The Challenge of Managing Diabetes in Pregnancy in Far North Queensland:

What does the future hold?

Bronwyn Davis, RN, RM, CDE, Cairns Diabetes Centre, 2013
Aims of this presentation:

To discuss:

- the increasing incidence of GDM
- the effect of diabetes on pregnancy
- screening & management guidelines for GDM
- To share a case history on engaging Indigenous women in diabetes care
- the results audits on screening and pregnancy outcome in Cape York and Torres Strait Islands
Global Projections for the Diabetes Epidemic: 2003-2025

World
2003 = 194 M
2025 = 333 M
↑ 72%

NA
23.0 M
36.2 M
↑ 57.0%

EUR
48.4 M
58.6 M
↑ 21%

EMME
19.2 M
39.4 M
↑ 105%

SEA
39.3 M
81.6 M
↑ 108%

AFR
7.1 M
15.0 M
↑ 111%

SACCA
14.2 M
26.2 M
↑ 85%

WP
43.0 M
75.8 M
↑ 79%

M = million; AFR = Africa; NA = North America; EUR = Europe; SACCA = South and Central America; EMME = Eastern Mediterranean and Middle East; SEA = South-East Asia; WP = Western Pacific
Age-adjusted Percentage of U.S. Adults Who Were Obese or Who Had Diagnosed Diabetes

Obesity (BMI ≥30 kg/m²)
- 1994
- 2000
- 2007

Diabetes
- 1994
- 2000
- 2007

Obesity in Pregnancy

- 52% of Aussie women obese
- 35% of women aged 25-35 obese
- Obesity linked to increasing prevalence of GDM
- Greater obstetric risk
  
  Higher rates of:
  - induction
  - slower cervical dilatation
  - prolonged labour
  - medical intervention
  - caesarean section
Conclusions: Obesity and GDM were independent risk factors of perinatal complications. The effect of the worldwide obesity and diabetes epidemic is extending into the next generation.
Obesity in pregnancy equates to increased risk for obesity in childhood.
Normalisation of obesity in children & general population
Type 2 Diabetes in Pregnancy – A growing concern

- TYPE 2 EPIDEMIC
- more women of child-bearing age have type 2 diabetes
- increasing number of women with type 2 diabetes in pregnancy

Foetal Risk & Diabetes

Closure of neural tube
Heart development
Fusion of palate
B-cell and islet development
Organogenesis

Gestation in weeks

0 10 20 30 40
First Trimester Second Trimester Third Trimester

LGA > 90th percentile
AGA
SGA < 10th percentile

Foetal Growth

B-cell and islet development
Foetal Abnormalities & Pre-existing Diabetes

- Birth defects occur in 1-2% of the general population
- In type 2 diabetes there is a 11 fold increase in the incidence of birth defects associated with poor glycaemic control
- Abnormality rates have been reported at 5-10% (some reports as high as 15%) in women with pre-existing diabetes
- Common defects in DIP
  - Neural tube
  - Cardiac
  - Musculoskeletal
  - Genito-urinary

Cheung et al., 2005, Dunn, 2005, Macintosh et al. 2006
The last half of the embryonic period (from 4-8 weeks) is the time when most organs are formed (organogenesis) and teratogens have their most damaging effects on the foetus.
Risks for Fetal Abnormality in Pre-existing Diabetes

Factors that increase the risks of fetal abnormality include:

- Poor attendance for pre-pregnancy counseling
- Poor glycaemic control pre-pregnancy and during organ development in the first trimester
- Late presentation for antenatal care
Risk of a major or minor anomaly according to periconceptional A1C.
Mean maternal glucose concentrations and infant mortality

Jovanovic L, Peterson CM, Management of the pregnant diabetic woman. Diabetes Care 1980
Peak postprandial glucose concentration and risk of macrosomia

Gestational diabetes is a common complication of pregnancy and is defined as

“any degree of glucose intolerance with onset or first recognition during pregnancy”
GDM: risks to mother and fetus

GDM has long been recognized as a risk factor for a number of adverse outcomes during pregnancy, including:

- excessive fetal growth,
- an increased incidence of birth trauma,
- and caesarean delivery, and
- neonatal metabolic abnormalities such as hypoglycemia, hyperbilirubinemia and polycythemia.
Gestational Diabetes Mellitus

- In low-risk populations with universal screening:
  - 1.9% (Sweden)
- In high-risk populations:
  - 13% (Torres Strait Island 2006)
- Anglo-Celtic women in Australia: 3.0%
- Indian women in Australia: 17%
- Increase of GDM follows the increase of T2DM
- Increasing incidence at Cairns Base Hospital
  - 342 (2008)
  - 459 (2011)
Pathophysiology

Gestational diabetes

Maternal hyperglycemia → Fetal hyperglycemia

Postpartum fetal hypoglycemia

↑ Fetal insulin

Fetal neurologic injury

Increased fetal metabolism; macrosomia

Pulmonary immaturity
Fetal Origins Hypothesis  
*Taylor PD Exp Physiol 2007;92:287*

Metabolic factors in the intrauterine environment (gluc, FFAs, TGs, inflammatory cytokines, insulin, hormones, growth factors, oxidative stress), have a profound effect on prenatal development and enhances susceptibility to later chronic disease.

- Early exposure: embryogenesis alters nutrient transport by placenta and gene expression of cytokines, hormones, GFs
- Mid: Alter number, growth, and function during organogenesis
- Later: Impact regulatory energy set points on brain and neuronal/metabolic pathways feed back loops, and mitochondrial function.
- Time when fetal fat accretion is most rapid
Controversy exists amongst experts whether:
- GDM not diagnosed often enough??
- mild elevations of blood glucose = no adverse events??

The objective of the HAPO study was to clarify risks of adverse outcomes associated with degrees of maternal glucose intolerance less severe than overt diabetes mellitus.

- 7 year international study
- Recruited approx. 25,505 pregnant women
- 15 centres in 9 countries including Australia
- 23,315 women completed the study

Principle investigator: Boyd E. Metzger, MD, Professor of Medicine, Division of Endocrinology, North-Western University Feinberg School of Medicine, Chicago 2008 HAPO study group
What did HAPO set out to tell us?

Much controversy surrounds glucose intolerance in pregnancy and possible risks to the fetus.

- Diagnosis of GDM should be based on criteria that predict future risk of maternal diabetes.
- Point at which elevated maternal blood glucose levels carries risk for foetus.
HAPO Key Findings......

The data show associations between increasing levels of fasting, 1-hour, and 2-hour plasma glucose obtained on oral glucose-tolerance testing and:

- birth weight above the 90th percentile
- Cord blood serum C-peptide level above the 90th percentile,

There were weaker associations between glucose levels and

- primary caesarean delivery
- clinical neonatal hypoglycaemia.

Some problems occurred even in ranges considered within normal range for pregnant women.
Fasting $\geq 5.1$
1 hour $\geq 10.0$
2 hour $\geq 8.5$

What is now needed - RCTs treatment trials using the suggested diagnostic criteria to define optimal management targets and assess pregnancy outcome.
ADIPS recommendations for GDM diagnosis - 2012

- High risk women screened with OGTT at first opportunity following conception
- Universal screening of all women with a standard 75g oral OGTT at 24–28 weeks

Recommendation: the diagnosis of GDM is made if one or more of these values are abnormal
Diagnosis of GDM in Australia

Old ADIPS guidelines
- Fasting $\geq 5.5$
- 2 hour $\geq 8.0$

New ADIPS guidelines
- Fasting $\geq 5.1$
- 1 hour $\geq 10.0$
- 2 hour $\geq 8.5$
Controversies over new diagnostic guidelines for GDM

- Medicalization of pregnancy
- Costs – expected 30% increase in workloads
- Benefits – less macrosomia, shoulder dystocia, PET, gest hypertension
- Treatment targets will need to change
- More women on insulin???
- Risks – treatment of mild hyperglycaemia may actually cause harm
- Would our efforts be spent better targeting obesity
Gestational Diabetes

Does screening and treatment of gestational diabetes reduce the rate of serious perinatal complications?
OGTT at 24-34 weeks
Treatment of mild GDM (WHO criteria for IGT)
Positive for glucose intolerance in pregnancy if
- fasting 5.5-7.8 mmol/L
- 2 hour 7.8-11.0 mmol/L

Intervention (524) and standard care (506) groups
Outcomes
- Decreased serious perinatal complications: death (0 vs 5), shoulder dystocia, bone fracture, nerve palsy
Treatment of mild GDM resulted in:

- ↓ LGA, macrosomia,
- ↓ shoulder dystocia,
- ↓ CS
- ↓ PET & gestational hypertension
Management of Diabetes during Pregnancy

- Diabetes Education
- Self blood glucose monitoring
- Diet
- Exercise
- Medication
Self Blood Glucose Monitoring

Tight control - BGL’S during pregnancy should remain within the normal range.

- Before breakfast $\leq 5.5$ mmol/L (4.5-5.0)
- 2 hours post prandial $\leq 7.0$ mmol/L (6.0-6.5)
- Blood sugars should be monitored daily with a 4 point profile

ADI PS New treatment targets
- Fasting $< 5.0$
- 1 hour $< 7.4$
- 2 hour $< 6.7$
Healthy diet during pregnancy

Healthy diet which provides nutritional needs for mother and baby

- Low in fat
- Quality carbohydrates,
- High in fibre
- Diet rich in iron, folate and calcium, omega 3 FA (pregnancy requirements for fetal growth)
- Low in added sugars
- Small frequent meals
- Obese women may need less
# Weight Gain in Pregnancy

<table>
<thead>
<tr>
<th>Pre-pregnancy BMI</th>
<th>Estimated Wt gain</th>
</tr>
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<tbody>
<tr>
<td>Healthy wt range 19.8-26 kg/m²</td>
<td>11.5 to 16 kg</td>
</tr>
<tr>
<td>Underweight 19.8 kg/m²</td>
<td>12.5 to 18 kg</td>
</tr>
<tr>
<td>Overweight 25 to 29.9 kg/m²</td>
<td>7 to 11.5 kg</td>
</tr>
<tr>
<td>Above &gt; 29 kg/m²</td>
<td>6 kg</td>
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</table>
Insulin Therapy

- Basal / bolus insulin
- eg Fast acting pre meals / intermediate or long acting pre bed
- Insulin is self administered and given in the abdomen or legs
- Insulin pens most commonly used.
- Insulin must be adjusted according to a pattern in blood sugar levels (increasing insulin as pregnancy progresses).
Oral Hypoglycaemic Agent Use in Pregnancy

- It is generally recommended that OHA’s are ceased prior to or once pregnancy is confirmed.
- Metformin was being used and anecdotally appears to be safe in pregnancy - MIG trial, 2009 – confirms safety for use in GDM.
- Metformin helps overcome insulin resistance and is useful when women are on large doses of insulin.
Diabetes / Obstetric Management

- Best management – combined diabetes/obstetric multidisciplinary team
- Tight blood glucose control – treat aggressively
- Pre-existing DM – screen for fetal anomalies
- Timing of delivery based on obstetric and/or fetal indications
- Intensive care nursery facilities may be required
This infant was macrosomic, weighed 4583 g, was delivered 1 month prematurely, had all of the signs of an infant of a diabetic mother (hypoglycemia, hypocalcemia, hyperbilirubinemia), and died of respiratory distress 2 days after this photograph was taken.

Macrosomia

Macrosomic infant of diabetic mother A newborn macrosomic infant of a diabetic mother. The main abnormalities are disproportionate growth with a plethoric appearance and excessive fat accumulation. Courtesy of G Cabrera-Mesa, MD.
Foetal Growth and Diabetes

fig 5-3. Three babies, same gestational age, weigh 600, 1400, and 2750 grams, respectively, from left to right. They are plotted on Fig. 5-2 at points A, B, and C.
Lactation

- Probably decreases the risk of developing T2DM in the GDM mothers
- Probably decreases the risk for the offspring to get both T1 and T2DM

GDM recurrence & conversion to type 2

- Recurrence rate at next pregnancy
  - 35.6% - 70%

- Future T2DM
  - 6 wk post partum: 2.8%
  - 28 yr post partum: 70%

- Increased risk for the offspring to have obesity and future T2DM

The Future for Women following GDM

- Longitudinal studies > 5 years 20% - 65% develop type 2 DM
- 17% - 42% develop IGT (pre-diabetes)
- Severity of GDM (insulin use) correlates with subsequent Diagnosis type 2 DM
- The earlier the diagnosis of GDM – the sooner the progression to type 2
- OGTT at 6 – 12 weeks post partum recommended

Strehlow & Mestman. 2005. Prevention of T2 DM in Women with a Previous History of GDM. Current Diabetes Reports. 5:272 - 277
The Future for the Infant!
“The fetal growth curve”

- Barker Hypothesis - suggests:
  - low birth weight predicts subsequent physiological disturbances in adult life
  - Intrauterine growth restricted infants have been reported at risk for hypertension, type 2 DM, impaired glucose tolerance and insulin resistance.

- Pedersen Hypothesis - suggests LGA infants are also at risk.

- Lowest risk between 3000 - 4000 g

Jovanovic L. 2004 Diabetes Care
Cape York and Torres Strait Island Diabetes in Pregnancy Project

Purpose:
To improve maternal and infant outcomes for women with diabetes during pregnancy living in rural and remote areas of Cape York & Torres Strait Islands
Objectives

- To implement a universal GDM screening protocol
- To implement GDM/DiP management guidelines
- To complete chart audit
- To develop GDM care plan and recall system (FERRET)
- To collect routine pregnancy data (FERRET / eVici)
- To provide workshops for doctors/nurses/midwives & health workers in screening and management of GDM/DiP
- To develop service provider/client education package
Key Performance Indicators

- Number of women screened for GDM
- Number of women requiring insulin therapy during pregnancy
- Maternal and neonatal outcomes – ADILPS criteria
- Postpartum OGTT follow-up
- Number of health providers completing DIP workshops
- Assessment of knowledge attainment by health providers pre and post workshop
Development of Educational Resources for Indigenous Women
# AUDIT Outcomes

<table>
<thead>
<tr>
<th></th>
<th>TSI</th>
<th>Cape York</th>
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</thead>
<tbody>
<tr>
<td><strong>No. of Women screened (%)</strong></td>
<td>86</td>
<td>99</td>
</tr>
<tr>
<td><strong>GDM &amp; DIP (%)</strong></td>
<td>4.3</td>
<td>13.3</td>
</tr>
<tr>
<td><strong>GDM (%)</strong></td>
<td>3.5</td>
<td>8.7</td>
</tr>
<tr>
<td><strong>Type 2 (%)</strong></td>
<td>0.8</td>
<td>4.6</td>
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## Maternal Outcomes

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<tr>
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<tbody>
<tr>
<td>Age (yrs)</td>
<td>33</td>
<td>32</td>
<td>33</td>
<td>29</td>
</tr>
<tr>
<td>Parity (n)</td>
<td>4.5</td>
<td>2.2</td>
<td>1.8</td>
<td>1.9</td>
</tr>
<tr>
<td>Booking Wt (kg)</td>
<td>94</td>
<td>90</td>
<td>87</td>
<td>71</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>29</td>
<td>25</td>
<td>15</td>
<td>42</td>
</tr>
<tr>
<td>Alcohol (%)</td>
<td>0</td>
<td>5</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Previous miscarriage (%)</td>
<td>56</td>
<td>44</td>
<td>15</td>
<td>12.5</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>18</td>
<td>29</td>
<td>61</td>
<td>25</td>
</tr>
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</table>
## Insulin use in pregnancy

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</thead>
<tbody>
<tr>
<td><strong>GDM Insulin</strong>&lt;br&gt;Use no. (%)</td>
<td>0/9 (0)</td>
<td>7/16 (44)</td>
<td>5/12 (42)</td>
<td>17/29 (58)</td>
</tr>
<tr>
<td><strong>Type 2 DIP</strong>&lt;br&gt;Insulin Use no. (%)</td>
<td>2/2 (100)</td>
<td>8/9 (88)</td>
<td>1/3 (33)</td>
<td>4/5 (80)</td>
</tr>
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</table>
## Neonatal Outcomes

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</thead>
<tbody>
<tr>
<td>Gestation at delivery (wks)</td>
<td>39</td>
<td>39</td>
<td>37</td>
<td>38</td>
</tr>
<tr>
<td>Birth wt (gms)</td>
<td>4014</td>
<td>3650</td>
<td>3259</td>
<td>3323</td>
</tr>
<tr>
<td>C-section (%)</td>
<td>18</td>
<td>48</td>
<td>50</td>
<td>44</td>
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</table>
# Neonatal Outcomes

<table>
<thead>
<tr>
<th></th>
<th>TSI</th>
<th>Cape York</th>
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</thead>
<tbody>
<tr>
<td>Hypoglycaemia (%)</td>
<td>25</td>
<td>45</td>
</tr>
<tr>
<td>Respiratory distress (%)</td>
<td>22</td>
<td>14</td>
</tr>
<tr>
<td>Congenital Malformation (%)</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Stillbirth (no.)</td>
<td>0</td>
<td>0</td>
</tr>
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## Post Partum Follow-up

<table>
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<tr>
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<th>Cape York</th>
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</thead>
<tbody>
<tr>
<td>% of GDM women followed up post partum</td>
<td>2/9</td>
<td>10/16</td>
</tr>
<tr>
<td></td>
<td>22%</td>
<td>62%</td>
</tr>
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</table>
## Patient Information & Recall System (FERRET)

<table>
<thead>
<tr>
<th></th>
<th>TSI</th>
<th>Cape York</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>2006</td>
<td>2008</td>
</tr>
<tr>
<td>GDM Care Plan</td>
<td>47%</td>
<td>52%</td>
</tr>
<tr>
<td>GDM Follow-up Plan</td>
<td>6%</td>
<td>13%</td>
</tr>
<tr>
<td>Type 2 Diabetes Care Plan</td>
<td>55%</td>
<td>80%</td>
</tr>
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</table>
Sustainability

- Staff in rural and remote centres educated in GDM/DIP screening and management guidelines – PCCM, CDM

- Combined telehealth sessions with Integrated Women’s Health Unit CBH, Diabetes Centre and Cape York and Torres Strait Health Centres for client consultation and staff education

- Finalisation and dissemination of educational resources
  Funding sought & gained for printing of more resources

- Additional FTEs for a diabetes midwifery educator and dietitian for Cairns Diabetes Centre

- Development of a midwifery led GDM clinic

- Telehealth case conference / client consult sessions
Conclusions

- Diabetes and pregnancy = high risk pregnancy
- Need multidisciplinary team input for management
- Diabetes in pregnancy/GDM more difficult to manage in rural and remote communities
- Staff turnover great in these areas
- Need standard guidelines
- R & R communities need links with tertiary centre - telehealth
- Need better systems for follow-up
Thank You

Questions?