Type 2 diabetes: preparing for pregnancy

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This section discusses the immediate management and investigation of an acute presentation in general practice. It is inspired by, but not based on, a real patient situation.

Penny is a 38-year-old Caucasian woman with type 2 diabetes diagnosed six months ago. She has recently married a man with older children and is considering becoming pregnant for the first time. Her body mass index (BMI) is stable at 31 kg/m^2 (class 1 obesity range), and her HbA_{1c} level is 6.9% (52 mmol/L) while taking metformin extended release 1 g at night. She has well-controlled hypertension for which she takes combined perindopril and indapamide daily. She has had a low level of microalbuminuria and the urinary albumin to creatinine ratio is 4.5 mg/mmol. Given Penny's medical conditions, she wants to know what the risks are to her and for the baby if she became pregnant, and how she can best prepare for a pregnancy. She stopped taking the oral contraceptive pill about two months ago and has just experienced her first natural period. She has booked a prolonged appointment with you to discuss her concerns.

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Penny is worried about difficulty in falling pregnant. What do you begin by telling Penny about fertility at her age?

Answer: In women around this age, there is at best about a 60% chance of conceiving naturally within 12 months. As Penny has had no previous pregnancies, a history should be taken for gynaecological conditions influencing fertility, such as symptoms of endometriosis (when not taking the oral contraceptive pill), polycystic ovarian syndrome (which is associated with diabetes, weight gain and hypertension) and pelvic infection. If it is likely that she has any of these conditions she should have the relevant basic investigations carried out and discussion should take place about referral to a gynaecologist/obstetrician without delay. If Penny wishes to try to get pregnant naturally she should be reminded that failure rates for both natural pregnancy and IVF increase exponentially from the mid 30s onwards. She and her husband should discuss whether they could afford or would choose IVF if she did not conceive naturally. If the answer is yes, then referral should be made if she is not pregnant within six months of trying. It is reasonable (should Penny wish) to refer her for an infertility review straight away because this may save delay later.

Penny needs to understands the ovulation cycle, when to maximise conception and that she would be considered to have a high-risk pregnancy (as she would be an elderly primigravida and has diabetes, hypertension and obesity). There are significant medical complications for both Penny and the baby, in addition to fertility issues and risk of miscarriage. The baby has an almost double risk (3.2%) of serious congenital abnormalities (especially neurological and cardiac) when the maternal HbA_{1c} is 6.9% periconceptionally (see Table).[1] The average rate of major birth abnormalities is approximately 2% in Australia. The higher the HbA_{1c} is around conception, the greater the risk of abnormalities. Penny will need careful monitoring throughout the pregnancy, especially regarding her blood glucose control and blood pressure, as well as fetal wellbeing. She should plan to deliver in a major centre specialising in high-risk pregnancies that has available a special care nursery, preferably at least level 2.

What risks do Penny's medical problems pose to her and the developing baby?

Answer: The following risks apply:

- ***Obesity:*** increased risk of infertility (use of metformin may decrease this risk by regulating ovulation), greater than recommended maternal weight gain (from decreased mobility, increased appetite), clotting disorders, pneumonia, increased maternal and fetal mortality, increased birth complications (shoulder dystocia and caesarean section).
- ***Diabetes:*** maternal urinary infection, developing retinopathy, increased risk of miscarriage, birth deformities, intrauterine growth retardation (placental abruption, insufficiency), oligo- or polyhydramnios, macrosomia, shoulder dystocia, caesarean section, stillbirth, neonatal hypoglycaemia requiring intensive care, poor feeding, abnormal glucose tolerance later in life in the offspring.
- ***Hypertension:*** increased risk of pre-eclampsia and eclampsia, decreased maternal renal function, increased intrauterine growth retardation, oligohydramnios, placental abruption and fetal loss. ACE inhibitors increase the risk of damage to developing fetal kidneys and should be ceased before conception.

As Penny will be an older mother, it should also be noted there is an increased risk of twins.

What investigations would you arrange for Penny (whether or not she is referred for IVF immediately)?

Answer: Penny needs to have the following basic tests carried out straight away: rubella IgG, varicella IgG, a general medical review (especially cardiac and breast examination), a Pap smear if due and a current assessment of her diabetes control (HbA_{1c}, testing her blood glucose level [BGL] several times a day both premeal and postmeal), thyroid-stimulating hormone level, iron studies and kidney function, including urinary albumin and electrolytes.

Penny needs to commence folic acid 5 mg daily (not taken with tea) to reduce the incidence of neural tube defects (without great evidence the higher dose of 5 mg rather than 0.5 mg is advised for women with diabetes due to the higher rates of neural tube defects seen in their offspring). Measurement of spot urinary iodine levels are unreliable and unnecessary. As Penny does not have thyrotoxicosis, she should be advised to take iodine 150 µg daily (usually obtained in a combination of 150 µg iodine and 0.5 mg folic acid) in addition to the 5 mg folic acid. If her ferritin level is low-normal or low, she should have at least 200 mg of elemental iron orally daily, at least 30 minutes before a meal, with a small amount of fresh fruit or juice. Expensive prepregnancy multivitamins are not necessary if Penny has a well-balanced diet. Multivitamins that are not specifically for pregnancy may contain vitamin A so they are contraindicated just before and during pregnancy.

The anti-Müllerian hormone test, which is an indication of ovarian reserve, may be arranged. However, given her age, Penny would be expected to have a reduced ovarian reserve and hence a reduced level of anti-Müllerian hormone. This test is best left to the IVF specialists, if required, as it will not change management.

What other specialist referrals might be necessary for Penny?

Answer: Penny should be referred to an endocrinologist or a diabetes team experienced in diabetes and pregnancy as soon as possible and preferably well before she conceives. Members of the diabetes team that may assist Penny in optimising her diet, exercise, weight and glycaemic control ahead of pregnancy include a diabetes educator, a dietitian and, if possible, an exercise physiologist. She should be advised to use barrier contraception until her BGLs are optimised (aim for HbA_{1c} close to 6.0% if this can be safely achieved with minimal tendency to hypoglycaemia). Penny needs a formal eye assessment before pregnancy. If Penny has a strong family history of early ischaemic heart disease, consideration of referral to a cardiologist is wise.

Penny asks what can be done medically to increase her chances of a healthy pregnancy.

Answer: Penny should commence an appropriate exercise program and try to lose weight through a sensible low-cholesterol, low-glycaemic index, portion-controlled diet. This will help stabilise her BGLs, increase her fertility and improve her general fitness pending the birth. It should be mentioned that healthy weight loss takes time to achieve and Penny should aim to lose approximately 1 to 2 kg a month. This will need to be continued under medical guidance. She will need to balance the time it takes to lose weight against her declining fertility.

Penny should self-monitor her capillary BGLs at least four times daily most days, aiming prepregnancy for premeal levels of below 6.1 mmol/L (the definition of an impaired fasting glucose level) and a two-hour postmeal level below 7.5 to 8.0 mmol/L. (Note that the target BGL range will be lower during pregnancy.) Metformin therapy needs review about whether it should be ceased, but it may be safely continued into early pregnancy. If she had been on any other noninsulin hypoglycaemic treatment(s), these should be ceased prior to pregnancy. If required, targeted insulin therapy should be commenced to achieve target glycaemic control. As perindopril needs to be ceased, another medication, such as methyldopa, labetalol or oxprenolol which are suitable for use during pregnancy, should be commenced and blood pressure monitored.[2] Indapamide should be ceased before pregnancy because it is associated with electrolyte disturbances, intravascular hypovolaemia and urinary incontinence (especially later in pregnancy).

Table. Maternal HbA_{1c} and risk of major congenital abnormalities in offspring[1]

Initial maternal HbA_{1c} (%)	Major abnormalities (%)*
≥13.9	20.1
13.2	17.0
12.5	14.4
11.8	12.1
11.1	10.1
10.4	8.4
9.7	7.0
9.0	5.8
8.3	4.8
7.6	3.9
6.9	3.2
6.2	2.7
5.5	2.2

*Background population: approximately 2% risk of major malformations.

Penny asks what weight gain to aim for to achieve a healthy pregnancy outcome.

Answer: The greater the starting body weight, the lower the weight gain that is desirable. In a normal pregnancy, a woman with a BMI in the healthy weight range should gain between 10 and 14 kg. This amount is the weight of the placenta and baby at term, the amniotic fluid, increased fluid retention in the mother and the increased weight of the breasts and the uterus. As Penny's prepregnancy BMI is in the obese range, the pregnancy weight gain should be only 5 to 9 kg.[3] Throughout pregnancy, she should continue to have careful portion control, a low-glycaemic diet and to exercise sensibly. The aim is not for her to lose weight throughout the pregnancy, but to eat appropriately and healthily and to exercise as she can. Periodic dietitian review should be encouraged.

Penny has heard that caesarean section is safer for the baby. What do you tell her?

Answer: Overall risks are increased due to Penny's diabetes and obesity, with potential fetal and maternal complications. If obstetrically appropriate at the time, Penny may choose a trial of labour and vaginal delivery. This will depend on the fetal presentation, anticipated cephalo-pelvic size and placental function being normal near delivery. Delivery should be arranged close to term taking the blood pressure, glycaemic control as well as fetal size and wellbeing into account. However, particular risks

of this plan include a failed induction and need for semi-urgent caesarean section and an increased risk of shoulder dystocia for the baby. She may choose an epidural for pain relief and this could be an advantage if an urgent caesarean section became necessary, but there is an increased likelihood of need for forceps with use of an epidural.

Penny may also choose to have an elective caesarean section because she may not have another successful pregnancy, given the fact she is an elderly primigravida with no obstetric record and with significant medical conditions. However, Penny is at higher risks of complications from caesarean section (such as wound healing, venous thrombosis and pulmonary emboli, wound, urine and respiratory infection). Her baby may require medical attention for respiratory distress of the newborn (RDS) and may have initially poorer attachment following a caesarean. Some women in this situation may feel that elective induction and trial of labour holds a less predictable outcome than an elective caesarean in this specific situation. This, however, is the woman's informed choice.

Penny is keen to know the regularity of follow up required by endocrine and obstetric care during her pregnancy. What do you tell her?

Answer: High-risk pregnancies such as this would be monitored for congenital abnormalities, fetal growth and wellbeing at the 18-week morphological ultrasound. Later, wellbeing ultrasounds should be carried out for fetal growth, amniotic fluid amount and placental function every two to four weeks starting between 28 and 30 weeks. It is important that Penny sees an obstetrician regularly during her pregnancy. The obstetrician or obstetric registrar would normally review her at least every two weeks from 28 weeks' gestation and weekly from at least 34 weeks' until delivery (more frequently if complications develop). If Penny's blood pressure becomes problematic during pregnancy or labour, a renal physician may become involved.

Penny will need to have a regular review by the endocrinologist throughout pregnancy as her BGLs and insulin requirements will continue to change. Ideally she should already have seen the endocrinologist prior to conception. She should then be seen two to four weekly from early pregnancy until 26 to 28 weeks' gestation, and then at least every two weeks until delivery. From 24 weeks' there is a more marked increase in maternal insulin requirements. Insulin therapy is usually needed, even in women with well-controlled diet-treated diabetes before pregnancy. If Penny has problems maintaining optimal glycaemic control, she may need to be seen more often and may generally benefit from additional review by the diabetes educator as well as the dietitian. In the last few weeks of the pregnancy, Penny may need to be seen at least weekly. The delivery plan should be discussed between the diabetes and obstetric teams by 36 weeks or sooner if the blood pressure starts to rise. If a preterm delivery is needed, antenatal corticosteroids will generally be given to prevent respiratory distress syndrome in the infant. Admission is required for all women with diabetes who are given antenatal corticosteroids as the corticosteroids will lead to a great increase in insulin requirement, usually involving need for intravenous insulin infusion for up to 72 hours after the first corticosteroid dose.

Outcome: Penny's HbA_{1c} level improved to 6.3% before she conceived naturally some four months later. Her blood pressure was well controlled on methyldopa. The nuchal scan and antenatal screening for chromosomal defects were all normal and showed a low risk of pre-eclampsia. Penny and her husband chose to have chorionic villus sampling, which was normal. A 19-week fetal ultrasound showed a normal appearing male fetus and the placenta also appeared normal. To maintain blood glucose targets, Penny required rapid-acting insulin with breakfast and isophane insulin before bed from 18 weeks' gestation. By late third trimester she was needing a total of 190 units of insulin per day. Her albuminuria did not increase during pregnancy and Penny developed no retinopathy. Her son James was born after an elective caesarean under epidural at 38.5 weeks. He weighed 3652 g and had a normal appearance with no malformations; his apgar scores were 7 at one minute and 9 at five minutes. His abdominal girth was in the upper of the normal range as was his length; his head circumference was at the 50th centile. Penny commenced breastfeeding just after delivery and plans to continue breastfeeding for the health of the baby and to aid her weight loss. Both Penny and the baby went home on day five. Penny's BGLs remained stable between 4.5 and 9 mmol/L after delivery. At discharge she was on treated with diet alone and she was advised to test her BGLs pre- and postprandially twice a day one to two days per week. She was encouraged to report any significant rise in the BGLs to her GP or the endocrinologist /hospital endocrinology registrar. She has a follow-up appointment with the endocrinologist at eight weeks' postpartum. Penny has been given information about the intrauterine device as contraception for when she sees the obstetrician or obstetric registrar at about six weeks' postpartum. ET

Practice points

- Pregnancies need to be planned in patients with diabetes; any associated medical conditions or complications need to be appropriately managed before and during the pregnancy.
- Patients with diabetes are at increased risk of a variety of complications during pregnancy and delivery, including infertility, an increased risk of congenital abnormalities, miscarriage and stillbirth, infections, intrauterine growth retardation, polyhydramnios, placental abruption and insufficiency, macrosomia, shoulder dystocia and neonatal hypoglycaemia.
- Referral of women with diabetes to an endocrinologist is required prior to conception as strict control of blood glucose levels before and into early pregnancy reduces risk of congenital abnormalities and fetal loss. Specialised diabetes and obstetric care is needed throughout pregnancy.
- Patients with diabetes require a formal eye assessment before and during pregnancy to ensure they do not develop or experience worsening retinopathy.

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References

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COMPETING INTERESTS: None.