

Routine antenatal screening



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A screening test is defined as one that is targeted at an asymptomatic population to improve the health of that population by the early detection of disease. The World Health Organisation's Principles of Screening include the ability to detect the disease in the asymptomatic phase; availability of a test with high sensitivity and specificity; an available treatment for the condition and evidence of improved outcome with treatment; acceptability of the test to the population; and cost-efficiency.¹

Several screening tests are currently performed throughout the course of a normal pregnancy. The following is an overview of the background and evidence base behind these investigations.

The antenatal screen

Tests performed at the first antenatal visit, in conjunction with a detailed history and physical examination, aim to detect early any variations from normal such that potential adverse sequelae to the mother or her fetus can be avoided or minimised. These should be undertaken with the woman's informed consent, after adequate explanation of the implications, limitations and consequences of the investigations. Current RANZCOG recommendations for tests to be performed antenatally on all women include:

- blood group and antibody screen
- full blood picture
- rubella antibody status
- syphilis serology
- hepatitis B serology
- hepatitis C serology
- HIV serology
- urine culture².

An article published in the *Medical Journal of Australia* in 2002 addressing the uniformity of antenatal screening throughout Australia concluded that while recommendations for syphilis testing were consistent and evidence-based, guidelines for screening of HIV and Hepatitis C were highly variable. It found that antenatal care recommendations vary widely throughout Australia and are not always consistent with national policies or research evidence.³

Blood group and antibody screen

There is little doubt regarding the valuable role of blood group and antibody screening at initial presentation, with repeat screening at 28 weeks for rhesus negative women.⁴ A positive antibody screen suggests the fetus is at risk for haemolytic disease and that further diagnostic measures are required. The value of repeat screening of rhesus positive women to detect other antibodies is less clear and the RANZCOG guidelines recommend this be done 'at the discretion of the clinician'.²

Full blood picture

Iron deficiency anaemia in pregnancy poses increased risk to both mother and fetus, while severe anaemia (Hb < 7g/dL) is associated with increased maternal mortality. All women should be screened at booking for anaemia (Hb < 11g/dL), with further investigation into the cause as indicated. Iron deficient women should be advised iron supplementation of 30 to 120mg per day until the anaemia is corrected.⁵ Prophylactic iron supplementation in pregnancy is more controversial. The *Cochrane database* shows no improvement in fetal or maternal outcomes using this approach. Selective treatment of iron deficiency anaemia in women who can have their haemoglobin status followed up is preferable to the routine use of iron.⁶

Rubella antibody status

The rubella virus causes a self-limiting infection in most adult hosts but, during pregnancy, can result in spontaneous miscarriage, growth restriction and fetal death. Features of congenital rubella syndrome include deafness, cataracts, cardiac malformations and neurological impairment. As there is no antenatal treatment available, prevention of maternal infection is the best strategy to avoid these outcomes.⁷ The incidence of rubella infection, including congenital rubella, has fallen by 99.6 per cent since the introduction of the rubella vaccine.⁸ Ideally, all susceptible women would be vaccinated pre-pregnancy (and avoid conception for one month post-vaccination). Women found to be susceptible in pregnancy should be warned against contact with anyone possibly infected and be offered vaccination after delivery. Postpartum vaccination programs have been shown to significantly reduce rubella susceptibility in seronegative women in subsequent pregnancies.⁷

Syphilis serology

Transplacental infection with *treponema pallidum* is associated with several adverse outcomes such as preterm birth, low birth weight, perinatal death, congenital anomalies and active congenital syphilis. The risk of these outcomes can be almost completely eliminated by universal early antenatal screening and appropriate antibiotic therapy.⁹ Despite its low yield, the United States Centres for Disease Control and Prevention recommend that all pregnant women be screened, as the cost and morbidity of testing is low and the benefit of detection and treatment high for both mother and child. Repeat serology in high-risk populations at 28 weeks and again at delivery is recommended and reinforced in the RANZCOG guidelines.^{9,2} Testing should be performed with a specific *treponema*

pallidum assay, as the non-specific assays are less likely to detect latent infection.²

Hepatitis B serology

There are more than 350 million hepatitis B virus (HBV) carriers worldwide, of whom one million die annually from liver disease. In Australia and New Zealand, the carrier rate is between 0.1 and 2.0 per cent. The incidence of progression from acute to chronic infection is highest with perinatally acquired infection, at a rate of around 90 per cent.¹⁰ The opportunity to provide almost complete protection against perinatally acquired infection makes antenatal identification of HBV carriers critical. Testing for surface antigen should be performed at booking in all women and repeated in high risk groups. Neonates of seropositive mothers can then receive immunoglobulin as soon as is feasible after birth and commence a course of vaccination. This approach is cost-effective even at a population prevalence for HBsAg as low as 0.06 per cent.¹¹

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Hepatitis C serology

The routine testing of all women for hepatitis C, although recommended by RANZCOG, is one of the more controversial aspects of routine screening in pregnancy. This contention is acknowledged in the college statement on antenatal screening.² The Centres for Disease Control and Prevention recommend against routine screening in pregnancy, advising testing be reserved for those in high-risk groups. Initial evaluation is with an antibody test, followed by HCV RNA quantification.¹² The risk of perinatal transmission is up to ten per cent in RNA positive women, but carries a significantly higher risk of progression to chronic liver disease than does hepatitis B infection. Current consensus opinion is that hepatitis C infection is not an indication for caesarean section, nor a contra-indication for breastfeeding. There is currently no neonatal intervention such as immunoglobulin to lower the risk of transmission, nor is there a vaccine available.¹¹

HIV serology

Obstetric intervention in HIV positive women in the form of antiretroviral therapy, caesarean section and avoidance of breastfeeding significantly reduces the rate of perinatal transmission from around 30 per cent to one or two per cent. Reproductive-aged women represent the fastest growing group with new HIV infection, the majority of which is acquired through heterosexual contact. Regardless of perceived risk, all women should be offered screening for HIV (with appropriate counselling and informed consent), to allow for optimal care throughout pregnancy and prevention of transmission.¹³ The RANZCOG guidelines also recommend repeat testing in all women at 28 weeks gestation.² Initial screening is with an enzyme immunoassay, followed by a confirmatory test such as a Western blot, HIV RNA level and CD4 lymphocyte count.¹³

Urine culture

Asymptomatic bacteriuria occurs in two to ten per cent of sexually active women, but is more likely to progress to pyelonephritis in the pregnant population. Urinary tract infection is associated with an increased risk of preterm birth, low birth weight and perinatal mortality. Antibiotic therapy for culture-confirmed bacteriuria significantly reduces the risk of these complications.¹⁴ Screening of all pregnant women with culture of a mid-stream specimen of urine is therefore recommended by the RANZCOG guidelines. Other authorities have suggested that screening could be limited to those populations where the incidence of asymptomatic bacteriuria is greater than five per cent to enhance cost-effectiveness.¹⁵ Other tests which can be considered in women with risk factors, but are not recommended as part of routine screening in pregnancy include:

- cervical cytology
- testing for vitamin D deficiency
- screening for haemoglobinopathies
- varicella, CMV and toxoplasmosis serology
- chlamydia screening
- thyroid function testing².

Routine antenatal ultrasound

The RANZCOG guidelines recommend that all women be offered an obstetric ultrasound for assessment of fetal morphology and placental localisation prior to 20 weeks gestation², yet the benefit of routine ultrasound screening in pregnancy remains a topic of debate.¹⁶ Several studies have evaluated this question, looking mainly at the ability of routine ultrasound to detect fetal anomalies in an unselected population, the impact on perinatal outcome and the cost-benefit of such an approach.¹⁷

The Helsinki trial in the late 1980s found that routine ultrasound screening significantly increased the detection of anomalies and was associated with reduced perinatal mortality. The detection rate of malformations varied significantly depending on whether the ultrasound was performed at a tertiary centre or peripherally. The RADIUS trial of the early 1990s showed a significant increase in the detection of fetal anomalies but, in contrast, no improvement in perinatal outcome. A cost-benefit analysis using data from the trial concluded that routine screening was associated with significant savings only if the ultrasound was performed in a tertiary centre. The Eurofetus trial of the late 1990s is the largest study of routine ultrasound in an unselected population. It found an overall sensitivity for the detection of anomalies of 56 per cent, with higher detection rates for major compared with minor abnormalities.¹⁷

Overall, these data suggest that it is ethical and cost-effective to offer routine screening if a targeted examination is performed by an experienced operator in a centre with high rates for detection of fetal anomaly, at a gestational age that allows for good visualisation of fetal anatomy, with the option of legal termination if required.^{17,18}

Screening for gestational diabetes

Screening for gestational diabetes is recommended by the RANZCOG guidelines in all pregnant women.² Testing is recommended between 26 and 28 weeks gestation with a glucose challenge test, followed by a fasting, two-hour glucose tolerance test if abnormal. The diagnosis of gestational diabetes is made if the fasting glucose level is higher than 5.5mmol/l, or the two-hour level is higher than 8.0mmol/l by Australian criteria, or higher than 9.0mmol/l by New Zealand criteria.¹⁹

Until recently, there was a paucity of level one evidence to demonstrate that the screening for and treatment of gestational diabetes improves perinatal outcome. The findings of the landmark ACHOIS (Australian Carbohydrate Intolerance Study in Pregnant Women) study provided convincing evidence to support the treatment of gestational diabetes, with a significant reduction in the rate of perinatal complications in the intervention group compared with controls. The results also strengthened the case for universal screening, given the prevalence of the condition and high rate of adverse outcome in the non-intervention group.²⁰

Focus then shifted from whether to screen and treat, to the threshold to be used as a marker of need for intervention. This issue was addressed by the HAPO (Hyperglycemia and Adverse Pregnancy Outcome) study, which examined the relationship between hyperglycaemia and adverse outcome. The results indicated a strong, linear association between maternal glucose levels and outcomes such as macrosomia, rate of caesarean section and neonatal hypoglycaemia. There was no obvious threshold at which risk increased, which contributes to the universal lack of consensus on the diagnostic criteria for gestational diabetes.²¹ A *Cochrane review* to assess the effects of different methods of screening for gestational diabetes on subsequent management and maternal and infant health is currently in progress.²²

Screening for group B streptococcus

Group B streptococcus (GBS) has previously been identified as one of the leading infectious causes of neonatal morbidity and mortality. The use of intrapartum prophylaxis with penicillin has led to a significant decline in the incidence of early-onset GBS disease since its introduction. Both risk-based and screening-based approaches have been used. The former involves the use of intrapartum antibiotics when one of a group of defined risk factors is present, while screening involves the collection of a low vaginal/anorectal swab from all women at around 36 weeks gestation, with intrapartum treatment for those with a positive culture.²³

In a large retrospective study, it was found that the culture-based strategy was almost 50 per cent more effective than the risk-based approach in the prevention of early-onset GBS disease, with no significant increase in antibiotic usage.²⁴ Based on this result, in 2002, the Centres for Disease Control and Prevention published guidelines recommending universal screening for GBS in pregnancy.²⁵ The RANZCOG guidelines support the screening-based approach, but recommend that where it is impractical or inappropriate to obtain swabs, the risk-based strategy be adopted.²³

Conclusion

When supported by evidence, screening tests in pregnancy play a valuable role in the prevention or early detection and treatment of disease through appropriately timed intervention, to improve outcomes for women and their babies.

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