A lot of early cases of diabetes are totally asymptomatic. Many people with diabetes will be diagnosed only if health professionals and general public remain alert to the possibility that they may have diabetes. The symptoms and signs of diabetes are summarised in Table 1.

Table 1. Symptoms and Signs of Diabetes

Symptoms
• Increased thirst • Passing a lot of urine, especially at night (may lead to bedwetting in children and incontinence in older people) • Extreme tiredness and lethargy • Weight loss despite increased appetite • Genital itching • Itchy skin rash • Blurred vision • Tingling, pain and numbness in feet, legs or hands • Sore or burning mouth
Signs
• Persistent or recurrent infections, such as skin infections, oral or genital thrush, mouth ulcers and urinary tract infections • Signs of microvascular complications, such as diabetic retinopathy detected by an optometrist during a routine eye check; foot ulcers; loss of sensation in the lower limbs; or impotence • Signs of cardiovascular disease, such as: high blood pressure; manifestations of dyslipidaemia (abnormal blood lipids), such as xanthoma; absent foot pulses

Diabetes can also be identified in general population by using the risk-based approach.

Table 2. Risk-based Screening for Type 2 Diabetes in General Population[1-5]

Who should be screened	What should be done?	How often?
1. Age ≥ 45 years 2. Anyone with any of the following risk factors for type 2 diabetes: ➢ Family history (first-degree relatives) of diabetes ➢ Overweight and obese subjects • BMI 23 to <25 kg/m^2 is classified as overweight and BMI ≥ 25 kg/m^2 is classified as obese for Chinese adults living in Hong Kong. For most Asian adults including Chinese, central obesity is defined as waist circumference of ≥ 90 cm for men and ≥ 80 cm for women. ➢ Previous impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) ➢ Hypertension ➢ Metabolic syndrome ➢ Clinical cardiovascular disease (e.g. coronary heart disease, stroke, peripheral vascular disease) ➢ Presence of other cardiovascular risk factors (e.g. high LDL-C, low HDL or high TG, smoking, physical inactivity)	<u>Fasting plasma glucose (FPG)</u> ● If FPG < 5.6 mmol/L, diabetes is unlikely in low risk subjects ● The diabetic range for FPG is ≥ 7 mmol/L. For asymptomatic person, an additional HbA1c or plasma glucose test result with a value in the diabetic range is required (Note 1) ● If FPG ≥ 5.6 and < 7 mmol/L, a 75 gram oral glucose tolerance test (OGTT) or HbA1c can be considered, particularly if there is high clinical suspicion of diabetes <u>HbA1c (Note 2 and Note 3)</u> ● An HbA1c of 6.5% is recommended as the cut point for diagnosing diabetes. For asymptomatic person, an additional HbA1c or plasma glucose test result with a value in the diabetic range is required (Note 1) ● A value of less than 6.5% does not exclude diabetes diagnosed using glucose tests <u>OGTT (Note 4 and Note 5)</u> ● The diabetic range for 2-hour post-load glucose level is ≥ 11.1	If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing, e.g. every 12 months, depending on initial results and risk status.

➢ Women with history of gestational diabetes mellitus / delivery of a macrosomic baby weighing ≥ 4 kg ➢ Polycystic ovarian syndrome ➢ Long term systemic steroid therapy	mmol/L. For asymptomatic person, an additional HbA1c or plasma glucose test result with a value in the diabetic range is required (Note 1) ● OGTT may be considered when the FPG is 6.1 to 6.9 mmol/L and/or A1C is 6.0% to 6.4%. OGTT may also be considered when the FPG is 5.6 to 6.0 mmol/L and/or A1C is 5.5% to 5.9% and suspicion of type 2 diabetes or IGT is high	

Note 1 For symptomatic cases, FPG ≥ 7 mmol/L or random glucose ≥ 11.1 mmol/L confirms the diagnosis. The American Diabetes Association (ADA) and World Health Organization (WHO) have also adopted HbA1c ≥ 6.5% as a diagnostic criterion. Diagnosis of diabetes in an asymptomatic person should not be made on the basis of a single abnormal plasma glucose or HbA1c value. At least one additional HbA1c or plasma glucose test result with a value in the diabetic range is required. The diagnosis should be made by the best technology available, avoiding blood glucose monitoring metres and single-use HbA1c test kits.

Note 2 The use of HbA1c can avoid the problem of day-to-day variability of glucose values, and importantly it avoids the need for the person to fast and to have preceding dietary preparations. However, HbA1c may be affected by a variety of genetic, haematologic and illness-related factors. Some of the factors that influence HbA1c and its measurement are listed in Table 3.

Note 3 Measurement of HbA1c should be standardized and done in accredited laboratories under Hong Kong Laboratory Accreditation Scheme (HOKLAS) which can be found from the website https://www.itc.gov.hk/en/quality/hkas/conformity_assessment_bodies/hoklas.html.

Note 4 The OGTT should be performed as described by the WHO, using a glucose load containing the equivalent of 75 gram anhydrous glucose dissolved in water.

Note 5 The ADA and WHO have recommended the use of glycated haemoglobin (A1c) to screen and diagnose diabetes (A1c ≥ 6.5% indicating diabetes[2,5] and 5.7-6.4% indicating prediabetes[2]) . While this strategy can mitigate the inconvenience, pre-analytical error and intra-individual variance of 75g OGTT, potential pitfalls can exist, for example in subjects with anaemia and haemoglobinopathy, and these can confound the result interpretations[6].

Table 3. Some of the factors that influence HbA1c and its measurement*
(Adapted from Gallagher et al [7])

1. Erythropoiesis Increased HbA1c: iron or vitamin B12 deficiency, decreased erythropoiesis. Decreased HbA1c: administration of erythropoietin, iron or vitamin B12; reticulocytosis, chronic liver disease.
2. Altered Haemoglobin Genetic or chemical alterations in haemoglobin: haemoglobinopathies, HbF, methaemoglobin, may increase or decrease HbA1c.
3. 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.
4. Erythrocyte destruction Increased HbA1c: increased erythrocyte life span: splenectomy. Decreased HbA1c: decreased erythrocyte life span: haemoglobinopathies, splenomegaly, rheumatoid arthritis or drugs such as antiretrovirals, ribavirin and dapsone.
5. Assays Increased HbA1c: hyperbilirubinaemia, carbamylated haemoglobin, alcoholism, large doses of aspirin, chronic opiate use. Decreased HbA1c: hypertriglyceridaemia. Variable HbA1c: haemoglobinopathies.

* Some of the above interfering factors are “invisible” in certain of the available assays

The diagnostic criteria recommended by the WHO and ADA are summarised in Table 4 and Table 5 respectively for reference.

Table 4. WHO Recommendations for the Diagnostic Criteria for Diabetes and Intermediate Hyperglycaemia [5,8]

Diabetes§	
Fasting plasma glucose **or** 2 hours plasma glucose* **or** HbA1c#	≥7.0mmol/L (126mg/dL) ≥11.1mmol/L (200mg/dL) ≥6.5%
Impaired Glucose Tolerance (IGT)	
Fasting plasma glucose **and** 2 hours plasma glucose*	<7.0mmol/L (126mg/dL) ≥7.8 mmol/L and <11.1mmol/L (140mg/dL and 200mg/dL)
Impaired Fasting Glucose (IFG)	
Fasting plasma glucose **and** (if measured) 2 hours plasma glucose*	6.1 to 6.9mmol/L (110mg/dL to 125mg/dL) <7.8mmol/L (140mg/dL)

§ The diagnosis of diabetes in an asymptomatic person should not be made on the basis of a single abnormal plasma glucose or HbA1c value. At least one additional HbA1c or plasma glucose test result with a value in the diabetic range is required, either fasting, from a random sample, or from the oral glucose tolerance test (OGTT). The diagnosis should be made by the best technology available, avoiding blood glucose monitoring meters and single-use HbA1c test kits (except where this is the only option available or where there is a stringent quality assurance programme in place). It is advisable to use one test or the other but if both glucose and HbA1c are measured and both are "diagnostic" then the diagnosis is made. If one only is abnormal then a further abnormal test result, using the same method, is required to confirm the diagnosis.

* Venous plasma glucose 2 hours after ingestion of 75g oral glucose load. If 2hours plasma glucose is not measured, status is uncertain as diabetes or IGT cannot be excluded.

\# HbA1c can be used as a diagnostic test for diabetes providing that stringent quality assurance tests are in place and assays are standardised to criteria aligned to the international reference values. A value of less than 6.5% does not exclude diabetes diagnosed using glucose tests.

Table 5. ADA Diagnostic Criteria for DM[2]

1. Fasting plasma glucose ≥ 7.0 mmol/L (126 mg/dL). Fasting is defined as no caloric intake for at least 8 hours.* **or**
2. 2 hours plasma glucose ≥ 11.1 mmol/L (200 mg/dL) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 gram anhydrous glucose dissolved in water.* **or**
3. In a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis, a random plasma glucose ≥11.1 mmol/L (200 mg/dL). **or**
4. HbA1c ≥ 6.5 %. The test should be performed in a laboratory using a method that is National Glycohemoglobin Standardization Program (NGSP) certified and standardised to the Diabetes Control and Complications Trial (DCCT) assay.*

* In the absence of unequivocal hyperglycaemia, the diagnosis of diabetes requires two abnormal test results in the diabetic range from the same sample (i.e. fasting plasma glucose and HbA1c from same sample) or in two separate test samples. If using two separate test samples, it is recommended that the second test, which may either be a repeat of the initial test or a different test, be performed without delay. If two different tests (such as HbA1c and FPG) are both above the diagnostic threshold when analysed from the same sample or in two different test samples, this also confirms the diagnosis. On the other hand, if a patient has discordant results from two different tests, then the test result that is above the diagnostic cut point should be repeated, with consideration of the possibility of HbA1c assay interference.

Reference:

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