Definition, Classification and Diagnosis of Diabetes Mellitus

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Definition

Diabetes mellitus is a general term for heterogeneous disturbances of metabolism for which the main finding is chronic hyperglycaemia. The cause is either impaired insulin secretion or impaired insulin action or both.

Classification

Type 1 Diabetes

- β-cell destruction which leads to absolute insulin deficiency
- Usually mediated by immune mechanisms
- LADA (latent autoimmune diabetes in adults) is classified as type 1 diabetes.

Type 2 Diabetes

- Can range from predominant insulin resistance with relative insulin deficiency to prevailing defective secretion with insulin resistance.
- Is frequently associated with other problems of the so-called metabolic syndrome

Other Specific Diabetes Types

- Diseases of the exocrine pancreas (e. g. pancreatitis, cystic fibrosis, hemochromatosis)
- Endocrinopathies (e. g. Cushing syndrome, acromegaly, pheochromocytoma)
- Drug induced (e. g. glucocorticoids, neuroleptics, alpha-interferons, pentamidine)
- Genetic defects of the β-cell function (e. g. MODY forms)
- Genetic defects of insulin action
- Other genetic syndromes which can be associated with diabetes
- Infections
- Rare forms of auto-immune mediated diabetes

Gestational Diabetes

Glucose tolerance impairments that first appear or are first diagnosed during pregnancy.

Diagnostic Criteria

Important

Only standardised, quality assured laboratory methods may be applied when venous plasma glucose and HbA1c are measured. The current gold standard for diagnosing diabetes is measurement of glucose in venous plasma. This measurement can be accurate only if glycolysis is inhibited in the blood sample as soon as the sample is drawn. This can be done in two ways. Either the blood tube is stored on ice and the blood is centrifuged within 30 minutes, or glycolysis in the tube is effectively inhibited by appropriate additives (citrate plus fluoride; fluoride by itself is not sufficient). The glucose levels stated in the practice guidelines apply to venous plasma. (These levels correspond to the recommendations of the *Deutsche Gesellschaft für Klinische Chemie und Laboratoriumsmedizin* (DGKL) and the *Deutsche Diabetes Gesellschaft* (DDG)).

Diabetes Mellitus

- HbA1c ≥ 6.5 % (≥ 48 mmol/mol)
- Random plasma glucose ≥ 200 mg/dl (≥ 11.1 mmol/l)
- Fasting plasma glucose ≥ 126 mg/dl (≥ 7.0 mmol/dl)
- OGTT 2-hour glucose in venous plasma ≥ 200 mg/dl (≥ 11.1 mmol/l)

These guidelines have been recommending the use of HbA1c for diagnosing diabetes since 2010. This became possible through international standardisation of the measurement method. On the other hand, epidemiological investigations in recent years have shown that the specificity of HbA1c

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Bibliography
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≥ 6.5 % is high enough to justify a diagnosis of diabetes and the sensitivity of HbA1c < 5.7 % is high enough to justify exclusion of a diagnosis of diabetes. For these reasons, HbA1c is suitable as a primary diagnostic tool for excluding diabetes with great certainty and for making a diagnosis of diabetes in some cases. When the HbA1c level lies between 5.7 and 6.4 %, these guidelines recommend that diabetes and prediabetes be diagnosed by measuring glucose in accordance with traditional criteria. See **Fig. 1, 2** in the annex for the recommended diagnostic approach. The HbA1c level cannot be applied to making a diagnosis if an inaccurate HbA1c level is to be expected due to any of the factors stated in **Table 2**.

See **Table 4** for details on OGTT and **Table 1** for differential diagnostic criteria for type 1 and type 2 diabetes.

Impaired Fasting Glucose

IFG for fasting glucose levels from 100-125 mg/dl (5.6 mmol-6.9 mmol/l) in venous plasma.

Impaired Glucose Tolerance

IGT for 2-hour plasma glucose in the OGIT in the range of 140-199 mg/dl (7.8-11.0 mmol/l) with fasting glucose < 126 mg/dl (< 7.0 mmol/l).

Gestational Diabetes

The OGTT diagnostic criteria given in **Table 3** are based on the recently published results of the HAPO study. The differences to the previous borderline values are small, but but now gestational diabetes is indicated if any one (rather than at least two) of these values is exceeded.

Annex

Table 1 Differential Diagnostic Criteria for Type 1 and Type 2 Diabetes.

	Type 1 Diabetes*	Type 2 Diabetes
Manifestation age	Mostly children, adolescents and young adults	Mostly middle and old age
Onset	Acute to subacute	Usually gradual
Symptoms	Frequently polyuria, polydipsia, weight loss, fatigue	Frequently no complaints
Body weight	Usually normal	Usually overweight
Predisposition to ketosis	Pronounced	None or only slight
Insulin secretion	Reduced or none	Below normal to high, qualitatively always impaired
Insulin resistance	None (or only low)	Often pronounced
Frequency in patient's family history	Usually negative	Typically positive
Concordance with identical twins	30 to 50 %	Over 50 %
Heredity	Multifactorial (polygenetic)	Multifactorial (most likely polygenetic, but genetic heterogeneity is possible)
Associated with HLA (leukocyte antigen) system	Present	Not present
Antibodies associated with diabetes	Approx. 90-95 % at onset (GAD, ICA, IA-2, IAA)	None
Metabolism	Unstable	Stable
Response to insulin secretion stimulating antidiabetics	Usually none	Usually good at first
Insulin therapy	Required	Usually not required until insulin secretion has decreased after years of disease

* The LADA (latent autoimmune diabetes of adults) is associated with slower loss of beta cell function. Rapid failure of oral antidiabetics is to be expected. Analysis of GAD antibodies is recommended for cases of suspicion of LADA.

1.	Haemoglobin variants (HbS, HbE, HbF, HbC, HbD and others) the extent of the distortion depends on the method to determine HbA1c
2.	Conditions with increased or decreased lifetime of the erythrocytes (haemolytic anaemia, iron deficiency anaemia, blood formation in the context of anaemia treatment, liver disease, kidney disease)
3.	Chemical modifications of haemoglobin uraemia (carbamylated Hb), high dosage long-time therapy with acetylsalicylic acid (acetylated Hb)
4.	Inhibition of glycation (e. g. long-time therapy with ascorbic acid or vitamin E) the clinical significance of this phenomenon has not been studied well
5.	Pregnancy

Table 2 Conditions which can lead to an inaccurate measurement of the HbA1c level.

	Venous plasma	
	mg/dl	mmol/l
Fasting	≥ 92	≥ 5.1
60 min.	≥ 180	≥ 10.0
120 min.	≥ 153	≥ 8.5

Table 3 Diagnosis of Gestational Diabetes. Diabetes is present if one or more of the criteria in the table are fulfilled.

Procedure for the 75 g OGTT pursuant to WHO guidelines
Test must be performed in the morning – after 10 – 16 hours abstention from nutrients (and alcohol) – after at least 3 days of a diet rich in carbohydrates (≥ 150 g carbohydrates per day) – while sitting or lying down (no muscular effort), no smoking before or during the test
At time 0 drink 75 g glucose (or equivalent quantity of hydrolysed starch) dissolved in 250 – 300 ml water within 5 minutes. – children 1.75 g/kg body weight (at most 75 g) – take blood samples at times 0 and 120 minutes. – store and process the samples properly.
Test is contraindicated in case of a previous diagnosis of diabetes mellitus, gastric or intestinal resection, any gastrointestinal disease with changed resorption, or any intercurrent disease.

Table 4 Oral Glucose Tolerance Test (OGTT).

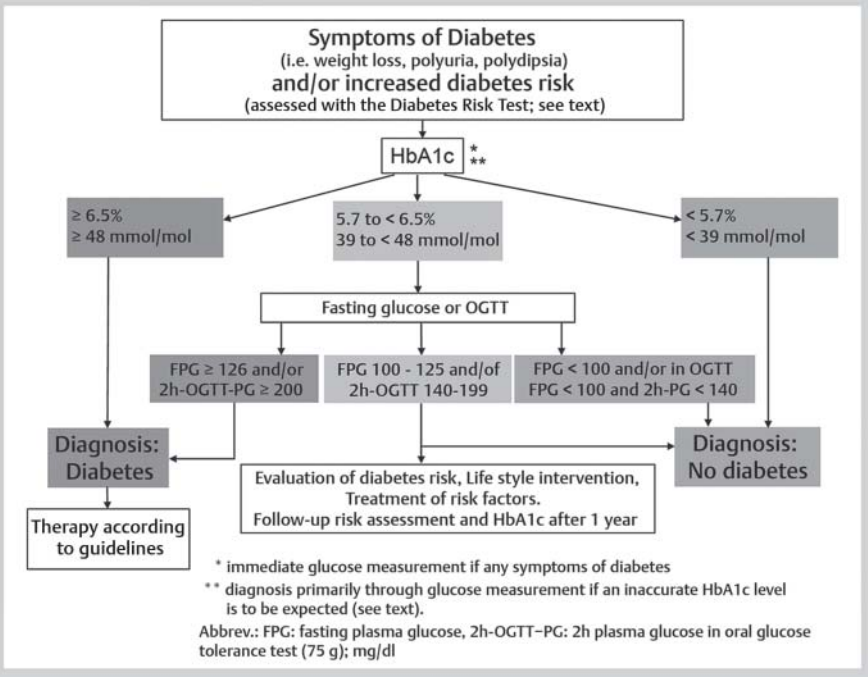

Fig. 1 Diagnostic Flowchart (glucose mg/dl).

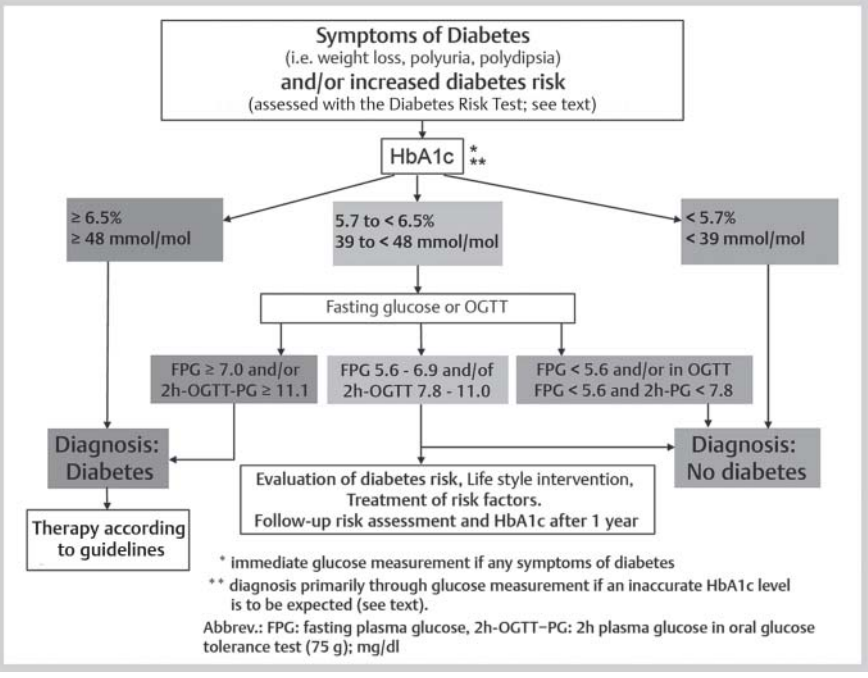

Fig. 2 Diagnostic Flowchart (glucose mmol/l).