Routine laboratory testing during pregnancy

Most general practitioners no longer offer lead maternity care, however, may still be involved with the initial confirmation of pregnancy and first laboratory tests and general care during pregnancy. The following article provides guidance on appropriate testing in early pregnancy, throughout pregnancy and information about common changes to testing reference ranges during pregnancy.

Blood tests included in the first antenatal screen

When a woman becomes pregnant, it is recommended that she receives a range of standard investigations. A first antenatal screen is required even if the woman is considering termination of pregnancy.

The "first antenatal screen" may be requested by the GP at the first appointment when pregnancy is confirmed, and the results later forwarded to the chosen Lead Maternity Carer (LMC). If the woman is likely to enrol with a LMC in the near future, the tests can be delayed, at the patient's request, until her first appointment with the LMC.

Tests included in the first antenatal screen include:

- Complete blood count
- Blood group and antibody screen
- Rubella antibody status
- Syphilis serology
- Hepatitis B serology
- HIV

Prior to all laboratory testing in pregnancy, information should be provided to the pregnant woman about why the test is recommended, the implications of both a positive or negative result, the risk of disease transmission to the foetus (if relevant) and how the results will be delivered. Verbal consent (or decline) should be documented in the patients notes.[1]

Although the first antenatal screen usually occurs early in pregnancy, it may be requested at any stage of pregnancy, i.e. if a women presents for the first time late in pregnancy, she should still receive a first antenatal screen.

Complete blood count

A complete blood count (CBC) gives information on a number of haematological parameters, but generally in pregnancy the most useful are the haemoglobin, platelets and white blood cell count. Most laboratories will provide pregnancy adjusted reference ranges to enable easier interpretation.

Very low or high haemoglobin levels are associated with increased foetal risk.[2] Gestational age should be taken into account when assessing haemoglobin, as levels decrease during pregnancy due to haemodilution caused by increased plasma volume.[2] The lower limit for haemoglobin is usually 115 g/L, but for pregnant women the lower limit is usually reported as 100 g/L.

Iron deficiency anaemia is the most frequent haematological concern during pregnancy and is usually characterised by decreased haemoglobin, mean cell volume (MCV) and mean cell haemoglobin (MCH) levels. When iron deficiency is suspected, a measurement of serum ferritin should be used to confirm the diagnosis.[2]

Changes in platelet levels are frequently seen during pregnancy. A decrease in the platelet count is more common than an increase and is most obvious in women who had low levels prior to becoming pregnant. Platelets usually decrease as a result of haemodilution, and this can become more pronounced as the pregnancy progresses from the second to third trimester.[3] A platelet level of 150 x 10^9/L or less is abnormally low and should be discussed with a haematologist.

Elevated platelets levels during pregnancy are generally a reactive response to the pregnancy and do not usually suggest a clinical problem. However, due to the slightly increased risk of clotting, it would be advisable, when platelet levels are higher than 600 x 10^9/L, to discuss results with a haematologist.

The total white cell count will frequently be elevated in pregnancy due to increased numbers of neutrophils. Neutrophils can also demonstrate a "left shift" (increased number of band neutrophils). However, this neutrophilia is not usually associated with infection or inflammation.

The total white cell count can also be misleading in pregnant women and should be interpreted with care, e.g. elevated neutrophils with a low lymphocyte count may produce a total white count that falls within the reference range. Therefore the absolute count of each cell type is more useful than the total white cell count.

Blood group and antibody screen

Identifying ABO blood group, rhesus D status and red cell antibodies in pregnant women is important to prevent "haemolytic disease of the newborn" in subsequent pregnancies.

If the foetus is rhesus D-positive (and the mother is negative), the mother may form anti-D antibodies, which may affect a subsequent rhesus D-positive foetus. Anti-D antibodies can be formed during a range of situations, including amniocentesis, chorionic villus sampling (CVS), external cephalic version (ECV), bleeding during the pregnancy, major abdominal trauma and late miscarriage.

Haemolytic disease of the newborn in subsequent pregnancies, can be avoided by antenatal prophylaxis of commercial anti-D in the second and third trimesters, and post-natally.[2]

Rubella antibody status

All pregnant women should be screened for rubella antibodies. Contracting rubella during pregnancy presents a high risk of harm to the foetus. Congenital Rubella Syndrome occurs when the rubella virus infects the developing foetus, especially during the first trimester when up to 85% of affected infants will be born with a birth defect, e.g. deafness, eye defects, heart defects, mental retardation. The risk of birth defects is decreased when infection occurs after 20 weeks gestation.[4]

The aim of screening is to identify women who have not been immunised or have diminished immunity and are susceptible to contracting rubella, so they can be immunised in the postnatal period to protect future

Maternity care funding for general practice

Within the funding of primary maternity services in New Zealand, a clinician who is not the lead maternity carer may access funding for one pregnancy-related visit during the first trimester. In general practice, this funding may be used, for example, when a patient presents for confirmation of pregnancy and the first antenatal screen.

N.B. Consultations regarding a potential pregnancy are not eligible for this funding if pregnancy is not confirmed.

pregnancies.[2, 5] Rubella vaccination cannot be given during pregnancy (as it is a live vaccine) and if a mother contracts rubella during pregnancy there is no way to prevent transmission to the infant.[2]

Rubella antibody titres should be measured at each pregnancy as levels may decline and fall below protection levels. This is more often seen in people only exposed to the virus through immunisation.[6]

Interpreting low rubella titres in previously immune women

A rubella antibody level greater than 10 IU/mL usually indicates protection from the disease, however, re-infection with rubella has still been reported in women with antibody levels above 15 IU/mL. Therefore, pregnant women with rubella antibody levels less than 15 IU/mL should be advised to avoid coming into contact with people with rubella. Women with antibody levels less than 25 IU/mL, who have received only one dose of MMR, can be advised to have a second dose after delivery.[7]

Syphilis serology

All pregnant women should be screened for syphilis.[2] Mothers infected with syphilis can experience long-term morbidity and the complications for pregnancy are significant; 70 to 100% of infants will be infected and one-third will be stillborn.[2] In recent years rates of syphilis in New Zealand have been increasing (2006–2009).[8] However, latest surveillance data show that although syphilis infection is still a concern, rates now appear to be decreasing.[9]

Mother-to-child transmission of syphilis in pregnancy is associated with non-immune hydrops (a life-threatening condition of severe oedema in the foetus and newborn infant), intrauterine growth retardation, malformations and perinatal death. Infected infants, who do survive, often have long-term disabilities.[2]

Universal screening for syphilis in newly pregnant women is recommended by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG). Women who test positive can then receive prophylactic antibiotic treatment. Penicillin is a safe and effective treatment for syphilis in pregnancy and can prevent congenital syphilis.[10]

The RANZCOG recommends that a treponemal test, e.g. Treponema pallidum particle assay (TPPA), is used to screen for syphilis as this can detect primary or secondary infection.[6]

Hepatitis B serology

Up to 85% of infants born to mothers infected with hepatitis B (particularly mothers who are HBeAg positive, i.e. with active infection), will become carriers and will be more likely to develop chronic liver disease, including cirrhosis, liver failure or liver cancer.[2, 11] Transmission of the hepatitis B virus from mother to infant can be prevented by administration of the hepatitis B vaccine and immunoglobulin to the infant at birth, therefore screening is important.[11, 12]

Women who are at increased risk of acquiring hepatitis B, e.g. women with sexual partners who are hepatitis B positive or intravenous drug users, are recommended to be vaccinated during pregnancy.[5]

HIV screening

All pregnant women should be screened for HIV. Women who are HIV positive can be given treatment to reduce the risk of HIV being transmitted to their infant (risk reduced from 32% to less than 1%).[1] Interventions to reduce mother-to-child transmission of HIV infection include antiretroviral therapy, elective caesarean section delivery and the avoidance of breastfeeding.[1, 2]

Any person undergoing a HIV test should be properly counselled about the implications of the test and the results, including how they wish to receive the results.

If a patient is considered at risk for HIV, hepatitis C screening should also be considered.

Best Practice Tip: In some DHB regions, HIV testing is automatically included as part of the antenatal screen, while in others, mothers must "opt on" for screening. The standard tick box for first antenatal screen does not always include HIV screening. Practices may wish to alter their electronic lab form to include an HIV tick box as a reminder to counsel patients on HIV screening and to add the test to the standard screen.

Additional testing in early pregnancy

Consider checking varicella antibody status in pregnant women with no (or uncertain) history of illness (i.e. chicken pox or shingles) or vaccination.[6] Contracting varicella during pregnancy is associated with a significant risk of harm to both mother and infant. There is a 0.7–2% risk of congenital varicella syndrome if varicella is contracted by the mother between eight and 20 weeks gestation.[13] Congenital varicella syndrome can cause blindness, growth retardation, limb and cranial malformations, delayed development, mental retardation, spontaneous abortion or foetal death. Contracting varicella between 25 to 36 weeks gestation increases the risk of the infant developing herpes zoster infection (shingles) after birth.[13] There is a 17–30% risk of serious disease in a newborn infant if the mother contracts varicella between five days before birth and two days after.[13]

As with the rubella vaccine, varicella is a live vaccine so cannot be given during pregnancy. Mothers with no (or diminished) immunity to varicella should consider immunisation to protect subsequent pregnancies.

If a mother with no history of varicella (and/or an absence of antibodies) is exposed to varicella during pregnancy, she may be offered either immunoglobulin (Zoster Immunoglobulin-VF) within 96 hours of exposure or acyclovir at the onset of symptoms. Treatment should be discussed with an infectious diseases physician. Zoster Immunoglobulin-VF is also recommended for:[14]

- Newborn infants who's mother has had chicken pox seven days before to seven days after delivery (not shingles)
- Hospitalised pre-term infants who's mothers have no history of chicken pox

A cervical smear may be considered at the first antenatal visit if the woman would be due for a routine test during the pregnancy (because as the pregnancy progresses, it may cause more discomfort to perform the test).[6] This is recommended by the RANZCOG who also states that there is no evidence that performing a smear is harmful to the foetus during pregnancy.[6] However, other countries such as the United Kingdom recommend that in most cases pregnant women should not have a cervical screening test, as pregnancy can make the results of the test more difficult to interpret and potentially inaccurate.[15] The decision whether to perform a routine cervical screening test during pregnancy should be based on clinical judgement and patient preference, taking into consideration factors such as previous abnormal smear results and time since last test.

Testing for chlamydia and gonorrhoea should be considered for those who may be at increased risk based on age (e.g. less than 25 years) and sexual history.[6]

Vitamin D is required for normal bone growth development in the foetus. Mothers with known vitamin D deficiency, or who are at risk for deficiency (e.g. dark skinned women, women who wear a veil) should receive vitamin D supplementation (cholecalciferol) without the need for testing.

For further information see "Vitamin D supplementation: navigating the debate", BPJ 36 (Jun, 2011).

N.B. Screening for toxoplasmosis or CMV infection during pregnancy is not routinely recommended in New Zealand.

Blood tests included in the second antenatal screen

At 26–28 weeks gestation, a second round of blood tests, commonly referred to as the "second antenatal" tests, is advised for pregnant women. In most cases the LMC will arrange these tests.

The second antenatal screen includes:

- 50 g glucose tolerance test (the "polycose" test)
- CBC
- Blood group antibodies

Screening for gestational diabetes

Gestational diabetes affects 5–8% of pregnant women and is associated with hypertensive disorders, macrosomia, shoulder dystocia, increased rates of caesarean delivery and the development of maternal diabetes later in life.[5, 16]

In New Zealand, it is recommended that testing for gestational diabetes occurs for all women between 26

and 28 weeks of gestation. Women at particularly high risk of gestational diabetes may be tested earlier.[17] Factors which increase the risk of gestational diabetes include; gestational diabetes in a previous pregnancy, family history of diabetes, belonging to a high risk ethnic group for diabetes, e.g. Māori, Pacific or South Asian (Indian).[17]

A 50 g glucose tolerance test (the polycose test) is used to screen for gestational diabetes. A 50 g glucose load is given to the non-fasting patient, and a glucose level is determined after one hour. Women with an elevated result should be followed up with a 75 g oral glucose tolerance test (OGTT).

Women who have had gestational diabetes during pregnancy should undergo an OGTT six to eight weeks after delivery. Even if not found to have diabetes at this time, women who have had gestational diabetes have an increased risk of developing type 2 diabetes within 15 years,[18] and should be screened with a fasting glucose test every one to two years.[17]

Repeat CBC and antibody screening

The CBC should be repeated at 28 weeks gestation, in particular to check haemoglobin and platelet levels (see commentary in previous section on how to interpret and manage these levels in pregnancy).

Antibody screening should also be repeated at 28 weeks gestation, to ensure no additional antibodies have developed. While blood group testing does not need to be repeated for subsequent pregnancies, the antibody screen should still be repeated.[2, 6]

Additional tests during pregnancy

Sub-clinical urine infection

It is recommended that all women have a mid-stream urine culture at the time of the first antenatal screen, again at the second antenatal screen and then at 36 weeks gestation, to exclude a sub-clinical urine infection (asymptomatic bacteriuria). Asymptomatic bacteriuria occurs in 2% to 10% of pregnancies and can lead to maternal pyelonephritis and may contribute to low birth-weight infants and pre-term birth (≤ 37 weeks).[19]

Screening for Group B Streptococcus

Group B streptococcal (GBS) infection is a significant cause of serious neonatal infection. Approximately 15–25% of women will be carriers, and one in 200 of these women will have infants who develop neonatal sepsis.[20]

Women may have a vaginorectal culture collected at 35 to 37 weeks gestation. Swabs may be collected by the patient, who has been instructed to swab the lower vagina first, and then rub the swab over the floor of the perineum to the anus, i.e. in a front-to-back direction. If positive for GBS, the mother should receive intrapartum antibiotic prophylaxis.[20]

Risk factors for GBS that would identify the need for intrapartum antibiotic prophylaxis include:[20]

- Pre-term labour, gestation ≤ 37 weeks
- Prolonged rupture of membranes ≥ 18 hours
- Maternal fever ≥ 38°C
- Previous GBS infected infant (prophylaxis required in all subsequent pregnancies)
- GBS bacteriuria during pregnancy (prophylaxis required in all subsequent pregnancies)

Testing for Down syndrome and other genetic conditions

Screening for Down syndrome, other chromosomal abnormalities and neural tube defects is offered to all pregnant women in New Zealand and testing can occur in either the first or second trimester of pregnancy.

Women need to be provided with enough information to make an informed decision about screening. Information should include the following:

- Reassurance that screening is voluntary
- Details of which screening options are available, the tests involved, the timing of the tests and where to go to get the tests
- Limitations of the tests, e.g. not all infants with the condition(s) being tested for will be identified, false positives are possible, testing is for specific conditions only and other abnormalities may be present
- Pamphlets explaining the different screening options are available from the National Screening Unit: **www.nsu.govt.nz**

First trimester screening is based on the combination of results of the following tests:

- Pregnancy-associated plasma protein A (PAPP-A)
- Beta-human chorionic gonadotropin (βhCG])
- Nuchal translucent (NT) scan

The PAPP-A and βhCG tests must be taken between nine and 13 weeks gestation (ideally between 10 and 12 weeks), and the NT scan carried out after 11 and before 14 weeks gestation.

Second trimester screening can be offered to all women who present after 14 weeks gestation but before 20 weeks, who have not completed first trimester screening (bloods are ideally taken between 14 to 18 weeks gestation). This serum screen measures βhCG, alpha-fetoprotein (AFP), unconjugated oestriol (μE3), and inhibin A.

If the results of either first or second trimester screening indicate an increased risk of foetal abnormalities, the mother should be referred to an obstetrician.

N.B. Women can only access one publically funded screening option. If they have the first trimester screening option, the blood tests will be fully funded and there is no cost to the patient, however, the NT scan may have a part-charge. The second trimester blood tests will be fully

Summary of routine antenatal tests

Laboratory	
Initial tests "First antenatal"	☑ CBC ☑ Blood group and antibodies ☑ Rubella ☑ Syphilis ☑ Hepatitis B serology ☑ HIV ☑ Urine culture
26–28 weeks "Second antenatal"	☑ CBC ☑ Polycose ☑ Antibodies ☑ Urine culture
35–37 weeks Group B streptococcal (GBS) infection (if risk factors)	☑ Vaginal swab ☑ Urine culture
Testing for genetic conditions (only one option applies)	
First trimester screening 11– <14 weeks	☑ NT scan ☑ Blood tests for PAPP-A, βhCG (3–4 days before scan)
Second trimester screening 14–18 weeks	☑ βhCG ☑ AFP ☑ μE3 ☑ Inhibin A

funded providing the women has not already accessed the first trimester screening. All sections of the laboratory referral form need to be filled out (including maternal age and weight, gestation and family history) to allow for an accurate risk prediction.

Woman at increased risk of foetal chromosomal abnormality, i.e. aged 35 years and over or have a family history of chromosomal disorder, should be referred to an obstetrician early in their pregnancy, to discuss the option of chorionic villus sampling (CVS) or amniocentesis.

CVS is usually performed at 11–12 weeks gestation and amniocentesis at 14–18 weeks gestation. These tests allow a more accurate prenatal diagnosis of chromosomal abnormality, but are associated with an increased risk of harm to the foetus including; infection, amniotic fluid leakage and miscarriage.

An ultrasound scan is offered to all pregnant women at 18–19+ weeks gestation to check foetal anatomy for any abnormalities.

Changes to reference ranges during pregnancy (adapted from Kyle, 2008)[21]

Analyte	Effect of pregnancy	Notes
Alpha-fetoprotein (AFP)	↑	Peaks in last trimester
Alkaline phosphatase (ALP)	↑	Marked increase due to placental izoenzyme
Blood volume	↑	Increases by 20–30%
Ca125 (tumour marker)	↑	2–2.5 times increase in first trimester
Cholesterol	↑	Up to 40% increase
Creatinine clearance	↑	
ESR	↑	Increasing to 30–60 mm/hr as pregnancy progresses
Iron binding	↑	Significant increase
White blood count	↑	May increase to 15–18 x10^9/L
CRP	↑	
Haemoglobin	↓	Decreases as a result of haemodilution due to greater blood volume
FT4	↓	May decrease up to 20% in late pregnancy
TSH	↓	Often decreases first trimester, but then returns to normal levels

ACKNOWLEDGEMENT: Thank you to **Dr Karine Baker**, Obstetrician and Gynaecologist, Southern DHB for expert guidance in developing this article.

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