Diabetes Type 2, Diagnosis Pathogenesis

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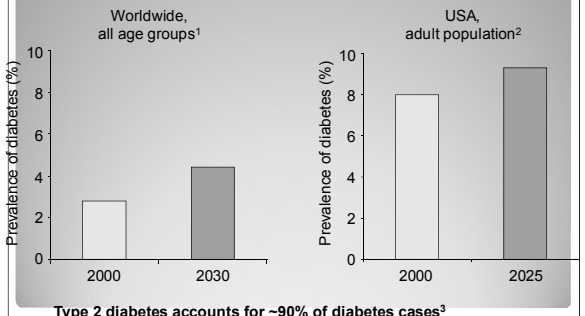
Prevalence of type 2 diabetes in different South African population groups:

Population	Region (number of participants)	Prevalence (%)	Age range (years)	Reference
African	Cape Town, urban (729)	8.0	30 +	Diabet Care 1993;16:601
African	QwaQwa, rural (853)	4.8	25 +	S Afr Med J 1995;85:90
	Mangaung, urban (758)	6.0		
African	Durban, urban (479)	5.3	15 +	S Afr Med J 1993;83:641
Coloured	Cape Town, urban (200)	28.7	65 +	S Afr Med J 1997;87 (suppl 3):364
Coloured	Cape Town, peri-urban (974)	10.8	15 - 86	Diabet Med 1999;16:946
European	Durban, urban (396)	3.0	15 - 69	S Afr Med J 1994;84:257
Indian	Durban, urban (2479)	13.0	15 +	Diabet Care 1994;17:70

Prevalence of Diabetes

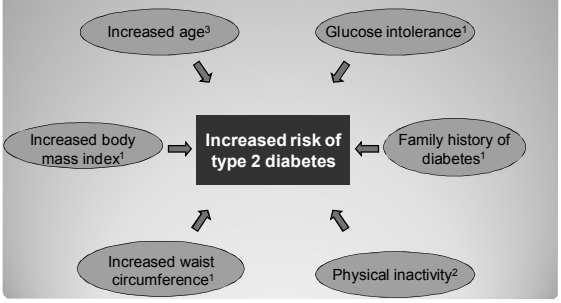
Type 2 diabetes is a growing epidemic



Type 2 diabetes accounts for ~90% of diabetes cases[3]

[1]Wild S, et al. Diabetes Care 2004; 27: 1047–53.
[2]International Diabetes Federation. http://www.eatlas.idf.org/Prevalence/index.cfm?data=table&tableId=16. Accessed November 23, 2005.
[3]World Health Organization. http://www.who.int/mediacentre/factsheets/fs138/en/index.html Accessed October 27, 2005.

Risk factors for type 2 diabetes



[1]Ohlson LO, et al. Diabetologia 1988; 31: 798–805.
[2]Manson JE, et al. Lancet 1991; 338: 774–8.
[3]Wild S, et al. Diabetes Care 2004; 27: 1047–53.

Diagnosis

Diagnostic Criteria for DM2

Fasting plasma glucose (FPG)	≥ 7.0 mmol/l[a]
or	
2-h plasma glucose (2PG) OGTT[b]	≥ 11.1 mmol/l during
or	
HbA1c	≥ 6.5%[c]
or	
Random plasma glucose (RPG) if classic symptoms or hyperglycaemic crisis[d]	≥ 11.1 mmol/l

[a]In the absence of unequivocal hyperglycaemia (and in asymptomatic individuals), criteria a-c should be confirmed by repeat testing (on another day) preferably by the same test.
The classic symptoms of diabetes include polyuria, polydipsia and weight loss.
[a] Fasting is defined as no caloric intake for at least 8hr.
[b] The test should be performed as described by the World Health Organisation using a glucose load containing the equivalent of 75-g anhydrous glucose dissolve in 250ml water ingested over 5 minutes.
[c] Provided that the test method meets stringent quality assurance criteria, the assay is standardized to criteria aligned to the international reference values (NGSP certified and standardized to the DCCT assay), and that there are no conditions present which preclude its accurate measurement (Appendix2 and 3).
[d] Random (casual) is defined as anytime of day without regard to time of last meal. The classic symptoms of hyperglycaemia include polyuria, polydipsia and weight loss).
Hyperglycaemic crisis refers to diabetic ketoacidosis or hyperosmolar non-ketotic hyperglycaemia.

Classification of Diabetes

Type 1

- Destruction of beta cells
  - Autoimmune (ICA, anti-GAD, anti-Insulin)
  - Idiopathic
- Absolute deficiency of insulin
- Not all patients with late onset of diabetes have type 2 diabetes

Type 2

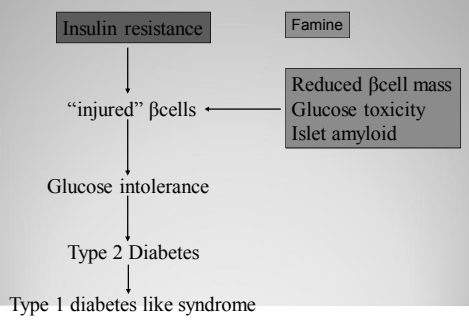
- Variable degrees of insulin deficiency and resistance
- No specific test for type 2 diabetes
- Keto-acidosis does not exclude type 2 diabetes

Classification of Diabetes (cont)

- Genetic defects of beta-cell function or insulin action
- Diseases of the pancreas
- Endocrinopathies
- Drug or chemical induced
- Infections
- Genetic syndrome associated
- Gestational

Pathogenesis

Pathogenesis of DM2



Type 2 diabetes is a chronic, progressive disease

- Glycaemic control typically shows gradual deterioration[1]
- Combination therapy and/or exogenous insulin is frequently required, even if the initial response to monotherapy is good
- Early use of combination therapy may be advantageous[2]

[1]Turner RC, et al. JAMA 1999; 281: 2005–12.
[2]Canadian Diabetes Association. Can J Diabetes 2003; 27(Suppl 2): S1–152.

- Inheritance thought to be polygenetic
- Due to strong association with obesity it is believed that genes predisposing to obesity are associated with DM2 as well
- A strong interplay between genetic and environmental factors exist in the development of diabetes

Genetics of Type 2 Diabetes

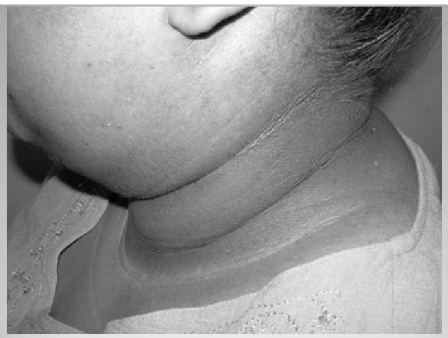
- Familial clustering suggests strong genetic component
- Monozycotic twins have 60 – 90% concordance
- Risk of developing DM2 in siblings of a diabetic patient is 10 – 33% vs. 5% for general population
- Offspring of a woman with DM2 have a 2 to 3 times higher risk than that of men

Genetics of Type 2 Diabetes

- Constellation of abnormalities often seen together:
  - Hyperinsulinaemia
  - Impaired glucose tolerance
  - Hypertension
  - Increased plasma TGs
  - Decreased HDL cholesterol
  - Truncal obesity
- Indicates an increased risk for DM2 and atherosclerotic disease

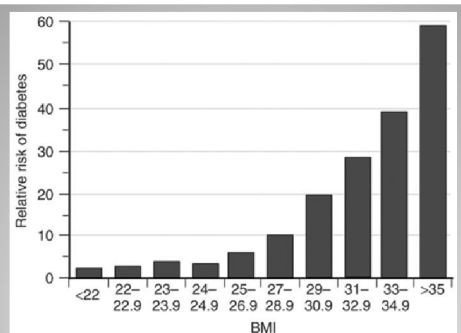
Insulin Resistance Syndrome

(Syndrome X, Reaven's Syndrome, Metabolic Syndrome)



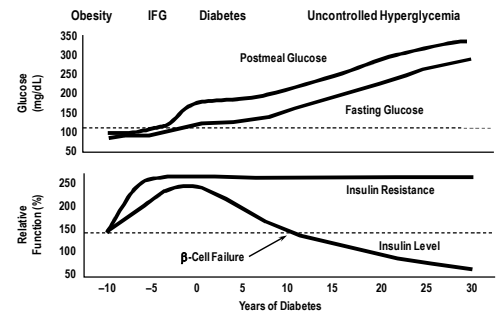
Acanthosis Nigricans

Abdominal Obesity



Risk of Diabetes in Obesity

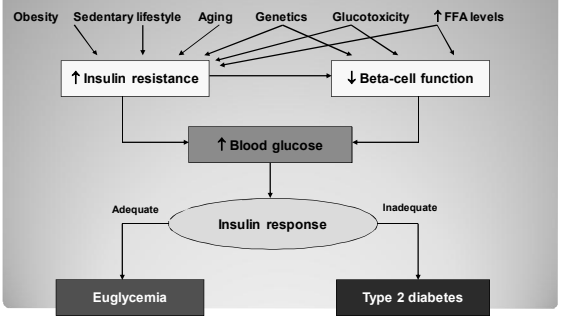
Progression of Type 2 Diabetes



IFG = impaired fasting glucose

Graph adapted from International Diabetes Center (IDC), Minneapolis, Minnesota.

Pathophysiology of Type 2 Diabetes



The Laboratory in Diagnosis and Control of Diabetes Mellitus

Diagnostic

OGTT
Fasting blood glucose

Assessment of Glycaemic Control

Random blood glucose
HbA_1C
Fructosamine

Lab tests in Diabetes Mellitus

- Indications
  - Diagnosis when Blood glucose values are equivocal
  - Diagnosis during pregnancy
  - Epidemiological setting to screen for DM and IGT
- Precautions
  - Preceding 3 days of unrestricted diet and usual exercise
  - Overnight fast of 8 –14 h
  - Smoking not permitted during test

OGT Test

- Method
  - Collect fasting blood sample
  - Drink 75 g glucose in 250 ml water over 5 min
  - Children 1.75 g glucose per kg body weight
  - Blood samples to be collected 2 h after glucose load
- If glucose determination cannot be done immediately the sample should be collected in a tube containing sodium fluoride

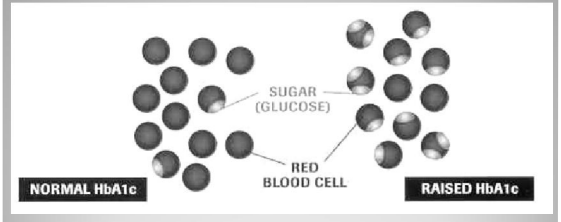
OGT Test (Cont)

- SMBG (Self monitoring of blood glucose) - recommended
- Lab glucose or finger prick glucose done at the clinic – not recommended any more

Random Blood Glucose

- Urine glucose testing are not recommended any more and have been replaced by SMBG
- Urine ketones or blood ketones – essential to test for in type 1 diabetic patients. The presence of ketones indicate impending keto-acidosis
  - Indicated in acutely ill patients or when the blood glucose is consistently higher than 16.7 mmol/l

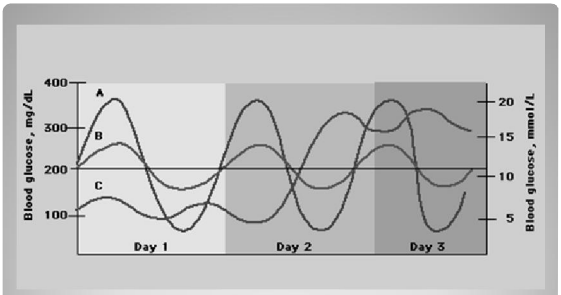
Urine Tests



HbA_1C

Factors influencing HbA1c

Erythropoiesis • Increased HbA1c: iron, vitamin B12 deficiency, decreased erythropoiesis. • Decreased HbA1c: administration of erythropoietin, iron, vitamin B12, reticulocytosis, chronic liver disease.
Altered haemoglobin • Genetic or chemical alterations in haemoglobin: haemoglobinopathies, HbF, methaemoglobin, may increase or decrease HbA1c
Glycation • Increased HbA1c: alcoholism, chronic renal failure, decreased intra erythrocyte pH. • Decreased HbA1c: aspirin, vitamin C and E, certain haemoglobinopathies, increased intra-erythrocyte pH. • Variable HbA1c: genetic determinants.
Erythrocyte destruction • Increased HbA1c: increased erythrocyte life span: splenectomy • Decreased A1c: decreased erythrocyte life span: haemoglobinopathies, splenomegaly, rheumatoid arthritis or drugs such as antiretrovirals, ribavirin and dapsone.
Assays • Increased HbA1c: hyperbilirubinaemia, carbamylated haemoglobin, alcoholism, large doses of aspirin, chronic opiate use. • Variable HbA_{1c}: haemoglobinopathies. • Decreased HbA_{1c}: hypertriglyceridaemia.



Glucose Fluctuations with the Same HbA1c Level

- Monitoring of glycaemic control in diabetic patients
  - <7% Good control
  - 7 – 10% Fair control
  - 13 – 17% Poor control
- When the mean annual HBA1C is < 1.1 X ULN, renal and retinal complications are rare, But complications occur in > 70% of cases if the annual HbA1c is > 1.7 X ULN

HbA_1C use

- May rise within 1 week if glucose is high, but may take 2 – 4 weeks to fall after the glucose is controlled
- The 30 days before test contributes ~ 50% of the glycated Hb and that 90 – 120 days before ~ 10%
- An 1% increase or decrease of HbA1C relates to an average blood glucose change of 1.6 mmol/l

HbA_1C Test