (RPR, TPPA) and child (RPR, TPPA, EIA IgM).
Consider:
- lumbar puncture for cell count, protein, glucose and syphilis serology.
- ophthalmologic exam if child has symptoms/signs of congenital syphilis.
- long bone X-rays.
- Syphilis PCR of foetal/placental tissue.
- histopathology of umbilical cord.
- PCR testing of amniotic fluid, placenta or cord.

Treat with benzylpenicillin 50mg/kg IV or IM (bd if <7d old, tds if 8-30d and qid if >1 month old) for 10d.

May be able to shorten treatment if above investigations normal.
Notify Health Department on Notifiable Infectious Diseases form.
Follow-up review and serology (RPR, TPPA, EIA) at 3 and 6 months (see appendix 3).
Consultation with Microbiologist.
Summary of guidelines (current Northern Territory CDC Guidelines for investigation and treatment of infants at risk for congenital syphilis in the Northern Territory; July 2005)

ASSESSMENT AND MANAGEMENT OF CONGENITAL SYphilis

ASSESS MATERNAL STATUS AT DELIVERY; if seronegative, baby remains “No risk”

TREATED PRIOR TO PREGNANCY AND ALL OF THE FOLLOWING
- Documented adequate treatment and response prior to pregnancy and
- All antenatal and delivery tests performed this pregnancy and
- All RPRs during pregnancy and at delivery are stable and no higher than 1:4 and
- No risk of reinfection late in pregnancy

MOTHER SEROPOSITIVE ELA, TPHA or FTA positive
NB if no antenatal care, evaluate carefully re high risk

MOTHER TREATED ADEQUATELY FOR SYphilis DURING PREGNANCY
- Treatment with adequate penicillin regime completed 30 days before delivery and
- No possibility of reinfection (eg partner treated) and
- 2 titre drop in RPR or maintaining low stable titre after treatment (Late Latent)

ANY ONE OF:
- Treatment not completed 30 days before delivery
- Likelihood of reinfection high
- No or inadequate treatment
- Treatment with non-penicillin regime
- If treated, no adequate and documented response to treatment

HIGH RISK
- Collect venous blood sample from mother and baby for syphillis serology and
  Examine baby

LOW RISK
- Collect venous blood from mother and baby and compare the RPRs
- Baby RPR > 4 times maternal RPR?
- NO

*TREAT WITH BENZATHINE PENICILLIN G 37.5 Mg (50,000 units)/Kg IM AS SINGLE DOSE

*Complete Congenital Syphilis Register form and send to your local CDC for all cases treated, in order for follow-up to be arranged.
### APPENDIX 1. Possible combinations of syphilis serology with interpretations

<table>
<thead>
<tr>
<th>R.P.R.</th>
<th>T.P.P.A.</th>
<th>F.T.A. IgG</th>
<th>EIA IgM</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>POS</td>
<td>POS</td>
<td>POS</td>
<td>POS</td>
<td>Syphilis of any stage: treated or untreated.</td>
</tr>
<tr>
<td>POS</td>
<td>POS</td>
<td>POS</td>
<td>NEG</td>
<td>Secondary, Latent or Tertiary Syphilis: treated or untreated.</td>
</tr>
<tr>
<td>POS</td>
<td>NEG</td>
<td>POS</td>
<td>POS</td>
<td>Primary Syphilis. Repeat serology until diagnosis established. This combination rarely occurs.</td>
</tr>
<tr>
<td>POS</td>
<td>NEG</td>
<td>NEG</td>
<td>NEG</td>
<td>False positive non-treponemal test (see below for causes)</td>
</tr>
<tr>
<td>NEG</td>
<td>POS</td>
<td>NEG</td>
<td>NEG</td>
<td>Early Primary Syphilis. Repeat serology until diagnosis established.</td>
</tr>
<tr>
<td>NEG</td>
<td>POS</td>
<td>NEG</td>
<td>POS</td>
<td>1) Treated Syphilis; or 2) Old untreated Syphilis.</td>
</tr>
<tr>
<td>NEG</td>
<td>POS</td>
<td>POS</td>
<td>NEG</td>
<td>1) Primary Syphilis; or 2) Late latent/Tertiary Syphilis; or 3) Early Re-infection; or 4) False Positive Treponemal test (see below for causes); Repeat serology until diagnosis established.</td>
</tr>
</tbody>
</table>

### Causes of false positive syphilis serology tests:

<table>
<thead>
<tr>
<th>Non-Treponemal specific tests (RPR)</th>
<th>Treponemal specific tests (TPPA, FTA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral:</td>
<td>Infectious mononucleosis</td>
</tr>
<tr>
<td>Varicella</td>
<td></td>
</tr>
<tr>
<td>Infectious mononucleosis</td>
<td>Bacterial:</td>
</tr>
<tr>
<td>Measles</td>
<td>Lyme borreliosis</td>
</tr>
<tr>
<td>Mumps</td>
<td>Relapsing fever</td>
</tr>
<tr>
<td>Viral hepatitis</td>
<td>Leptospirosis</td>
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<tr>
<td>HIV</td>
<td>Leprosy</td>
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<tr>
<td>Bacterial:</td>
<td>Malaria</td>
</tr>
<tr>
<td>Pneumococcal pneumonia</td>
<td>Systemic lupus erythematosus</td>
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<tr>
<td>Scarlet fever (GpA Strep)</td>
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<tr>
<td>Mycoplasma infections</td>
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<tr>
<td>Chancroid (Haemophilus ducreyi)</td>
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<tr>
<td>Lymphogranuloma venereum (Chlamydia trachomatis)</td>
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<tr>
<td>Psittacosis (Chlamydia psittaci)</td>
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<tr>
<td>Relapsing fever (Borrelia spp)</td>
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<tr>
<td>Rickettsial infections</td>
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<tr>
<td>Leptospirosis</td>
<td></td>
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<tr>
<td>Infective endocarditis</td>
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<tr>
<td>Tuberculosis</td>
<td></td>
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<tr>
<td>Leprosy</td>
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<tr>
<td>Protozoal:</td>
<td></td>
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<tr>
<td>Malaria</td>
<td></td>
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<tr>
<td>Trypanosomiasis</td>
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<tr>
<td>Pregnancy</td>
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<tr>
<td>Chronic liver disease</td>
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<tr>
<td>Injection drug use</td>
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<tr>
<td>Malignancy (advanced)</td>
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<tr>
<td>Myeloma</td>
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<tr>
<td>Multiple transfusions</td>
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<tr>
<td>Connective tissue disease</td>
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<tr>
<td>Advanced age</td>
<td></td>
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</table>
APPENDIX 2. Oral penicillin desensitisation protocol (Table 2.21 Antibiotic Guidelines 2006)

<table>
<thead>
<tr>
<th>Step (at 15-minute intervals)</th>
<th>Phenoxythemethylpenicillin solution (mg/mL)</th>
<th>Volume (mL)</th>
<th>Dose (mg)</th>
<th>Cumulative dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.05</td>
<td>0.05</td>
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<tr>
<td>2</td>
<td>0.5</td>
<td>0.2</td>
<td>0.1</td>
<td>0.15</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>0.4</td>
<td>0.2</td>
<td>0.35</td>
</tr>
<tr>
<td>4</td>
<td>0.5</td>
<td>0.8</td>
<td>0.4</td>
<td>0.75</td>
</tr>
<tr>
<td>5</td>
<td>0.5</td>
<td>1.6</td>
<td>0.8</td>
<td>1.55</td>
</tr>
<tr>
<td>6</td>
<td>0.5</td>
<td>3.2</td>
<td>1.6</td>
<td>3.15</td>
</tr>
<tr>
<td>7</td>
<td>0.5</td>
<td>6.4</td>
<td>3.2</td>
<td>6.35</td>
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<tr>
<td>8</td>
<td>5.0</td>
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<tr>
<td>9</td>
<td>5.0</td>
<td>2.4</td>
<td>12</td>
<td>24.35</td>
</tr>
<tr>
<td>10</td>
<td>5.0</td>
<td>4.8</td>
<td>24</td>
<td>48.35</td>
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<td>11</td>
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<td>98.35</td>
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<td>50</td>
<td>2</td>
<td>100</td>
<td>198.35</td>
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<tr>
<td>13</td>
<td>50</td>
<td>4</td>
<td>200</td>
<td>398.35</td>
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<tr>
<td>14</td>
<td>50</td>
<td>8</td>
<td>400</td>
<td>798.35</td>
</tr>
<tr>
<td>15</td>
<td>Observe for 30 minutes; if no reaction, administer 1.8g of benzathine penicillin IM</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Precautions for desensitisation

Where there is a life-threatening history of drug hypersensitivity, ensure desensitisation occurs in a hospital setting with adrenaline and resuscitation facilities available.

Desensitisation is absolutely contraindicated where there is a history of drug-induced epidermal necrolysis (Stevens-Johnson syndrome and variants).

Where non–life-threatening features (e.g. rash) have occurred, graded desensitisation may occur on an outpatient basis with regular observation and telephone contact available, and with an action plan for hypersensitivity reactions in place (e.g. administration of an oral antihistamine such as cetirizine 10 mg). In the event of such a reaction, the desensitisation schedule should pause pending further discussion with the medical team, after which a slower dosage escalation, together with regular dosing with an oral antihistamine, may be advised.

Morbidity associated with desensitisation may be reduced by premedication with an oral antihistamine. In higher-risk settings, regular corticosteroids may also be added (e.g. prednisolone or prednisone 0.25 to 0.5 mg/kg orally daily).
APPENDIX 3: Follow up of positive cases (WA STI Guidelines 2006)

SYPHILIS FOLLOW-UP CHART*

RPR rising, or clinical signs of syphilis
Give penicillin and seek specialist consultation

RPR not fallen by four-fold or more
Repeat RPR 12 months after treatment

RPR fallen by four-fold or more

RPR not fallen by four-fold or more
Seek specialist consultation

RPR fallen by four-fold or more

RPR more than 1:16
Seek specialist consultation

RPR 1:16 or less
No further follow-up

RPR 1:16 or less
No further follow-up

RPR more than 1:16
Repeat RPR 12 months after treatment

* Adapted from the Central Australian Rural Practitioners Association 2003, Standard Treatment Manual, 4th edn, CARPA, Alice Springs.
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11. UpToDate 16.2 (2008)

National Standards – 1- Care provided by the clinical workforce is guided by current best practice
Legislation - Nil
Related Policies - Nil
Other related documents – Nil

RESPONSIBILITY
Policy Sponsor | Nursing & Midwifery Director OGCCU
Initial Endorsement | November 2001
Last Reviewed | September 2014
Last Amended | September 2017
Review date | September 2017

Do not keep printed versions of guidelines as currency of information cannot be guaranteed.
Access the current version from the WNHS website.