Diabetes mellitus and abnormal glucose tolerance

Table 1: Maternal diabetes: Intrapartum monitoring and early neonatal care

Maternal diabetes	Intrapartum maternal / fetal monitoring	Early neonatal care
Type 1 Diabetes mellitus	**Once labour is established:** > Commence hourly glucometer readings > Commence 5 % glucose infusion at 100 mL/ hour > Set up insulin infusion (see chapter 92) > Continuous electronic fetal monitoring	> A neonatologist or neonatal registrar should be informed of the delivery > The baby's first blood glucose level should be obtained by 1 hour of age (see chapter 80) > The baby should be fed within the first hour after birth > Many babies will have hypoglycaemia, requiring transfer to the nursery and blood glucose monitoring (see chapter 80)
Type 2 Diabetes mellitus	**Once labour is established:** > Commence hourly glucometer readings > If the blood glucose is ≥ 8 mmol / L over a two hour period, and delivery is not imminent, commence an insulin / glucose infusion > Continuous electronic fetal monitoring	
Gestational diabetes on insulin or metformin	**Once labour is established:** > Commence 2 hourly glucometer readings > Continuous electronic fetal monitoring if diabetes was poorly controlled antenatally or there is suspected fetal macrosomia or associated growth restriction or other indication	
Gestational diabetes (well controlled on diet) Last reviewed 06/08/12	**Once labour is established:** > Commence 2-4 hourly glucometer readings, providing that the initial value is normal (glucose 4-7 mmol / L) > More frequent blood glucose level monitoring may be required if hyperglycaemia is noted > If the blood glucose in labour is ≥ 8 mmol / L over a two hour period, and delivery is not imminent, commence an insulin / glucose infusion > Continuous electronic fetal monitoring if diabetes was poorly controlled antenatally or there is suspected fetal macrosomia or associated growth restriction or other indication	

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Introduction

- Tight control of blood glucose levels before and in the first weeks of pregnancy reduces the risk of malformation. Tight control is defined as maintaining a blood sugar between 5.6 and 6.7 mmol / L (Farrag, 1987; Walkinshaw, 2006)
- Continued tight control later in pregnancy facilitates normal fetal growth and normal vaginal birth after spontaneous labour (Langer et al, 1991)
- Treatment of pregnant women, with gestational diabetes (see below) with dietary advice, glucose monitoring and insulin as needed, reduces serious perinatal morbidity and may also improve maternal quality of life (Crowther et al. 2005)

Diabetes mellitus

Preconception counselling

- Aim for review by the woman's physician or general practitioner

Explain:

Control of blood glucose

- Reasons for and benefits of optimal blood glucose and glycosylated haemoglobin levels in pregnancy

Risks associated with poor control

- Congenital malformations
- Pregnancy complications including preeclampsia, polyhydramnios, preterm birth, macrosomia and / or growth restriction, intra-uterine fetal death, shoulder dystocia
- Operative delivery or caesarean section
- Care of the newborn including risk of hypoglycaemia (and therefore need for monitoring blood glucose levels), jaundice, respiratory distress

Outline preconception management plan

- If poor control, advise against pregnancy and offer contraception advice for interim period until good control obtained.
- Aim for HbA1c < 7 % and ideally < 6 %.
- Arrange dietitian review
- Review / identify complications of diabetes, especially retinopathy and nephropathy
- Consider need for consultation e.g. ophthalmologist review
- Instruct on the use of a menstrual calendar
- Commence folate 5 mg daily ideally at least 6 weeks before conception
- Consider need for iodine and vitamin D supplementation

Antenatal care

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- Early referral to high risk care with physician and obstetrician
- Plan birth in a hospital with at least a level 4 nursery facility

First Visit

Bloods

- Routine booking bloods
- Glycosylated haemoglobin (HbA1c)
- Thyroid function test (Type I diabetes)
- Electrolytes, liver and renal function tests, urate
- Random glucose

Urine

- Early morning spot urine for albumin / creatinine ratio

Medications

- Review medications
- Some oral hypoglycaemic agents are contraindicated and need to be ceased e.g. thiazolidinediones (glitazones), repaglinide
- Ongoing treatment with metformin and sulfonylureas is currently the subject of research: they should not be used in pregnancy without guidance from a physician / endocrinologist
- Insulin may be needed to improve glucose control
- Starting or switching to insulin should be done in collaboration with a physician / endocrinologist to avoid periods of hyperglycaemia during critical stages of fetal growth and development

Education

- Reinforce dietary advice and appropriate blood glucose monitoring
- Advise on the likely need for additional / increased insulin
- Involve diabetes educator

Referral

- Arrange dietitian referral
- Arrange ophthalmologist referral

Subsequent review

- Usually 2 to 4 weekly

Fetal surveillance

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- Review maternal HbA1c, renal function and proteinuria results after first visit. Confirm gestational age
- At 12 weeks gestation offer nuchal translucency assessment and serum screening
- 19-20 week morphology ultrasound (document that the woman has pre-gestational diabetes on the request form)
- In the absence of a tertiary perinatal ultrasound service, a fetal echocardiogram may be of value with women with markedly elevated (>10 %) HbA1c (at 22-24 weeks)
- Consider further scans for growth / liquor volume in the third trimester

Consider umbilical artery blood flow measurement if:

- Evidence of microvascular (nephropathy or proliferative retinopathy) or macro vascular disease.
- Hypertension (essential or pre-eclampsia)
- Intrauterine growth restriction
- Smoker

Blood glucose monitoring

- Four times a day: before breakfast (fasting) and two hours after the start of each meal
- Aim for blood glucose between:
  - 3.5 – 5.5 mmol / L before breakfast (fasting)
  - 4 - 7 mmol / L two hours after a meal
- Women with type 1 diabetes, who have been adjusting their insulin dose on the basis of pre-prandial blood glucose levels, may continue to monitor in this way. It has been shown, however, that perinatal outcome is better with control based on post prandial glucose values

Antenatal admission

- Consider if complications arise
- Consider if glycaemic control is poor
- Women with poor glucose control should have contact with a neonatologist, as neonatal morbidity can be anticipated

Timing of delivery

Await spontaneous labour (up until 40 weeks) if:

- Blood glucose control remains satisfactory
- Normal fetal growth
- There is no polyhydramnios or other complication of pregnancy (e.g. pre-eclampsia)

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Plan induction of labour if:

- Poor glycaemic control at 38^{+0} weeks
- Polyhydramnios
- Macrosomia
- No spontaneous onset of labour by term
- Birth should occur before 40^{+6} weeks of pregnancy
- Betamethasone 11.4 mg (x 2 ampoules of 5.7 mg) x 2 doses 24 hours apart should be given if delivery required before 35+0 weeks of gestation. Admission for additional insulin and glucose monitoring (for further information, refer to the PPG 'Insulin') : consult physician / endocrinologist

Method of delivery

- Vaginal birth if fetal weight is < 4000 grams as clinically indicated
- Consider elective caesarean section if estimated fetal weight is ≥ 4250 grams because of the increased risk of shoulder dystocia (Conway and Langer, 1997)

Intrapartum care

Type 1 diabetes

- Normal labour management
- Continuous electronic fetal monitoring
- Care of the woman with type 1 diabetes in labour should be in consultation with the physician/endocrinologist
- If induction of labour is to be performed, modify usual insulin regimen the day before in consultation with the physician / endocrinologist
- On the morning of induction, if not already in labour, the woman can be given a light breakfast and, in consultation with the physician / endocrinologist, a dose of short acting (Novorapid® or Humalog®) insulin
- If labour is not established by lunch time, a further light meal and soluble insulin may be considered, in consultation with the physician / endocrinologist, with a further 2 hours post prandial glucometer reading
- Avoid prolonged labour and water overload – if ordered, Syntocinon® should be administered in 0.9 % sodium chloride
- Consider the need for second IV access
- Be aware of the increased risk of shoulder dystocia

Insulin regimen

- Once in labour, a 5 % glucose infusion should be commenced at a constant rate [1 litre per 10 hours (i.e. 5 g glucose / hour)]
- At the same time an insulin infusion (Actrapid) should be set up in accordance with insulin infusion guideline. (for further information, refer to the PPG 'Insulin infusion')
- Determine blood glucose hourly using blood glucometer and / or laboratory determinations and adjust insulin infusion with the aim of keeping blood glucose between 5.5 and 7 mmol / L

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Type 2 diabetes

- If induction of labour is planned, the pre-existing insulin regimen is continued until labour is established or no later than midnight on the day of admission. Further insulin management will be according to guidelines below
- If metformin is being used, this can be continued until labour is established
- Routine blood glucose monitoring to continue until labour is established
- On the morning of induction, if not already in labour, the woman can be given a light breakfast and, if insulin is being used, a dose of short acting insulin in consultation with the physician / endocrinologist
- If labour is not established by lunch time, a further light meal with metformin and / or short acting insulin may be considered, in consultation with the physician / endocrinologist
- Once labour is established, hourly glucometer readings should be taken
- If the blood glucose in labour is ≥ 8 mmol / L over a two hour period, and delivery is not imminent, an insulin / glucose infusion should be commenced (for further information, refer to the PPG 'insulin infusion'
- Two intravenous access lines will be required to accommodate the glucose / insulin infusions and mainline / Syntocinon® infusions
- Syntocinon® should be administered with 0.9 % sodium chloride to prevent hyponatraemia into a mainline of 0.9 % sodium chloride (for further information, refer to the PPG 'Syntocinon infusion regimen')
- Normal labour management
- Continuous electronic fetal monitoring
- Be aware of the increased risk of shoulder dystocia

Neonatal management

- A neonatologist or neonatal registrar should be informed of the delivery
- The baby should be fed within the first hour after birth
- Many babies will have hypoglycaemia, requiring transfer to the nursery and blood glucose monitoring
- The baby's first blood glucose level should be obtained by 1 hour of age
- Other morbidities e.g. polycythaemia, jaundice, hypocalcaemia, respiratory distress syndrome (RDS) also occur, further emphasising the need for nursery observation and management

Postpartum care

Maternal

- Send placenta for histopathological examination
- Women with Type 1 or Type 2 diabetes need to maintain a diabetic diet and to continue glucose monitoring as pre-labour
- There is an immediate fall in maternal insulin resistance after delivery of the placenta

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Normal vaginal birth

- After birth, insulin infusion can be ceased in women with Type 2 diabetes
- After birth, for women with Type 1 diabetes, cease insulin infusion and recommence subcutaneous insulin (long acting and / or short acting, depending on when birth occurs) as prescribed by the physician / endocrinologist.
- Recommence usual diet
- Once the insulin infusion is ceased, recommence routine blood glucose monitoring
- Physician / Endocrinologist follow up as indicated

Caesarean section

- Women with type 1 diabetes should continue with an insulin infusion and dextrose infusion until the woman is ready to resume oral intake
    - Subcutaneous insulin can then be reintroduced, using the pre-pregnancy regimen, or often at smaller doses, if breastfeeding, as per physician / endocrinologist orders
    - Recommence routine blood glucose monitoring
- Women with type 2 diabetes who had required an insulin infusion can cease this after birth and may recommence oral hypoglycaemic agents (if required pre-pregnancy)
    - Recommence routine blood glucose monitoring

Breastfeeding

- Thiazolidinediones are NOT recommended for breastfeeding women
- Recent studies have indicated the use of metformin during breastfeeding is safe (Briggs et al. 2005). Similarly, only very small quantities of modern sulphonylurea drugs (eg glibenclamide and glipizide) are excreted into breast milk, and previous concerns may have been misplaced (Glatstein et al. 2009)
- Encourage breastfeeding. The increased energy demands may require less insulin than usual for a woman with pre-existent insulin dependent diabetes

Neonatal

- (for further information, refer to the PPG 'neonatal hypoglycaemia')

Gestational diabetes and glucose intolerance in pregnancy

Introduction

- There is no single test of glucose tolerance which is accepted internationally for use in pregnancy to detect abnormal glucose tolerance. In Australia, the standard test is a 75 gram 2 hours oral glucose tolerance test (including a fasting level) to detect and define gestational diabetes (Hoffman et al. 1998)

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Diabetes mellitus and abnormal glucose tolerance

Definitions

Glucose intolerance

- A glycaemic response to a standard oral glucose tolerance test that is intermediate between a normal and a diabetic result with onset or recognition during the present pregnancy (WHO 1985)

Gestational diabetes mellitus

- Carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. This definition applies regardless of whether insulin is used for treatment and whether the condition persists after pregnancy or not (Gabbe and Graves 2003)

Diagnosis

Screening tests

- The Australasian Diabetes in Pregnancy Society (ADIPS) recommends universal screening to detect abnormal glucose tolerance in pregnancy (Hoffman et al. 1998)

Oral glucose challenge test (OGCT)

- Taken at 26 - 28 weeks gestation
- A non-fasting 50 gram glucose drink is given to the pregnant woman
- After one hour venous blood is taken
- A one hour venous blood glucose level of ≥ 7.8 mmol / L indicates the need for an oral glucose tolerance test (OGTT)

Oral glucose tolerance test (OGTT)

- May be performed at any time during pregnancy if symptoms and signs of abnormal glucose tolerance e.g. excess thirst; polyuria, polyhydramnios, macrosomia
- Consider an early test (around 12-16 weeks of gestation) for women with a past history of gestational diabetes if a recent OGTT has not been performed
- Women with known glucose intolerance outside pregnancy may be considered to have gestational diabetes from the time of conception and therefore a repeat OGTT is not required
- Ensure a normal diet containing at least 300 grams of carbohydrate is consumed for three days before the test
- Performed after an 8 hour fast (food and fluids)
- Obtain fasting venous blood glucose
- A 75 gram glucose drink is then given to the pregnant woman, who should remain seated and non smoking
- Measure venous blood glucose at two hours
- A fasting glucose ≥ 5.5 mmol / L or a glucose ≥ 7.8 mmol / L two hours after the glucose drink indicates the need for dietary advice, and home glucose monitoring

Although the ADIPS consensus statement refers to ≥ 8 mmol / L for diagnosis of gestational diabetes, level I evidence refers to a 2 hour glucose value ≥ 7.8 mmol / L and indicates benefits of treatment for these women (Crowther et al. 2005)

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Alternative diagnostic tests

Alternative diagnostic tests include capillary blood glucose monitoring (fasting and postprandial – see below) over a number of days, particularly if there has been previous intolerance of glucose loading

The random venous blood glucose screening test is not a particularly sensitive method for diagnosis of GDM, but a result of ≥ 7 mmol / L indicates the need for a 75 gram oral glucose tolerance test (OGTT) or for capillary blood glucose monitoring

Management

Gestational diabetes / Glucose intolerance of pregnancy

Referral to diabetic educator / high risk pregnancy / medical care for:

- Dietary advice
- Home blood glucose monitoring education
- Commencement of treatment as indicated
- Occasionally, the woman may require admission for further assessment if blood glucose is over 11 mmol / L despite monitoring and treatment, or if poor compliance with diet is an issue

Blood glucose monitoring and indications for treatment

Blood glucose monitoring

- Four times daily: before breakfast (fasting) and two hours after the start of each meal (e.g. if the woman starts a meal at 1300 hours, the test should be taken at 1500 hours)
- Aim for blood glucose between:
    - 3.5 – 5.5 mmol / L pre breakfast (fasting)
    - 4 - 7 mmol / L two hours after a meal
- If good control is achieved as above, testing may be reduced to
    - Twice daily at varying times
- If values continue to be well controlled
    - Once daily at varying times
- There is debate as to whether lower targets should be used: these are currently under discussion

Indications for more intensive treatment

- Treatment will be considered if:
    - Fasting values are ≥ 5.5 mmol / L once or more a week
    - Post prandial values ≥7.5 mmol / L twice or more a week are recorded in the absence of dietary non compliance

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Diabetes mellitus and abnormal glucose tolerance

Insulin treatment

- Refer to physician / endocrinologist for individualised management
- Usually a combination of short acting (Actrapid®, Novorapid®, Humalog®) and intermediate acting (protophane) insulins, although a basal bolus regimen with a very long acting (glargine) insulin may be used
- Start with approximately 0.5 units per kilogram bodyweight

Metformin

- The MiG trial (2008) showed that use of metformin gives comparable outcomes to insulin in the management of women with gestational diabetes. Women treated with metformin had offspring with less severe neonatal hypoglycaemia. They gained less weight during pregnancy and lost more weight after delivery. Women preferred treatment with metformin. Follow up of the offspring to date has shown no difference between those whose mothers were treated with insulin and those whose mothers were treated with metformin
- Although promising, there is no long-term follow-up of children born to mothers who took metformin during pregnancy.
- The use of metformin in pregnancy is therefore not currently endorsed by regulatory authorities or professional bodies, including the Australian Diabetes in Pregnancy Society. Although no adverse effects have been demonstrated, metformin does cross the placenta, leading authorities to be very cautious in their recommendations.
- Nonetheless, metformin is used for the treatment of gestational diabetes in many centres around Australia and New Zealand
- Metformin could be considered for use in women who have failed non-drug treatments and who either refuse or are unable to take insulin. The mother should be educated about the potential risks, benefits and areas of uncertainty so that an informed decision can be made.
- Use of metformin should only be in consultation with a physician / endocrinologist with specialised knowledge of its use in pregnancy

Metformin treatment

- Refer to physicians for individualised management
- Start with standard metformin 500 mg 1 – 3 times a day, depending on the glucose profile
- Long acting (XR) metformin may be considered, particularly at night for those with fasting hyperglycaemia, and may be better tolerated
- Insulin may be added to metformin treatment where control is not achieved with metformin

Side effects

- Gastrointestinal effects, usually nausea, vomiting and or diarrhoea, occur in up to 8 % of women taking metformin in pregnancy. These usually settle over a few days and / or with reduction of the dose. Two percent of women in the MiG trial were unable to continue with metformin

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Intrapartum care

- If induction of labour is planned, the last dose of the long acting insulin, if being used, should be given the night before
- If metformin is being used, this can be continued until labour is established
- Routine blood glucose monitoring to continue until labour is established
- On the morning of induction, if not already in labour, the woman can be given a light breakfast and, if insulin is being used, a dose of short acting insulin in consultation with the physician / endocrinologist
- If labour is not established by lunch time, a further light meal with metformin and / or short acting insulin may be considered, in consultation with the physician / endocrinologist
- Once labour is established, at least 2 hourly glucometer readings should be taken if the woman is taking insulin or metformin. If gestational diabetes has been well controlled with diet alone, glucometer readings may be taken every 2-4 hours once labour is established, providing that the initial level is normal (glucose 4-7 mmol / L). More frequent blood glucose monitoring may be required if hyperglycaemia is noted (see table 1)
- If the blood glucose in labour is ≥ 8 mmol / L over a two hour period, and delivery is not imminent, an insulin / glucose infusion should be commenced
- Two intravenous access lines will be required to accommodate the glucose / insulin infusions and mainline / Syntocinon® infusions
- Syntocinon® should be administered with 0.9 % sodium chloride to prevent hyponatraemia
- Normal labour management
- Continuous electronic fetal monitoring if maternal diabetes is poorly controlled or there is suspected fetal macrosomia or growth restriction associated with the maternal diabetes or other obstetric complications requiring continuous EFM (see table 1)
- Be aware of the increased risk of shoulder dystocia

Neonatal management

- A neonatologist or neonatal registrar should be informed of the delivery
- The baby should be fed within the first hour after birth
- Many babies will have hypoglycaemia, requiring transfer to the nursery and blood glucose monitoring
- The baby's first blood glucose level should be obtained by 1 hour of age
- Other morbidities e.g. polycythaemia, jaundice, hypocalcaemia, respiratory distress syndrome (RDS) also occur, further emphasising the need for nursery observation and management

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Postpartum follow up

- Send placenta for histopathological examination
- The woman with gestational diabetes may resume a normal diet after birth, but will need advice on maintaining a healthy diet

Glucose profile on day 3-4 post partum

- Some assessment of ongoing glucose intolerance should occur in the week after birth. Options include:
  - Fasting and 2 hours post prandial capillary BGL (4 measurements in total)
  - A single fasting blood glucose level up to day 4 or before discharge (venous blood sample, not capillary)

Fasting values > 6 mmol / L or postprandial values 8 - 11 mmol / L

- Suggest continuing impaired glucose tolerance / fasting hyperglycaemia. These women should continue to give attention to their diet and be encouraged to exercise and obtain an optimal weight

Fasting values > 7 mmol / L or postprandial values >11 mmol / L

- Suggest ongoing diabetes. A diabetic diet should be reinstituted and the woman should be reviewed by the physician / endocrinologist before discharge

Fasting values < 6 mmol / L or postprandial values of < 8 mmol /L

- Normal. These women should continue to give attention to their diet and be encouraged to exercise and obtain an optimal weight

Follow-up

- All women with gestational diabetes should have a glucose tolerance test at 6-12 weeks post partum
- The Gestational Diabetes Recall Register should be offered (if the woman has not already been recruited to this) to facilitate long-term follow-up
- Advice should be given about the increased risk of type 2 diabetes, as well as the high (40 - 70 %) risk of recurrent gestational diabetes in any future pregnancy
- Emphasis should be placed on maintaining a healthy diet with regular exercise, bringing weight into the normal range, as the only established way of reducing the long-term risk of diabetes
- Offspring of women with diabetes, both pre-existing and gestational, are at increased risk of obesity and developing diabetes
- Contraception: progestogen-only contraception (including progestogen-only pills, Implanon implants and Depo-Provera injections) is associated with an earlier onset of type 2 diabetes in women with previous gestational diabetes (Kjos 2000). The combined oral contraceptive pill does not have this effect and may be used for women who are not breastfeeding
- Consideration may be given to a Mirena intra-uterine device for contraception

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Subsequent pregnancy

- Pre-conception advice and assessment of glucose tolerance should be offered before any further pregnancy is undertaken, otherwise at 1-2 year intervals

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Useful web site:

Organisation of teratology information specialists. Diabetes and pregnancy. Available from URL: http://www.otispregnancy.org/pdf/diabetes.pdf

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Abbreviations

ADIPS	Australasian Diabetes in Pregnancy Society
BGL	Blood glucose level
EFM	Electronic fetal monitoring
e.g.	For example
et al.	And others
g	Gram(s)
GDM	Gestational diabetes mellitus
HbA1c	Glycosylated haemoglobin
Hb	Haemoglobin
mg	Milligram(s)
mmol / L	Millimol(s) per litre
OGCT	Oral glucose challenge test
OGTT	Oral glucose tolerance test
%	Percent
RDS	Respiratory distress syndrome
WHO	World Health Organisation

Version control and change history

PDS reference: OCE use only

Version	Date from	Date to	Amendment
1.0	18 Dec 06	18 Oct 07	Original version
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