LIPID DISORDERS

Background

LIPID disorders are important for three reasons:
• They contribute to cardiovascular disease, still the number one cause of death in our society, by aggravating atherosclerosis.
• They are common and are treatable, mainly with statins, which have revolutionised preventive medicine in the last few decades.
• In Australia, more than a million adults take lipid-modifying drugs, at an annual cost of about $1.1 billion to the PBS.

Indications for lipid-modifying drugs
The indications for using lipid-modifying drugs are to:
• Reduce the incidence of CVD through primary and secondary prevention.
• Reduce itching in obstructive jaundice, due to deposition of bile acids in the skin, by the use of bile-acid sequestrants (resins).
• Prevent acute pancreatitis, a potentially fatal complication of very high triglyceride (TG) levels (>11mmol/L).
• Induce regression of lesions caused by high levels of low-density lipoprotein.

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The author

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Lipid disorders

How to treat

Clinical presentation

Symptoms of lipid disorders
Most lipid disorders are asymptomatic. Symptoms may arise from associated comorbidities, some of which are caused by the lipid disorder (eg, angina from coronary atherosclerosis secondary to high LDL-C levels; acute abdominal pain from acute pancreatitis secondary to high TG levels).

Signs of lipid disorders
Most lipid disorders are not detectable clinically unless extremely high levels of lipids are present, generally for a prolonged period.

Eruptive xanthomas
Very high TG levels (usually >5mmol/L and often >20mmol/L) may present with eruptive xanthomas. These are painless, tender small maculopapular lesions with a yellowish centre, surrounded by an area of erythema. Eruptive xanthomas generally occur on extensor surfaces of the elbows, lower back, buttocks and limbs. They may persist for several weeks until TG levels are lowered, after which they can completely resolve over a few weeks.

Lipemia retinalis
Examination of the fundi in these patients may reveal the presence of yellow-white, creamy fundal vessels due to the presence of TG-rich lipoproteins, especially chylomicrons.

Planar xanthomas
Uncommonly, very high levels of intermediate-density lipoproteins (IDLs), as occurs in familial dyslipoproteinemia (type III disorder; see below), may result in xanthomas that are yellowish, flat linear lesions occurring along the creases of the palms.

Other xanthomas
Very high levels of LDL-C result in premature and extensive deposition of LDL-C in the cornea, tendons, eyelids and skin, resulting in arcus senilis, tendon xanthomas, xanthelasmas and cutaneous (tuberoous) xanthomas (figures 1-7). These lesions suggest the presence of familial hypercholesterolaemia or other genetic disorders resulting in a similar phenotype (see below). A very early arcus senilis may be difficult to see without using a hand torch to reflect light obliquely from the edge of the cornea. It is seen as a very faint, milky, thin arcuate opacity. It is readily seen, however, with a slit lamp.

Table 1: Criteria for reimbursement of lipid drugs for those patients not at very high risk

<table>
<thead>
<tr>
<th>Patient category</th>
<th>Lipid levels for PBS subsidy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus (not high-risk)</td>
<td>TC &gt;6.5mmol/L</td>
</tr>
<tr>
<td>Aboriginal or Torres Strait Islander Hypertension</td>
<td>TC &gt;6.5mmol/L or TC &gt;6.5mmol/L and HDL-C &lt;1mmol/L</td>
</tr>
<tr>
<td>HDL-C &lt;1.0mmol/L</td>
<td>TC &gt;6.5mmol/L</td>
</tr>
<tr>
<td>Familial hypercholesterolaemia identified by:</td>
<td>If aged ≤18 at treatment initiation, LDL-C &gt;4mmol/L</td>
</tr>
<tr>
<td>DNA mutation</td>
<td>If aged &gt;18 at treatment initiation:</td>
</tr>
<tr>
<td>Tendon xanthomas in the patient or a first- or second-degree relative</td>
<td>• LDL-C &gt;5mmol/L, or</td>
</tr>
<tr>
<td>Family history of symptomatic CHD:</td>
<td>• TC &gt;6.5mmol/L, or</td>
</tr>
<tr>
<td></td>
<td>• TC &gt;5.5mmol/L and HDL-C &lt;1.0mmol/L</td>
</tr>
<tr>
<td>Patients not eligible under the above criteria:</td>
<td>TC &gt;7.5mmol/L or TG &gt;4mmol/L</td>
</tr>
<tr>
<td>Men aged 35-75</td>
<td>Patients not otherwise included</td>
</tr>
<tr>
<td>Postmenopausal women aged up to 75</td>
<td>TC &gt;8mmol/L or TG &gt;4.5mmol/L</td>
</tr>
</tbody>
</table>

HDL-C = high-density lipoprotein–cholesterol; LDL-C = low-density lipoprotein–cholesterol; TC = total cholesterol; TG = triglycerides
Interpreting lipid profile patterns

There are three common kinds of lipid disorders:

- **Hypercholesterolaemia**: high TC and LDL-C levels with normal or slightly raised triglycerides (Frederickson types I and IIa).
- **Combined hyperlipidaemia**: high TC plus high TG levels; LDL-C may be normal or increased (Frederickson types III and IV).
- **Hyperm triglyceridaemia**: high triglyceride level with normal or low LDL-C (Frederickson types IV and V).

In patients with combined hyperlipidaemia and hypertriglyceridaemia, a reciprocal relationship often exists between HDL-C and TG levels.

Occasional patients have isolated HDL-C levels (>0.9mmol/L in men and >1.0mmol/L in women), with other lipid levels relatively normal.

Others have hyper-alpha-lipoproteinaemia, with levels of HDL-C of 2.0-2.2mmol/L. These patients generally have a ‘longevity syndrome’, but in about 10% LDL-C levels are also high. Another subgroup of patients with high HDL-C levels appears to have dysfunctional HDL, which is not protective for atherosclerosis. The pattern of lipid profile may suggest an underlying aetiology, which may be primary (genetic) or secondary (acquired) (table 2).

Other tests

Sometimes it is useful to measure special lipids, such as lipoprotein (a) [Lp(a)], apoA-1 or apoB. Lp(a) is usually ordered in young patients with premia CVD, or those who have a family history of premature CVD. Lp(a) is a highly heritable lipoprotein, structurally related to LDL and plasminogen, with prothrombotic and proinflammatory properties.

Normal values for Lp(a) are <0.3g/L. Levels <0.3g/L are associated with increased CVD relative risk of 20-30%, depending on which isoform is evaluated. Patients with very high levels (often >3g/L) experience spontaneous recurrent arterial and venous thrombosis affecting multiple vascular beds. Statins are relatively ineffective in lowering Lp(a) levels, whereas some patients respond to nicotinic acid.

Lower LDL-C targets should be achieved in patients with elevated Lp(a), and antithrombotic therapy considered.

ApoB and apoA-1 are the major proteins of LDL and HDL, respectively. Their measurement is widely available, accurate and inexpensive using immunoassays with validated international reference standards. Many studies have shown that apoB and apoA-1 levels are better CVD risk discriminators than LDL-C and HDL-C levels, and they also predict the extent and severity of atherosclerosis more reliably.

Each molecule of LDL and triglyceride-rich lipoproteins (very low-density lipoprotein [VLDL], VLDL remnants and LDL) has one apoB molecule, so levels of apoB measure the atherogenicity of plasma. Some patients have high apoB levels and normal LDL-C levels because of the presence of triglyceride-rich lipoproteins, especially in diabetes.

The recent Canadian lipid guidelines include a target apoB level of <0.8g/L, although target apoA-1 levels have yet to be recommended.

Measurement of apoB is most useful in mixed hyperlipidaemia in the presence of small dense LDL-C, when apoB may determine the presence of these particles.

### Hypercholesterolaemia

- Total cholesterol (TC) = 7.0mmol/L
- HDL-C = 1.0mmol/L
- TG = 5.5mmol/L

LDL-C may be measured in non-fasting plasma in which TG levels are <1.0mmol/L and direct methods are available. Remind the patient to maintain their usual diet and fast overnight for 12 hours, allowing water only as required. Medications should be taken at the usual times. Advise against alcohol intake for 48 hours before the test (otherwise TG may be elevated acutely).

### Combined hyperlipidaemia

- Total cholesterol (TC) = 7.0mmol/L
- HDL-C = 1.0mmol/L
- TG = 1.1mmol/L

### Hypertriglyceridaemia

- TG often >4.5mmol/L
- TC increased
- LDL-C near-normal or reduced (direct assay)
- HDL-C reduced

### Combined hyperlipidaemia

- TG increased
- TC increased
- LDL-C variable (direct assay)
- HDL-C reduced

### Isolated low HDL-C

- HDL-C low
- Near-normal TG, TC, LDL-C

### High HDL-C

- No specific gene identified
- Dysproteins (HRT)
- Alcohol
The downstream products of MVA include ubiquinones, which function in mitochondrial dioxidation pathways through coenzyme Q10 (CoQ10), and geranyl and farnesyl pyrophosphates, the latter playing important roles in cell signalling and function, which may elucidate the pleotropic effects of these. These effects are not obviously directly related to lipid effects (and include immunomodulation and improved transplant survival). Ubiquinones may be involved in statin myopathy, although this is debated. Clinical trials of CoQ10 supplements are conflicting. Statins are first-line drugs for all lipid disorders except for TG >4.5mmol/L and isolated HDL-C <1.0mmol/L, when preferred drugs are fibrates or nicotinic acid (in countries where extended-release nicotinic acid is available). For every 1.0mmol/L reduction in LDL-C level (see figure 8, page 29) there is about a 23% reduction in the risk of major coronary events and about a 21% reduction in the risk of major vascular events over a five-year period. Larger reduction in LDL-C levels and initiation of therapy produce larger reductions in vascular disease risk. These benefits are likely to represent a class effect and to occur for each statin.

Prescribing statistics
• Prescribe the dose of a given statin sufficient to achieve target LDL-C level, thereby avoiding dose titration. This strategy can improve compliance.
• Obtain a baseline history of muscle aches, pains, cramps and stiffness, as these are the most frequent adverse effects of statins.
• Check baseline levels of CK and transaminases, as these can be increased with statins and may reflect muscle or liver cell injury. Repeat after 8-12 weeks of initial therapy (and at the same period after dose up-titration). Levels should then be repeated annually, or for CK if unexplained musculoskeletal symptoms (MSS) occur.
• Dose adjustment may be necessary with renal impairment (for statins with pre-dominantly renal excretion, such as nimoprazole and simvastatin) or hepatic impairment (for statins predominantly metabolised by the liver such as pravastatin, simvastatin and fluvastatin).
• Use lower doses for elderly women and others with low muscle mass. MSS and CK should be monitored more frequently in these patients (eg, every 4-6 monthly).
• Use caution in treating patients with recognised myopathy or previous MSS (whether or not statin-related). MSS and CK should equal page 32.
Table 5: How to manage adverse events with statin therapy

<table>
<thead>
<tr>
<th>Event</th>
<th>Initial treatment</th>
<th>Subsequent treatment</th>
<th>Long-term treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased transaminase levels (AST, ALT)</td>
<td>Withdraw or reduce statin dose if CK &lt;3 ULN</td>
<td>Repeat CK after 1-2 weeks; withdraw, use lower dose if symptoms persist</td>
<td>Monitor more frequently (six monthly)</td>
</tr>
<tr>
<td>Myalgia (pain, stiffness) with CK &lt;3 ULN</td>
<td>Continue statin; check secondary cause and treat if indicated*</td>
<td>Repeat CK after 1-2 weeks; if CK &lt;3 ULN, reduce dose or change statin</td>
<td>Consider non-statin if statin intolerant</td>
</tr>
<tr>
<td>Myalgia with CK &lt;3 ULN</td>
<td>Withdraw statin; check secondary causes and treat if indicated</td>
<td>As above</td>
<td>As above</td>
</tr>
<tr>
<td>Myositis (more severe symptoms, including weakness with CK &gt;3-10 ULN)</td>
<td>As above</td>
<td>As above</td>
<td>Monitor symptoms more frequently; check CK if occur; advise patient to report symptoms and stop statin immediately if occur</td>
</tr>
<tr>
<td>Rhabdomyolysis (severe symptoms, CK &gt;10 ULN with myoglobinuria and impaired renal function)</td>
<td>As above; Rehydration</td>
<td>Monitor renal function and CK, refer to renal feltemarked recommended</td>
<td></td>
</tr>
</tbody>
</table>

Table 5 summaries how to manage adverse events with statin therapy.

Ezetimibe

Ezetimibe is added to statin therapy when target LDL-C is not reached even with maximally tolerated statin doses. It is also used to lower LDL-C levels for patients intolerant of statins. Ezetimibe is well tolerated and safe in long-term therapy and has some effects on non-LDL-C lipids.

Ezetimibe is a competitive inhibitor of the intestinal sterol transporter protein (NPC1L-1), which is responsible for uptake of cholesterol and some plant sterols. It is also used in the rare disorder beta-sitosterolemia, in which plant sterols are not excreted and accumulate in tissues, including the arteries. Ezetimibe lowers LDL-C by about 20%, due to increased hepatic LDL receptor activity. This does not increase bile-acid excretion (as do bile-acid sequestrants) but does inhibit cholesterol synthesis in the liver (as do statins).

Ezetimibe plus statin therapy can reduce LDL-C by >70% in responsive patients, with greater reduction of TC, LDL-C, apoB, and TG and increased HDL-C compared with statin alone. Greater reduction in high-sensitivity (hs)CRP levels, N-terminal pro-BNP, and edematous leg rash to a given dose of statin is equivalent to three doses of a maximally tolerated dose of statin, with each doubling reduces LDL-C by about 6% (‘rule of 6x’).

Flushing

Flushing tends to decrease at night, then twice daily, increasing by 1-2 tablets every 4-7 days, depending on tolerability. Flushing tends to decrease with longer use but is often expected (including sudden and intolerable in higher doses (>1.5g/day). Prior treatment with slow-release aspirin may improve cutaneous flushing and compliance with nicotinic acid.

Drugs causing secondary lipid disorders

Current medications need to be checked in patients with lipid disorders, and offending drugs reduced in dose, stopped or changed to alternatives. These include anabolic steroids (HDL-C, glucocorticosteroids, beta blockers, smoking, alcohol, resins (cholesterolamine, colestipol, oestrogens, oral contraceptives, diuretics (TGT) and protease inhibitors (TGT, LDL-C, HDL-C)).

Familial hypercholesterolaemia

Familial hypercholesterolaemia (FH) is inherited as an autosomal dominant disorder, affecting 50% of progeny, males and females equally. It occurs in 1:200-500 of the population, though in some ethnic groups (eg, Lebanese) it may be as high as 1:80. FH is associated with loss of receptors in cutaneous blood vessels. FH is metabolised to nicotinic acid, which has vitamin B3 activity. Initial treatment effects are modest, with further increases in dose over five years to prevent one CVD event was 20. These are preceded by further fibrate trials showing that CVD benefit with fibrate therapy is confined to those with high and low LDL-C levels.

The ACCORD-Lipid study compared treatment with simvastatin plus fenofibrate to simvastatin alone in about 5000 subjects with diabetes, and noted the hypothesis that raising LDL-C level with fibrate therapy provides additional CVD benefit to statin therapy alone.*

The only patient group to benefit from fenofibrate was the 30% of the cohort with ‘marked dyslipidaemia’. These patients had raised TG levels (>2.3mmol/L) and low HDL-C levels (<0.9mmol/L). The primary endpoint (fatal CVD) and secondary endpoints (CVD, all-cause death, myocardial infarction, and total mortality) were not different between the two groups. The ACCORD-Lipid study was stopped early due to increased risk of mortality.

Ezetimibe plus statin therapy can reduce LDL-C by >70% in responsive patients, with greater reduction of TC, LDL-C, apoB, and TG and increased HDL-C compared with statin alone. Greater reduction in high-sensitivity (hs)CRP levels, N-terminal pro-BNP, and edematous leg rash to a given dose of statin is equivalent to three doses of a maximally tolerated dose of statin, with each doubling reduces LDL-C by about 6% (‘rule of 6x’).

Fibrates

Fibrates have wide-ranging effects because of multiple gene activation and repression. With LDL-C levels, these include the following potentially beneficial changes:

• Increased apoA-1 synthesis.
• Significantly reduce triglycerides.
• Potentially beneficial changes: these include the following gene activation and repression effects because of multiple effects (eg, increased fibrinogen, pro-thrombotic tendency, increased CRP).
• Central abdominal obesity
• Impaired glucose metabolism
• Increased LDL-C
• Atherogenic lipoproteins
• Reduced HDL-C
• Increased LDL-C
• Atherogenic dyslipidaemia: increased apoA-1 and small dense LDL reduced HDL-C increased TG (TG and TG-rich lipoproteins.

Possible contributors to residual risk in patients on statin therapy

• Cigarette smoking
• Uncontrolled hypertension
• Impaired glucose tolerance
• Reduced physical exercise
• Central abdominal obesity
• Increased LDL-C
• Myocardial ischaemia
• Left ventricular hypertrophy
• Chronic obstructive pulmonary disease
• Increased TG
• High density lipoprotein (HDL)-C
• Increased LDL-C

High HDL-C with high LDL-C

Patients with high levels of HDL-C as well as LDL-C are a dilemma to clinicians because they often have a normal cholesterol:HDL-C ratio. Most appear to be at low CVD risk, as expected by the ratio, but a subgroup has subclinical atherothrombosis (shown by carotid ultrasound and coronary calcium scoring) and should be treated with statins.

How well are we doing with lipid management?

A recent Australian study showed there is still a long way to go for all patients to be treated according to national guidelines:

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Treatment rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with CVD or diabetes</td>
<td>Of those with established CVD or diabetes, 42% were untreated and only 58% of those being treated reached target LDL-C levels.</td>
</tr>
<tr>
<td>Patients with diabetes or cardiovascular disease</td>
<td>Of those without CVD or diabetes, 38% achieved target LDL-C levels, and 31% of patients with high CVD risk did not receive lipid treatment for primary prevention.</td>
</tr>
</tbody>
</table>

These figures are similar to those published from Europe, the UK and the US over the past decade.

Residual risk

Residual risk refers to CVD events that occur despite statin therapy. In controlled trials, statins reduce CVD events by 30–40% compared with placebo, reaching 40–60% in women. The two important implications of residual risk are that statins are not the complete answer to prevention of CVD, and that other therapies must also be considered and possibly be subjected to appropriate clinical trials.

Possible contributing factors are listed in the box (left). Lifestyle measures as a means of improving residual risk are likely to be significant. These include:

• Stopping smoking.
• Increasing aerobic capacity through exercise.
• Losing excess weight and mass through diet and exercise.

The role of alcohol needs to be re-evaluated. Studies have shown that alcohol reduces cholesterol.

Many GPs recommend a glass of red wine daily to minimise CVD risk. However, alcohol is a ‘double-edged sword’, capable of increasing CVD risk through increased TG levels and aggressive drinking. TG levels TG and TG-rich lipoproteins, aggravation of hypertension, and possible other harmful effects.

Increased HDL-C levels may counteract these effects, and may have pleiotropic and anti-inflammatory effects. Recent recommendations to limit alcohol to 20g/day in men and 10g/day in women appear appropriate. It may also be appropriate to restrict consumption of alcohol in those with TG >1.5mmol/L.

Residual risk may be reduced by interventions that lower TG levels. TG-rich lipoprotein clinical trials are in progress to determine the relative benefits of these two strategies.

When to refer

Some lipid disorders are difficult to manage because of genetic factors (eg, isolated low HDL-C and FH with extremely high LDL-C levels) or because of environmental factors (uncontrolled diabetes, excess alcohol). Referral to a lipid clinic or specialist is often appropriate, as well as the help of patients with statin-associated myositis or rhabdomyolysis.
Lipid disorders—9 July 2010

1. Which TWO statements are correct?
   a) Statins effectively treat the pruritus of hypercholesterolaemia
   b) Lipid-lowering drugs are indicated for the prevention of pancreatitis due to very high triglyceride (TG) levels
   c) Patients with symptomatic CVD or a family history of premature CVD are eligible for PBS-subsidised lipid-lowering drugs only if total cholesterol (TC) level is >5.5 mmol/L
   d) Patients aged >60 years, with DM or a history of premature CVD are eligible for PBS-subsidised lipid-lowering therapy irrespective of their lipid levels

2. Which TWO statements are correct?
   a) Eruptive xanthomas tend to occur in those with very high low-density lipoprotein–cholesterol (LDL-C) levels
   b) Lipaemia retinalis is due to the presence of TG-rich lipoproteins
   c) The presence of arcus senilis, tendon xanthomas or xanthelasma is associated with familial hypercholesterolaemia
   d) Fasting is required before lipid blood testing to avoid high postprandial total TC levels

3. Which TWO statements are correct?
   a) The Friedewald formula used to calculate LDL-C level is valid when TG is <4.5 mmol/L
   b) LDL-C level may be measured in non-fasting plasma if direct methods are available
   c) In patients combined with hyperlipidaemia (CHL) and hypertriglyceridaemia (HTG), a reciprocal relationship often exists between HDL-C and TG levels
   d) Patients with hyperalphalipoproteinaemia (elevated apoA-1) level, tend to have low levels of HDL-C

4. Which THREE statements are correct?
   a) Secondary causes of hypercholesterolaemia include hypothyroidism and myeloma
   b) Familial dysalphalipoproteinaemia is suspected when TG level is raised and TC level is normal
   c) Insulin resistance disorders and alcohol excess are common secondary causes of CHL
   d) Isolated low HDL-C level is associated with cigarette smoking and a high-carbohydrate diet

5. Which TWO statements are correct?
   a) Lipoprotein (a) is protective against CVD
   b) Statins are effective in lowering LDL levels
   c) ApoB and apoA-1 may be better CVD risk discriminators than LDL-C and HDL-C
   d) LDL and triglyceride-rich lipoproteins (very low-density lipoproteins and intermediate-density lipoproteins) contain apoB

6. Which TWO statements are correct?
   a) Measurement of apoB is most useful in combined hyperlipidaemia to detect the presence of small dense LDL-C
   b) ApoB-1 is protective against CVD
   c) For patients with very high CVD risk, the target level of LDL-C is <3.0 mmol/L
   d) For patients with low CVD risk, the target level of LDL-C is <2.0 mmol/L

7. Which TWO statements are correct?
   a) The fire-and-forget treatment strategy has the disadvantage of being more expensive than a treat-to-target strategy
   b) A modified fire-and-forget strategy stratifies patients into higher and lower five-year CVD risk groups, with a different standard treatment for each group
   c) When compared with an intensive treat-to-target strategy, the modified fire-and-forget strategy prevents fewer CVD events and deaths
   d) For TG levels >1.7 mmol/L, the nature of LDL particles changes from large and light (safely) LDL to small and dense (harmful) LDL

8. Which TWO statements are correct?
   a) Non-HDL-C is a measure of atherogenic cholesterol, when high TG makes the Friedewald formula inaccurate
   b) Lowering TG levels may provide benefit in reducing CVD risk, independent of lowering LDL-C and raising HDL-C levels
   c) The reduction in CVD absolute risk with multiple risk factor interventions is similar across the age spectrum
   d) Fish oils are the most effective dietary supplement to lower LDL-C level

9. Which TWO statements are correct?
   a) Fenofibrate is the first-line pharmacotherapy for TG level >4.5 mmol/L
   b) For elevated LDL-C level sufficiently responsive to a statin alone, ezetimibe is the drug of first choice in combination with the statin
   c) With statins, start with a low dose and titrate up as needed
   d) No dose adjustment of statin is necessary in patients with low muscle mass

10. Which TWO statements are correct?
    a) If a patient on a statin has myalgia and CK level >3 × upper limit of normal, the statin should be continued
    b) Additional reduction in CVD risk by adding a fibrate to statin therapy is confined to patients with high TG and low HDL-C levels
    c) Nicotinic acid reduces TG and LDL-C, and increases HDL-C levels
    d) Patients with raised LDL-C and HDL-C levels and a normal total cholesterol ratio do not need treatment with a statin

References
Available on request from: julian.mcAllan@greenbusiness.com.au
Online resources
www.theheart.org.au—the best site for CVD issues
Heart Foundation, for local references
www.heartfoundation.org.au

Next Week
The next How to Treat looks at pelvic organ prolapse in women, which is a major cause of reduced quality of life in older women particularly. Advances in conservative and surgical management are examined. The authors are Dr David Knight and Dr Peter Scott, senior staff specialists in obstetrics and gynaecology, Canberra Hospital, and clinical lecturers in obstetrics and gynaecology, Australian National University, Canberra, ACT.

Instructions
Complete this quiz online and fill in the GP evaluation form to earn 2 CPD or PDP points. We no longer accept quizzes by post or fax. The mark required to obtain points is 80%. Please note that some questions have more than one correct answer.

Online only

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