

Preconception counselling: serendipitous and targeted approaches

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Key points

- Advice regarding timing and preparation for pregnancy is advisable for all women.
- Most advice given to women will not be in the context of a formal 'preconception' consultation, so any opportunity should be used (serendipitous approach).
- Women with pre-existing morbidities should be offered advice in general terms well before they may be considering pregnancy, and more specifically when pregnancy is a possibility (targeted approach).
- Most interventions and modifications need to be in place at the time of conception to benefit the formation of a fetus.

Taking a serendipitous approach to discuss future pregnancy with women of childbearing age who present to your practice will optimise their chances of having a healthy baby. A targeted approach is appropriate for women who present specifically for preconception counselling or those with health issues that may affect a pregnancy.

Pregnancy is a life-changing event and a time when a woman has the maximum impact on her (future) child. Most women are very motivated to do the best for their child, and pregnancy can provide the impetus women may need to optimise their lifestyle and health. However, making lifestyle changes once a pregnancy has been confirmed is often too late.

The majority of organogenesis occurs from embryonic days 18 to 40 (menstrual dates four weeks four days to seven weeks five days) and is the time when the embryo is most sensitive to external insults. The implication of this is that improvements to a woman's health and lifestyle need to be optimised before, rather than after, she conceives. The World Health Organization estimates that almost half of all pregnancies

are unplanned, making this aim difficult to achieve.

Therefore, preconception counselling needs to be undertaken with either a serendipitous approach (aimed at all woman of childbearing age) or targeted approach (aimed at those women who either present asking for advice in anticipation of pregnancy or have underlying medical problems that may affect a pregnancy and can be better dealt with beforehand).

SERENDIPITOUS APPROACH

The following encapsulates the knowledge that is relevant to all women embarking on a pregnancy. It is equally relevant to women in the targeted group as it is to those who are approached serendipitously.

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Age

Maternal age (and, to a lesser extent, paternal age) has an impact on a woman's ability to conceive and have a successful pregnancy. Despite the advances in reproductive technologies, women (and their partners) may need to be reminded of the 'biological clock'. By the age of 40 years, fertility has halved compared with that of a 25-year-old woman and the probability of having a miscarriage is higher than the probability of a live birth. Women who have problems that may impact on their reproductive performance, such as endometriosis or polycystic ovary syndrome, should be advised not to delay pregnancy unduly.

In semen analyses from men older than 50 years, a clear decline in the volume, motility and morphology of the sperm has been seen. The risk of miscarriage, and possibly some genetic mutations, increases in women with partners in this age group.

Dietary advice

Common sense suggests that a well-balanced diet is a good basis on which to start a pregnancy to ensure that all the substrates necessary for early fetal development are present. Some dietary supplementation of particular vitamins and minerals is advised in some or all women planning to conceive.

Folic acid

Folate is known to play an important role in the closure of the neural tube. Following studies in the early 1980s, the Medical Research Council conducted a randomised controlled trial that showed that the risk of neural tube defects could be dramatically decreased (by about 70%) in women with a previously affected child by taking 4 mg folic acid preconceptually.¹ A subsequent study showed a similar reduction in women in their first pregnancy when taking a multivitamin containing 0.8 mg folic acid.² A more recent review confirms the benefit of folic acid

in the prevention of neural tube defects.³

However, as the neural tube is closed (or not) by embryonic day 26, folic acid supplementation needs to have been commenced before the onset of pregnancy – preferably at least one month beforehand.

The Australian Federal Government recommendation is that all pregnant women have an additional 400 µg/day folic acid commenced at least one month before conception and for three months after, in addition to a dietary intake of ideally 600 µg/day.⁴ Extra folic acid – 120 µg per 100 g (about three slices of bread) – is now present in bread flour in Australia.⁵

A dosage of 5 mg/day is recommended for women who have previously had a fetus or child with a neural tube defect, who have spina bifida themselves or whose partner or a close relative has a neural tube defect. Women who are taking antiepileptic medication may also be advised to commence a higher dose of folic acid preconceptually.

Iodine

Severe iodine deficiency during pregnancy is a known cause of congenital hypothyroidism and mental retardation. There is now growing recognition that milder iodine deficiency may also be related to cognitive deficits. Mild iodine deficiency has been consistently found in all studies of pregnant women living in Australia and New Zealand.⁶ The mandatory addition of iodised salt in bread that occurred in late 2009 may not sufficiently increase iodine intake to meet the requirements of pregnant women, and Food Standards Australia New Zealand has recommended that pregnant women take a daily dietary supplement containing 150 µg/day of iodine.⁵ However, no published studies have yet examined the effect of iodine supplementation in pregnancy on the clinical outcomes of mothers or babies in regions with mild iodine deficiency.

Calcium

Calcium supplements more than halves a woman's overall risk of developing pre-eclampsia compared with placebo in all women but particularly in those at high risk of pre-eclampsia (risk reduction of 78%) and those with a low dietary intake of calcium.⁷ Current Australian advice (since 2006) is that an intake of 1000 mg/day (equivalent to just over three glasses of milk) for women be encouraged, and that there is no need for additional supplementation.

Iron

Iron supplementation is often recommended for pregnant women. Iron deficiency is unlikely to affect the developing fetus except in cases of severe anaemia. However, given the additional demands of pregnancy on the mother's iron stores, commencing pregnancy with adequate stores is wise.

Vitamin D

Low vitamin D levels occur more notably in the winter months and in those women with reduced exposure to sunlight – that is, dark-skinned women, veiled women or those who spend most of their days indoors. Low levels of vitamin D may be associated with growth restriction and preterm birth of the fetus and rickets in children. In pregnant women, low vitamin D levels have been linked to hypertension, pre-eclampsia and poorer glycaemic control in women with gestational diabetes.⁸ If a woman's serum 25-hydroxyvitamin D level is less than 50 nmol/L (some would say less than 75 nmol/L), prescription of 1000 to 2000 IU/day cholecalciferol is recommended.

Weight

There is much interest in and concern expressed about the obesity epidemic facing the western world, including Australia.^{9,10} Being obese is known to increase the risk for almost all complications

in pregnancy. These include difficulty in conceiving, miscarriage, fetal anomalies, stillbirth, gestational diabetes, pre-eclampsia, thromboembolic disease, caesarean section, postpartum haemorrhage, wound infection and maternal mortality.

Although some women may lose weight in early pregnancy because of nausea, many will overeat to counteract the nausea, and once into the second and third trimesters may eat more than required in the belief they are 'eating for two'.

A weight-loss program in pregnancy is not acceptable to many women, and may have the effect of depriving the mother and fetus of vital nutrients if not very carefully monitored. Hence, the best time to address the issue of weight loss and appropriate diet is before pregnancy (or between pregnancies). How this is best achieved is not always clear;¹¹ however, programs incorporating a combination of dietary advice, exercise and psychological support would appear to be the most likely to succeed.

In morbidly obese women for whom the above regimen has been unsuccessful, bariatric surgery may be considered before pregnancy. This will help in reducing weight, but will require closer attention to dietary requirements and supplements both before and during pregnancy. Delaying pregnancy until dietary stability is reached is recommended. Additional folic acid supplementation is suggested before and during pregnancy in these women.

Substance use and abuse

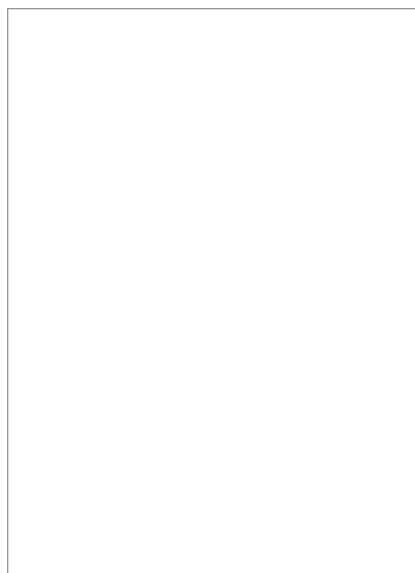
Alcohol

Alcohol is a known teratogen. Whether there is a safe level of alcohol intake in pregnancy is unknown and hence advice for women hoping to become pregnant should be to avoid alcohol in pregnancy. Current Australian guidelines from the National Health and Medical Research Council state that: 'for women who are

pregnant or planning a pregnancy, not drinking is the safest option'.¹²

Cigarettes

Cigarette smoking in pregnancy is associated with miscarriage, fetal growth restriction, stillbirth and placental abruption. Smoking cessation is strongly advised but, like weight loss, is more difficult to achieve.



Nicotine replacement therapy has been shown to help in smoking reduction and is best implemented before pregnancy.¹³ Advising and helping the woman's partner to stop smoking at the same time can be beneficial, both for the woman herself and the home environment for the newborn child.

Illicit drugs

Preconception counselling should include advice about stopping the use of illicit drugs. However, as cessation is often not achievable, harm minimisation should be the goal.

For those women addicted to narcotics, stabilisation on a methadone program is recommended. For those stabilised on buprenorphine, continuation may be appropriate although its safety in pregnancy has not been demonstrated.

Discussion with or referral of the patient to a specialist clinician or unit is advisable. Stopping or reducing use of other drugs is wise.

Cocaine use is particularly harmful at any stage of a pregnancy because of its vasoconstrictive properties. 'Party drugs', due in particular to the lack of information of drug content, should be avoided. Marijuana, although not a known teratogen, is also best stopped before pregnancy. It may be that cigarette smoking (that almost invariably accompanies illicit drug use) is as dangerous to the pregnancy as the illicit drugs themselves.

The *National Clinical Guidelines for the Management of Drug Use During Pregnancy, Birth and the Early Development Years of the Newborn* is a useful resource.¹⁴

Caffeine

Caffeine has been linked to miscarriage but the evidence is not consistent. Women seeking advice should be recommended to minimise their daily caffeine intake to no more than two caffeine-containing drinks (including soft drinks that contain caffeine).

Medications

A thorough assessment is required in a preconception discussion to decide whether prescription drugs are able to be ceased, reduced temporarily, reduced for the duration of the pregnancy or continued throughout. This is always a balance between potential risks to the fetus by continuing, and risks to the mother by stopping, the medication.

Although many women are keen to stop all medications during pregnancy, they need to be reminded that a successful pregnancy requires a healthy mother.

Psychotropic medication (in particular antidepressants) is one of the groups of drugs some women are keen to stop before pregnancy. Again this needs to be discussed in light of risks to the mother should she cease the medication.

A useful resource when discussing this is the Perinatal Psychotropic Medicine Information Service (www.ppmis.org.au).

Over-the-counter medications

Cold and flu medications are often best avoided during pregnancy. The vasoconstrictive effects of some nasal decongestants may theoretically interfere with intrauterine vasculature, although the systemic dose is likely to be small. NSAIDs are best avoided in pregnancy due to a possible increased risk of miscarriage and, at a later stage of pregnancy, their effects on the fetal kidneys and cardiovascular system.¹⁵

Although paracetamol is thought to be safer (having a different mechanism of inhibiting prostaglandin synthesis), recent data suggest that a rethink in certain groups of women, particularly those at high risk of pre-eclampsia, may be wise.¹⁶

Complementary and alternative medicines

Most complementary and alternative medicines are best avoided in early pregnancy unless the benefits are thought to outweigh any potential risks to the fetus. Little is known about the safety profile of many of these therapies, whereas others are known to have abortifacient and oxytocic effects.

Immunisation and infectious diseases

The ninth edition of the *Australian Immunisation Handbook* states:¹⁷ 'The need for measles, mumps, rubella, varicella, diphtheria, tetanus and pertussis vaccination should be assessed as part of any preconception health check. Where previous vaccination history or infection is uncertain, relevant serological testing should be undertaken to ascertain immunity. Influenza vaccine is recommended routinely and pneumococcal vaccination is recommended for women with risk factors, including cigarette smoking.

Women receiving live viral vaccines must be advised against falling pregnant within 28 days of vaccination.'

Vaccination is available and advisable for some infectious diseases. However, there are no vaccinations for some infectious diseases, but knowledge of the woman's immunity status may be helpful.

Influenza

All women who are planning a pregnancy and are likely to be in the second or third trimester during the flu season should be vaccinated. Evidence from the H1N1 2009 pandemic in Victoria showed that pregnant women were more susceptible to severe disease even without comorbidities.¹⁸

Varicella

About 85% of women will already be immune to chickenpox. However, due to the possibility of severe fetal and maternal effects of varicella infection it is advisable that immunity is checked before pregnancy. Those women who are not immune should be vaccinated.

Rubella

Fortunately, most women who grew up in Australia have been vaccinated against rubella during childhood. Levels of rubella immunoglobulin G should still be tested and repeat vaccination given if levels have dropped. Immigrant women are a group who may not have received immunisation and need testing and vaccination if appropriate.

Pertussis

Although not a known teratogen, pertussis is particularly problematic in newborn babies. As there has been a recent upsurge in pertussis in the Australian community, women and their partners are advised to be revaccinated immediately after the birth or, better still, before a pregnancy. A combined diphtheria, pertussis and tetanus vaccine is available and recommended to all who have not had a booster vaccination in adulthood

Human papillomavirus

In preconception discussions with younger women, HPV vaccination should be offered. This will reduce their own risk of HPV infection (at which they are at risk through unprotected sexual intercourse), and potentially minimise the (albeit small) risk of infection of the neonate. Fewer cervical abnormalities will mean fewer ablative procedures to the cervix and possibly less chance of cervical insufficiency and subsequent preterm birth that may result from this treatment.

Parvovirus

There is no vaccine to prevent parvovirus infection. This condition can cause temporary fetal anaemia and/or myocarditis, which can occasionally lead to fetal death, or the need for an intrauterine blood transfusion. About one-half of those women in the reproductive age range will be immune to the virus before pregnancy. It may be worth testing for immunity in those women at high risk (e.g. those in contact with children) to be able to reassure at least half of them should they come in contact with parvovirus during pregnancy. There is no role for routine antenatal screening for parvovirus.

Cytomegalovirus

Cytomegalovirus is another infectious disease for which there is no vaccine available but which has the potential to cause abnormalities in the fetus. Some doctors would advise testing for immunity to reassure some women, and to forewarn other women to take particular precautions during pregnancy. Cytomegalovirus is present in the secretions and urine of infected individuals, who are often children, so basic hygiene is required when changing nappies, etc. This is particularly relevant to childcare workers and those women with young children who attend daycare. Unfortunately, evidence of past

infection does not ensure that there is no chance of fetal infection, either due to reinfection or infection with a different serotype.

Toxoplasmosis

Maternal infection with toxoplasmosis may cause fetal abnormalities and there is no vaccine available. However, Australia is not a high-prevalence country. Advice to prevent infection includes avoiding uncooked meat, unwashed raw vegetables and cat faeces. Routine testing for immunity is not advised.

Pap smears

It is very important to ask when the woman last had a Pap smear. If the two-year screening interval is likely to fall during the pregnancy, repeating the Pap smear before, rather than during, the pregnancy is advisable. Pregnancy does not increase the risk of cervical abnormalities, but it does hamper the ability to diagnose and treat abnormalities if they are found.

TARGETED APPROACH

For those women who present requesting information shortly before embarking on a pregnancy, taking a thorough history is mandatory to help elicit those conditions known to impact or be impacted upon by pregnancy. Performing the routine blood and urine tests normally taken in early pregnancy (full blood count; blood group and antibody screen; syphilis, rubella, hepatitis B and C, HIV and varicella serology; and a midstream urine examination for microscopy and culture) is worthwhile. Exclusion of other sexually transmitted diseases such as chlamydia and gonorrhoea is recommended when clinically appropriate.

For those women with pre-existing medical conditions, a specific appointment with the physician managing their condition is advisable. Referral of the woman to an obstetrician with a

particular interest in maternal medicine may also be helpful.

The underlying principle is always to optimise the woman's health and minimise any potentially harmful treatments before commencing a pregnancy.

Diabetes

Diabetes is possibly the most common condition for which preconception counselling is advised. Poorly controlled diabetes is known to increase congenital abnormalities by a factor of two or three, resulting in about a 6 to 7% chance of fetal abnormality. If maternal blood glucose levels are tightly controlled before and during the early stages of pregnancy, this risk returns to the baseline risk.

Blood glucose levels should be 5.0 mmol/L or less during fasting and 6.7 mmol/L or less two hours after meals. The target level for glycated haemoglobin (HbA_{1c}) is less than 6%.

Although there is still debate, oral hypoglycaemic medication should be stopped before conception in most cases and insulin commenced as required. Lipid-lowering drugs should also be ceased before conception. The need for renoprotective antihypertensive agents such as ACE inhibitors and angiotensin receptor blockers should be reassessed because these are contraindicated in pregnancy.

Thyroid disease

Appropriate thyroid hormone levels are essential for normal brain development. Women with hypothyroidism should have their thyroid-stimulating hormone levels checked before pregnancy and during each trimester of pregnancy. The dose of replacement thyroxine should aim to keep the thyroxine levels in the high-normal range.

In women with hyperthyroidism, surgery should be performed before pregnancy if it is an appropriate solution. For those requiring medication,

propylthiouracil is preferable to carbimazole in the first trimester.¹⁹

Epilepsy

Epilepsy is another area in which preconception rationalisation of treatment is essential. Women with epilepsy have a two to three times increased risk of:

- maternal morbidity and mortality
- major congenital abnormality
- long-term developmental delay in the infant.

Polydrug therapy is known to increase the risk of congenital malformations and sodium valproate use has the highest association with malformations.

In any woman with epilepsy considering pregnancy, preconception assessment should include whether she needs to continue her treatment. For those women who have been symptom free for a long time, consideration should be given to a trial period without drug therapy before conception. For those taking multiple drugs, trying to reduce treatment to a single drug is worthwhile.

For women taking sodium valproate who are best kept on this drug, reducing the dose to the lowest possible for seizure control is advisable. Where possible, carbamazepine is the drug of choice, preferably at a dose under 400 mg/day.

Although it is hoped that some of the newer drugs are less teratogenic, there has been insufficient use to confirm this. However, a recent study suggested that lamotrigine at a dose less than 300 mg/day had the lowest rate of malformation when compared with carbamazepine, sodium valproate and phenobarbitone.²⁰

All women taking antiepileptic medication are advised to take 5 mg of folic acid preconceptually, although evidence from registries does not show that this higher dose protects against neural tube defects. Hence, for women with epilepsy, it is vital that pregnancies are planned and appropriate contraception used

until their epilepsy and treatment are optimised.

Cardiac disease

Young women with a broader range of surgically corrected congenital cardiac anomalies are now reaching childbearing age. Acquired cardiovascular problems, such as ischaemic heart disease, are an increasing problem during pregnancy as the pregnant population ages and lifestyle factors increase the risk for cardiovascular events.

Before pregnancy, both these groups of women need appropriate assessment by their cardiologist (if they have one) and an obstetrician with an interest in maternal medicine.

Hypertension

Women who need to continue taking their antihypertensive medications should be changed to and stabilised on methyldopa or labetalol before embarking on pregnancy. Calcium-channel blockers (e.g. nifedipine) are suitable second-line agents. ACE inhibitors, angiotensin receptor blockers and direct renin inhibitors should not be used in pregnancy. ACE inhibitors were once thought to only cause problems in the second and third trimesters of pregnancy; however, recent studies have suggested an increase in the risk of abnormalities in fetuses exposed to ACE inhibitors in the first trimester.²¹

The blood pressure target should be 140 to 150 over 90 to 100 mmHg.

Respiratory diseases

Asthma is the most common respiratory disease that may cause problems during pregnancy. Optimisation of treatment is required. Most asthma medications are appropriate to continue throughout pregnancy.

Phenylketonuria

With the early detection of phenylketonuria by neonatal heel prick test and

effective management, many women with the condition are now reaching reproductive age. Many women will have relaxed their restrictive diet during their teenage years. For those hoping to become pregnant, it is essential that they resume their strict diet, because the build up of phenylalanine will have the same damaging effect on the fetal brain that it would have had on their own brain had they not had the benefit of an appropriate diet in childhood.

Systemic lupus erythematosus

Pregnancy is best undertaken during a quiescent phase of systemic lupus erythematosus. In any preconception assessment, even if the disease is quiescent, it is wise to test for coexisting antibodies including antiphospholipid antibodies, lupus anticoagulant and the SSA and SSB (anti-Ro and anti-La) antibodies, because their presence may have implications for the fetus and the pregnancy itself. The SSA and SSB antibodies are associated with an increased chance of neonatal lupus and/or congenital heart block.

Other medical illnesses

Pre-existing renal, hepatic and other diseases also require assessment and input from medical and obstetric specialists in the relevant field. For those women requiring an organ transplant, it is often advisable to delay pregnancy until after

a successful transplant has occurred. Again, this needs to be discussed with her managing physician.

Most major maternity departments in Australia have clinics or specialists available to advise and assist women (and their GPs) in these preconception discussions.

Genetic diseases

In women with a family history of a genetic syndrome it is worthwhile confirming the inheritance and likely impact on any offspring. Referral to a clinical geneticist is appropriate. Preconception partner testing is advisable for women known to be a carrier of an autosomal recessive trait (e.g. cystic fibrosis and thalassaemia).

Certain ethnic groups may wish to avail themselves of testing for inherited disorders common in their community (e.g. Tay-Sachs disease, Canavan disease and familial dysautonomia in Ashkenazi Jews).

Some couples will want testing for inherited diseases if there is no family history. Tests for cystic fibrosis and Fragile-X syndrome are two of the more commonly available.

CONCLUSION

The GP plays a vital role in preconception counselling to help women achieve the best outcomes for their baby and

themselves. It is worth keeping in mind that there are some women who may be advised against pregnancy until or unless their problem improves. **MT**

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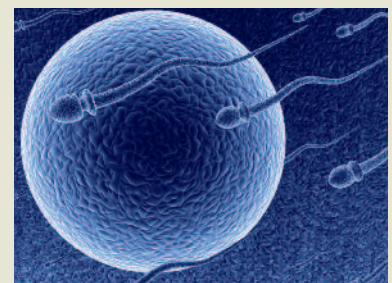
A list of references is available on request to the editorial office.

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COMPETING INTERESTS: None.

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