Treatment of Gestational DM and DM in Pregnancy

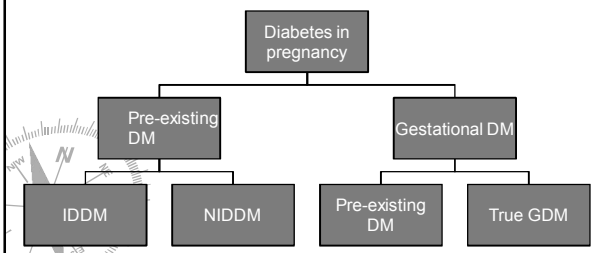
Physiological changes

- Fasting glucose levels decreased
- Serum levels increased after a meal.
- Doubling of insulin production
- Anti–insulin hormones:
  - Human placental lactogen
  - Glucagon
  - Cortisol

Physiological changes

- Renal tubular threshold decrease
- In normal pregnancy starvation leads to a breakdown of triglyceride, this leads to liberation of fatty acids and ketone bodies.

Classification in pregnancy



Pre-gestational Diabetes

Pre-gestational Diabetes

- Complicates about 0.2 to 0.5% of pregnancies
  - 35% type 1 DM
  - 65% type 2 DM
- Becomes more prominent due to delayed age of child bearing
- Problem: effects of high blood glucose starts at conception and implantation, this continue until the postpartum period

Effect of pregnancy on pre-existing DM

- Increase need of Insulin
- Deterioration of nephropathy
- 2 fold increased risk of deterioration in retinopathy
- Hypoglycaemia more common
- Women with autonomic neuropathy experience deterioration of their symptoms.

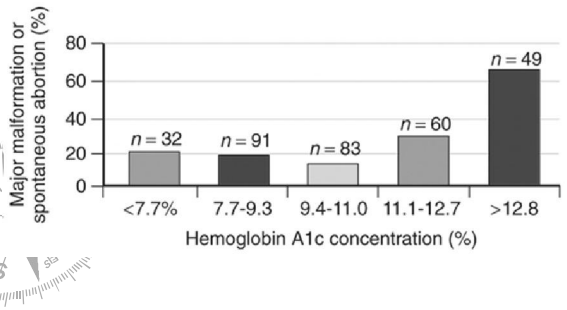
Effect of DM on pregnancy:

- Increased risk of miscarriage
- Increased risk of pre-eclampsia (1% increase in HbA1C cause a 60% increase in risk of PET)
- DM nephropathy associated with normochromic normocytic anemia, severe oedema and proteinuria.
- Increased c/section rate
- Increased risk of infection.

Effects on Fetal Development

- Effects of poor glycaemic control in first trimester:
  - Increased risk of spontaneous abortion
  - Increased risk of congenital abnormalities
  - Growth restriction
- Because women frequently do not know they are pregnant during fetal organogenesis, they must be counseled before pregnancy and optimal glycaemic control must be achieved

Glycaemic control vs. risk of fetal abnormalities and abortion



Risk for congenital abnormalities

Anomaly	Ratios of incidence compared with control population
Caudal regression	252
Spina bifida, hydrocephalus, or other CNS defect	2
Anencephalus	3
Heart anomalies (includes septal defects and transposition of the great vessels)	4
Anal or rectal atresia	3
Renal anomalies	5
Agenesis	6
Cystic kidney	4
Ureter duplex	23
Situs inversus	84

Effects on Fetal Development

- During the second and third trimesters the most common abnormalities in the fetus are stillbirth and Macrosomia

Maternal Risks (1)

- Patients with uncontrolled pre-gestational diabetes are at increased risk of progression of diabetic vasculopathy
- Diabetes In Early Pregnancy study
- Retinopathy:
  - Preexisting no retinopathy – 10% progressed
  - Preexisting mild retinopathy – 22% progressed
  - Preexisting severe retinopathy – 55% progressed

Chew EY Diabetes Care 1995; 18: 631

Maternal Risks (2)

- Risk factors identified for progression of retinopathy during pregnancy:
  - Baseline retinopathy
  - Elevated HbA1c at conception
  - Elevated HbA1c followed by rapid normalization of blood glucose
  - Diabetes longer than 6 years
  - Proteinuria
- Patients planning pregnancy with severe pre-proliferative or proliferative retinopathy should receive laser photocoagulation

Maternal Risks (3)

- Pregnancy does not increase the risk of future nephropathy and does not adversely affect the fetus, unless kidney function is impaired before pregnancy
- Creatinine clearance usually increase in normal pregnant women. 30% diabetic patients with nephropathy CC declines and 30% does not show the increase in CC expected

Maternal Risks (4)

- Patients with proteinuria before pregnancy, this may progress significantly during pregnancy.
- First trimester proteinuria > 250g / 24h is linked to third trimester nephrotic syndrome
- Proteinuria should be measured pre-pregnancy to prognosticate risk.
- Be aware of hypertension: results in intrauterine growth retardation and fetal demise

Reece EA. Am J Obstet Gynecol 1988; 159: 56

Contra indications for pregnancy:

- Ischaemic heart disease
- Untreated proliferative retinopathy
- Severe gastroparesis
- Severe renal impairment

Gestational Diabetes

Gestational diabetes mellitus:

- Definition: National Diabetes Data Group (1985)
  - Carbohydrate intolerance of variable severity with onset or first recognition during the present pregnancy.

Clinical features:

- Asymptomatic and develop in the 2nd or 3rd trimester
- More commonly diagnosed in women:
  - A family history of DM
  - Previous large-for-gestational-age infants
  - Obesity
  - Advanced maternal age
  - Certain ethnic groups

Importance of GDM:

- Women dx with GDM at increased risk for type 2 DM
- Some women have pre-existing DM
- GDM is associated with adverse pregnancy outcome

Diagnosis of Diabetes Mellitus !!!!Confusion!!!!

Organization	*Glucose load for OGTT*	*Time (mmol/l)*			
		Fasting	1h	2h	3h
NDDG	100g	5.8	10.6	9.2	8.1
ADA	100g or 75g	5.3	10	8.6	7.8
WHO	75g	7.8		11.1	
ISGGDM	75g	>5.1	>10	>8.5	

NDDG – National Diabetes Data Group

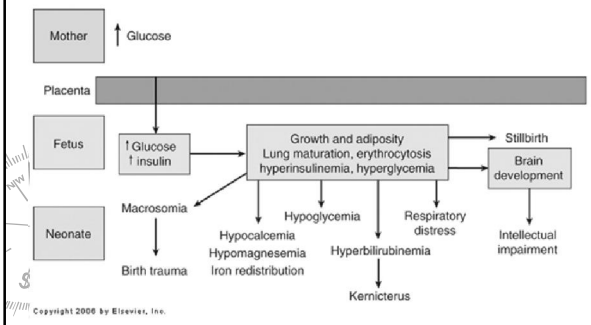
Diagnosis of GDM

- The criteria for the diagnosis of diabetes (OGTT)
  - Fasting>5.1 mmol/L or
  - 1-h PG >10mmol/L or
  - 2-h PG >8.5 mmol/L

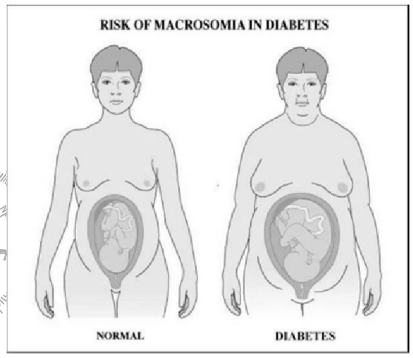
Fetal complications of DM

- Increased neonatal mortality
- Increased perinatal mortality
- Macrosomia
- Late stillbirth
- Premature delivery
- Neonatal hypoglycaemia
- Polycytheamia
- Jaundice

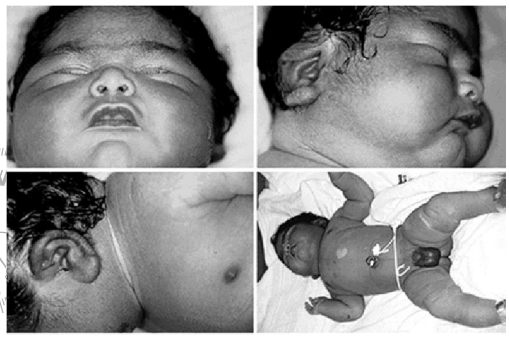
Pederson Hypothesis



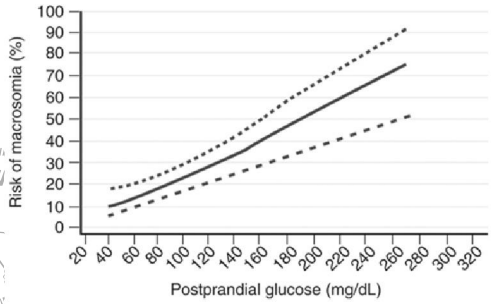
Macrosomia



Macrosomia



Macrosomia



mmol/L = mg/dl ÷ 18

Screening:

Clinical risk factors:

- Previous GDM
- Family history of DM
- Previous macrosomic baby
- Previous unexplained stillbirths
- Obesity
- Glycosuria
- Polyhydramnios
- Large-for-gestational-age infants
- Certain ethnic groups.

Why Treat?

Women with mild GDM:

fasting glucose < 7.8 mmol/l and

2 h post prandial glucose of 7.8 – 11.1 mmol/l

Results:

- Less perinatal infant complications in treatment group (1 vs 4%).
- Less macrosomia (10 vs 29%)
- Higher rate of neonatal ICU admissions (71 vs 61%)
- No difference in CS rate (31 vs 32%)
- Higher rate of labour induction (39 vs 29%)
- No difference in neonatal metabolic complications

2005 NEJM Growther CA et al:

Three Pillars of Treatment

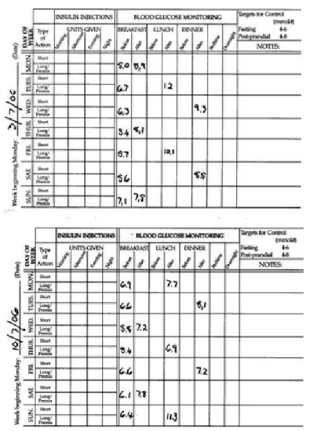
- Nutritional therapy
- Glucose monitoring
- Medical therapy

Nutritional Therapy

- All patients should receive nutritional counseling
- Aims:
  - Achieve normoglycaemia
  - Prevent ketosis
  - Provide for adequate weight gain
  - Contribute to fetal well being

Glucose Monitoring

- Patients with GDM should monitor and keep diary of measurements
  - Facilitates recognition of patterns
- When to monitor is still uncertain:
  - Consensus on measurement upon awakening in morning
  - Before / 1h after / 2h after meals uncertain



Targets!

	Fasting	***Post-prandial***
American College of O & G	5.3	1h: 7.2 – 7.8 2h: 6.7
American Diabetes Association	5.8	1h: 8.6 2h: 7.2

Note: Numerous other targets are suggested

HbA1c

- Should be measured more frequently in pregnancy
  - To check accuracy of self monitoring
  - Track trends
- Aim for a HbA1c of <5%
  - Increase in RBC formation in pregnancy, thus increased volume of RBC's and smaller fraction of glycated HB

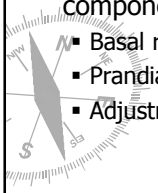
Normal non-pregnant: 4 – 6% normal pregnant: 4 – 5%

Medical Therapy

- When glycaemic control cannot be achieved with nutritional therapy alone
- 2 Options:
  - Insulin
  - Oral agents

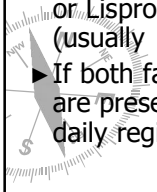
Insulin

- Dose varies and need to be adjusted for each individual (The majority of cases will control on between 50 and 90 U/d)
- All insulin regimens consist of Three components:
  - Basal requirements
  - Prandial requirements
  - Adjustments



Insulin

- If fasting hyperglycaemia start with intermediate acting NPH insulin before bedtime (usual starting dose 0.2 u/kg/d)
- Post prandial hyperglycaemia start regular or Lispro or Aspart insulin before meals (usually 1 – 1.5 U/10g meal carbohydrates)
- If both fasting and prandial hyperglycaemia are present start on a basal bolus or twice daily regimen



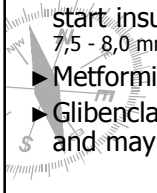
Oral Agents

- Increase in the prevalence of GDM makes use of oral agents more attractive
- Metformin is safe in pregnancy (MiG trial)
- There are currently evidence accumulating towards the use of certain sulphonylureas (Glibenclamide) during pregnancy.

Diabetic Medicine 2006; 23: 223

Management summary:

- Diet advice the same as for DM
- Obese women get a calorie reduced diet
- Home glucose monitoring
- Persistent hyperglycaemia an indication to start insulin. Fasting > 5,5 mmol/l or post prandial > 7,5 - 8,0 mmol/l
- Metformin safe
- Glibenclamide does not cross the placenta and may be an alternative

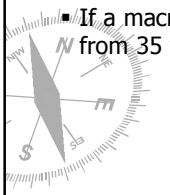


Obstetric Management:

- Early dating scan
- 11 - 14 weeks nuchal translucency scan
- 20 – 22 weeks detail anatomy scan
- Regular growth scans in the 3rd trimester
- Pregnancies not allowed to continue past 40 weeks

Obstetric management:

- Kalafong protocol:
  - If not macrosomic and good control:
    - Deliver at 38 weeks and if not confirm at 38 weeks with a positive PG
  - If a macrosomic fetus or poor control do PG from 35 weeks and deliver if mature

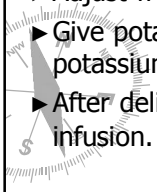


Intrapartum management:

- Women on oral or with low insulin dose, do not need continuous insulin therapy.
- Women with large insulin needs continuous - insulin therapy.
- Women with GDM require a formal OGTT 6 weeks after delivery

Intrapartum management:

- IV dextrose infusion 500ml/8hr with short acting insulin and aim for capillary glucose of 5-8mmol/l
- Adjust frequently according to control.
- Give potassium replacement or check potassium regularly.
- After delivery of the placenta half the insulin infusion.



Summary

- Diabetes are becoming more common, also during pregnancy
- Management should be aggressive to prevent maternal and fetal complications
- Diagnosis and targets levels are uncertain
- Oral agents are becoming more fashionable during pregnancy