

# STANDARDS, LIMITS AND CONDITIONS FOR ORDERING AND INTERPRETING SCREENING AND DIAGNOSTIC TESTS<sup>1</sup>

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<sup>1</sup> Formerly *Guidelines for Ordering and Interpreting Diagnostic Tests*

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## **STANDARDS, LIMITS AND CONDITIONS FOR ORDERING AND INTERPRETING SCREENING AND DIAGNOSTIC TESTS**

The following are the College of Midwives of BC's standards for the screening and diagnostic tests which midwives are able to order, collect and interpret in the community, hospital or other sites of midwifery practice. This list is inclusive. Midwives may not order any other tests unless changes are made to the Standards, Limits and Conditions.

Midwives are expected to refer to the CMBC Indications for Discussion, Consultation and Transfer of Care document. Midwives are expected to recognize circumstances when it is appropriate to order diagnostic tests that are normally associated with low risk obstetrics. Midwives must consult with appropriate physicians when lab results indicate pathology.

The following list includes clinical circumstances in which midwives would be expected to order or perform diagnostic tests. The list includes both standardized and typical Reference Ranges for each test.

<b>Standard Reference Range</b> <b>Typical Reference Range*</b>
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Typical reference range means that laboratories can have different reference norms; most laboratories will provide the reference range on each laboratory report. If the reference range is not provided, the midwife should consult with the pathologist of the local lab facility or hospital. Management decisions on clinical data should be based upon local Reference Ranges where these differ from those provided in this guideline.

### **Note on Universal Precautions:**

Midwives should adopt a practice of universal blood and body fluid precautions when obtaining specimens. Protective clothing, latex gloves (or the equivalent), protective eye and/or face wear should be worn where indicated. Soap and water should be used to clean accidental exposure to skin. Surface spillage of fluids should be removed with a hypochlorite solution 1:100-1:10. Sharps should be carefully handled and disposed of in appropriate disposal containers. In the event of injury, the wound should be allowed to bleed, washed thoroughly, and the accident should be reported and followed up by an occupational healthcare provider.

### **Lab Referrals**

Midwives may order labs for clients admitted to hospital and refer clients to fee-for-service outpatient labs for all laboratory medicine tests outlined in this standard. For more information on current lab reference schedule and MSP fee codes, go to:  
<http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/laboratory-services-diagnostic-services/laboratory-services/practitioner-information/midwives>.

**1.a A midwife may order, collect samples for and interpret the report of the following maternal screening and diagnostic tests:**

**Actim Partus**

Actim Partus is an immunological rapid test to estimate the risk of preterm delivery. It detects phosphorylated form of insulin-like growth factor binding protein (IGFBP-1) in cervical fluid samples. Phosphorylated IGFBP-1 is the tissue form of IGFBP-1 produced by the decidual cells, and it is released in the cervical canal when the cervix matures.

Several studies indicate that the level of phosphorylated IGFBP-1 rises considerably as the cervix matures.

**Clinical Indications:**

Actim Partus can be used to assess whether preterm labor is imminent. A negative test result is a safe indication that imminent delivery or delivery within 7-14 days is highly unlikely.

The test is most useful when patients are symptomatic, gestational age is between 22 and 34 weeks and membranes are intact.

- 22 to 34 weeks gestation
- Threatened preterm labour (regular uterine contractions 10 minutes apart or less and/or pelvic pressure)
- Intact amniotic membranes
- Cervical dilation of 3 cm or less
- Reassuring fetal assessment

**Contraindications:**

- EGA <22 weeks or >34 completed weeks
- Preterm PROM
- Cervix >3 cm dilation
- Cervical cerclage
- Vaginal bleeding

*\*IGFBP-1 is not detected in urine or seminal fluid, therefore recent intercourse does not affect the Partus test results*

*\*Blood and amniotic fluid contains elevated levels of phosphorylated IGFBP-1, therefore Partus samples should be essentially free of blood and amniotic fluid to avoid false positive results.*

**Specimen Collection:**

The sample of cervical fluid is collected from the endocervix with a swab provided in the test package, ideally before digital exam to preserve cervical fluid. However, prior digital exam is not a contraindication to performing this test. After collection, the swab should be immediately transferred to the Specimen Extraction Solution while mixing the swab in the tube for 10 seconds. Dip the dipstick in the sample solution and keep it there until the liquid front reaches the result area. Remove the dipstick from the sample and let it develop for 5 minutes in horizontal position. Immediate testing is recommended, however if necessary the sample can be stored for up to 4 hours prior to testing.

The absence of *ph*/GFBP-1 in cervical secretions of those who are symptomatic and between 20 and 36 weeks gestation presenting with preterm contractions and intact membranes may be a reassuring sign that the likelihood of imminent preterm birth/delivery (PTB/PTD) is low before 35 weeks of gestation and within 7 days from testing. A negative *ph*GFBP-1 test result might rule out imminent PTB/PTD in up to 94% of this population who are symptomatic.

Due the small sample sizes, variable design, and eligibility criteria, the validity and reliability of these results are limited<sup>2</sup>.

A rapid Actim Partus testing device allows for results within 5 minutes. Specimens held during ongoing assessments (i.e. for contractions or other signs of labour) and not processed within four hours of collection must be discarded.

A positive Actim Partus result is an indication for physician consultation.

Please see Fetal fibronectin (fFN) for an additional rapid testing device to assist in determining possible preterm delivery.

### **Blood Glucose**

Used to screen for or diagnose glucose intolerance or diabetes and to monitor serum levels in daily management of diabetes. The efficacy and ethics of screening for gestational diabetes mellitus (GDM), and subsequent treatment and cost effectiveness continues to be debated<sup>3</sup>.

### **Gestational Diabetes testing options and diagnostic criteria**

There is strong evidence to support treatment when GDM is detected. However, there is insufficient evidence to demonstrate what types of screening can improve maternal and infant health outcomes<sup>4</sup>. The midwife will consider the unique health history, clinical judgment, community standards and guidelines (PSBC, SOGC and CDA) in determining when testing should be offered. An informed choice discussion including risks and benefits of testing or not versus diagnosis and treatment should take place. Tests for determining blood glucose include fasting random, HbA1C, 1-hour gestational screen (50 gram), 2-hour postprandial, 2-hour glucose tolerance test (75 gram).

Risk factors for Gestational Diabetes include:

- age >35
- member of a high risk population (Aboriginal, Hispanic, South Asian, Asian, African)
- pre-pregnant body mass index (BMI) >30 kg/m<sup>2</sup>
- previous history of GDM or glucose intolerance
- pre-diabetes
- family history of diabetes in first-degree relative
- history of GDM-associated adverse pregnancy outcomes, macrosomia, previous stillbirth, congenital abnormalities
- current fetal macrosomia or polyhydramnios
- history of polycystic ovary syndrome

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<sup>2</sup> Akercan F, Kazandi M, Sendag F, Cirpan T, Mgoyi L, Terek MC, et al. Value of cervical phosphorylated insulin like growth factor binding protein-1 in the prediction of preterm labor. *Journal of Reproductive Medicine* 2004, 49(5), 368-72.

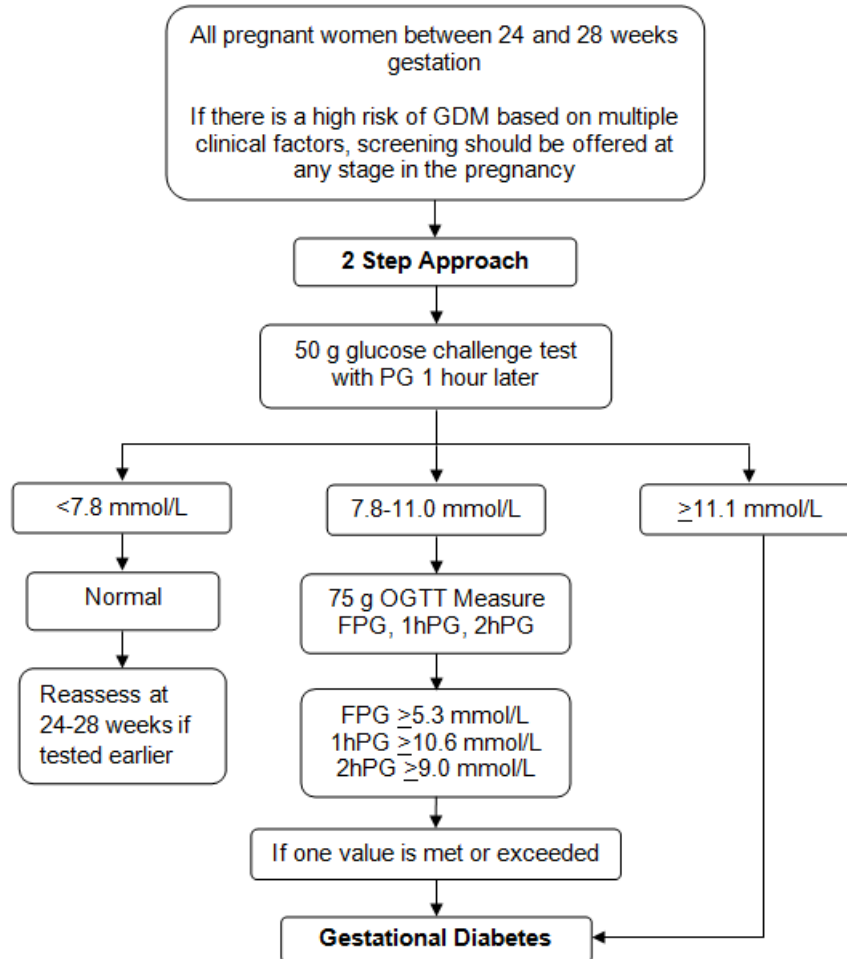
<sup>3</sup> Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, 2013. [Cochrane Database Syst Rev](#). 2010 Jul 7;(7):CD007222. doi: 10.1002/14651858.CD007222.pub2

### 1. Routine screening 2 Step Approach

Routine screening for pregnancies between 24 and 28 weeks gestation with the 50 gram oral glucose tolerance test followed by a plasma glucose (PG) 1 hour later.

See figure 1 below.

**Typical Reference Range\***: less than 7.8 mmol/L (140 mg/dL)<sup>5</sup>



**Figure 1, (Adapted from CDA 2013, Clinical Practice Guidelines)** *1hPG*, 1-hour plasma glucose; *2hPG*, 2-hour plasma glucose; *FPG*, fasting plasma glucose; *GDM*, gestational diabetes mellitus; *OGTT*, oral glucose tolerance test; *PG*, plasma glucose

or

### 2. Routine screening 1 Step Approach

Routine screening for all pregnancies between at 24-28 weeks of gestation with the fasting plasma glucose screen and with the 75 gram oral glucose tolerance test.

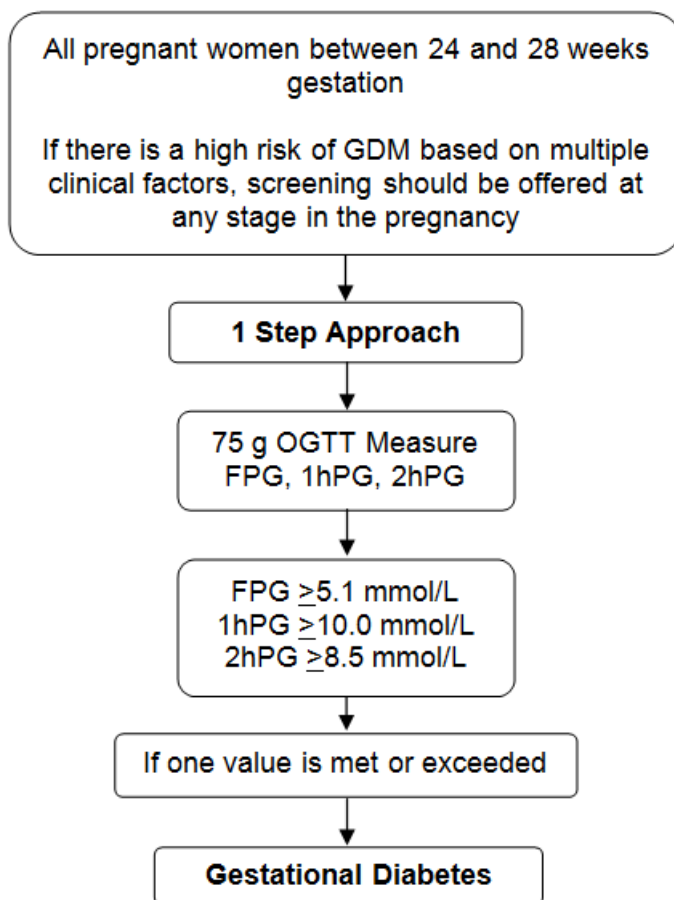
See figure 2 below.

<sup>5</sup> CDA, Clinical Practice Guidelines – Chapter 36: Diabetes in Pregnancy 2013

GDM is diagnosed if 1 value is met or exceeded<sup>6,7</sup>.

If at high risk for GDM based on multiple clinical factors (please refer to risk factors), screening should be offered at any stage in the pregnancy.

**Standard Reference Range:** less than (fasting) 5.1 mmol/L; (1 hour) 10.0 mmol/L; (2 hours) 8.5 mmol/L).



**Figure 2, (Adapted from CDA 2013, Clinical Practice Guidelines)** *1hPG*, 1-hour plasma glucose; *2hPG*, 2-hour plasma glucose; *FPG*, fasting plasma glucose; *GDM*, gestational diabetes mellitus; *OGTT*, oral glucose tolerance test; *PG*, plasma glucose.

Fasting PG or random PG or HbA1C

High risk: offer fasting PG or random PG or HbA1C with first prenatal bloodwork. These tests may be offered during pregnancy.

**Typical Reference Range\*:** HbA1C less than or equal to 6.5% at any time during pregnancy; FPG -less than or equal to 7.0 mmol/L; Random PG less than 11.1 mmol/L if reconfirmed by FPG or HbA1C.

<sup>6</sup> Perinatal Services BC (PSBC) 2010

<sup>7</sup> International Association of Diabetes and Pregnancy Study Groups (IADPSG) 2010

HbA1c (Haemoglobin A1c): First trimester glucose and glycosylated haemoglobin measurements may be used for counseling purposes about the risk of congenital abnormalities if there are risk factors as listed above, or if there is pre-existing diabetes. Achieving and maintaining a preconception value of less than 7% may decrease the risks of congenital malformation.

The risk of malformations is increased in infants of diabetics in the range of 4-10%<sup>8,9</sup>.

The HbA1C blood test is more effective in evaluating blood glucose control since results gives an average of blood glucose level over a two to three month period. These HbA1C readings do not fluctuate as routine blood tests do through the course of an average day.

If diagnosed with gestational diabetes, referral to a diabetic clinic or an endocrinologist for dietary and exercise counseling and instructions on the use of glucose self-monitoring is required. If glycemic control cannot be maintained, immediate referral to an endocrinologist or internal medicine specialist is indicated. Midwives can refer to the *Guidelines for the Management of Gestational Diabetes Mellitus*. If diagnosed with gestational diabetes, a repeat OGTT screen at or after 6 weeks postpartum should be done.

**The following tests remain optional, test availability and reference range may vary according to different labs<sup>10</sup>.**

#### Random blood glucose

Can be ordered in the evaluation of carbohydrate metabolism and diabetes mellitus. Random sugars are convenient, as a same day random blood glucose can be done in the clinic using a glucometer or at the lab to rule out pathology in the presence of glycosuria or other signs and symptoms of diabetes; however, a fasting and two-hour postprandial specimen may be more reliable in evaluating glucose control.

**Typical Reference Range\*:** 3.3-11.0 mmol/L

#### Fasting blood glucose

A fasting blood glucose can be ordered in combination with the 2-hour postprandial blood glucose test below.

Fast for 8 hours prior to test.

**Typical Reference Range\*:** 3.3-5.5 mmol/L

#### 2-hour postprandial blood glucose

Blood should be collected in the morning after an overnight fast and standard meal. The meal should be completed within 15-20 minutes. Specimen should be collected 2 hours from beginning of meal.

**Typical Reference Range\*:** 3.3-11.0 mmol/L

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<sup>8</sup> November JOGC 2007- SOGC Clinical Practice Guideline – Teratogenicity Associated with Pre-Existing and Gestational Diabetes

<sup>9</sup> HAPO is an acronym for Hyperglycemia and Adverse Pregnancy Outcome, a study that attempted to identify poor perinatal outcomes where blood sugar levels did not classify them as gestational diabetic (GDM).

<sup>10</sup> Reference Range - BC Life Labs Medical Laboratory Services June 2013



### **Blood Group and Type with Antibody Screen**

Human blood is grouped according to the presence or absence of blood group antigens (ABO). Found on the surface of red blood cells, these antigens can trigger the body's production of antibodies. Blood groups are identified for blood donation and blood transfusion. In addition, blood can be classified as either Rh-positive or Rh-negative in the presence or absence of the D antigen on the red blood cell membrane. The D antigen, Rh1 (D), is important to identify in pregnancy as fetal maternal hemorrhage of an Rh+ fetus to an individual who is Rh- can contribute to maternal antibody production. Maternal antibodies can, in turn, cross the placenta into the fetal circulation and attack the Rh+ fetal blood cells. This condition can be prevented if Rh- and a dose of RhIg is received at 28 weeks gestation and another dose within 72 hours of the birth of an Rh+ infant.

Blood Group, Type with antibody screen should be routinely ordered at the beginning of all pregnancies. If Rh-negative, information of the risks and the potential benefits of Rh immune globulin should be provided. Canadian Blood Services requests follow-up specimens at 24-26 weeks. If Rh-negative, Rh immune globulin should be offered after a miscarriage, amniocentesis, ECV, any trauma or an APH, and at 28 weeks gestation, and within 72 hours after the birth if the newborn is Rh-positive.

Postpartum Rh immunization can occur, even when RhIg has been administered, if a fetal maternal transfusion exceeds 30 mL. Therefore, those who are Rh-negative who have given birth to an Rh-positive infant should also have a Rosette test and/or a Kleihauer-Betke test to determine the presence of fetal blood in their circulation.

Antibody screening determines Rh-antibody levels and should be repeated every pregnancy.

**Standard Reference Range for Group:** A, B, AB, O.

**Standard Reference Range for RH1 D Type:** positive or negative.

**Standard Reference Range for Antibody titer:** negative is 0 (no antibody detected).

### **Incidence of Blood Group and Rh Type**

<b>Blood Group</b>	<b>% Rh–</b>	<b>% Rh+</b>
O	6.6	37.4
A	6.3	35.7
B	1.5	8.5
AB	0.6	3.4

### **Cervical and Vaginal Cultures and Smears (Including Sensitivities where Relevant)**

Canadian Guidelines on Sexually Transmitted Infections (STIs) – 2010 Edition published by Health Canada is highly recommended as a reference text for all midwives. Contact the Community Acquired Infections Division, Public Health Agency of Canada, Ottawa. Fax: 613-957-0381

Canadian STI Treatment Guidelines (2010) are available at: [www.publichealth.gc.ca/sti](http://www.publichealth.gc.ca/sti).

Site	Common Pathogens sought	Tests performed
Vagino-anorectal	Group B Streptococcus	Vagino-anorectal culture
Vagina	Bacterial vaginosis	Stained smear
Cervix	Chlamydia trachomatis Neisseria gonorrhoea	Chlamydia examination Cervical culture
First-catch urine	Chlamydia trachomatis Neisseria gonorrhoea	Nucleic acid amplification test (NAAT)*

***\*If testing is done by methods other than NAAT and sexual contact occurred < 48 hours prior to testing, tests may be falsely negative. Nucleic acid amplification testing (NAAT) should be used for screening asymptomatic individuals. Due to increased sensitivity of NAAT over culture, both gonococcal culture and NAAT may be indicated.***

Please ensure that the site of origin and the clinical condition for each genital specimen is clearly noted to ensure appropriate processing. The lab reserves the right to reject a specimen if either of these criteria are not indicated.

The following BC Ministry of Health document offers recommendations that should be followed when collecting samples to be submitted for laboratory diagnosis.

Recommendation	Explanation
<b>Use only the collection kit approved by the laboratory providing the assay</b>	Neisseria gonorrhoea and chlamydia trachomatis are sensitive to swabs or media not intended for collection of these pathogens. Collection kits are both technique and manufacturer specific. Collection kits provided for immunoassay cannot be used for culture or molecular diagnosis. Collection kits provided for one laboratory may be invalid for another laboratory if they use an assay from another manufacturer.
<b>Swabs must include cells from the patient in order to be an adequate sample</b>	When collecting samples from the female genital tract, both <i>N. gonorrhoea</i> and <i>C. trachomatis</i> are optimally collected by swabbing the cervical os. For those who have had a hysterectomy, submission of vaginal swab may be acceptable. Use only warm water for lubricating the speculum. It is important to remove excess mucus from the cervix with a dry swab before collecting the sample.
<b>Separate tests require separate samples</b>	<ul style="list-style-type: none"> <li>• Insert a sterile swab 1–2 cm into the endocervical canal, rotate 180° and withdraw for collection of columnar epithelial cells for diagnosis of Chlamydia trachomatis and Neisseria gonorrhoeae. The choice of swab should be based on the type of testing being done; consult with the laboratory providing the service.</li> <li>• A vagino-anorectal swab collected in pregnancy cannot be used to test for any organisms other than Group B streptococcus. Unfortunately this requires multiple samples being collected. Almost all laboratories will accept these multiple samples using a single requisition. If in doubt about a specific clinical situation, consult with the laboratory before collecting the samples.</li> </ul>

<p><b>Some laboratories require both a swab and microscopic slide for examination</b></p>	<p>Swab collection kits used for culture of <i>N. gonorrhoea</i>, <i>chlamydia trachomatis</i>, yeast, bacterial vaginosis, trichomonos and group b streptococcus often come in either charcoal, clear gel or amplified DNA assay media<sup>11</sup> to improve pathogen survival. Some laboratories request that the clinician also produce a smear for microscopic analysis at the time of sample collection. If both are requested, make the microscopic smear before putting swab in the transport medium.</p>
<p><b>Storage requirement</b></p>	<p><i>N. gonorrhoea</i> are extremely sensitive to low temperature.</p> <p><i>CMBC Note: BC Biomedical laboratories wrote “This only pertains to charcoal-containing transport media where the yield on N. gonorrhoea is improved if swabs are kept warm. On the other hand, for the clear transport media used by BC Biomedical Laboratories, the opposite is true – refrigeration greatly improves the survival of the GC organism” (BC Biomedical Laboratories Ltd, Physician’s Newsletter, September 2000, vol III, issue 3).</i></p> <p>Remember to <b>CHECK WITH YOUR LAB</b> for collection, storage and transport criteria.</p>
<p><b>Ensure that samples are transported to the laboratory quickly</b></p>	<p>If culture samples are unlikely to reach the laboratory within 24 hours they may not be worth collecting, unless special transport techniques are used. Some laboratories will provide fresh culture media for direct inoculation and a transport kit including a CO<sub>2</sub> generating tablet for the detection of <i>N. gonorrhoea</i> by culture. These kits prolong the survival of <i>N. gonorrhoea</i> and improve recovery.</p> <p><i>C. trachomatis</i> are sensitive to room temperature. Samples collected for culture must be transported at 4° C.</p> <p>Samples for detection of <i>C. trachomatis</i> by immunoassay or by molecular techniques are stable for a longer period of time and are more likely to survive transport.</p>
<p><b>Urine samples can be used for chlamydia and gonorrhoea</b></p>	<p>First voided urine is the best sample for testing. Urine samples for <i>C. trachomatis</i> and <i>N. gonorrhoea</i> testing are approved for nucleic acid testing for both males and females. NAATs are the most sensitive and specific and should be used whenever possible for urine, urethral, and cervical specimens; blood and mucous can affect NAAT performance<sup>12</sup>.</p> <ul style="list-style-type: none"> <li>• Both <i>C. trachomatis</i> and <i>N. gonorrhoea</i> can be detected from a single specimen in some NAATs.</li> </ul> <p><b>Urine - first-void nucleic acid amplification test (NAAT)</b></p> <ul style="list-style-type: none"> <li>• The patient should not have voided for at least 2 hours, but having done so does not preclude testing. A first-void urine</li> </ul>

<sup>11</sup> LifeLabs. Microbiology specimen handling & collection instructions. Doc. #8231, Ver #2.0 Aug 18, 2010 Retrieved March 27, 2012.

<sup>12</sup> <http://www.phac-aspc.gc.ca/std-mts/sti-its/guide-lignesdir-eng.php>

	<p>(FVU) may be collected at any time and may also be termed a first-catch urine (FCU).</p> <ul style="list-style-type: none"> <li>• Provide the patient with a leak-proof container.</li> <li>• Ask the patient to collect <i>only</i> the first 10–20 mL of urine into the container and to cap it tightly.</li> </ul>
<p><b>Consult with the laboratory before collecting samples for <i>T. vaginalis</i></b></p>	<p>Diagnostic assays for <i>T. vaginalis</i> differ between laboratories. For best recovery of <i>Trichomonas</i>, samples intended for culture require inoculation into special transport medium at the time of collection. Samples intended for saline wet mount require rapid transmission to the laboratory. Samples for latex agglutination or microscopic slide examination are not affected by transport.</p>
<p><b>Vagino-anorectal samples that are taken for detection of Group B streptococci can be collected using a single swab.</b></p>	<p>Swabs that are not being transported immediately should be refrigerated, but not frozen. The value of collecting swabs should be questioned if they are not likely to be set up for culture within 3 days of collection. Some laboratories may provide special transport medium (LIM) for vagino-anorectal swabs for Group B Streptococcus search. This medium is highly selective, and must be used only for Group B Streptococcus search. LIM medium cannot be used for transport of any other samples, including vaginal or rectal swabs for any other pathogens.</p> <p>Vagino-anorectal swabs are significantly superior to vaginal or rectal swabs alone for the detection of Group B Streptococcus.</p> <p>Anorectal swabs collected for detection of <i>N. gonorrhoea</i> are of no diagnostic value if contaminated with feces.</p>

**Bacterial vaginosis is not an STI.** It is characterized by a major change in vaginal flora from a predominance of lactobacillus to a large mix of anaerobic bacteria with little lactobacillus. Symptoms of bacterial vaginosis may include scanty, thin, homogeneous, milky, gray or white, malodorous discharge with a fishy odour, which may become worse after intercourse. Occasionally copious discharge with vaginal irritation, pruritis, with labial burning or pain is reported. However, 50% will remain asymptomatic. If the specimen is being sent to the lab for analysis, the swab should be collected from the lateral walls of the vagina. Alternatively, a specimen may be examined by doing a wet prep in the clinic. Examination of vaginal secretions will produce a positive KOH “whiff” test (fishy), a pH >4.5 and microscopic exam will reveal clue cells and little to no WBCs, although clue cells will be absent in up to 40% who have BV. BV infections have been associated with premature birth, preterm rupture of membranes and postpartum endometritis. Screening for BV may be of benefit at 12 to 16 weeks if the pregnancy is at risk (previous premature rupture of membranes, low birth weight, miscarriage, stillbirth, endometritis, premature delivery).

There is no consensus to screen or treat bacterial vaginosis if asymptomatic during pregnancy. If symptomatic, testing and treatment for BV is indicated. If at risk for preterm birth, routine screening for and treatment of bacterial vaginosis may be beneficial. A test of cure should be repeated one month post treatment. The treatment of choice is an oral course of metronidazole 500 mg twice daily for seven days or clindamycin 300 mg twice daily for seven days (SOGC, 2008).

**Chlamydia** is the most prevalent STI in North America. It is associated with pelvic inflammatory disease, infertility, ectopic pregnancy, premature rupture of membranes, preterm birth and postpartum infections such as ophthalmia neonatorum and neonatal pneumonia. Fifty percent of the population infected with chlamydia have no symptoms. Symptoms include mucopurulent discharge from the cervix, cervical edema and congestion with exstrophy of the columnar epithelium cells. During pregnancy, regardless of risks, screening for chlamydia is recommended early in pregnancy. A cervical swab is preferred, as chlamydia does not infect squamous epithelial cells. The specimen for gonorrhea should be obtained before taking the specimen for chlamydia. Labs can test for chlamydia using a number of procedures. A test currently in wide use is the polymerase chain reaction (PCR). This test provides significantly increased sensitivity over older methods such as EIA (enzyme immunoassay). Check local labs for methodology and test procedure available.

To obtain a cervical specimen:  
Insert a speculum to view the cervix;  
Remove overlying vaginal secretions;  
Insert a sterile cotton tipped swab 1 to 2 cm into the endocervical canal and rotate;  
Rotate for 10-30 seconds and withdraw, avoiding contact with vaginal walls;  
Place the swab in transport medium;  
Detection may be enhanced by using a Cytobrush. (The use of the cytobrush is not recommended during pregnancy)<sup>13</sup>.

Store swabs in refrigerator at 2-8° C until they can be transported. Specimens must reach lab within 4 days of collection.

All partners who have had sexual contact with the index case within at least 60 days prior to diagnosis, parents of infected neonates, must be located, clinically evaluated and treated with the same regimen as the index case.

#### Test for Cure:

Repeat testing for chlamydia is not routinely indicated in the non-pregnant population if a recommended treatment is given and taken and symptoms and signs disappear and there is no re-exposure to an untreated partner. Where symptoms persist, infection with other pathogens and a non-infective etiology should be considered.

Repeat testing is advisable for all children and those who are pregnant or when compliance is difficult to assess or if an alternative treatment regime has been used. This should be collected 3-4 weeks after completion of appropriate treatment. Culture or amplified nucleic acid tests are recommended.

#### Reporting:

Chlamydia infections must be reported by labs and primary care providers to the local public health authorities.

**Gonorrhea** is caused by the gram negative bacteria, *Neisseria gonorrhoea*. A large number of those infected with gonorrhea also have chlamydia and less frequently, also trichomonas. Gonorrhea is associated with prematurity, preterm rupture of membranes, pelvic inflammatory disease, infertility, endometritis and neonatal gonorrhea ophthalmia, which can cause

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<sup>13</sup> BC Cancer Agency December 2010

blindness. There may be no symptoms or there may be a combination of the following: lower abdominal pain, urethritis with tenderness, urinary frequency, and dysuria, purulent discharge from Skene's or Bartholin's glands or the urethra, tenderness of the Skene's or Bartholin's glands, yellow, purulent or mucopurulent vaginal discharge, or a history of metrorrhagia and menorrhagia. Diagnosis is by culture. Screening for chlamydia and gonorrhoea should be done during pregnancy where current or past history reveals STI risk behaviour. The specimen should be collected from the cervix. The specimen for gonorrhoea should be obtained before taking the specimen for chlamydia.

Charcoal medium cultures must be stored at room temperature. However, some labs use Ayres medium, and these must be stored in the refrigerator. Both culture techniques are effective. Neonates born to those infected with gonorrhoea must be tested and treated. Check with your local labs to determine transport medium and storage recommendations.

Test of cure is not routinely indicated in the non-pregnant population if a recommended treatment is given and taken and symptoms disappear and there is no re-exposure to an untreated partner. Follow up testing is recommended if the infection occurs in pregnancy and should be carried out approximately 4-5 days after the completion of therapy.

#### Reporting:

Gonococcal infections must be reported by labs and primary care providers to the local public health authorities.

Either of the following methods may be used to identify and manage those whose newborns might be at increased risk of **Group B Streptococcal disease**:

- Universal screening at 35-37 weeks gestation with a single combined vaginal-anorectal swab and the offer of intrapartum chemoprophylaxis to all who are GBS-colonized ;
- No universal screening, but intrapartum chemoprophylaxis if identified risk factors are present. This strategy should also be used in cases where universal screening is the policy, but either was not done or the test results are not available. Risk factors include:
  - Pre-term labour (<37 weeks gestation);
  - Term labour (>37 weeks gestation);
    - Prolonged rupture of membranes. (Neonatal benefits are optimally achieved if antibiotics are given at least 4 hours prior to delivery);
    - Fever during labour (>38° C orally);
  - Previous delivery of a newborn with GBS disease regardless of current GBS colonization status;
  - Previously documented GBS bacteraemia (SOGC, 2004).

**Trichomonas Vaginalis** is an anaerobic protozoan, is primarily sexually transmitted and frequently coexists with other STIs such as gonorrhoea, chlamydia and monilia. Symptoms include pruritis with a malodorous, copious, frothy or non-frothy, white/yellow-green/gray discharge which may be thin or thick. The odour may be fishy and a "whiff" test may be positive. The vagina may be inflamed, excoriated, with petechiae (strawberry patches) on the vaginal walls or cervix. There may be dysuria, dyspareunia or postcoital bleeding. Severe cases may cause significant pelvic and lower abdominal pain and tender inguinal nodes. There may be no symptoms but the parasite can be found in the vagina, cervix, bladder, urethra, or Skene's or Bartholin's glands. If the specimen is being sent to a lab for analysis, it

should be collected using a speculum without lubricant. The mucosa of the posterior vagina may be swabbed and placed into saline for transport to the lab. Specimen should not be refrigerated.

Alternatively, a direct microscopic examination for motile trichomonads may be done in the clinic (wet preparation). Wet mount may be negative in 30%-50% of the population with trichomonas. Vaginal pH is >4.5, "fishy" odour is sometimes present. On microscopic examination trichomonads are seen and WBC's are >10/hpf.

Reporting:

Trichomonas Vaginalis must be reported by labs and primary care providers to the local public health authorities.

**Yeasts (Candidiasis)** – Candida albicans is a common cause of fungal vaginal infection that 75% will experience at least once in their lifetime. Candida is rarely sexually transmitted. Its occurrence rate almost doubles in pregnancy. Predisposing factors include current or recent use of antibiotics, pregnancy, corticosteroids, poorly controlled diabetes mellitus, and immunocompromise. Symptoms include itch, external dysuria, vaginal discharge, and introital dyspareunia. Discharge is white, clumpy and adherent. Erythema and edema of the vulva, vagina and/or introitus may be evident.

Lab diagnosis includes pH <4.5, negative whiff test, wet mount with 10% KOH shows budding yeast and/or pseudohyphae.

Vaginal cultures for yeast are not routinely indicated and a positive culture by itself does not confirm candidiasis. A smear showing hyphae and inflammation is more specific.

When vulvitis is present without vaginitis, consider vulvar culture for yeast. Follow-up is not necessary unless signs and symptoms persist or reappear.

### **C Reactive Protein**

C-reactive protein (CRP) is an acute phase reactant synthesized in the liver that increases in inflammatory conditions, including sepsis. The level of CRP rises when there is inflammation throughout the body.

Maternal and/or neonatal CRP and white blood cell counts (WBC) are simple blood tests. CRP and WBC are markers for predicting early onset neonatal infection or determining the presence of infection in newborns in situations such as when there has been prolonged rupture of membranes or where the time period for intrapartum antibiotic prophylaxis administered to those who are GBS positive is less than 4 hours.

The overall incidence of neonatal sepsis ranges from one to five cases per 1000 live births. The risk for sepsis increases from 1 to 4 percent in neonates born where there is a maternal infection of chorioamnionitis. Group B streptococcal (GBS) bacteriuria during the current pregnancy, prior delivery of an infant with GBS disease, and maternal colonization are some risk factors for early-onset GBS sepsis. The risk of sepsis increases with decreasing gestational age and birth weight. Group B streptococcus (GBS) and Escherichia coli (E coli) are the most common causes of neonatal early-onset sepsis (EOS). In very preterm infants, the incidence of EOS with E coli is higher than with GBS.

Although an elevated CRP greater than 1 mg/dL is 90 percent sensitive in detecting neonatal sepsis, its poor specificity makes it a poor predictor for neonatal sepsis, as CRP is elevated in other noninfectious inflammatory conditions (eg, maternal fever, fetal distress, stressful delivery, meconium aspiration). In addition, CRP is not a sensitive test at birth because it requires an inflammatory response to increase its level. A single measurement of CRP soon after birth is not a useful marker in the diagnosis of neonatal sepsis. Serial CRP values however are useful in supporting but not confirming a diagnosis of sepsis. The isolation of a pathogen from a blood culture is the only method to confirm the diagnosis of neonatal sepsis. CRP testing is one amongst other laboratory findings that are used to identify infants with a high suspicion for sepsis, who are treated until culture results are available.

If the CRP level remains persistently normal, neonatal bacterial sepsis is unlikely<sup>14</sup>. If the CRP level is initially elevated then drops, it is an indication that the inflammation or infection is subsiding and/or responding to treatment. Infants with elevated CRP levels that decrease to <1.0 mg/dL 24 to 48 hours after the start of antibiotic therapy typically are uninfected and generally do not require further antibiotic treatment.

**Standard Reference Range:** <1 mg/dL

### **Cytomegalovirus Antibody**

CMV is a herpes virus that infects most people eventually. The mean age at the time of infection in adults is 29 years. The disease is spread by intimate contact with infected secretions, including breast milk, cervical mucous, semen, saliva and urine. CMV antibodies have been found in 40% to 100% of the adult population. More than 90% of primary infections are clinically silent. Congenital CMV can lead to low birth weight, microcephaly, intracranial calcifications, chorioretinitis, mental and motor retardation, sensorineural deficits, hepatosplenomegaly, jaundice, hemolytic anemia, and thrombocytopenic purpura. As with other herpes virus exposure, primary infection is more serious than recurrent, but both can lead to congenital infection. It is the most common cause of perinatal infection and occurs in 0.5-2 % of newborns. IgG and IgM testing may be done for those who may have been exposed to cytomegalovirus. Cord blood and urinalysis can be collected from the neonate at birth.

Primary infection can be diagnosed by detecting IgM CMV antibody. Recurrent infection is not usually accompanied by IgM antibody. There is no effective treatment for maternal infection. Neonates infected with CMV are treated supportively. Babies infected with CMV may continue to shed the virus for some time.

**Standard Reference Range:** Negative. If neither IgG nor IgM antibodies to the organism are detected, there has not been exposure, or the specimen was collected prior to an immune response. If IgM is detected, there was exposure to the organism and an immune response is developing. If IgG is detected and no IgM, there is immunity to the organism but this does not necessarily indicate there is currently an infection.

### **Fetal Blood Screen (Kleihauer-Betke) & Rosette Test**

The Kleihauer-Betke is performed as an aid in diagnosis of fetomaternal hemorrhage for those who are either Rh-positive or Rh-negative. The test is conducted during the postpartum if Rh-negative to *quantify* fetomaternal hemorrhage and determine required dosage of Rh immune globulin. Also performed during the antepartum period on those who have had invasive

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<sup>14</sup> *Treatment and outcome of sepsis in term and late preterm infants:* Retrieved Sept 16, 2014 from Up to Date.



procedures such as amniocentesis, an APH, miscarriage or trauma. A positive antepartum test is an indication for physician consultation.

A Rosette test is a *qualitative* test that detects Rh-positive fetal cells in the Rh-negative maternal circulation and is often used instead of the Kleihauer-Betke. It is used in situations where during pregnancy there is known Rh-negative status and the newborn is known Rh-positive. Quantitation of a fetomaternal hemorrhage is not possible by using a rosette test alone. The specimen should be collected shortly after birth.

**Standard Reference Range:**

Kleihauer-Betke: Negative – no fetal cells in circulation.  
Rosette: Negative for fetal blood; no Rh-positive fetal red blood cells detected.

**Fetal Fibronectin (fFN)**

fFN is a glycoprotein produced by the chorionic membranes that is known to have a role in binding the chorionic membranes to the adjacent maternal deciduas. It can be found in cervical and vaginal secretions until 22 weeks gestation. However, it is not normally present between 22 weeks and 34 weeks in the absence of premature effacement and dilation of the cervix.

Indications for fFN testing:

- 24 to 34 weeks gestation
- Threatened preterm labour (regular uterine contraction 10 minutes apart or less and/or pelvic pressure)
- Intact amniotic membranes
- Cervical dilation of 3cms or less
- Reassuring fetal assessment

Contraindications:

- EGA <24 weeks or >34 completed weeks
- Preterm PROM
- Cervix >3 cm dilation
- Cervical cerclage
- Vaginal bleeding
- Vaginal exam, vaginal ultrasound, or vaginal intercourse in the previous 24 hours

Specimen collection:

fFN specimens are collected using a Fetal Fibronectin Kit such as the ADEZA kit. The required equipment includes the swab, collection tube, tube cap, test cartridge and an instrument based system to perform the fFN test. The speculum exam must be done without the use of lubricants as these can alter the predictability of the test.

How to collect the fFN specimen:

- 1) During speculum exam, with no lubricant, lightly rotate the swab across the posterior fornix of the vagina for 10 seconds.
- 2) Remove the swab and immerse the tip into the buffer in the tube. The shaft of the swab is scored, snap the end off even with the top of the tube.
- 3) Align the shaft with the hole in the tube cap and push down; this will seal the tube. Check to be sure the shaft is aligned to avoid leakage.

A rapid fFN testing device allows for results within one hour. Specimens held during ongoing assessments (i.e. for contractions or other signs of labour) and not processed within eight hours of collection must be refrigerated (2-8 degrees Celsius) and assayed within three days of collection.

A positive fFN is an indication for physician consultation.

Please see Actim Partus for an additional rapid testing device to assist in determining possible preterm delivery.

### **Genetic Screening**

The purpose of prenatal genetic screening is to identify pregnancies at increased risk of chromosome disorders or structural anomalies. BC has a serum-based approach to prenatal genetic screening, with nuchal translucency (NT) (see Ultrasound in section 3 of the Standards) added for those at higher risk of having a fetus with Down syndrome or trisomy 18 and for those with multiple gestations. Serum integrated prenatal screen (SIPS), integrated prenatal screen (IPS), quad marker screen (Quad), maternal serum alpha-fetoprotein (MSAFP), non-invasive prenatal test (NIPT), and detailed second trimester ultrasounds are some of the options available<sup>15</sup>. Reliability of serum testing is dependent on accurate determination of gestational age. A thorough informed choice discussion should be a part of offering genetic screening options. Additional information and requisitions for serum genetic screening in BC can be found at [www.bcprenatalscreening.ca](http://www.bcprenatalscreening.ca).

#### **Serum Integrated Prenatal Screen (SIPS)**

SIPS involves both first trimester pregnancy-associated plasma protein A (PAPP-A) and second trimester quad markers (AFP, uE3, hCG and inhibin-A) measured in two separate blood tests. PAPP-A is collected between 9 and 13+6 weeks (best 10-11+6 weeks), and the quad marker test between 15 and 20+6 weeks (best 15+2-16+6 weeks) and results are available within 10 days of the second test. Samples are taken locally and sent to the Prenatal Biochemistry Lab for analysis.

*For pregnancies which have had an early dating ultrasound – the best time for the Part 1 blood draw is at 10+2 weeks gestation. For pregnancies where there is no early ultrasound available – the best time for the Part 1 blood draw is at approximately 11 weeks gestation. Waiting until 11 weeks will not delay results as they are not available until after the Part 2 sample has been received.*

#### **Integrated Prenatal Screen (IPS)**

IPS involves a first trimester serum PAPP-A and a nuchal translucency (NT) ultrasound, followed by second trimester serum quad markers. The timing for serum markers is the same as for SIPS and the NT is done between 11 and 13+6 weeks (best 12-13+3 weeks). Nuchal translucency is only available at specific centres and access is prioritized for those at higher risk of Down syndrome or trisomy 13, 18 or 21 and for those with multiple gestations. Results are available within 10 days of the second blood test.

#### **Quad Screen (formerly Maternal Serum Screening MSS)**

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<sup>15</sup> PSBC Obstetric Guideline 17: Prenatal Genetic Screening 2014

This screen measures the following second trimester serum markers: human chorionic gonadotropin (HCG), alpha-fetoprotein (AFP), unconjugated estriol (uE3) and inhibin A. The timing for serum quad markers is the same as for the second SIPS serum test between 15-20+6 weeks (best at 15+2-16+6 weeks). This test may be offered to those who enter care after 13+6 weeks to assess relative risk of the fetus being affected with open neural tube defects or trisomy 13, 18 or 21. Samples are taken locally and sent to the Prenatal Biochemistry Lab for analysis. Results are available within 10 days.

### **Maternal serum alpha-fetoprotein (MSAFP)**

This screen measures second trimester maternal serum AFP to screen for open neural tube defects (ONTDs) such as anencephaly, spina bifida and myelomeningocele. While also measured as a part of SIPS, IPS and the Quad screen, MSAFP alone is available for singleton pregnancies who have had a first trimester screen (PAPP-A, free beta hCG and NT ultrasound) and/or chorionic villus sampling (CVS). If declining SIPS, IPS or Quad for Down syndrome and trisomy 18 screening but screening for ONTDs is requested, MSAFP alone can be measured, however the detection rate of open neural tube defect is only 70%. This screen should be limited to those with a BMI > 40, or with limited access to a quality 18-20 week ultrasound. A detailed ultrasound at 18-20 weeks gestation has a higher detection rate for neural tube defect. The timing for MSAAFP is the same as for SIPS, IPS and the Quad screen, between 15 and 20+6 weeks (best 15+2 - 16+6 weeks). Results are available within 10 days of the blood test.

***TWO prenatal biochemistry lab requisitions are needed for SIPS/IPS testing – one for each blood draw. The first requisition must be filled in completely, including early ultrasound information if available, weight and diabetes status. The second requisition must include information to identify the patient and any updated information, such as an ultrasound performed after the first blood draw.***

***For Quad or serum AFP alone: the patient will be going once to the lab:***

***- To be drawn between 15 to 20+6 weeks gestation (best at 15+2 - 16+6 weeks).***

***ONE Prenatal Biochemistry Lab requisition is needed for this testing. Reference ranges are dependent on gestational age.***

### **Non-Invasive Prenatal Test (NIPT)**

NIPT measures cell free fetal DNA circulating in maternal blood and tests for Down syndrome, trisomy 18, trisomy 13, and sex aneuploidy. The detection rate for Down syndrome is >99% accuracy with less than 0.1% false positives; the detection rate for trisomy 18 is approximately 98% with less than a 0.1% false positive rate. NIPT requires one blood sample to be drawn any time after 9-10 weeks gestational age, depending on indication and NIPT vendor.

NIPT can be ordered by Registered Midwives. It is available as funded first-line genetic screening for those who have had a previous trisomy 13, 18 or 21 pregnancy, and as second-line screening for those with a positive SIPS/IPS/QUAD screen or with a risk of Trisomy 21 greater than one in 300 based on results of screening and ultrasound markers of aneuploidy. NIPT is also available as a private-pay option as an alternative to SIPS/IPS/QUAD screening.

### **Hematocrit**

Used to evaluate anemia, blood loss, hemolytic anemia, polycythemia and state of hydration. Test is performed on blood collected in capillary tubes from venipuncture, finger or heel pricks.

<b>Typical Reference Range*:</b>	(%) First Trimester	31.0 - 41.0
	Second Trimester	30.0 - 39.0
	Third Trimester	28.0 - 40.0

Note: HCT may not be reliable immediately after even a moderate loss of blood, IV bolus infusion or a transfusion. If blood is drawn from a capillary puncture and a microhematocrit is done, values are slightly higher. Normal hydraemia of pregnancy slightly decreases hematocrit.

### **Hemoglobin**

Used to evaluate anemia, blood loss and response to iron therapy. This test is recommended in the first and third trimester. It is performed on blood collected from venipuncture or finger prick. Used more commonly than hematocrit.

**Typical Reference Range\*:** 114-143 g/L

Note: Hemoglobin concentration falls in pregnancy due to normal pregnancy hydraemia. Where iron deficiency is suspected, serum ferritin is the test of choice.

### **HbA1c (haemoglobin A1c) – Please see Blood Glucose section**

### **Hepatitis**

Hepatitis is an infectious process that causes inflammation of the liver. Hepatitis B is the most common cause of hepatitis compared to Hepatitis A and C. Forty-five percent of Hepatitis B is sexually transmitted. Infants born to those who are HbsAg positive are at high risk of infection. Infants born to those with Hep A and C are at less risk. Screening for HbsAg is strongly recommended for all pregnancies, especially those at risk. An HBsAg positive result indicates either current infection or a chronic carrier state. All children born to those who are HBsAg positive or going home to a household where there is an HBsAg positive member should be actively AND passively immunized.

An anti-HBs positive screen indicates immunity to the virus acquired as a result of previous infection or vaccination. If symptomatic for active infection, screen for HBsAg and referral to a physician for immediate follow-up should be made.

Hepatitis A is most commonly transmitted through contaminated food or fecal-oral household contamination. While there are no chronic carriers and perinatal transmission is not an issue, Hepatitis A infection poses particular risk to those co-infected with HCV or HIV. If IgM-HAV positive, a current infection may be present and a referral to a physician for follow-up should be made.

While perinatal transmission of Hepatitis C occurs much less efficiently than with Hepatitis B, it does occur. For those at high risk of infection, such as those with a history of blood transfusion prior to 1992 or of intravenous drug use, should be offered anti-HCV testing and appropriate counseling. It should be noted that the absence of anti-HCV does not exclude active Hepatitis C. If acute infection is suspected, a referral to a physician should be made with advice that testing should be repeated within three to six months.

When a hepatitis infection is suspected to have been parenterally transmitted, HIV testing is also strongly recommended. (Canadian STI guidelines, 2010.)

**Standard Reference Range:** Negative.

**Herpes Simplex Virus Serology** (*updated November 2017*)

Herpes simplex virus is categorized into two types: herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2). Both are highly infectious and incurable. HSV-1 is primarily transmitted by oral contact and usually causes orolabial herpes (cold sores) but is increasingly implicated in genital herpes, causing up to 45% of new outbreaks in BC (2017). HSV-2 is almost entirely sexually transmitted and causes genital herpes.

Genital herpes outbreaks at time of labour and primary genital herpes outbreaks during the third trimester of pregnancy can result in serious morbidity and mortality for the newborn. Up to 70% of newborns with neonatal herpes are born to those without a history of genital herpes. Consequently, comprehensive screening for genital herpes in both the pregnant client and their partner should be done in early pregnancy.

With a history of genital herpes in the pregnant client, HSV serology is not required; but counseling about suppressive antiviral therapy starting at 36 weeks, the risks of transmission of HSV to the neonate at birth, and mode of delivery is strongly advised. **With a history of genital herpes in the partner but not in the pregnant client**, there is a significant risk of primary infection in pregnancy. Non-type specific HSV IgG serology may be offered to confirm possible prior exposure, but counselling and clinical management should be the same regardless of results given the prevalence of HSV-1 in the population (66% globally in those under the age of 50). Midwives should counsel the couple on safer sex practices including abstinence from oral and/or genital sexual contact and judicious condom use, and consider referral to a family physician or nurse practitioner to consider suppressive therapy for the partner for the duration of the pregnancy (Canadian STI Guidelines, 2010).

Type-specific serology

Type-specific serology is used to differentiate between HSV-1 and HSV-2 infections, though not where on the body the outbreak has occurred. It is typically not indicated in pregnancy, but may be of limited use in determining past exposure in the pregnant client if the partner has a history of genital herpes confirmed by type-specific serology.

Non-type specific serology

Non-type specific serology can assist in determining whether or not someone has been exposed to herpes of any kind at some point in their life. **Positive non-type specific serology indicates previous oral or genital infection, and negative non-type specific serology confirms no prior exposure.** Those who are pregnant and do not have a history of HSV but have a partner with genital HSV should have HSV serology ordered to determine risk of acquiring genital HSV in pregnancy as early in pregnancy as possible. If serology is negative, it should be repeated at 32 to 34 weeks' gestation.

**Standard Reference Range:** Negative or Positive

**Human Immunodeficiency Virus Antibody**

It is estimated that 40,000 to 50,000 Canadians are infected with HIV. Seroconversion usually occurs by 12 weeks but may take up to 6 months. During pregnancy, HIV testing and counseling should be offered. Refer to the Pre-Test Counseling Discussion for HIV Infection (Canadian STI Guidelines, 2010). Testing should only be carried out with consent and if HIV testing is declined, document refusal and the reason for it.

***The midwife must consult a physician who will initiate antiretroviral therapy for those who are HIV positive during pregnancy.*** Initiation of antiretroviral therapy during pregnancy is critical for the survival of infants born to those infected with HIV because it markedly reduces the risk of maternal-fetal transmission from 25% to <1% (Canadian STI Guidelines, 2010).

**Standard Reference Range:** Negative.

<b>Clarify</b>	<ul style="list-style-type: none"> <li>➤ Confidentiality of HIV testing &amp; counseling</li> <li>➤ Testing options available (i.e., nominal, non nominal, anonymous)</li> <li>➤ The test is for antibodies to HIV – it is not a test for AIDS</li> <li>➤ The majority of persons produce detectable antibodies within 3 months</li> <li>➤ A non-reactive or negative test may mean no infection or too soon to detect antibodies</li> <li>➤ A positive test means infection with HIV – the person is infectious to others through unprotected sexual contact, blood or breast milk</li> <li>➤ An indeterminate result means another test needs to be performed</li> <li>➤ HIV is NOT casually transmitted through sweat, tears or saliva</li> <li>➤ Transmission risks are: direct blood to blood contact, sharing needles or syringes and sexual contact: anal sex (very high risk); vaginal sex (high risk); oral sex (low risk)</li> <li>➤ Transmission of infection during pregnancy, at birth or via breast milk</li> <li>➤ Recipient of blood or blood products in Canada before November 1995 (elsewhere risk will vary depending upon testing of donated blood)</li> </ul>
<b>Discuss</b>	<ul style="list-style-type: none"> <li>➤ Specific risks, sexual and otherwise</li> <li>➤ If pregnant, discuss availability of therapy to decrease the risk of in utero transmission (decreased by 80%)</li> <li>➤ Whether future testing will be necessary</li> <li>➤ Risk reduction behaviors: consistent use of latex condoms; avoidance of casual/anonymous/unprotected sex; no sharing of needles, syringes or injection drug use equipment</li> </ul>
<b>Explore</b>	<ul style="list-style-type: none"> <li>➤ Psychological implications of testing: coping mechanisms for either result; support systems available (personal, community, medical) should be known</li> </ul>
<b>Explain</b>	<ul style="list-style-type: none"> <li>➤ The need to return for test result and schedule the post test counseling – visit and obtain agreement for follow up appointment if patient fails to return</li> <li>➤ Post test counseling procedure (see STI guidelines)</li> <li>➤ Partner notification and reporting requirements for HIV infection (depends on jurisdiction and availability of anonymous testing)</li> </ul>

## Pap Smears

The Pap smear is the most effective screening method for the detection of cervical cancer and its precursors. It is recommended for all who are or have ever been sexually active. The specimen should be obtained in accordance with the BC Cancer Association guidelines:

1. Print name and date of birth on the frosted end of the slide using a lead pencil and complete cytology requisition.
2. Gently insert a prewarmed speculum to visualize cervix.
3. Gently cleanse the cervix with cotton swab if obscured with discharge or secretions.
4. Identify extent of transformation zone and probable squamocolumnar junction.

**If squamocolumnar junction visible:** Rotate a spatula through 360° once to obtain a single specimen. Smear on slide. *Applying a fixation agent is now recommended.*

**If squamocolumnar junction not visible:** First use a spatula for the exocervical specimen, then if necessary use the elongated end of the spatula for the endocervical sample. Use of a cytobrush is not recommended during pregnancy<sup>16</sup>. Place both specimens on a single slide and *fix immediately*.

### Cautions:

- If a clinically suspicious lesion is seen, refer for biopsy immediately.
- If menstruation or infection is present reschedule exam.

**Frequency of screening:** Women between the ages of 25 to 60 should be screened for cervical cancer every three years. With cytological abnormalities, screening should continue according to laboratory recommendations. Pregnancy does not affect the recommendations for screening frequency.

## Parvovirus (B19 Infection)

Also known as erythema infectiosum (fifth disease) and/or slap cheek disease.

An acute contagious viral infection characterized by mild symptoms and a maculopapular rash beginning on cheeks and spreading to trunk and extremities. Disease is caused by human parvovirus B19. Occurring mostly during spring months and outbreaks commonly occur among children and adolescents. Spread appears to be by the respiratory route. This infection can also occur without signs or symptoms.

Parvovirus B19 can be transmitted transplacentally, sometimes resulting in stillbirth or severe fetal anemia with hydrops fetalis. The risk of fetal death is <10% after maternal infection in the first half of pregnancy and is even lower in the second half. Parvovirus B19 may have some similar features to rubella and other enteroviruses. There is no effective treatment for maternal infection. Recommendations have been made for serial testing of the fetus by ultrasound.

### Parvovirus B19 Serology

Anti-B19 IgG and IgM testing may be done for those who may have been exposed to Parvovirus B19.

**Standard Reference Range:** The presence of IgM specific antibody in the late acute or early phase strongly supports the diagnosis. If IgM is detected (reactive), exposure to the organism

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<sup>16</sup> BC Cancer Agency December 2010

and the development of an immune response can be confirmed. If IgG is detected (reactive), and no IgM (non reactive), immunity to the organism can be confirmed and indicates that a current infection is not present. Non-reactive IgG signifies no immunity to parvo virus.

Note: The PHSA stores the serum of all specimens collected in early pregnancy until after the due date. Midwives can request an anti-B19 IgG and IgM titre if there has been contact with parvovirus and immunity is unknown.

### **Platelet Count**

Included in a complete blood count (CBC), platelets play a role in clot formation. Thrombocytopenia is an abnormal blood condition in which the platelet numbers are reduced. It is usually caused by a breakdown of tissue in bone marrow linked to certain tumor diseases or an immune response. Low platelets are a common cause of bleeding disorders and are also part of HELLP syndrome. Thrombocytosis or high platelets may be due to postpartum, exercise, myeloproliferative syndromes, rebound following thrombocytopenia, rapid blood regeneration after bleeding episode, hemophilia, iron deficiency, asplenic, infections, inflammatory or malignant disease.

<b>Typical Reference Range*:</b>	First Trimester	174-391 x 109 /L
	Second Trimester	155-409 x 109 /L
	Third Trimester	146-429 x 109 /L

### **Pregnancy Test (Blood and Urine)**

#### Qualitative (urine)

Test detects levels of HCG in urine. First morning voided urine preferred. Specimen should be delivered to the lab immediately following collection and kept refrigerated.

**Standard Reference Range:** Positive or negative. Negatives may occur early in pregnancy, ectopic pregnancy or threatened abortion when HCG levels are not yet within the range detected by the test. Negative results may also occur in specimens with specific gravity <1.010, due to dilution of HCG down to an undetectable range.

#### Qualitative Beta HCG (Serum)

Used to confirm pregnancy or diagnose early ectopic pregnancy.

**Standard Reference Range:** Concentrations of  $\beta$ -HCG in the non-pregnant population are usually <5 IU/L. Levels between 5IU/L and 25 IU/L may indicate pregnancy. Test is considered positive when  $\beta$ -HCG is >25 IU/L.

Correlation with other clinical findings (e.g. LMP, pelvic exam) should be sought in evaluating the determined  $\beta$ -HCG levels. Values for  $\beta$ -HCG generally peak during the first trimester and decline slowly throughout the remainder of pregnancy. Causes for increased  $\beta$ -HCG other than pregnancy include choriocarcinoma, hydatidiform mole, ovarian cancer, cancers of the breast, lung, kidney, GI tract, pancreas, liver, malignant melanoma, and sarcoma. Drugs such as Pergonal and Clomid can cause false positives. In a normal pregnancy, the test is expected to become positive within 3 days of implantation.

#### Quantitative Beta HCG (Serum)

Reserved for non-routine detection of HCG, e.g. ectopic pregnancy, threatened abortions, miscarriages, or very early pregnancy. Sequential measurements may be required in some clinical circumstances. Normal  $\beta$ -HCG levels do not rule out ectopic pregnancy. Chorionic



gonadotropin assays may be used to support the diagnosis of ectopic pregnancy. Ectopic gestations do not develop or secrete HCG as do intrauterine pregnancies. Abnormal HCG levels coupled with transvaginal ultrasound detect many ectopic pregnancies prior to rupture.

**β-HCG quantitative, serum levels Standard Reference Ranges:**

	IU/L
Pregnancy (single fetus) 1 <sup>st</sup> week	<25
2 <sup>nd</sup> week	<200
3 <sup>rd</sup> week	50-2,000
1 <sup>st</sup> trimester (reach a peak between 60-90 days after the last menstruation)	15,000-100,000
2 <sup>nd</sup> trimester	3,000-60,000
3 <sup>rd</sup> trimester	500-40,000
Postpartum 14 days	Levels may be detectable in this period
Non-pregnant female	<5
Trophoblastic disease	The presence of measurable β-HCG in plasma or serum is consistent with the presence of trophoblastic tissue which signifies disease.
Other HCG-producing tumors	As for trophoblastic disease
Negative	All values <5

**Red Blood Cell Morphology**

An evaluation of red blood cells in the preliminary investigation of anemia. Red Cell Morphology is performed by making a thin smear of whole blood on a glass slide and staining it. The slide is then placed under a microscope and the red cells (erythrocytes) are examined to for their size characteristics, colour (deepness of red as an indicator of hemoglobin content), unusual shape, presence of nuclei, and mixtures of normal and abnormal. This examination is generally performed by a hematopathologist in conjunction with an examination of the white cells. There are no absolute abnormal ranges used in morphology as the examination is subjective.

In assessing red cells, the Red Cell Indices (Mean Corpuscular Volume, Mean Corpuscular Hemoglobin) is done automatically as part of a Hematology Panel. If these and the hemoglobin and hematocrit are normal in a person in whom no other disease is suspected, there is very little chance that there is anything wrong with their hematology picture. In such cases a RBC Morphology is not necessary. If there is abnormality in these parameters, the examination is automatically extended to include a morphology, and therefore this test does not require a specific order. These blood smears are routinely examined by a hematopathologist when they are done. Red Cell Morphology appears in Schedule 2 to ensure that labs are authorized to perform a morphology on blood work ordered by a registered midwife and to report those results to the midwife.

**Rubella Antibody (IgG- Immune Status)**

Used to evaluate rubella immune status. Primary rubella exposure in the first trimester will result in a fetal infection rate of 80%. Fetal infection is less common when exposure occurs later in pregnancy. During pregnancy, those without immunity or who acquire primary rubella

should be counseled on the risks of exposure. If spontaneous abortion does not occur, then surviving infants may have cardiac defects, hearing problems, cataracts and experience significant developmental delays. They are highly infectious at birth and should be isolated.

**Standard Reference Range:**  $\geq 10$  IU/mL Rubella IgG indicates immunity.

Blood is sent to PHSA for testing. If antibodies are not detected during pregnancy, there is susceptibility to infection and follow up should be done accordingly. If exposed to rubella during pregnancy and antibodies are detected within the first 2 weeks after exposure, risk of damage to the fetus is considered to be negligible. If no antibody is detected, a subsequent serum specimen obtained 2 weeks later should be sent to the laboratory to determine whether a fourfold rise in antibody titre has occurred. If non-immune to rubella and pregnant, immunization should be offered in the immediate postpartum period. Pregnancy should be avoided for three months after immunization.

### **Serum Ferritin**

This test is ordered to evaluate microcytic anemia and iron storage diseases. It should not be ordered during iron therapy.

**Typical Reference Range\*:**  $>12$  mcg for adult females.

Serum ferritin is one of the most reliable indicators of total body iron stores. High serum ferritin levels may be associated with inflammation, liver disease, megaloblastic anemia, hemolytic anemia, thalassaemia, iron overload and malignant diseases. Very high levels indicate iron overload.

### **Serum B12**

This is the standard test to evaluate B12 (cobalamin) deficiency. Because the test measures total rather than metabolically active B12, test results should always be interpreted in the light of clinical symptoms.

**Typical Reference Range\*:** 150-600 pmol/L. Using this value, the following interpretation is recommended:

<75 pmol/L	Deficiency highly likely
75-150 pmol/L	Probable deficiency
150-220 pmol/L	Low probability of deficiency (3-5%)
>220 pmol/L	Deficiency rare

The most common cause of B12 deficiency is food-cobalamin malabsorption. Oral B12 supplementation is the treatment of choice in most cases. For those with significant neurological symptoms, referral to a physician for assessment and parenteral B12 therapy should be made. The most serious cause of B12 deficiency is lack of intrinsic factor resulting in pernicious anemia. If pernicious anemia is suspected, referral to a physician for appropriate follow-up should be made. (Investigation and Management of Vitamin B12 and Folate Deficiency, BCMA and MSP Guidelines and Protocols Advisory Committee, 2002.)

### **Sickle Cell Solubility (Sickle Cell, Sickle Prep, Sickledex)**

Used in the detection of sickling hemoglobins; the evaluation of hemolytic anemia; undiagnosed hereditary anemia, morphologic (sickle like) abnormalities on peripheral blood

smear. For those with a positive sickle cell screen test, further evaluation with alkaline Hgb electrophoresis, acid electrophoresis, Hb F studies and family studies is recommended.

**Standard Reference Range:** Negative.

### **Hemoglobin electrophoresis**

This test is performed when a disorder associated with abnormal haemoglobin (hemoglobinopathy) is suspected. Many different types of hemoglobins can be evaluated, the most common being A1, A2, F, S, and C. The test is used primarily to diagnose diseases involving abnormal forms of hemoglobin production, such as in sickle cell anemia and thalassemia.

### **Thalasaemia/hemoglobinopathy**

The thalassemias are a group of inherited blood disorders caused by abnormal production of hemoglobin which can present in varying degrees of anemia, hypochromic microcytosis and sometimes elevated ferritin. They are more common in people from South East Asia, India, the Middle East, Mediterranean countries, and Africa. Persons with alpha or beta Thalassemia trait are usually asymptomatic, while homozygotes are significantly affected. Screening tests include a hematology panel (CBC), blood film examination (morphology), haemoglobin H body preparation and high performance liquid chromatography (HPLC) and polymerase chain reaction (PCR) assays. Clinical information, including ethnicity and family history, is valuable in the interpretation of the haemoglobin analysis. Genetic counselling is advised if both genetic contributors are positive for Thalassemia trait.

### **Swabs for Culture and Sensitivities**

Midwives may collect swabs for culture and sensitivity for screening or when indications warrant during the prenatal, intrapartum and postpartum period. Included are screening swabs for antibiotic resistant organisms (ARO), vaginal, cesarean section wounds that are suspicious of infection, episiotomies or perineal tears that appear infected etc. A prenatal ARO swab is indicated for those with a previous history of Methicillin-resistant Staphylococcus Aureus (MSRA) or other ARO; for those who are in close contact with a health care worker in an institution where AROs are a problem; and for those who are at risk (homeless, those with problematic substance use, or a previous hospital admission).

Swabs should be sent to the local lab for analysis and a referral made to a physician for treatment in the event that an infection is identified.

If no evidence of infection is found but non-symptomatic ARO carrier status is determined, the midwife should reinforce hand hygiene and encourage antiseptic bathing and/or topical therapy. If signs of infection are identified, a referral to a physician should be made. Re-swabbing is indicated following decontamination management to establish carrier status. Treatment should be discontinued if subsequent culture and sensitivity is negative.

### **Stool culture for infectious diarrhea**

In most cases of mild diarrhea, etiology is usually viral in nature, while in severe diarrhea and if associated with fever and bloody stools, etiology is usually bacterial. Parasites are a common cause of chronic infectious diarrhea. Norovirus and rotavirus are the most common gastrointestinal viruses associated with hospital and community related outbreaks.

Microbiology laboratories may test stool specimens submitted for bacterial culture routinely for the following: Campylobacter, Salmonella, Shigella, E. Coli. Local laboratories may be consulted for information on pathogens routinely tested.

**C. difficile toxin testing is not part of a routine stool culture and may need to be specifically requested. See criteria below.**

### **Clostridium difficile**

C. difficile is a gram positive, anaerobic, spore-forming bacillus that is responsible for development of antibiotic associated diarrhea and colitis. C. difficile colitis is one of the most common nosocomial infections.

C. difficile infection may manifest as mild to moderate diarrhea, with or without abdominal cramping to life threatening colitis, sepsis and bowel perforation. In rare circumstances, C. difficile can be fatal<sup>17</sup>. C. difficile colonization may manifest in asymptomatic carriers. Approximately 20% of individuals acquire C. difficile during hospitalization.

#### Indications for testing:

C. difficile should be suspected in any individual presenting with diarrhea who has received antibiotics within the previous 2 months and/or when diarrhea occurs 72 hours or more following hospitalization<sup>18</sup>. In most circumstances, diarrhea develops during or shortly following the start of antibiotics. As many as 25-40% of individuals may not become symptomatic for as long as 10 weeks after completion of antibiotic therapy.

Symptoms may include: Anorexia, cramping, abdominal pain, dehydration, fever, malaise, mild to moderate watery diarrhea which is rarely bloody.

**C. difficile toxin testing is not part of a routine stool culture and needs to be specifically requested<sup>19</sup> in the following circumstances:**

#### **Severe Diarrhea (of any duration)**

- fever >38.5 C
- profound systemic illness/toxicity
- hemodynamic instability
- greater than 6 diarrheal episodes per day for greater than 5 days
- bloody stools\*

*\*(with severe diarrhea where Clostridium difficile-associated disease (CDAD) is not suspected, bloody stools are usually tested for Escherichia coli)*

#### **Mild, Moderate Diarrhea (greater than 5 days duration)**

- recent (<3 months) or current antibiotic use
- recent hospitalization
- patient with a previous confirmed or suspected current episode of Clostridium difficile-associated disease (CDAD)

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<sup>17</sup> Public Health Agency of Canada. *Fact Sheet – Clostridium difficile (C. difficile)*. July 29, 2011. Retrieved April 25, 2012 from [www.publichealth.gc.ca](http://www.publichealth.gc.ca).

<sup>18</sup> Faten N Aberra, MD. *Clostridium Difficile Colitis*. Retrieved April 25, 2012 from Medscape.

<sup>19</sup> Guideline for Ordering Stool Specimen, March 16, 2009: Retrieved April 25, 2012 from [www.BCGuidelines.ca](http://www.BCGuidelines.ca)

- severe abdominal pain
- if Clostridium difficile-associated disease (CDAD) is suspected

Specimen Collection:

**Collection and Transport of Stool Specimens**

- For bacterial stool cultures such as C. difficile toxin testing: one stool specimen is sufficient in most cases and must be submitted to the lab as soon as possible.
- For viral pathogens: one stool specimen in a sterile container is sufficient in most cases.  
Viral stool cultures are tested for suspected viral gastroenteritis outbreaks and are not routinely tested. The local Medical Health Officer should be consulted.

All relevant clinical history should be included on the laboratory requisition.

***Please check your local lab for specific specimen collection kits and instructions***

Toxin detection is essential for the diagnosis of CDAD and may be performed by various methods. Culture of C. difficile alone is not diagnostic as non-toxin producing strains may be a part of the normal enteric flora.

Repeat or alternative testing may be required for patients with negative toxin results who have a high clinical suspicion of CDAD.

Stool culture is the most sensitive testing option (sensitivity 90-100%) although results can be slow and may lead to a delay in diagnosis. Other options for testing for C. difficile are available but have a lower sensitivity rate: Glutamate dehydrogenase enzyme immunoassay (EIA) (sensitivity 85-100%) however a positive test using this method will need to be confirmed with a subsequent assay, real time PCR may be used to detect the C. difficile gene toxin, stool cytotoxin test (sensitivity 70%-100%).

**Note: If initial C. difficile toxin test is negative and clinical suspicion is high, or if there are concerns regarding the timing of specimen collection and transport to the laboratory, consult the laboratory as additional testing may be indicated.**

**Standard Reference Range:** Negative

A physician consult is required with a positive result for C.difficile or with any other identified pathogens associated with infectious diarrhea.

**Syphilis Serology**

The spirochete Treponema Pallidum causes the sexually transmitted disease syphilis. Congenital syphilis is a serious infection and may leave debilitating sequelae. Universal screening during pregnancy is a standard of care in BC and should be done early in pregnancy. In the absence of prenatal care, you should screen at birth and delay discharge from hospital until screen results are available. Screening using non-treponemal tests such as RPR, VDRL, ART, RST EIA and TRUST determine the presence of reagin, antibodies to nontreponemal phospholipid antigens. Rarely, non-syphilitic conditions can give rise to false positive screening including acute bacterial or viral infections, pregnancy and even the common cold. A positive screen indicates the diagnostic test should be carried out, usually the FTA-ABS test (Fluorescent Treponemal Antibody ABSorbed) which uses treponemal antigens. Those at increased risk for syphilis include: youth <25 years of age, injection drug

users, commercial sex workers, street youth, and those originating from or who have had sex with a person from a syphilis endemic area (Canadian STI Guidelines, 2010).

**Standard Reference Range:** Negative

Syphilis must be reported to the local public health authorities in all provinces/ territories. Follow up testing is required. The regime is dependant upon the stage of syphilis. Infants born to those treated for syphilis must have pediatric assessment and follow up testing.

**Thyroid Stimulating Hormone & Free Thyroxin** (updated May 2018)

Thyroid Stimulating Hormone (TSH) and Free Thyroxin (fT4) are thyroid function tests used to detect thyroid disorders. Because of a possible connection between untreated overt maternal hypothyroidism and neuropsychological impairment in the offspring, TSH testing is indicated in pregnancy (ideally in the first trimester) in those with risk factors for thyroid disease:

- Age >30 years
- More than two prior pregnancies
- History of pregnancy loss, preterm delivery or infertility
- Type 1 diabetes or other autoimmune disorders
- BMI  $\geq$ 40
- History or current symptoms of thyroid disease
- Family history of autoimmune thyroid disease or dysfunction
- History of head or neck radiation or prior thyroid surgery
- Known thyroid peroxidase antibody positive or presence of goiter
- Currently taking levothyroxine replacement
- Use of amiodarone or lithium, or recent administration of an iodinated radiologic contrast

TSH in the first trimester should be slightly below the typical, non-pregnant reference range, and gradually return to normal in the second and third trimesters. If TSH results are outside of the trimester-specific reference range, fT4 levels should be ordered. FT4 should be normal or slightly below normal levels throughout pregnancy due to changes in binding proteins during pregnancy. Controversy exists regarding whether or not to treat subclinical hypothyroidism in pregnancy (elevated TSH, normal fT4).

**Trimester-Specific Reference Ranges, Pregnant:**

For the management of thyroid disease during pregnancy and postpartum, trimester-specific, population based reference ranges for TSH should be referenced. If the laboratory does not provide trimester-specific reference ranges for TSH (mU/L), contact the laboratory to verify the method used and correlated method-specific upper limit of normal for the 1<sup>st</sup> trimester of pregnancy (Abbott vs. Non-Abbott method). Generally, the following reference ranges can be used:

	<b>First Trimester</b>	<b>Second Trimester</b>	<b>Third Trimester</b>
<b>TSH mU/L</b>	0.1-2.5 mU/L (Abbott method- i.e. LifeLabs)  0.1-3.1 mU/L (Non-Abbott method- i.e Hospital labs)	0.3- 4.5 mu/L	0.3- 4.5 mu/L

<b>fT4</b>	within the lower 10 <sup>th</sup> % of the non-pregnant reference range, in conjunction with a normal TSH.
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**Typical Reference Ranges, Non-Pregnant:**

TSH- 0.3- 5.5 mU/L

Free T4- 11-22 pmol/L

Note: If taking Levothyroxine, TSH and fT4 levels should be monitored three to four weeks after each dose adjustment. When equilibrium is achieved, TSH alone should be monitored every two to three months. Results of ongoing monitoring should be copied to the physician to facilitate co-management.

**Thyroid Peroxidase Antibodies (TPO Antibodies)** *(updated September 2018)*

Thyroid peroxidase antibodies (TPOAb) are elevated in 2% to 17% of the pregnant population and help distinguish between autoimmune-mediated and other thyroid disease. Elevated TPOAb are associated with an increased risk of developing hypothyroidism during pregnancy and postpartum thyroiditis; in euthyroid individuals with known elevated TPOAb, serum TSH should be ordered every four weeks until 20 weeks, once in the third trimester and again at 6-12 weeks postpartum.

There is no evidence to support routine screening for TPOAb in pregnancy or following a single abnormal TSH level. However, TPOAb should be ordered in the following clinical situations by the midwife at the same time as medical consultation is considered and initiated:

- enlarged thyroid (goiter);
- repeatedly or profoundly abnormal TSH or FT4 levels; and
- with symptoms of thyroid dysfunction in an individual with a known non-thyroid-related autoimmune condition, such as systemic lupus erythmatosus, rheumatoid arthritis or pernicious anemia.

**Standard Reference Range:** ≤ 35 IU/mL

**Toxoplasmosis Antibody**

For diagnosis of acute toxoplasmosis or congenital infections. Toxoplasmosis is caused by the protozoan toxoplasma gondii. It is found in uncooked meat and cat and dog feces.

Toxoplasma gondii can cause intrauterine death or significant disease in the neonate such as ocular disease, blindness, and developmental delay. Infection during pregnancy carries a 50% risk of infection for the fetus. The risks are higher if exposure occurs in the first half of pregnancy. If IgM is detected, there was exposure during pregnancy to the organism and an immune response is developing. If IgG is detected and no IgM, there is immunity to the organism but this does not necessarily signify there is a current infection. Cord blood, amniotic fluid and placental tissue can also be tested for the organism. Blood is analyzed at PHSA. If testing suggests acute or congenital infection, a physician consultation is indicated.

**Standard Reference Range:** Negative.

**Urinalysis** *(updated August 2017)*

Urinalysis includes assessment of specific gravity, pH, protein, glucose, blood, ketones, bilirubin, urobilinogen, leukocyte esterase and nitrites in the urine. Urinalysis may be offered to all pregnant clients in early pregnancy to screen for preexisting renal disease, but urinalysis

for glucose and protein by means of dipstick testing at each subsequent antenatal visit in low-risk pregnancies is not recommended.

Beyond initial screening, initiation of urinalysis should be based on the client’s presentation and chief complaint during pregnancy and labour. Intervention and further testing may be indicated with abnormal urinalysis results. If protein is found in the urine and there is suspicion of preeclampsia, more definitive testing (urine protein-creatinine ratio (UPCR)) is indicated.

**Standard Reference Range:**

<b>Test</b>	<b>Standard Reference Range</b>
Bilirubin	Negative
Blood	Negative
Glucose	Negative
Granular casts (/hpf)	0-2
Hyaline casts (/hpf)	0-2
Ketone	Negative, trace
Leukocyte esterase	Negative
Nitrite	Negative
PH	5-8
Protein	Negative, trace, +1
RBC (/hpf)	0-5
Specific gravity, adult	1.035
Urobilinogen	Negative
WBC (/hpf)	0-5

**Urine for Culture and Sensitivities**

During pregnancy, some suffer from asymptomatic bacteriuria, of which Group B Strep is one potential pathogen. A first trimester urine culture and sensitivity should be offered as the presence of asymptomatic bacteriuria is known to increase the risk of pyelonephritis and preterm labour. Identifying and treating pathogenic organisms can reduce this risk. This test should be ordered at the first prenatal visit and repeated at any time in pregnancy or the postpartum period when there is suspicion of urinary tract infection to isolate and identify potentially pathogenic organisms. Instruction in the technique for collecting a midstream urine or clean catch specimen should be provided. Specimens must be delivered to the lab within 2 hours of collection or refrigerated for up to 24 hours. Alternatively, going directly to the lab to provide the specimen there can be arranged.

**Standard Reference Range:** No growth or colony count <100 M CFU/L

**Urine Macroscopic and Microscopic**

When microscopic is ordered with urine macroscopic, a urine microscopic exam will only be performed if a positive macroscopic result is obtained.

**Varicella**

Zoster Serology is used to establish the diagnosis of varicella-zoster (chicken pox) infection or previous exposure to varicella-zoster.



Varicella is transmitted by direct contact and respiratory droplets and is highly infectious. Immunity to varicella is usually lifelong. If immunity cannot be documented by history, an IgG varicella serology should be obtained with the initial prenatal blood work.

If during pregnancy there is exposure to chicken pox and there is no immunity, a physician consultation should take place. It is recommended that varicella-zoster immune globulin (VZIG) be administered. This preparation is 60-80 percent effective in preventing infection if given within 96 hours of exposure. The usual dose is 125 units/10 kg of body weight. Monthly ultrasounds for surveillance of fetal well being are also recommended as there is a 1-2% chance the fetus could develop hydrocephaly or become intrauterine growth restricted. Infection of the neonate occurs in 10 to 20 percent of infants where there was maternal infection of acute varicella within the period from 5 days before to 2 days after delivery. Infection may result from hematogenous dissemination of virus across the placenta and/or from direct contact with viral shedding at a time when no antibody is present to provide passive immunity to the fetus. Newborns in this situation will require a consultation with a physician and VZIG (125 units) given immediately after birth is recommended. Exposed neonates are candidates for administration of VZIG anytime up to 3 months of age.

**Standard Reference Range:** If IgM is detected (reactive), there was exposure to the organism and an immune response is developing. If IgG is detected (reactive), and no IgM (non reactive), there is immunity to the organism but a current infection is not necessarily present. If IgG is not detected (non reactive), there is no immunity to chicken pox.

Note: The PHSA stores the serum of all specimens collected in early pregnancy until after the due date. Midwives can call the lab and request a varicella-zoster titre if there has been contact with chicken pox and immunity is unknown.

#### **Viral Swabs – Skin, Mucous Membranes, Vesicles (e.g. herpes)**

Special collection kits should be ordered from the PHSA. In those who are symptomatic, vesicular fluid is the preferred specimen for culture.

From vesicles, the fluid can be obtained by lifting the top from the vesicle and swabbing the lesion. From ulcers, warn that specimen collection may hurt. Swab the ulcer for culture and direct examination. For direct examination, obtain cellular material by firm swabbing or gentle scraping from the base of the lesion. For culture, use the swab and viral transport medium supplied with the collection kit from the lab. Use of other swabs may decrease likelihood of detection.

Do not collect specimens from those who are asymptomatic except for:

- during pregnancy at time of completion of an active clinical phase and diagnosis not previously confirmed;
- during labour if presenting with a history of genital ulcers or active lesions in order to identify neonates at high risk;
- a neonate born where there is a possible history of genital herpes at time of delivery.

For the detection of HSV in those who are asymptomatic:

In pregnancy: Use a swab moistened with viral transport medium. Rub clitoral hood, labia minora, labia majora, perineum and perianal region, and place swab in transport medium.

Newborn: Use a swab moistened with viral transport medium. Gently rub conjunctiva, insert into mouth and gently rub around the lips, external ear canal, umbilicus, axillae and groin, and place in transport medium.

Specimens should be collected at 24 and 48 hours after birth (Canadian STI Guidelines, 2010).

### **Viral Swabs – Nose, Throat, Mucous Membranes**

#### **Indications:**

If presenting at a visit with an influenza-like illness (ILI) such as H1N1<sup>20</sup>, the midwife may obtain an upper respiratory specimen, preferably with a nasopharyngeal swab, to assist in decision-making regarding the need for referral to medical care. If H1N1 infection is already confirmed to be wide spread in the community, swabbing may no longer be recommended. However, if no swab is done, and if another ILI develops, a second course of antiviral therapy will be recommended because immunity cannot be assured.

Because of the risks associated with influenza in pregnancy, anti-viral treatment is recommended for those who develop influenza-like illness (ILI), especially those in their second and third trimesters or within 4 weeks post-partum. Because antivirals are most effective if administered within 48 hours of symptom onset, treatment should be commenced without waiting for the swab result. Early treatment can help to reduce the risk of complications<sup>21</sup>. Treatment may be discontinued if the swab is negative.

A confirmed case of influenza is defined as detection by PCR, culture or four-fold rise in antibody titre based on acute compared to convalescent sera. In B.C., testing can be done at the BCCDC laboratories. Consult the BCCDC Laboratories and PSBC Guideline to ensure compliance with mandatory information required<sup>22, 23</sup>.

During influenza season, influenza testing should be obtained in the following patients:

- Immunocompetent outpatients who are at high risk for influenza complications who have an acute febrile respiratory illness and present within five days of illness onset.
- Immunocompromised outpatients with an acute febrile respiratory illness, regardless of time since illness onset.

If infection is confirmed or strongly suspected, consultation with a physician is required unless otherwise indicated by a symptom-based protocol established between the midwives and physician consultants in a given community. In a pandemic situation, how the consultation process takes place may be guided by this specific community-based protocol that takes into account the severity of the signs and symptoms, and the availability of medical resources.

#### **Specimens:**

Optimal specimens continue to be nasopharyngeal swabs (COPAN flocked swab). Non-flocked swabs are also acceptable. If there is no ready access to these swabs, the swabs and transport media used for genital herpes culture are acceptable.

***Please check your local lab for specific specimen collection kits and instructions.***

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<sup>20</sup> Public Health Agency of Canada. *About H1N1 Flu Virus*. February 24, 2012

<sup>21</sup> [www.publichealth.gc.ca](http://www.publichealth.gc.ca)

<sup>22</sup> [www.bccdc.ca/PHSALaboratories](http://www.bccdc.ca/PHSALaboratories)

<sup>23</sup> [www.perinatalervicesbc.ca/Guidelines.htm](http://www.perinatalervicesbc.ca/Guidelines.htm)

RT-PCR (conventional gel-based PCR, real-time RT-PCR, and multiplex PCR) 2 h NP swab, nasal or endotracheal aspirate, sputum, throat swabs can be utilized and all have varying degrees of sensitivity. High sensitivity and high specificity testing can differentiate between influenza types (A or B) and subtypes (including H1N1 influenza and avian H5N1 influenza).

One factor influencing sensitivity is the timing of tests in relationship to clinical symptoms. Viral shedding peaks at 24 to 48 hours of illness and then rapidly declines; little or no detectable viral replication occurs in the respiratory tract after 5 to 10 days in immunocompetent hosts. Reverse-transcriptase polymerase chain reaction (RT-PCR) is the most sensitive and specific modality for diagnosing influenza infection, yields relatively rapid results, and differentiates between influenza types and subtypes (including H1N1 influenza and avian H5N1 influenza).

***Although RT-PCR takes only 4 to 6 hours to perform, it often takes longer for results to be available since it may not be performed in-house and may be batched with other samples<sup>24</sup>.***

#### Specimen Collection Instructions:

- a. For personal protection, wear gloves, gown and eye protection
- b. Patients with copious discharge should be requested to gently clean nose by washing or use of tissue
- c. Incline patient's head to insert the cotton swab perpendicular to the face to a depth of 2-3 cm into the nostril. Swab around the inside of the nostril and along the floor of the nasal cavity by rotating the swab.
- d. Break or cut off shaft of the swab and place in accompanying vial of transport medium. Tighten lid.
- e. Label with patient's name and date of birth. Use the lab requisition for viral cultures (BCCDC Virology-Culture (HLTH 1811) requisitions) and include all medical mandatory information.
- f. Ensure that correct reachable phone numbers are included on the requisition.
- g. Follow regional protocols to ensure that the specimen is processed as quickly as possible. Standard transportation procedures used to transport to BCCDC can be utilized.

#### **Wet Preparation (for Fungus, Trichomonas, Clue Cells)**

Yeast, trichomonas and bacterial vaginosis may be diagnosed in clinics equipped with microscopes and where practitioners are experienced in the necessary techniques.

#### Preparation for wet mount:

- Place several drops of saline on a slide before collecting the specimen;
- Obtain the vaginal swab and use it to test the pH;
- Rotate the swab in the saline;
- Cover the saline preparation with a cover slip;
- Immediately examine by microscopy.

#### Potassium hydroxide (KOH preparation):

For a KOH preparation, use the same technique as for the wet mount except use 10% potassium hydroxide instead of saline.

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<sup>24</sup> Diagnosis of seasonal influenza in adults. Retrieved April, 2012 from Up To Date

## **White Blood Cell Count with Differential**

White blood cells (or leukocytes) fight infection and defend the body through phagocytosis, and also produce, transport and distribute antibodies as part of an immune response to a foreign substance. Used in the evaluation of anemia, infections, inflammatory diseases and other conditions. Any stressful situation that leads to increase in endogenous adrenaline production may cause a rapid (15-30 minute) increase in WBC count. WBC is normally elevated in pregnancy and during labour. The WBC is the total number of all types of white blood cells.

**Typical Reference Range\*:** 4.2-10.8 x 10<sup>9</sup>/L

The differential is the total count of circulating WBCs according to the five types of leukocytes, each of which performs a specific function:

<b>White Blood Cell Type</b>	<b>These cells function to combat:</b>
Neutrophils	Pyogenic infections (bacterial)
Eosonophils	Allergic disorders and parasitic infestations
Basophils	Parasitic infections
Lymphocytes	Viral infections
Monocytes	Severe infections, by phagocytosis

<b>Normal Values for Leukocyte Count</b>							
<b>Age</b>	<b>Bands/ STAB (%)</b>	<b>Segs/ Polys (%)</b>	<b>Eos (%)</b>	<b>Basos (%)</b>	<b>Lymphs (%)</b>	<b>Monos (%)</b>	<b>Metas (%)</b>
<b>&gt;18 years</b>	3-6	50-62	0-3	0-1	25-40	3-7	0-1
<b>EOS=eosonophils; Basos=basophils; Lymphs=lymphocytes; Monos=monocytes; Metas=metamyelocytes</b>							

## **Zika Virus**

Zika virus infection is caused by a virus which is primarily spread by the bite of an infected mosquito (*Aedes aegypti* and *albopictus*). Zika is a flavivirus, closely related to West Nile virus and dengue virus but has been associated with less severe clinical illness. Zika virus infection can be transmitted sexually and, if pregnant and infected, the virus can be transmitted to the fetus. Zika virus infection can cause microcephaly in newborns and a number of countries have reported an increase in the number of cases of Guillain-Barre Syndrome.

Symptoms can include: headache, fever, conjunctivitis, skin rash, joint and muscle pain. The illness is usually mild and only lasts a few days with the majority of those infected do not have symptoms. There is no medication or vaccine that protects against Zika virus infection.

## **Recommendations**

- Those who are pregnant or planning a pregnancy: a) avoid travel to countries with ongoing Zika virus outbreaks; and b) if travel can't be avoided, strict mosquito bite prevention measures should be followed due to an increased risk of serious health effects on the fetus;
- If travelling and returning from countries with ongoing Zika virus outbreaks and planning a pregnancy: a) wait at least two months before trying to conceive to ensure that any possible Zika virus has cleared the body;

- Zika virus can persist for an extended period of time in the semen, it is recommended from time of Zika Virus exposure to: a) use condoms during pregnancy; b) wait six months before conceiving by using condoms; c) use condoms with any partner for six months.

The following Table outlines the details for Zika Virus Testing.

<b>Presentation</b>	<b>Recommended Specimens</b>
<p><b>Acutely ill:</b></p> <p>1. Report <b>two or more symptoms consistent with Zika virus disease</b> (acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis) with onset during or within 2 weeks of travel AND</p> <p>2. Is <b>currently symptomatic</b> or <b>symptom onset</b> was in the previous 5-10 days.</p>	<p>1. 5 ml EDTA purple top blood tube for Zika virus RNA detection.</p> <p>2. 5 ml gold top serum separator tube for Zika virus serology.</p> <p>3. Urine for Zika virus RNA detection</p> <p>4. Nasopharyngeal swab for Zika virus RNA detection.</p> <p><b>Please provide both the travel and clinical history, including the date of onset of symptoms and indicate that samples are to be forwarded to the BCCDC Public Health Laboratory.</b></p>
<p><b>Recovered:</b></p> <p>1. Reported symptoms consistent with Zika virus disease with onset during or within 2 weeks of travel.</p> <p>2. No longer symptomatic, <b>and</b> symptom onset was more than 10 days ago.</p>	<p>5 ml gold top serum separator tube for Zika virus serology, collected <b>one month</b> after symptom resolution.</p> <p><b>Please provide both the travel and clinical history, including the date of onset of symptoms and indicate that samples are to be forwarded to the BCCDC Public Health Laboratory.</b></p>
<p><b>Asymptomatic:</b></p> <p>1. No symptoms consistent with Zika virus disease with onset during or within 2 weeks of travel</p>	<p>5 ml gold top serum separator tube for Zika virus serology, collected <b>one month</b> after return from Zika affected area.</p> <p><b>Please provide travel history, including the date of return, and indicate that samples are to be forwarded to the BCCDC Public Health Laboratory</b></p>

**Standard Reference range:** Non reactive

***This information is current as of May 2016. The information on Zika virus infection is evolving and is likely to change. For updated and additional information, refer to the following sources:***

<http://www.phac-aspc.gc.ca/phn-asp/2016/zika-eng.php>

[http://www.paho.org/hq/index.php?option=com\\_content&view=article&id=11585&Itemid=41688&lang=en](http://www.paho.org/hq/index.php?option=com_content&view=article&id=11585&Itemid=41688&lang=en)

<http://www.cdc.gov/zika/index.html>.

Committee to Advise on Tropical Medicine and Travel Recommendations, 17 March 2016.  
<http://www.healthycanadians.gc.ca/publications/diseases-conditions-maladies-affections/committee-statement-treatment-prevention-zika-declaration-comite-traitement-prevention/index-eng.php>

**1.b A midwife may order, collect samples for and interpret the report of the following newborn screening and diagnostic tests:**

**Bilirubin**

Total serum bilirubin or transcutaneous bilirubin is ordered for the evaluation of hemolytic disease and risk of kernicterus in the newborn. Hyperbilirubinemia is common and usually benign in term and late preterm newborns. Severe hyperbilirubinemia is uncommon but can potentially lead to acute and/or chronic encephalopathy. Kernicterus is a potential consequence of chronic bilirubin encephalopathy. While rare, kernicterus results in severe neurological damage for the infant.

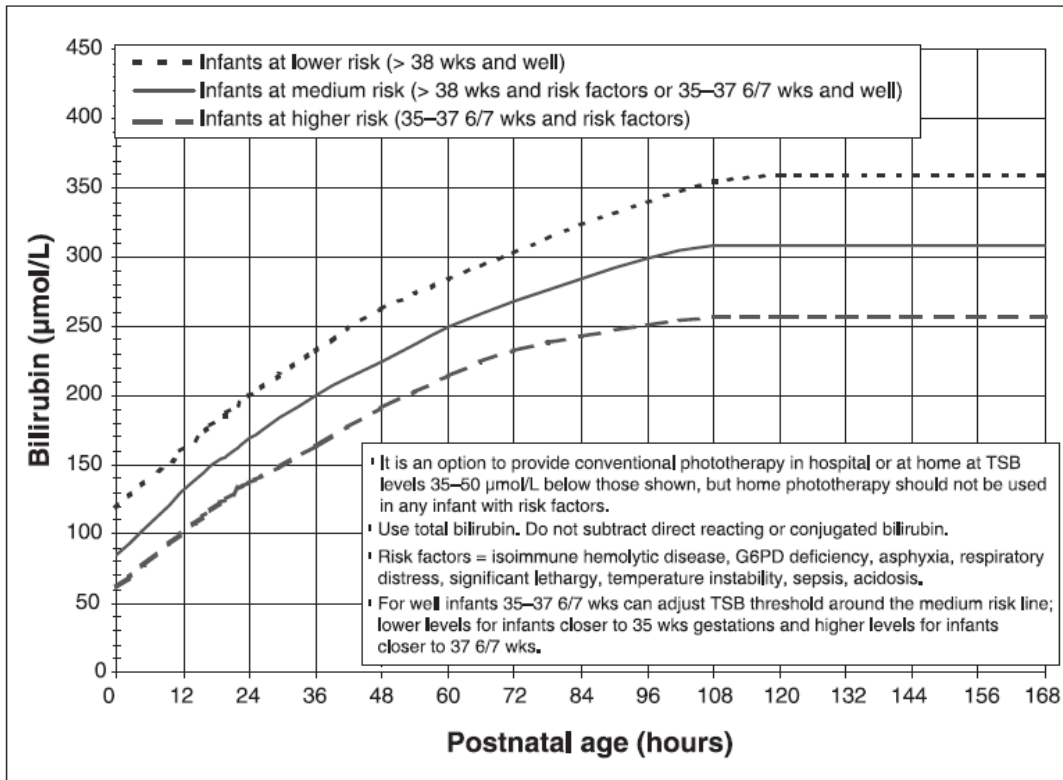
**Typical Reference Range\*:** Mild bilirubinemia greater than 150 µmol/L may occur in normal neonates. Elevations greater than 200 µmol/L may require phototherapy and at levels >300 µmol/L an exchange transfusion is rarely required. Severe hyperbilirubinemia is a total serum bilirubin concentration greater than 340 µmol/L during the first 28 days of life. Critical hyperbilirubinemia is a total serum bilirubin concentration greater than 425 µmol/L during the first 28 days of life.

Risk factors for severe hyperbilirubinemia are any visible jaundice at less than 24 hours of age, sibling with severe hyperbilirubinemia, visible bruising, cephalohematoma, male sex, maternal age greater than 25 years of age, ethnic background (Asian or European), exclusive and partial breastfeeding.

*Other investigations that may be warranted in the presence of hyperbilirubinemia and prior to treatment include: maternal and infant's blood group, neonatal coombs, Hgb, Hct, CBC, retic count and red cell morphology.*

All bilirubin results should be placed in the phototherapy graph to determine if phototherapy is indicated. See graph below or refer to the bilitool for total serum bilirubin measures:

<http://bilitool.org/>

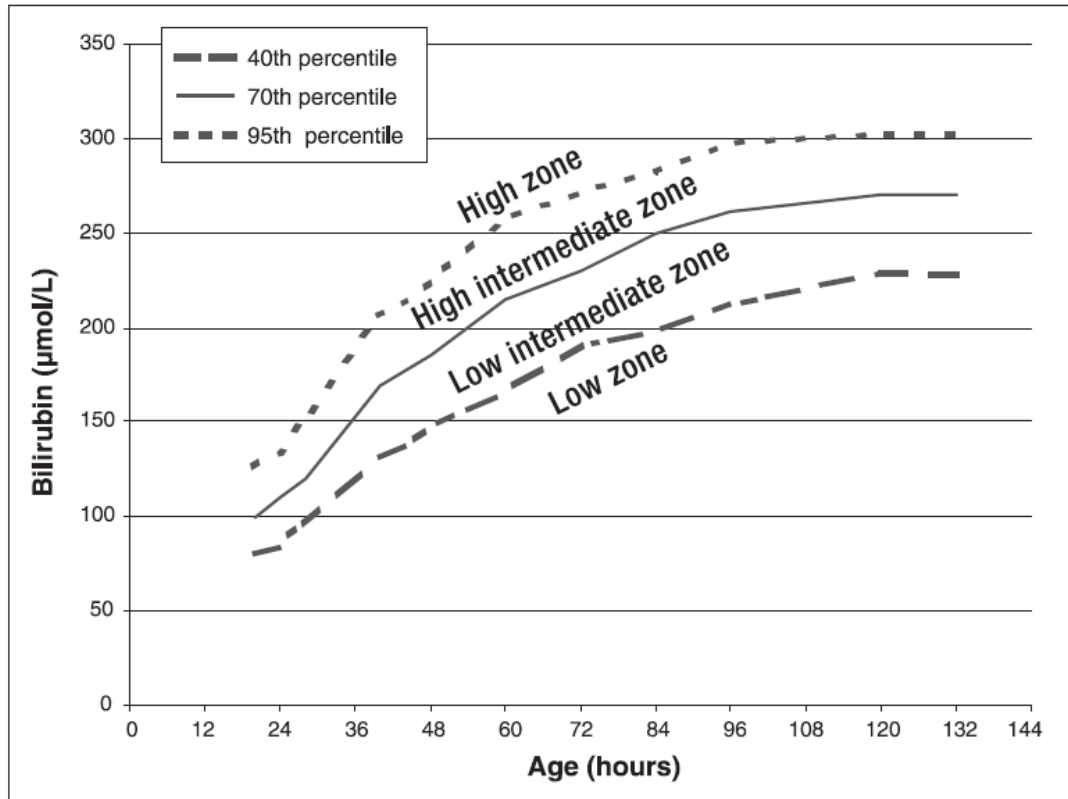


**Figure 2)** Guidelines for intensive phototherapy in infants of 35 or more weeks' gestation. These guidelines are based on limited evidence and the levels shown are approximations. Intensive phototherapy should be used when the total serum bilirubin (TSB) concentration exceeds the line indicated for each category

Midwives should also refer to their hospital protocols for the recommended management of neonatal hyperbilirubinemia. When intensive or conventional phototherapy is indicated, and after ordering or initiating phototherapy for the newborn, midwives must consult with a physician.

If phototherapy is not indicated, measurements should be placed on the graph according to the newborn age in hours. See graph below or refer to the bilitool for total serum bilirubin measures:

<http://bilitool.org/>



**Figure 1)** *Nomogram for evaluation of screening total serum bilirubin (TSB) concentration in term and later preterm infants, according to the TSB concentration obtained at a known postnatal age in hours. Plot the TSB on this figure, then refer to Table 4 for action to be taken*

A repeat total serum bilirubin within 24 hours is indicated if the results are within the high risk zone and no treatment is required. Midwives should also refer to their hospital protocols for the recommended management of neonatal hyperbilirubinemia.

**Blood Type and Rh Factor - see 1.a**

**Coombs**

Detects antigen – antibody complexes. The indirect coombs detects antibodies that react only through a potentiating medium. A direct coombs detects antigen antibody complexes on red blood cell membranes in vivo and in red blood cell sensitization. Coombs is indicated if maternal blood type is O, Rh negative or type unknown; if maternal blood type is Rh negative and newborn is Rh positive, or if maternal blood type is O and newborn A or B. It should be used for the diagnosis of hemolytic disease of the newborn, acquired hemolytic anemia, transfusion reactions, and RBC sensitization caused by drugs. An indirect coombs in pregnancy reveals maternal anti Rh antibodies.

**Standard Reference Range:** Negative.



### **Cord and Eye, Ear, and Gastric Fluid Culture**

Individual swabs from each surface area can be obtained if there is suspicion of sepsis. Care should be taken to culture for Chlamydia, G.C. and C & S in the presence of neonatal conjunctivitis. 10%-20% of neonatal conjunctivitis is caused by chlamydia, <1% by GC and a large number by staphylococcus aureas. Prophylactic erythromycin at birth does not always prevent neonatal ophthalmia. Consult with lab for proper collection of eye specimens for each test.

**Standard Reference Range:** Normal flora or no growth.

### **C Reactive Protein**

C-reactive protein (CRP) is an acute phase reactant synthesized in the liver that increases in inflammatory conditions, including sepsis. The level of CRP rises when there is inflammation throughout the body.

Maternal and/or neonatal CRP and white blood cell counts (WBC) are simple blood tests. CRP and WBC are markers for predicting early onset neonatal infection or determining the presence of infection in newborns in situations such as when there has been prolonged rupture of membranes or where the time period for intrapartum antibiotic prophylaxis administered to those who are GBS positive is less than 4 hours.

The overall incidence of neonatal sepsis ranges from one to five cases per 1000 live births. The risk for sepsis increases from 1 to 4 percent in neonates born where chorioamnionitis was present. Group B streptococcal (GBS) bacteriuria during the current pregnancy, prior delivery of an infant with GBS disease, and colonization are some risk factors for early-onset GBS sepsis. The risk of sepsis increases with decreasing gestational age and birth weight. Group B streptococcus (GBS) and Escherichia coli (E coli) are the most common causes of neonatal early-onset sepsis (EOS). In very preterm infants, the incidence of EOS with E coli is higher than with GBS.

Although an elevated CRP greater than 1 mg/dL is 90 percent sensitive in detecting neonatal sepsis, its poor specificity makes it a poor predictor for neonatal sepsis, as CRP is elevated in other noninfectious inflammatory conditions (eg, fever, fetal distress, stressful delivery, meconium aspiration). In addition, CRP is not a sensitive test at birth because it requires an inflammatory response to increase its level. A single measurement of CRP soon after birth is not a useful marker in the diagnosis of neonatal sepsis. Serial CRP values however are useful in supporting but not confirming a diagnosis of sepsis. The isolation of a pathogen from a blood culture is the only method to confirm the diagnosis of neonatal sepsis. CRP testing is one amongst other laboratory findings that are used to identify infants with a high suspicion for sepsis, who are treated until culture results are available.

If the CRP level remains persistently normal, neonatal bacterial sepsis is unlikely<sup>25</sup>. If the CRP level is initially elevated then drops, it is an indication that the inflammation or infection is subsiding and/or responding to treatment. Infants with elevated CRP levels that decrease to <1.0 mg/dL 24 to 48 hours after the start of antibiotic therapy typically are uninfected and generally do not require further antibiotic treatment.

**Standard Reference Range:** <1 mg/dL

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<sup>25</sup> *Treatment and outcome of sepsis in term and late preterm infants*: Retrieved Sept 16, 2014 from Up to Date.

## **Glucose**

Glucose levels may be indicated for infants who are sick, premature, have low birth weight, suffered hypoxia, hypothermia, are infants of diabetics, or display symptoms of hypoglycemia. Hypoglycemia occurs in 30-50% of infants of diabetics, and in the first 48 hours is characterized by a whole blood concentration of <2 mmol/L. The onset is usually within first 1-5 hours of life. Early feeds of breast milk are recommended.

Normal Newborn Blood Sugar Levels:

	<b>Hours of Age</b>	<b>Blood Sugar Levels</b>
Full Term	<72 hours	≥2.0 mmol/L
Full Term	>72 hours	≥2.5 mmol/L
Preterm	<24 hours	≥1.5 mmol/L
Preterm	>24 hours	≥2.0 mmol/L

**Typical Reference Range\*:** Up to 1 day: 3.3-5.6 mmol/L; 1-2 days 2.2-5.6 mmol/L; 2 days to adult: 3.3-7.0 mmol/L

## **Hematocrit**

Is part of the CBC and indirectly measures red cell mass. It is used to evaluate anemia, blood loss, hemolytic anemia, polycythemia and state of hydration. The test is performed on blood collected in capillary tubes from heel pricks or from a venous sample.

**Typical Reference Range\*:** <2 weeks of age 44%-64%  
>2 weeks-8 weeks 39%-59%

Note: HCT may not be reliable immediately after even a moderate loss of blood or a transfusion. If blood is drawn from a capillary puncture and a microhematocrit is done, values are slightly higher. Polycythaemia exists when the venous hematocrit is >65%.

## **Hemoglobin**

Is part of the CBC and is the main component of erythrocytes. It is responsible for the transport of oxygen and carbon dioxide. The oxygen combining capacity is directly related to Hgb. Hgb is used to evaluate anemia, blood loss and response to iron therapy. Test is performed on unclotted blood collected via venipuncture or heel prick. Used more commonly than hematocrit.

**Typical Reference Range\*:** 0-2 weeks 145-245 g/L  
2-8 weeks 125-205 g/L

## **Newborn Screening (Updated June 2017)**

In BC, newborn babies are screened for 22 rare but treatable disorders through neonatal blood.

Screening includes: Metabolic disorders Phenylketonuria (PKU), Maple Syrup Urine Disease (MSUD), Citrullinemia (CIT), Argininosuccinic Acidemia (ASA), Homocystinuria (Hcy), Tyrosinemia I (Tyr), Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD), Long-chain Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD), Trifunctional Protein Deficiency (TFP), Very-long chain Acyl-CoA Dehydrogenase Deficiency (VLCAD), Propionic Acidemia (PROP), Methylmalonic Acidemia (MUT), Cobalamin Disorders (Cbl A,B), Glutaric Aciduria Type 1 (GA I), Isovaleric Acidemia (IVA), and Galactosemia (GALT), Endocrine disorders

Congenital Hypothyroidism (CH) and Congenital Adrenal Hyperplasia (CAH), Hemoglobinopathies Sickle Cell Disease (HbSS), Sickle Cell/Hemoglobin C (HbSC) and Sickle Cell/ $\beta$ -thalassemia (HbS/ $\beta$ -thal), Cystic fibrosis (CF).

About 40 babies per year will be identified with one of these disorders. The most common disorders are: Congenital Adrenal Hyperplasia (CAH), Congenital Hypothyroidism (CH), Cystic Fibrosis (CF), Galactosemia, Medium-Chain Acyl-CoA Dehydrogenase Deficiency (MCAD) and Phenylketonuria (PKU).

The goal of screening is to prevent serious morbidity or death from a treatable disorder by identifying the infants affected prior to symptom appearance. Specimen collection is done by means of a blood dot collection card. All newborns should have a primary care provider designated prior to discharge to ensure prompt and appropriate follow-up of newborn screening results.

**Collection timelines:** Provincial guidelines for metabolic testing are established by the BC Newborn Screening Program and state:

1. Initial newborn screening specimen should be collected prior to hospital discharge and from all infants regardless of birth place between 24 and 48 hours of age (pre-term and term babies). Note: The need for repeat testing for phenylalanine is 3% when the specimen is obtained between 13 and 24 hours of age and 0.05% when collected after 24 hours of age. Galactosemia and hypothyroidism can be detected at any time.
2. If the initial specimen for newborn screening is collected prior to 13 hours of age due to early hospital discharge, a second specimen should be collected before 2 weeks of age. (Note: it is preferable to collect the initial specimen between 24 and 48 hours of age – see note from point #1.) The first blood screen will identify over 80% of disorders and will help to prevent life threatening events such as severe or potentially fatal bacterial infections in babies with galactosemia or significant metabolic crises in babies with medium-chain acyl-CoA dehydrogenase deficiency (MCAD), very-long chain acylCoA dehydrogenase deficiency (VLCAD) or maple syrup urine disease (MSUD). The 2nd screen optimizes detection of phenylketonuria (PKU), cystic fibrosis (CF) and homocystinuria (Hcy) which are time sensitive and cannot be reliably detected until 24 hours or more after birth.

**Early hospital discharge:** The BC Newborn Screening Program recommends that all infants should have initial screening prior to discharge from hospital regardless of age, as galactosemia and hypothyroidism can be detected at any time. However, because midwifery care is continuous from hospital to home, midwives may defer testing of infants born in hospital and discharged home within hours of birth to reduce intrusion to the infant.

If the newborn is born in hospital and discharged before 13 hours of age:

1. The discharging midwife who will be following the infant in the community should sign in the discharge orders that testing for the newborn is deferred. In addition, an informed deferral form should be signed by a parent and the midwife. These forms are health authority-specific and can be found on the PSBC Newborn Screening Program [website](#). This ensures that the primary care provider is aware that testing was not done in hospital. Midwives are potentially liable for missed cases if the infant does not have the testing done in the community.

2. If the midwife is aware and agrees to discharge the infant without blood dot card specimen collection, the BC Newborn Screening Program recommends that a plan for testing be discussed and clearly communicated, which would include how the testing will be done, by either a public health nurse or midwife visit to the home or return to hospital lab for testing.

**Community Collection:** If the midwife collects the blood dot card specimen in the community following early discharge or home birth, the BC Newborn Screening program recommends the following:

1. Collection of the newborn screening specimen between 24 and 48 hours of birth.
2. Shipment/couriering of newborn screening specimens within 24 hours of collection to ensure delivery to the BC Newborn Screening Lab within **72 hours of collection**. Check with your local hospital and lab facilities, and the BC Newborn Screening Lab to determine ways to optimize delivery times.
3. Review sample collection practices with collections staff and visit [www.newbornscreeningbc.ca](http://www.newbornscreeningbc.ca) for further sample collection guidelines.
4. Review sampling and specimen handling protocols to minimize the chance of sample contamination (ie; alcohol, water)

**Standard Reference Range:**

PKU (depends on age)	<2.5 mg/dl (negative)
Galactosaemia GPT	18.5-28.5 U/g of Hgb
Hypothyroid	>7.5 mcg/dl
MCAD	N/A
CAH	N/A
Cystic Fibrosis	High IRT with 0-2 CF mutation

For informed deferral forms, informed refusal forms and updates on newborn screening for health care providers, please refer to the PSBC Newborn Screening [website](#).

### **Pulse Oximetry Screening for Critical Congenital Heart Disease** *(added September 2018)*

Pulse oximetry screening (POS) is a safe, painless and noninvasive way to screen newborns for critical congenital heart disease (CCHD). CCHDs are structural heart defects associated with life-threatening hypoxia in newborns. CCHDs screening by POS include but are not limited to hypoplastic left heart syndrome, pulmonary atresia, total anomalous pulmonary venous return, tetralogy of Fallot, transposition of the great arteries, tricuspid atresia, truncus arteriosus, double outlet right ventricle, Ebstein's anomaly, interrupted aortic arch, and defects with single ventricle physiology. Although POS for CCHD is not universally implemented across British Columbia, it is standard of care in many BC hospitals and recommended by the Canadian Pediatric Society.

The goal of POS is to identify otherwise clinically undetectable cyanosis in the first 24-36 hour of life, to prevent serious morbidity or death from a treatable CCHD. It is estimated that up to 39% of infants with CCHD appear healthy after birth and may be discharged home prior to the development of cardiac murmurs or visible cyanosis. POS for CCHD has high specificity

(approximately 99.9%) and moderately high sensitivity (approximately 76.4%). Its false negative rate is 0.014%, false positive rate before 24 hours of life is 0.5% and false positive rate after 24 hours of life is 0.05%.

POS for CCHD augments, but does not replace, a thorough physical exam and cardiac assessment of the newborn by the midwife, including assessment of femoral pulses, heart sounds, etc.

**Screening eligibility, timing and location:**

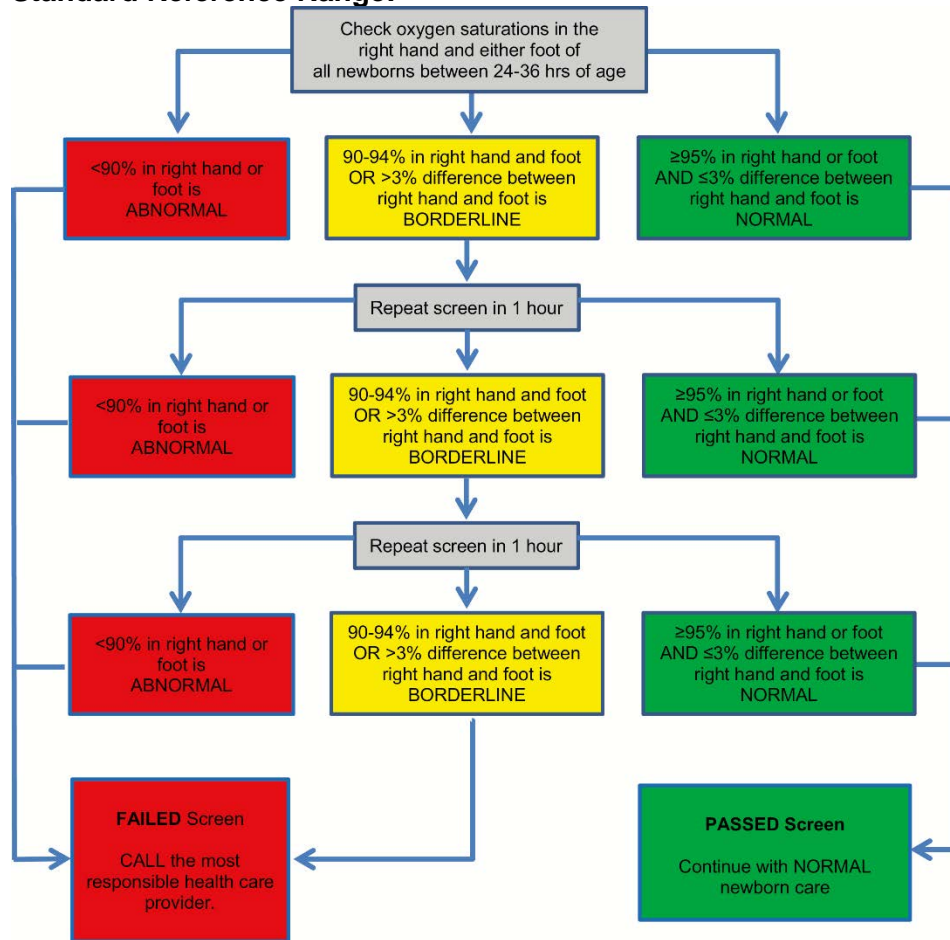
All newborns born after 34 weeks gestational age should have POS performed at 24-36 hours of life. For newborns born at home or discharged from the hospital prior to 24 hours of life, midwives should perform the POS for CCHD at 24-36 hours of life during a home or clinic visit.

**How to screen:**

1. Attach newborn pulse oximeter to right hand until a consistent saturation reading is achieved.
2. Attach newborn pulse oximeter to either foot until a consistent saturation reading is achieved.
3. Interpret results and act according to the standard reference range flow chart below.
4. Document findings in the medical record.

Pulse oximeters must be regularly serviced, calibrated, cleaned and disinfected between uses.

**Standard Reference Range:**



\* adapted from Narvey, M, Wong, KK, Fournier, A. (2017). Pulse oximetry screening in newborns to enhance detection of critical congenital heart disease. *Pediatrics & Child Health*. 22:8, (494-498).

**White Blood Cell Count with Differential**

White blood cells (or leukocytes) fight infection and defend the body through phagocytosis. They can also produce, transport and distribute antibodies as part of an immune response to a foreign substance. Used in the evaluation of anemia, infections, inflammatory diseases and other conditions. Any stressful situation that leads to increase in endogenous adrenaline production may cause a rapid (15-30 minute) increase in WBC count. The WBC is the total number of all types of white blood cells.

**Typical Reference Range\*:**

0-2 weeks	9.0-30.0 x 10 <sup>9</sup> /L
2-8 weeks	5.0-21.0 x 10 <sup>9</sup> /L

The differential is the total count of all circulating WBCs according to the five types of leukocytes, each of which performs a specific function. It is expressed as a percentage of the total number of leukocytes. The percentages indicate the relative number of each type of leukocyte in the blood.

White Blood Cell Type	These cells function to combat:
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Neutrophils	Pyogenic infections (bacterial)
Eosonophils	Allergic disorders and parasitic infestations
Basophils	Parasitic infections
Lymphocytes	Viral infections
Monocytes	Severe infections, by phagocytosis

Normal Values for Leukocyte Count							
Age	Bands/ STAB (%)	Segs/Pol ys (%)	Eos (%)	Basos (%)	Lymphs (%)	Monos (%)	Metas (%)
≤1 week	10-18	32-62	0-2	0-1	26-36	0-6	-
1-2 wk	8-16	19-49	0-4	0-0	38-46	0-9	-
2-4 wk	7-15	14-34	0-3	0-0	43-53	0-9	-
4-8 wk	7-13	1-35	0-3	0-1	41-71	0-7	-
>18 years	3-6	50-62	0-3	0-1	25-40	3-7	0-1
EOS=eosonophils; Basos=basophils; Lymphs=lymphocytes; Monos=monocytes; Meta=metmyelocytes							

**2. A midwife may order, perform and interpret the results of the following screening and diagnostic tests:**

**Blood Glucose: Adult and Newborn (Stix Method)**

Adult capillary glucose can be tested using a reagent stick with or without an automated glucose meter. Follow the directions of the manufacturer. Infant glucose monitoring requires sensitive analysis as the blood sugar levels are lower and have a smaller normal range. Note: Some institutions require neonatal blood sugars be drawn by the lab. Others use pediatric calibrated glucose meters. Adult calibrated glucose monitors are not sensitive enough for neonatal ranges and are not recommended. Check with your facility for neonatal glucose monitoring protocols.

**Typical Reference Range\* Adult:** 3.3-7.0 mmol/L  
critical values <2.2 mmol/L or >15.0 mmol/L

**Typical Reference Range\* Infant:** up to 1 day: 3.3-5.6 mmol/L;  
1-2 days: 2.2-5.6 mmol/L;  
2 days to adult: 3.3-7.0 mmol/L

**Normal Newborn Blood Sugar Levels**

	<b>Hours of Age</b>	<b>Blood Sugar Levels</b>
Full Term	<72 hours	≥2.0 mmol/L
Full Term	>72 hours	≥2.5 mmol/L
Preterm	<24 hours	≥1.5 mmol/L
Preterm	>24 hours	≥2.0 mmol/L

**External Fetal Monitoring**

External electronic fetal monitoring is indicated for fetal surveillance during the antenatal and intrapartum period for fetuses at increased risk. It is appropriate to maintain fetal surveillance in the low risk pregnancy by auscultation using a fetoscope or a doptone. Self awareness of daily fetal movements should also be encouraged in all pregnancies, with or without risk factors, starting between 26 and 32 weeks gestation. A decrease in perceived movement should be followed by fetal movement counting and if <6 movements are felt over a 2 hour period, this should be reported to the provider immediately.

Admission electronic fetal heart tracings are not recommended for healthy pregnancies in labour at term in the absence of risk factors for adverse perinatal outcome, as there is no evidence of benefit. The SOGC (2007) recommends that all low risk pregnancies receive one to one professional care along with intermittent auscultation of fetal heart tones throughout active labour and the second stage. See SOGC *Guideline for Fetal Surveillance* (2007).

If electronic fetal monitoring is warranted, professionals skilled in the interpretation of fetal heart rate patterns should be present in the birthing suite area. Regular updating of fetal surveillance skills is recommended by the SOGC.

**Standard Reference Range:** Baseline fetal heart rate 110–160 bpm  
Baseline variability 5–25 bpm  
The presence of accelerations above the baseline >15 bpm and >15 seconds



The absence of atypical or abnormal patterns including late decelerations and complicated variable decelerations.

Indications for the use of electronic fetal monitoring include:

- Inaudible or abnormal finding on intermittent auscultation
- Meconium stained amniotic fluid
- Dystocia/inadequate progress
- Prior to and following prostaglandin or oxytocin administration
- With epidural analgesia, although intermittent auscultation may be used with regional analgesia provided that a protocol is in place for frequent IA assessment (SOGC 2007)
- Any pregnancy assessed to be at risk for perinatal morbidity or mortality which may include:
  - IUGR
  - Oligohydramnios
  - Hypertension in pregnancy
  - Post term pregnancy
  - Antepartum/intrapartum hemorrhage
  - Medical complications (e.g. diabetes)
  - MVA/trauma
  - Morbid obesity
  - Preterm rupture of membranes
  - Preterm labour <36 weeks
  - Multiple gestation
  - Breech presentation

### **Ferning Test (Amniotic Fluid)**

The confirmation of membrane status is critical to appropriate interventions in the case of SRM with: prematurity, in the absence of progressive labour at term, or for chemoprophylaxis of GBS. If the diagnosis of rupture of membranes is not obvious the clinician should undertake to assess the presence of amniotic fluid from secretions that can be collected in the vaginal vault or suspicious fluid that can be collected outside of the vagina. Microscopic examination of amniotic fluid reveals a characteristic ferning pattern upon drying. Materials needed include high power microscope, glass slide, and slip cover.

### **Hemoglobin (Finger Prick Method)**

See 1 a. and b.

### **Non-Stress Test**

The NST is used as a method of fetal surveillance commonly used during the antenatal period when risk factors for adverse perinatal outcomes are present in the antenatal period. An electronic fetal monitor is employed. This non-invasive procedure usually takes <30 minutes but can take up to one hour.

An NST should be classified and documented. An atypical or abnormal test should be followed-up by a physician consultation at the time the classification is apparent. The evidence indicates the NST has poor predictive value for fetal well being much beyond the actual time in which the test is performed. (An NST is considered to have a negative predictive value for fetal/neonatal death of 99% within one week of testing. False positives are common.)

Non-stress testing and single pocket amniotic fluid assessment in otherwise healthy postdates pregnancies should begin between 41 and 42 weeks.

A Normal NST has the following characteristics:

- Baseline rate: 110–160 bpm;
- Variability: moderate variability of 6 to 25 bpm is expected, usually described in amplitude and frequency, >5 bpm <25 BPM > 4/min;
- Accelerations: at least two acceleration in 20 minutes, lasting 15 seconds with a peak at least 15 bpm above baseline rate (if the fetal heart does not meet this acceleratory response rate after 20 minutes in the term or near term fetus, the test should continue for another 20 minutes to account for the average period of non-REM sleep when variability is reduced);
- Decelerations: absent or occasional variable <30 seconds.

If the fetus lacks acceleration after 40 minutes, fetal monitoring should continue.

**Antepartum Classification – Non-Stress Test**

Parameter	Normal NST	Atypical NST	Abnormal NST
Baseline	110-160 bpm	100-110 bpm >160 bpm <30 min Rising baseline	Bradycardia <100 bpm Tachycardia >160 for >30 min Erratic baseline
Variability	6-25 bpm (moderate) ≤5 (absent/minimal) for <40 min	≤5 (absent/minimal) for 40-80 min	≤5 for ≥80 min ≥25 bpm >10 min sinusoidal
Decelerations	None or occasional variable <30 sec	Variable decelerations 30-60 sec duration	Variable decelerations >60 sec duration Late deceleration(s)
Accelerations Term Fetus	≥2 accelerations with acme of ≥15 bpm, lasting 15 sec <40 min. of testing	≤2 accelerations with acme of ≥15 bpm, lasting 15 sec. in 40–80 min.	≤2 accelerations with acme of ≥15 bpm, lasting 15 sec. in >80 min.
Preterm Fetus (<32 weeks)	≥2 accelerations with acme of ≥10 bpm, lasting 10 sec. <40 min. of testing	≤2 accelerations of ≥10 bpm, lasting 10 sec. in 40-80 min.	≤2 accelerations of ≥10 bpm, lasting 10 sec. in >80 min.
Action	FURTHER ASSESSMENT OPTIONAL Based on total clinical picture	FURTHER ASSESSMENT REQUIRED	URGENT ACTION/ REQUIRED assessment, physician consultation and further investigation (U/S or BPP).

**Pregnancy test (Urine)**

Follow directions of manufacturer. Tests usually reliable within 2-3 days of missed period.

**Urine (Dip Stick Analysis)**

Follow directions of manufacturer. Please see urinalysis – 1a(i).

### 3. A midwife may order and interpret the report of the following diagnostic tests:

#### **Amniocentesis** (updated May 2018)

Amniocentesis is a procedure that facilitates fetal cytogenetic diagnosis from amniotic fluid retrieved transabdominally after 14 weeks gestational age. Cytogenetic diagnosis from this procedure is only offered when the risk of diagnosis is greater than the risk of pregnancy loss following amniocentesis (0.5%-1%).

Amniocentesis is an option and/or indicated for those:

- ≥40 years of age on their due date;
- 35-39 years old, presenting ≥21 weeks gestation with no prior genetic screening;
- who have a positive Serum Integrated Prenatal Screen (SIPS), Integrated Prenatal Screen (IPS), Quad Screen (Quad) or Non-Invasive Prenatal Testing (NIPT);
- who are at risk for carrying a fetus with chromosome abnormalities;
- with a viable twin pregnancy who will be ≥35 years at time of birth;
- pregnant following in vitro fertilization with intracytoplasmic sperm injection (IVF with ICSI) without prior screening with IPS, SIPS or NIPT;
- following prenatal ultrasound detection of a fetal abnormality which is associated with an increased risk of fetal chromosomal abnormality.

Midwives may directly request amniocentesis for their clients. When amniocentesis is an option in pregnancy, the midwife must:

- facilitate an informed choice discussion regarding amniocentesis;
- consult as indicated as per *CMBC Indications for Discussion, Consult and Transfer of Care*;
- initiate a referral pathway to the appropriate consultant (obstetrician, perinatologist, or clinical medical genetics service) based on the indication for amniocentesis;
- communicate the results of the amniocentesis to the client; and
- organize follow-up care as required.

**Standard Reference Range:** Male (XY) or female (XX) karyotype with normal diploid complement

#### **Chorionic Villi Sampling (CVS)**

CVS is sometimes offered as alternative to amniocentesis. The procedure takes about 20-30 minutes to perform and can be done transabdominally or transvaginally.

CVS is available during pregnancy to those:

- presenting at <13+2 weeks gestation and ≥40 years of age on the due date without prior maternal serum screen testing;
- who are at risk for carrying a fetus with chromosome abnormalities;
- with multiple gestations who are >35 years old at expected date of delivery;
- pregnant following in vitro fertilization with intracytoplasmic sperm injection (IVF with ICSI) without prior screening with IPS or SIPS.

**Standard Reference Range:** Karotype results take at least 2-3 weeks. In certain clinical situations a rapid cytogenetic analysis using amniotic fluid for fluorescence in situ hybridization (FISH) (also known as AneuVysion Assay) allows geneticists to detect up to 90% of the chromosomal abnormalities associated with birth defects such as Down's syndrome.

The assay provides a result of the chromosome number for 13, 18, 21, X and Y in 3-4 working days. Full karyotype analysis is also done for the following:

- A fetal anomaly or pattern of anomalies detected on ultrasound is highly suggestive (>5%) of aneuploidy of chromosomes 13, 18, 21, or X or Y where rapid results are needed.
- Pregnancies present at 22-24 weeks with advanced maternal age (AMA) or AMA equivalent (positive maternal serum screen or ultrasound markers).
- Pregnancies present at ≥24 weeks with anomalies detected on ultrasound suggestive of aneuploidies where a rapid result is needed for delivery management.

	<b>Chorionic Villus Sampling (CVS)</b>	<b>Amniocentesis</b>
Time period for performing tests	11 – 13 <sup>+</sup>	≥15 weeks gestation
Sample	Placental villi	Amniotic fluid
Pregnancy loss rate	1 – 2 in 100 (1 – 2%)	1 in 200 (0.5%)
Other risks associated with this procedure	<ul style="list-style-type: none"> <li>• Bleeding, cramping, infection</li> <li>• Possible increased risk of fetal limb malformations (arms, legs, hands, or feet)</li> <li>• With no procedure, the risk is 1 in every 2000 to 5000 births; after CVS, the risk is 1 in every 1000 to 2000 births</li> <li>• Risk is primarily associated with CVSs done prior to 10weeks</li> <li>• Failure to obtain results due to insufficient sample or poor cell growth</li> </ul>	<ul style="list-style-type: none"> <li>• Bleeding, amniotic leakage, cramping, infection</li> <li>• Failure to obtain results due to insufficient sample or poor cell growth</li> </ul>
Result Turn-Around Time	2 weeks for full karyotype	<ul style="list-style-type: none"> <li>• 2 weeks for full karyotype</li> <li>• 2 – 3 days for Rapid Aneuploidy Detection (RAD) of chromosomes 13, 18, 21 and sex chromosomes done in high risk or late gestational age cases</li> </ul>

**Diagnostic Ultrasound** (updated May 2018)

Ultrasound is a useful tool for diagnosis and is indicated in variety of maternal and newborn clinical situations. Ultrasound offers diagnosis through visualization of maternal, fetal and newborn anatomy, amniotic fluid, placenta, umbilical artery and fetal cord Doppler study. Ultrasound can confirm gestational age, intrauterine pregnancy, spontaneous abortion, retained products of conception, abnormalities of the female reproductive system and

abnormalities of the newborn kidneys and hips. Ultrasound should be limited to a minimum and only ordered when medically necessary. Non-medical use of this technology, such as for the sole purpose of determining fetal sex, should not be encouraged<sup>26</sup>.

#### Routine First Trimester Ultrasound

A routine first trimester ultrasound between 7 and 14 weeks should be offered.

First trimester ultrasound may be of benefit:

- a. to date a pregnancy;
- b. for assessment of threatened abortion;
- c. to document fetal viability for incomplete abortion;
- d. prior to pregnancy termination;
- e. during diagnostic or therapeutic procedures requiring visual guidance (e.g. chorionic villus sampling) and prior to cervical cerclage placement;
- f. when multiple gestation is suspected, to allow for reliable determination of chorionicity or amnionicity;
- g. during suspected ectopic pregnancy, molar pregnancy, and for suspected pelvic masses;
- h. early assessment of anatomic development in situations of increased risk of major fetal congenital malformations;

#### Nuchal Translucency (NT) Ultrasound

NT ultrasound is available at specifically designated centres in BC for clients at higher risk of having a fetus with trisomy 13, 18 or 21 and or open neural tube defects (ONTDs), as well as in cases with multiple gestations.

Eligibility for NT ultrasound to be done in conjunction with first and second trimester serum markers as part of the Integrated Prenatal Screen (IPS) includes those:

- $\geq 35$  years old or older at EDD and are between 11 to 13+6 weeks gestation (eligibility based on client age may vary depending on region);
- with multiple gestation pregnancies;
- with a history of a child or fetus with trisomy 13, 18 or 21 and or open neural tube defects (ONTDs);
- who are HIV positive;
- pregnant following in vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI).

Nuchal translucency screening should only be offered as part of the IPS.

#### Routine Second Trimester Ultrasound

A second trimester ultrasound between 18 and 22 weeks' gestation should be offered. Second trimester ultrasound identifies the number of fetuses, the gestational age, the location of the placenta, assesses anatomy and screens for congenital fetal anomalies. If fetal sex has been determined, a patient's request for disclosure should be respected.

#### Non-Routine Ultrasound (all trimesters)

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<sup>26</sup> SOGC – Joint SOGC/CAR Policy Statement on Non-medical use of Fetal Ultrasound No. 304, February 2014.

Ultrasound may be recommended at additional times during pregnancy, for indications including but not limited to:

- Cramping and spotting or bleeding at any gestational age
- Symptoms consistent with a missed, threatened or incomplete abortion
- Inability to auscultate fetal heart rate after 12 weeks
- Symptoms consistent with hydatidiform mole
- Inappropriate symphysis fundal height (SFH)
- Amniotic fluid assessment
- Antepartum hemorrhage
- Follow up for diagnosed anomalies, multiple gestations, etc.
- As part of an obstetrical procedure such as amniocentesis, CVS, or external cephalic version
- Cervical length assessment (12-34 weeks) (transvaginal ultrasound recommended)
- Assessment of uterine fibroids or ovarian cysts
- Placental location if previously assessed as low-lying or previa (transvaginal ultrasound recommended)
- Serial growth measurement in suspected or diagnosed intrauterine growth restriction (IUGR)
- Confirmation of presentation as indicated
- Fetal assessment with a biophysical profile
- Fetal and placental assessment for: umbilical artery and fetal cord Doppler study for query IUGR or hypertension
- Follow up ultrasounds for maternal or fetal indications
- Identify retained products of conception

### Newborn Hip Ultrasound

A hip ultrasound should be organized to take place at six weeks of age for newborns considered at risk of developmental dysplasia of the hip (DDH). Risk factors include a history of clinical instability (positive click or clunk on Barlow-Ortolani exam), breech presentation at term or family history of DDH. Not all ultrasound clinics offer newborn hip ultrasound examination; midwives must be aware of local availability and referral pathways outside their region as required.

It is important to note that the ideal timing of the hip ultrasound coincides with when the client and newborn are typically discharged from care. Regardless of discharge status, the ordering midwife is responsible for following up on the results of the newborn hip ultrasound. If the ultrasound is abnormal, referral to an orthopedic pediatrician is required.

### Abnormal Ultrasound Results- Suggested Clinical Management

- Structural abnormality of the fetus requires a prompt referral to a tertiary care center for consultation/repeat examination before therapeutic abortion or other treatment is considered or offered. Information that false positives and false negatives do occur with varying frequency should be provided.
- Abnormalities detected by ultrasound may require consultation with and/or transfer to an obstetrician or pediatrician as per CMBC's *Indications for Discussion, Consultation and Transfer Care*.

- A transvaginal follow up ultrasound between 32 and 34 weeks or earlier should be done if the placenta is covering the os or is  $\leq 2$  cm from the internal os.
- Specific concerns or potential complications should be investigated in accordance with clinical judgment.

**4. A midwife may order the following tests during pregnancy. If results are abnormal, a physician consult is required.**

**24-Hour Urine for Protein**

Used to quantify proteinuria. Normally, the glomeruli prevent passage of protein from the blood to the glomerular filtrate. However, there are some physiologic conditions (e.g: exercise, fever) that can lead to proteinuria. The presence of protein in the urine is the single most important indication of renal disease. In pregnancy, kidney involvement with hypertension is prognostically a poor sign associated with a two-fold increase in perinatal mortality and the development of oliguria. If more than a trace of protein is found in two separate catches a 24-hour urine is indicated. Values are investigated in the presence of hypertension in pregnancy.

**Typical Reference Range\*:** In pregnancy: 0.2-0.3 g/day

**Albumin**

Albumin is synthesized in the liver and is the most abundant protein in human plasma. Albumin maintains the oncotic pressure of the blood and is essential to the blood's many transportation functions.

**Typical Reference Range\*:** 30-50 g/L. Hemodilution may lower albumin levels slightly, but normal pregnancy values are rarely below 26 g/L. Hypoalbuminaemia (<18 g/L) is indicative of severe pre-eclampsia.

**Bilirubin**

Bilirubin is the end result of hemoglobin breakdown and is removed from the body by the liver. Increased bilirubin comes from liver disease or from increased hemoglobin breakdown. Bilirubin is increased in the serum in liver disease or cholestasis.

**Typical Reference Range\*:**  $\leq 24$   $\mu\text{mol/L}$

**Blood Urea Nitrogen (BUN)**

Urea forms in the liver and, along with CO<sub>2</sub>, is the final product of protein metabolism. Rapid protein catabolism and impaired renal function will elevate BUN levels. Therefore, BUN is used as an index for glomerular function in the production and secretion of urea. Values are investigated in the presence of hypertension in pregnancy.

**Typical Reference Range\*:** For adults: 2.9-7.5 mmol/L

**Liver Function**

Liver involvement can occur in hypertensive disorders of pregnancy.

Alanine Aminotransferase (ALT) is an enzyme that occurs in high concentrations in the liver, with lower concentrations found in the heart, muscle and kidneys. ALT levels are used to determine liver disease and monitor the course of treatment for hepatitis. ALT is elevated in cholestasis of pregnancy.

**Typical Reference Range\*:** 5-35 u/L, significant findings >50 u/L

Aspartate Transaminase (AST) is an enzyme present in tissue with high metabolic activity such as heart, liver, skeletal muscles, kidney, brain, pancreas, spleen and lungs. The enzyme is released into the blood when injury or cell death occurs in these tissues. AST levels are used to evaluate liver and heart diseases.

**Typical Reference Range\*:** 10-30 u/L, significant findings >72 u/L

Lactic Acid Dehydrogenase (LDH) is an enzyme present in most cells in the body and becomes elevated in response to tissue damage. An increase in LDH levels commonly indicates inflammation of the liver. LDH is elevated in gestational hypertension.

**Typical Reference Range\*:** 140-280 u/L, significant findings >494 u/L  
Results outside of the reference range require immediate physician consultation.

### **Spot Urine Protein/Creatinine Ratio (UPCR)**

While a 24 hour urine collection remains the standard assessment of kidney involvement with hypertension in pregnancy, a urine protein/creatinine ratio of a single voided urine specimen can provide an accurate and rapid method for quantitation of proteinuria in suspected hypertensive pregnancies within a matter of hours. This test is considered to have reasonable accuracy for ruling out proteinuria of 0.3 g/day or more.

**Standard Reference Range:** Results <30 mg/mmol

### **Activated Partial Thromboplastin Time (aPTT)**

The aPTT test is used to evaluate coagulation status and often ordered in combination with other tests such as a PT test. It is generally ordered to monitor diseases such as hypertensive disorders of pregnancy, liver disease, injury, or to investigate the cause of bleeding or clotting episodes such as with recurrent miscarriages. It is also used to monitor heparin anticoagulant therapy. Coagulation factor deficiencies may be acquired or inherited. Several factors are vitamin K dependent. If a person has liver disease, for instance vitamin K deficiency, they may have one or more factor deficiencies. Inherited factor deficiencies may involve the quantity and/or function of the factor produced. Inhibitors may be antibodies that specifically target certain coagulation factors, such as Factor VIII antibodies, or they may be non-specific inhibitors, such as lupus anticoagulants that bind to chemicals called phospholipids found on the surface of platelets.

**Typical Reference Range\*:** 25-36 seconds

Please check with your local lab to ensure the capability of processing the aPTT test is available.

### **Fibrinogen**

Fibrinogen is an important plasma protein involved in the blood clotting mechanism. It is measured to determine the nature of bleeding disorders and to provide information about the body's ability to clot. It is generally ordered when there is unexplained bleeding, as well as monitoring other diseases such as hypertensive disorders of pregnancy and liver disease.

**Typical Reference Range\*:** 3.4-6 g/L



### **Prothrombin (PT) or International Normalized Ratio (INR)**

Prothrombin (PT) or INR is a test for coagulation which measures the time that it takes for blood to clot and a means to evaluate bleeding disorders. Prothrombin or factor II is one of the clotting factors made by the liver. Prothrombin time checks to see if different blood clotting factors (factors I, II, V, VII and X) are present. It is generally ordered to monitor diseases such as hypertensive disorders of pregnancy, liver disease or injury.

**Typical Reference Range\*:** 0.8-1.2 seconds

### **Serum Bile Acid** *(added September 2018)*

Serum bile acid concentrations reflect the ability of the liver to effectively excrete bile acids. Impaired excretion of bile acids is frequently the case in intrahepatic cholestasis of pregnancy (IHCP), a condition that occurs in 0.1% to 1.5% of pregnancies. Both increased and decreased sex steroid levels have been implicated in IHCP, but current research centers on the numerous mutations that have been identified in the genes that control hepatocellular transport systems. Whatever the inciting cause(s), bile acids are cleared incompletely and accumulate in plasma in IHCP. Clients who present with clinical symptoms of IHCP should have measurement of serum bile acid included in their initial laboratory investigations.

***Clients must fast for 10 hours prior to blood collection for serum bile acid.***

In British Columbia, serum bile acid samples are sent to BC Children's Hospital for processing in weekly batches. This may affect the timing of results availability. Initial clinical management and consultation based on presentation and other laboratory results should not be delayed when serum bile acid results are not immediately available.

**Reference Range (BC Children's Hospital): <10 umol/L**

### **Serum Creatinine** *(updated May 2018)*

A renal function test providing a rough approximation of glomerular filtration. Values are investigated in the presence of hypertension or suspicion of renal disease in pregnancy.

**Typical Reference Range\*:** in pregnancy: 45-90 µmol/L.

### **Serum Electrolytes**

Body function is intricately dependant upon several electrolytes. Hydration, medication and disease can alter the levels of electrolytes in circulation. Ranges are dependent upon age.

Adult normal ranges:

Calcium	<b>Typical Reference Range*:</b> 2.20-2.70 mmol/l
Chloride	<b>Typical Reference Range*:</b> 98-106 mmol/l
Phosphate	<b>Typical Reference Range*:</b> 0.87-1.45 mmol/l
Magnesium	<b>Typical Reference Range*:</b> 0.66-1.07 mmol/l
Potassium	<b>Typical Reference Range*:</b> 3.5-5.3 mmol/l
Sodium	<b>Typical Reference Range*:</b> 135-145 mmol/l

### **Serum Uric Acid**

A prognostic indicator in pregnancy-induced hypertension. Uric acid is formed from the breakdown of nucleonic acid and is an end product of metabolism. The kidneys excrete two thirds of uric acid and one third is excreted in the stool. Uric acid levels above the normal

range may indicate overproduction of nucleonic acids (gout), high production and destruction of cells (leukemia) or inability to excrete the substance produced (renal failure). In pregnancy uric acid levels outside the normal range are suggestive of preeclampsia, even in the absence of proteinuria.

**Typical Reference Range\*:** 214  $\mu\text{mol/L}$ -350  $\mu\text{mol/L}$

Values  $>350 \mu\text{mol/L}$  in particular are said to indicate poorer outcome.