Diabetes Type 2, Diagnosis Pathogenesis
DG van Zyl

Prevalence of diabetes (%)

2000 2020

Risk factors for type 2 diabetes

Increased age
Glucose intolerance
Increased body mass index
Increased waist circumference
Physical inactivity

Diagnostic Criteria for DM2

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

*In the absence of unequivocal hyperglycaemia in a symptomatic individual a diagnosis can be confirmed by typical symptoms plus a random plasma glucose ≥ 11.1 mmol/l or a 2-h plasma glucose ≥ 11.1 mmol/l. Diagnosis should be confirmed by repeat testing (at least 2 days later). This is important because fasting blood sugars ≤ 7.8 mmol/l may be seen in some people on a single occasion with intact glucose tolerance despite potential diabetes. This applies to other diagnostic tests, including HbA1c and OGTT.

Diabetes Type 2 is a growing epidemic
Prevalence of diabetes (%)

Worldwide, all age groups
USA, adult population

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**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)**

**Pathogenesis**

**Insulin resistance**

“injured” β-cells ➔ Reduced β-cells mass
Glucose toxicity
Islet amyloid

**Type 2 Diabetes**

**Famine**

**Type 1 diabetes like syndrome**

**Type 2 diabetes is a chronic, progressive disease**
- Glycaemic control typically shows gradual deterioration
- 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

**Pathogenesis of DM2**

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

**Genetics of Type 2 Diabetes**

- 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
- Monozygotic 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

Insulin Resistance Syndrome
(Syndrome X, Reaven’s Syndrome, Metabolic Syndrome)

- 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

Acanthosis Nigricans

Abdominal Obesity

Risk of Diabetes in Obesity

Progression of Type 2 Diabetes

Graph adapted from International Diabetes Center (IDC), Minneapolis, Minnesota.
Pathophysiology of Type 2 Diabetes

- Obesity
- Sedentary lifestyle
- Aging
- Genetics
- Glucotoxicity
- FFA levels

↑ Insulin resistance
↓ Beta-cell function
↓ Blood glucose

Euglycemia
Type 2 diabetes

The Laboratory in Diagnosis and Control of Diabetes Mellitus

Diagnostic
OGTT
Fasting blood glucose

Assessment of Glycaemic Control
Random blood glucose
HbA1C
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 (Cont)

- 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

Random Blood Glucose

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

- 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

HbA₁C

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: ascorbic acid, vitamin C and E, certain haemoglobinopathies, increased intra-erythrocyte pH.
- Variants HbA₁c: genetic determinants.

Erythrocyte destruction
- Increased HbA₁c: increased erythrocyte life span: splenectomy
- Decreased HbA₁c: decreased erythrocyte life span: haemoglobinopathies, splenomegaly, rheumatoid arthritis or drugs such as anticoagulants, thiazides and nitrates.

Assays
- Increased HbA₁c: hyperbilirubinaemia, carbamylated haemoglobin, alcoholism, large doses of aspirin, chronic gout.
- Decreased HbA₁c: haemoglobinopathies.
- Variable HbA₁c: genetic determinants.

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

Glucose Fluctuations with the Same HbA₁c Level

HbA₁C Test

- 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