

Glucose Metabolism and diabetes Mellitus

(V) ذوي استجابة عالٍ لسكر لأنهم يسهرون كميات
سوائل كثيرة بلا BV خصبير عندهم

١) كسبان نقيس السكر اول فحصة منجوله انه
فنتقيس ال *fasting blood glucose* او *Random*
normal range for random - 120 - 140
140 - 200 intolerance
> 200 diabetic

٢) *intolerance* معناها انه الانسولين بوجه
فا نتميز بضع الحلو كونه الي بياكله
ففي عنده مشكلة بكمية الانسولين
الي يتنفذ

٣) فحصة التراكمية *HbA1c* و *OGTT* همار منجوله للحواصل

٤) كلنا استجابة عال ال *kidney* لأنه أكبر Risk لل *chronic renal disease* همد استكري

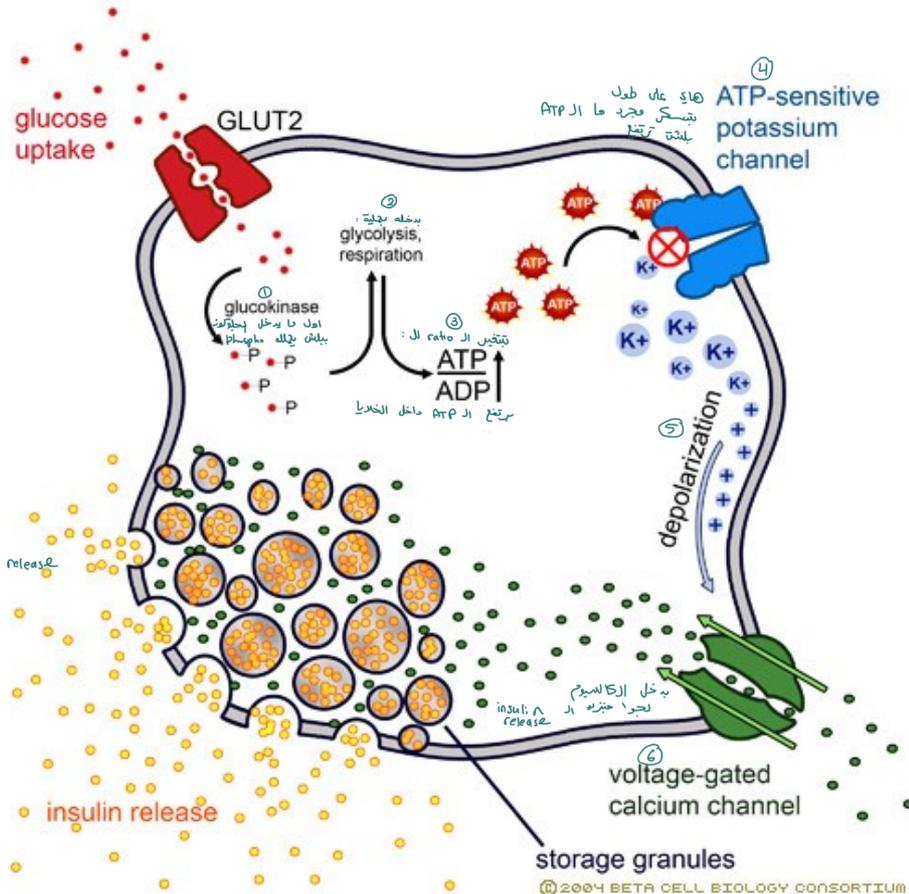
٥) في كمان *neuropathy* بي الحيلة عالجين واشون التروية اله

٦) بي الحيلة عالجين و الكوليسترول لأنه انا نتحققه عن مشكلة هرمون يعني اذا عندي مشكلة بالانسولين معناها عندي مشكلة بالهورمون بالتالي بالبروتينات والدهن كان

بعض ما الزايد ياكل على طول كميان الجلوكوز يدخل من GLUT-2 وهاي
 insulin independent يعني ما تحت علائط هب carrier تبعه على ال
 passive diff و conc. gradient

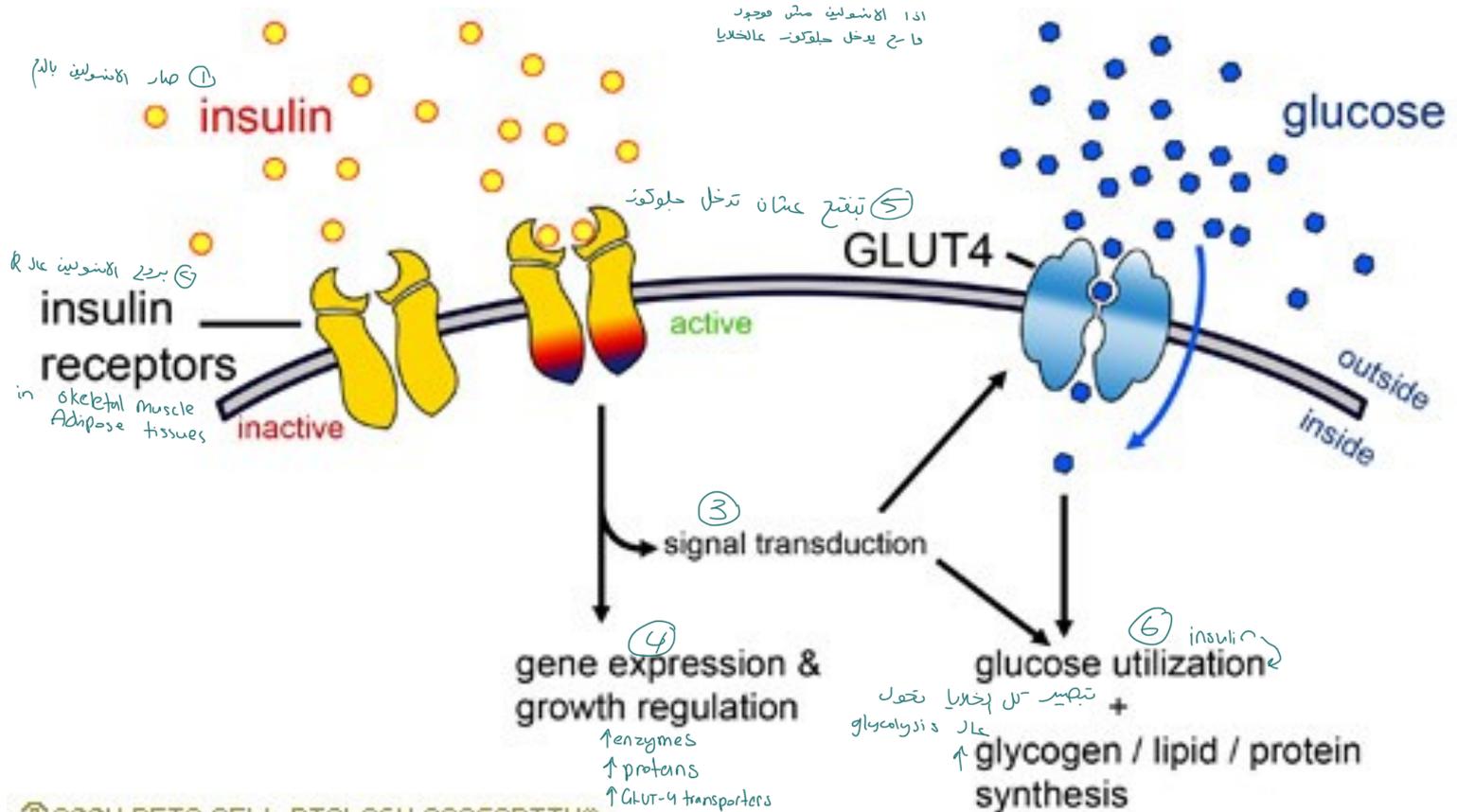
- دخل الجلوكوز بي غنا انزيم glucose kinase هادي واحد منه بالliver بيتا
 كبح الكبرهيرات الي مائلها كتيرة شوي تجرح للكبح و هاد الاتزيم هعبر
 ما له activity ↑ يعني الكمية الهضرة من الجلوكوز على طول
 بعلها phosphorylation ه ماد هعبر البنكرياس B-cells هاد الاتزيم
 بتصنف sensor للجلوكوز عشان انزل على قده انسولين

Effect of Insulin



↑ depolarization ↑ Ca²⁺ influx ↑ insulin release

Effect of Insulin



Effect of Insulin

- Carbohydrate
- Facilitates the transport of glucose into muscle and adipose cells
- Facilitates the conversion of glucose to glycogen for storage in the liver and muscle.
- Decreases the breakdown and release of glucose from glycogen by the liver
أحنا ما بنبترو وبنقوم بنفس الوقت بعين يا بنبترو يا بنبترو inh للوقت و Activation للتانية

- Protein precursor of gluconeogenesis
أحنا فنكسر البروتينات ومنتخدم المواد تبعها علشان اطلع Alanine ← Glucose → Pyruvate
- Stimulates protein synthesis

- Inhibits protein breakdown; diminishes gluconeogenesis
لما انا عندي خلوكوت كتير ليه اطلع كمان

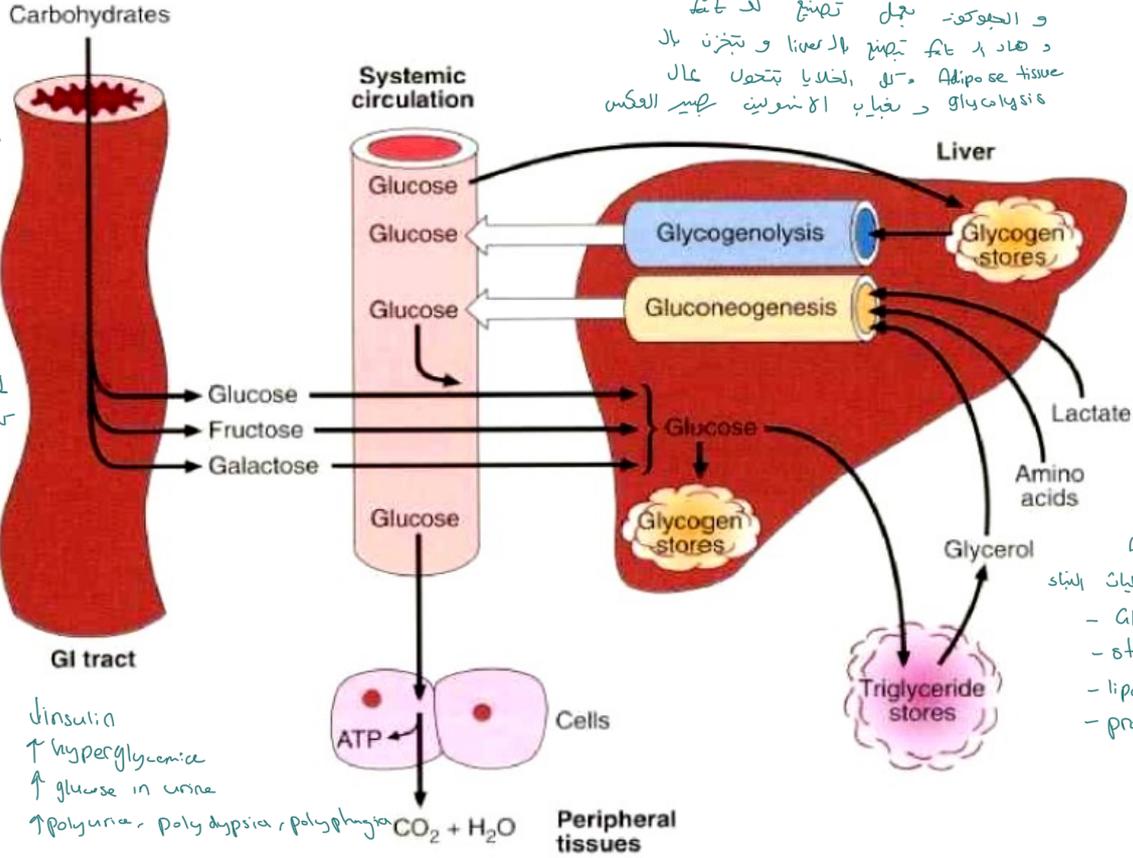
- Fat
- Stimulates lipogenesis- the transport of triglycerides to adipose tissue
- Inhibits lipolysis – prevents excessive production of ketones or ketoacidosis
سبب زفير مع الواحد سكرتي زح ينحف بسبب كتير كتير لأنه
فنتق انشولين بالتالي زح ينزق ال lipolysis وتكسير ال triglyceride
= البروتينات بالكيف انه يضربها جوماته فنتق ميتة من العجز وفضل ياكل

Insulin : Anabolic

- التناصح يكون عنده مقاومة انشولين يعني الانشولين بقتد عالي عنده يعني بقتد الاشولين
يرتبط عال R مع ما في signal transduction كاتبة يعني لازم بقتد تركيز الانشولين عالي جدا علشان
سويطين signal فغشاء انك العلكة للاحتمالية اكبر من الانشولين

Effect of Insulin

الانسولين يتساعه انه تفتح glycogen
والجوكوز- يفتح تفتح لاد تفتح
دهاد لاد تفتح بالاصغر وبتخزن بال
Adipose tissue- مثل الخلايا يتحول عال
glycogen و يفتح بالانسولين في العكس



جذب اللاحه
فا اكل الكبره
ينتقل للدم وبعد هيك
تتخزن عال شكل
glycogen, lipids
(Triglycerides)
و تتخزن بال
Adipose tissue-
لا الانسولين يقدر تاثير
كلتي يفتح تفتح
- Glucagon - Epinephrine
Cortisone, GH
هدهو للدم سيجعلها عكس
الانسولين ← Catabolic
فيكسرنا الlipid و يحوها
F.A و يحوها للدم
على ال metabolism
والاعه والبروتينات تتكسر
وهو كذا يتفتح منها جلوكوز
فال gluconeogenesis يتحسن
بوجود الحاله و الانسولين
تفتح و هدهو كذا يفتح
ماتالي hyperglycemia
دهاد لك يفتح عند مرض
السكره

الانسولين الابوليك
يقدر مؤثر على عمليات التمثيل
- Glycogen ↑
- store glucose
- lipogenesis
- protein synthesis

↓ insulin
↑ hyperglycemia
↑ glucose in urine
↑ polyuria - polydipsia, polyphagia

Introduction

Type 1 diabetes

المرض الفجائي المهم هو الأنسولين

- هاد لا يعنى انه جدا كثير مستحيل يصير معه Type 1
- Most frequently affects children and adolescents.
- Symptoms include excessive thirst, excessive urination, weight loss and lack of energy. + polydipsia polyuria
- Daily insulin injections required for survival.

Type 2 diabetes

عادة بعد الأربعين سنة

- هاد النوع ما يصير حاجة بس هو مرض بيبي عند الواحد فجأة
- هاد نوعه او على شرح بيبي هو بالذبح الحادى الانسولينى قاعد يتزل عنده شوي شوي من الحيلوتور قائم يرتفع شوي شوي فهرمون حاسوس ولسا ما يصل لمرحلة فوتة 150 وانه ملتش تطالع عنده باليونك بس هو يرتفع اذا بدو احسب له HbA1c راجد يكون اكثر عند الكويش
- Occurs mainly in adults.
- Usually people have no early symptoms.
- People may require oral hypoglycaemic drugs and may also need insulin injections.

الادوية بتتربط معه لأنه لسا الـ β -cells عنده سقالة و يمكن يوصل لمرحلة انه يصير ماخذ انسولين

- اخر طرح ال Type 2 يصير تربع زي ال Type 1 بتجده خلفه الـ β -cells كلها خربت و حالة سقالة

دمك استخدمه بالانسولين
ادا طالي عنده وال β -cells
تلات على فصاته diabetic

Diabetes mellitus

- Disease in which the body doesn't produce or properly use insulin, leading to hyperglycemia

نسبة الانتشار

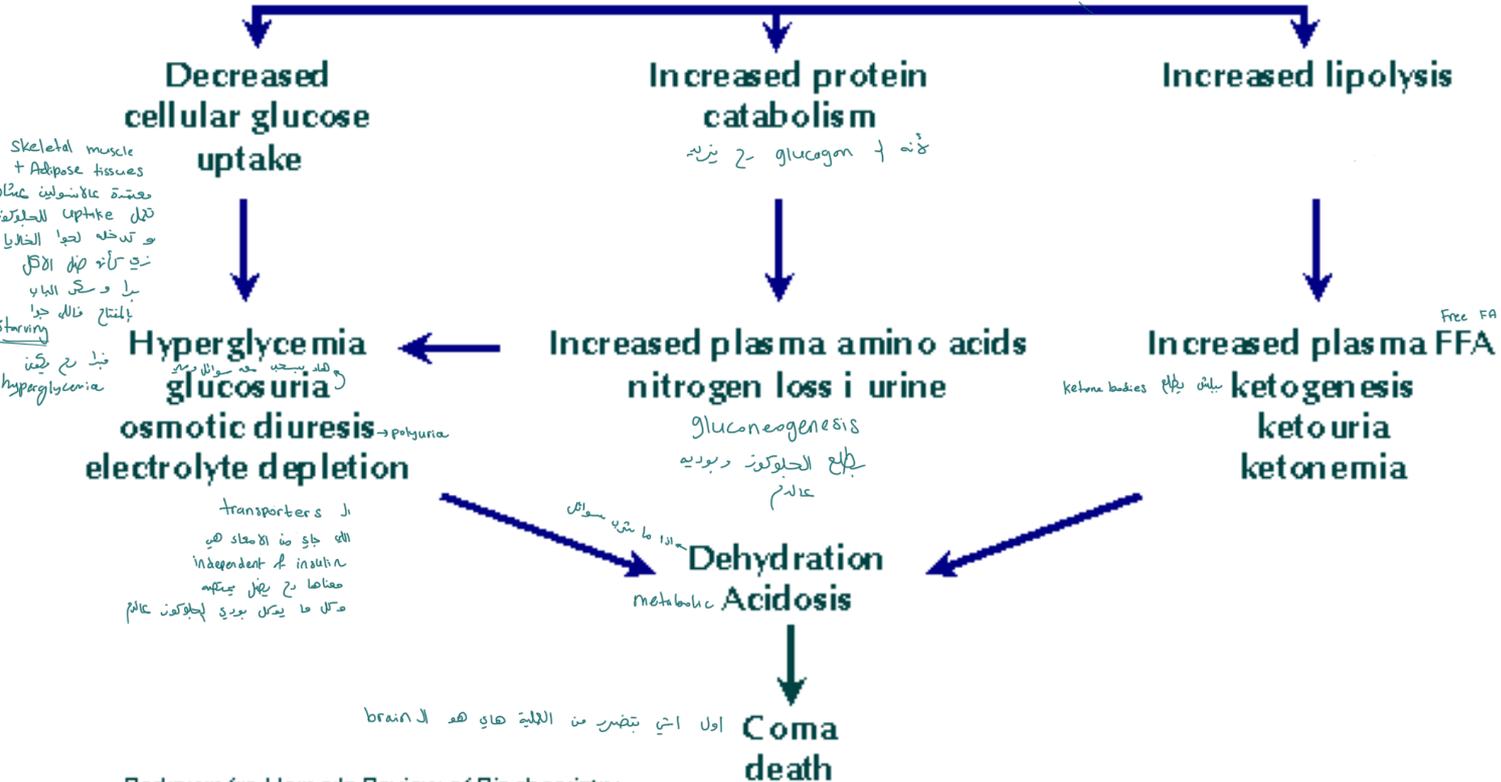
Main Features	IDDM Type 1	NIDDM Type 2
Epidemiology		
Frequency in Northern Europe	0.02-0.4% <i>North</i>	1-3%
Predominance	<u>N. European</u> <u>Caucasians</u>	<u>Worldwide</u> <u>Lowest in rural areas of developing countries</u>
	له دخل الجينات بين صبي الاشيخ الرئيسي يعني معدل يكوننا Polygenic + viral inf فلاونه هبشرة هي حبيبه سكره انه عنده استعداد وراثي	المناخه الريفيه تكون انتشاره اقل يعني ما عندهم سكره صحة انه اصل المدن كثير يستعمل Carbs و Acid و السكر الحبيب ما رح يلحقه عندهم السكره
Clinical Characteristics		
Age	<30yrs	>40yrs
Weight	<u>Low</u>	Normal or increased <i>obese</i>
Onset	<u>Rapid</u>	<u>Slow</u>
Ketosis	<u>Common</u>	<u>Under stress</u>
Endogenous insulin	<u>Low/absent</u>	<u>Present</u>
HLA associations	<u>Yes</u>	<u>No</u>
Islet cell antibodies	<u>Yes</u>	<u>No</u>
	اذا اخذ اشويك ونسبه ياكل طارد حذا Ketoadacidosis Very انه صبر	لأنها عنده اشويك معافا احتمالية لا Ketoadacidosis تكون اقل شوي من 1/2 ارتناجات السكره عنده في عندهم 200-400 و لكن يا عندهم يوصل 1000 واكثر
Pathophysiology		
Aetiology	Autoimmune destruction of pancreatic islet cells	Unclear. Impaired insulin secretion and insulin resistance
Genetic associations	Polygenic	Strong
Environmental factors	<u>Viruses and toxins implicated</u>	<u>Obesity, physical inactivity</u>
	واحد مصاب inf و تحقن الجوانت الميتش بمواجده cells من مصابهم β-cells (self cells)	↑ sugar consumption عند الجهر و ageing لخلايا البنكرياس و هي تتكسر و ما تقدر بدورها قبل عدمه مع لفتة ر الإا دخل بالوراثة بين العلية كلال عندها سكره تبتلع عنده الخلايا β-cells قليلة يعني ما لحت سكره بالجهر و عنده الخلايا عندهم تنافس ووصلت للسكر فيها وهو صغير كراته اندره طاشية له الرصون بتربك كان

المسبب

Diabetic Metabolism

Insulin Deficiency (and glucagon excess)

+ epinephrine, GH, cortisol



قلة بدمير hypoglycemia عند المرضي ؟
 اذا اخذت كمية قليلة او اشد الاذا رما اكل او اخذ الاكل
 والى ذلك تتوازن بسبب لحي راحة فحرق كثير سعرات
 وتقل معه السكر وتقل الناس الل... على انة ketogenic
 هدم يمكن كمية الكربوهيدرات عندهم قليلة والبروتين متوفر
 والفاكهة كلة ثام... الحلو كمنز قد اموه د ثام ولكن
 ال ثامه ما بعد احوله ليلا يكون معانها يمكن غير عنده
 ketone bodies + hypoglycemia

70-110 الزرمان
 110-125 prediabetic
 >125 diabetic

Hypoglycemia

hypoglycemia 50-55 < لحد ما عنده سكره
 الاعراض: تفرق، برودة، دوخة
 يتقال بيج الحقي - رجفة tremor
 propranol → mask symptoms

- Hypoglycemia involves decreased plasma glucose levels
- The plasma glucose concentration at which glucagon and other glycemic factors are released is between 65 and 70 mg/dL; at about 50 to 55 mg/dL, observable symptoms of hypoglycemia appear all related to the central nervous system.
- The release of epinephrine into the systemic circulation and of norepinephrine at nerve endings of specific neurons act in unison with glucagon to increase plasma glucose.
- Glucagon is released and inhibits insulin.
- Epinephrine is released, increases glucose metabolism and inhibits insulin.
- In addition, cortisol and growth hormone are released and increase glucose metabolism

اذا صوح سكره
 hypoglycemia
 بدمير عنده 90-50
 يليل عنده

الاعراض صاى كليا
 Epinephrine ال
 سرعة نقل للدم
 عشتان يرفع يرفع
 السكر مرة ثانية يرفع
 Glucagon و
 Epinephrine, cortisol
 GH
 عشتان يثامك الام
 ويثام السكر مرة ثانية
 عشتان صاى الاعراض يتكون
 CNS

TABLE 13-8 CAUSES OF HYPOGLYCEMIA

PATIENT APPEARS HEALTHY

No coexisting disease

Drugs

نتيجة تخفيض بالإنسولين

Insulinoma

Islet hyperplasia/
nesidioblastosis

Factitial hypoglycemia from
Insulin or sulfonylurea SE

Severe exercise

كأنه كمية الكربوهيدرات منخفضة عملية

Ketotic hypoglycemia

Compensated coexistent

Drugs/disease

PATIENT APPEARS ILL

Drugs

Predisposing illness

Hospitalized patient

الأشخاص الذين ما معهم سكري
لماذا ينزل عندهم السكر؟

Laboratory Testing in Diabetes

معلومات السكري تفرد بالوقت

○ Fasting morning venous glucose is the best initial test for diagnosing diabetes. *Fluoride tube for sample*

○ An oral glucose tolerance test is reserved for people with equivocal fasting glucose results.

انه بتعطيه و5% من التلوكسترين بدين بتفجعه السكر وبتشوف هل قدرة البنكرياس انه تخففه السكر بعد ساعتين كويسة ولا لا وانا ما زلت عنائه diabetic او prediabetic

○ Patients with impaired glucose tolerance or impaired fasting glucose benefit from lifestyle intervention and annual review.

بنتمنى على اكل نرجه انه يخفف الاديان تبعته يعني بدل حبتين كبار ختمهم الوجبة على طول اليوم لخص وجبات صغائر

if obese, loose weight and exercise

Alcohol x
smoke x

انه هو يرفع الالوسونيم

انه كل سنة فيجعه السكر حتى يتأكد انه ما عنده مشكلة

الفرابي، منطو كل ٣ الشهر او كل ٦ شهر وبتك ما اول مرة
normal: 5.6
Prediabetic: 5.6-6.5
diabetic: >6.5

○ HbA_{1c} is the best test of glycaemic control in diabetes.

و السكري كمان برنظم فيه ناس تزمه المشكلة + بالتحك بجل in ال glucosogenesis فيقول hypoglycemia

○ Patients with diabetes benefit from aggressive monitoring and management of all cardiovascular risk factors.

People at high risk of diabetes

Unfortunately the risk factors for diabetes, unlike those for cardiovascular disease, have not been quantified.

Factors associated with increased risk for diabetes include:

● الهندية عرقية اكتت للسكري

● Pacific or Indian ethnicity

● Increasing age

● **Metabolic syndrome**

● يعجز عن تحمّل جلوكوز ودهناته بعد ساعتين وما كان نازول

● Impaired glucose tolerance

● كمتكيسه مبايليه

● Polycystic ovary syndrome

● انا عمرها كبيره تك بغير عندها سكره حمل و ما يريح بعد الولادة

● History of gestational diabetes or having a baby over 4 kg

● كاهول لايم بيتجهوا عالسكر تهمهم

● Family history of diabetes

● Physical inactivity

● انا هع obese / overweight

● Increased BMI

● Central obesity *Apple shape or pear shape body*

● عشان هيك الا عندهم سكره دايا من ارتفاع الهيمته

● Hypertension *هدول اخده سكره ويا بس ههدول + الضغط كمين متكره باليه ههدول لايم بيتجهوا*

● Adverse lipid profile

● Elevated LFTs *Liver function test*

● Patients taking some drugs e.g. prednisone or anti-psychotic drugs (haloperidol, chlorpromazine, and newer atypical anti-psychotics). *corticosteroid*

People at high risk of diabetes

Three or more of the following risk factors listed below are required for a **diagnosis of metabolic syndrome**.

3 or more → ↑ metabolic syndrome ↑ diabetes ↑ CVD ↑ sub-fertility ↑ gout

Risk Factor	Defining Level
Waist circumference*	Men ≥ 100 cm Women ≥ 90 cm
Triglycerides	≥ 150 mg/dL
HDL cholesterol	Men < 40 mg/dL Women < 50 mg/dL
Blood pressure	SBP ≥ 130 or DBP ≥ 85
Fasting glucose	≥ 100 mg/dL

هذه هي
التي
تزيد
من
خطر
السكري
و
أمراض
القلب
و
الكلى
و
التهاب
المفاصل

2 risk factors are not sufficient for diagnosis of metabolic syndrome

People with the metabolic syndrome are at increased risk of diabetes, cardiovascular disease, sub-fertility and gout despite only moderate elevation in individual risk factors.

*It is likely that people of Indian ethnicity will have features of the metabolic syndrome at lesser waist circumferences than people of European or Pacific ethnicity.

الهندية لديهم محيط خصر أقل من الأوروبيين
Metabolic syndrome

Prevention and identification

Opportunities for prevention

Both impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) refer to metabolic stages intermediate between normal glucose homeostasis and diabetes, in which there is an increased risk of progressing to diabetes.

Who to test

Asymptomatic people without other known risk factors, Men (45 years) and women (55 years)

إذا عنده ال risk factors لازم يجهاد المر يلايش يبيشيك عالسكر عنده

People with one or more risk factors, Men (35 years) and women (45 years)

Testing for diabetes

- Fasting morning blood glucose is the best initial test.
- Urine glucose should not be used for diagnosis while HbA_{1c} can be used according to the new protocols

لأنه حتى شرط الجلوسن بال urac يعين عنده
سكرو حتى اذا الراه أكل كميات هائلة من السكر
يخرج سكر بال urac لأنه الحبة الي أكلها أكبر من
قدرة البكتريا على انه يتعامل معها

تكن تغير ال
life style
و نجد عن ال
diabetes
يعني بل فا صير
عنه السنة الجاي
يك بعد ٣-٤
سنين عنده انتبه
لحاله

People with symptomatic hyperglycaemia

Symptomatic hyperglycaemia may have an acute onset, usually in younger people with type 1 diabetes, or a more insidious onset, usually in older people with type 2 diabetes. The usual symptoms of hyperglycaemia are thirst, polyuria and weight loss but hyperglycaemia can also cause fatigue, lack of energy, blurring of vision or recurrent infections, such as candida.

*For people with symptomatic hyperglycaemia,
a single fasting glucose of ≥ 126 mg/dl*

OR

*a random glucose of ≥ 200 mg/dl
is diagnostic of diabetes.*

سبب لانم اتاك من التلخيمه
عن طريق اني بجلله فحه تاني

Action following fasting venous plasma glucose

Criteria have been recommended by ADA for the diagnosis of diabetes, IGT and IFG.

	Normal		Diabetes
Fasting glucose result	70 - 110 < 110	prediabetic 110-125	≥ 126 mg/dl
Interpretation	Normal result	IFG <i>impairment in fasting blood glucose</i>	Diabetic
Action	Retest in five years or three years for those at risk.	Assess with OGTT. <i>life style changes</i> Re-test <i>assessment every year</i> annually those with IFG or IGT	<i>كدم عشان أوك الفحص ارجع اعلمه الفحص بيوم تاني</i> Two results > 126 on two different days are diagnostic of diabetes. <u>OGTT is not required.</u> <i>فحص فasting blood glucose في يومين مختلفين</i>

Gestational diabetes mellitus

Gestational diabetes mellitus (GDM) increases the risk of many fetal and maternal complications in pregnancy and the development of type 2 diabetes later in life. Screening is currently recommended for all women between 24 - 28 weeks gestation.

عند الدكتورة النسائية

Screening for GDM using 50 gram load

If the one hour blood glucose is ≥ 190 mg/dL, a two hour OGTT is performed.

ال one hr one hour blood glucose ≥ 190 mg/dL مع 50g جلوكوز مع كاستة من ثوبين بعد ساعة يفحصونها السكر، إذا طبع فوق ال 190 فضاها عنده gestational diabetes و عشان اعلم Confirm بتلها 2 hr OGTT و يمكن اعلمها fasting blood glucose و اذا اسي من 105 فضاها gestational diabetes

OGTT for diagnosis of GDM ^{75g glucose}

A fasting glucose ≥ 105 and/or a 2 hour value ≥ 165 mg/dL is diagnostic of GDM.

← العلاج انشولين

سكري الحمل بتترتب عليه لطفل حجمه كبير تكون وزنه فوق ال 4 كيلو خالي بهيمير في هاي الحالة انه الام يكون يرتفع عندها السكر و لكن السكر منته واصل ال diabetes يعني ال اعصاب و blood fasting فوق ال 105 و هو الطبيب 110 بين 106-108 هاي gestational diabetes فهو بيبي بهيمير بس هو مش طبيير و هذا بتترتب عليه انه الطفل يخرج ما انزل بهيمير عنده severe hypoglycemia و اذا ما اكتشفنا هاي المشكله فكلنا نراي ال و طاقه و يمكن تكون المشكله بالنسبة للام انه يظل فيها حتى مع العلاج السكري خصوصاً اذا مبرها كبير بشوي

Interpretation of the glucose tolerance test

A 75 gram oral glucose tolerance test (OGTT) is used to follow up people with equivocal results who may have diabetes, IFG or IGT.

ال حالات بح نتيجة من هون

	Fasting mg/dL		2 hours post load mg/dL
Normal	< 110	and	< 140
IFG <i>Impaired fasting glucose</i>	110-125 ↑	and	< 140 <i>normal</i>
IGT <i>Impaired glucose tolerance</i>	< 126 <i>maybe impaired maybe normal</i>	and	140-200 ↑
Diabetes mellitus	≥ 126 ↑	<u>and/or</u>	≥ 200 ↑
GDM <i>Gestational</i>	≥ 105	and	≥ 165

Target level for HbA_{1c}

هنا مرتبة بحد CVDs، كل ما كان ال control على السكر اقل ما عنده control د ال HbA_{1c} ارتفاع

- Any sustained reduction of HbA_{1c} is worthwhile because there appears to be a direct relationship between cardiovascular risk and HbA_{1c}.
- The goal is to achieve an HbA_{1c} as low as possible, preferably less than 7.0%, without causing unacceptable hypoglycaemia.
- HbA_{1c} > 7% is a sign of inadequate control for most people.
- HbA_{1c} targets need to be individualised, taking into consideration the patient's age and co-morbidities.

فمثلا فحد HbA_{1c} كل 6 اشهر
او كل سنة
بين اذا اعطيت دوا لازم بعد 3 اشهر
انحصه وادا غيرتله اياه يرجع كمان 3 اشهر
بجمله النصف ه 5 اشهر او ما يعقل بجله بعد
6 اشهر

Stable diabetes	Test six monthly
Changes in treatment	Test no more than three monthly

فهيّة ل
Type 1
أكثر

Self monitoring blood glucose (SMBG)

○ People who take insulin should regularly self monitor blood glucose (3-4 times daily according to ADA).
هو عادةً يفحصه السكر قبل الوجبة و بحسب قدسيته انسولين كانم يأخذ و قدسيته ال ياتمنها تبعاً الوجبة و يأخذ على قدره انسولين بعدئذيه بمسح فحبه مرة تالية

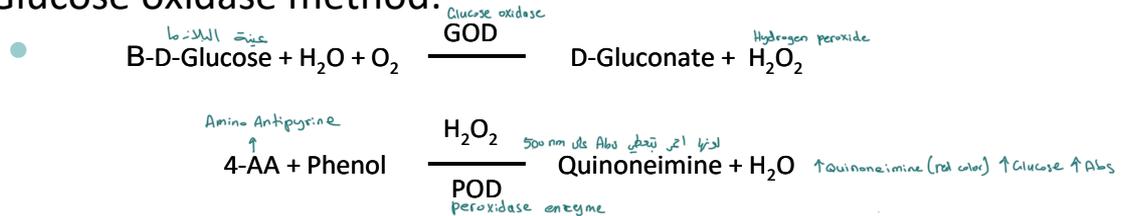
هناك اذا ياكلوا حبتين

○ For people with non-insulin treated type 2 diabetes testing is most useful if patients use the results to learn and alter behaviour, or medication.
له يفحصه كل فترة لما يحس أنه السكر مرتفع او اذا حاي عماله يركل اسني حلو برشح فحبه قبل ما يأكل الشطة صاني او اذا لعي رطهه برشح فحبه كان سانه قلنا تنزله السكر

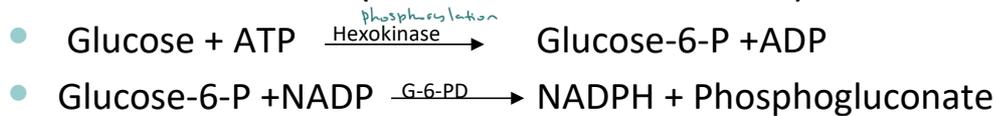
Methods of glucose measurement

① more common

○ Glucose oxidase method:

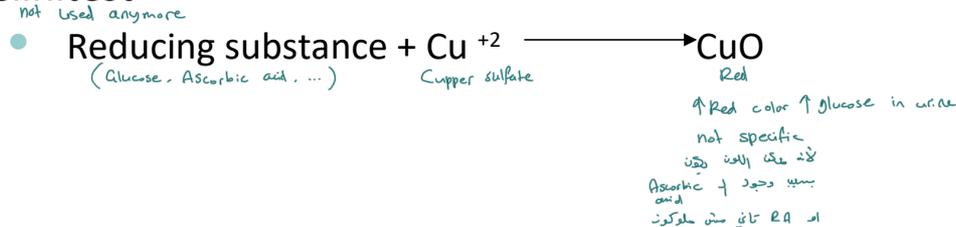


○ Hexokinase method (more accurate than GO):



↑ Glucose ↑ Abs
NADH Abs: 340 nm
متناسب طرديا مع glucose conc
↑ Glucose ↑ Abs

○ Clinitest



Methods of glucose measurement

يفضل ما يصير نفضله وهو ما عند carbs الامل

- The patient should be on a normal-to high carbohydrate diet and fasting for at least 10 hrs and not more than 16 hrs
- The test should be performed in the morning because of the hormonal diurnal effect on glucose
- The preferred specimen for glucose analysis is fluoride oxalate plasma
- Before and during performance of OGTT, the patient should not exercise, eat, drink (only water), or smoke
- In OGTT, the adult dose of glucose solution is 75 g and children receives 1.75 g/kg of glucose to a maximum dose of 75 g

اذا وزنه 20kg

يطلبه 35g

اذا وزنه 50kg

المفروضه 87.5g حلوكوز

من يتم الامتلاك ← 75g ببطيه

ساعة : 50g

ساعتين 75g

Serum ما يربط بأنه اذا بقي استقر عليه نمر ساعة اعمله coagulation عجين نغله centrifugation طول الدم ساعة وهم سبتهلك حلوكوز ف مع تعطيلها pseudohypoglycemia نلازم من بلزما استقر

الانولين مش كل الامتلاك نجما نفسه التركيز بالتالي تأثيره على حلوكوز مع بقاء صفاد

Measurement of glycosylated hemoglobin

- The specimen required is EDTA whole blood sample

ما يزيد بيلانزا وكا Serum

- Method based on structural differences

- Immunoassay (antibodies against the ^{glucose}glycated N-terminal of Hb)
 يتخذها جزء الاله من الهموتين مع الحليوكون و ريلاعورا Antibody و تستخدمها كاتم تكن 5-6 (HbA1c)
- Affinity chromatography (separated based on chemical structure using borate to bind glycosylated proeins.
 يكون في column فيه resin تكبد مربوط عليه مواد borates فهو يح يشيلك مع ال glycosylated Hb عا طه القادي بس ما يرتب عا طه القادي

- Methods based on charge differences:

دون في Charge بس الي فوق طه اعليا Charge

- Ion exchange Chromatography (positive charge resin bed)
- Electrophoresis (difference in charge) and size
- Isoelectric focusing (method uses isoelectric point for separation)
- HPLC (ion exchange column)

ارتباطه بال resin يكون مختلفا و ريلاعورا ال conc حسب ال AUC

له منسبته ال PH تكبد ال sln عا ال gel

اي بروتين عند ال isoelectric point تكبد اذا بيك
 ال PH عا نفس ال isoelectric point ... هاد ما عليه
 Charge و تكبد هين تتركش عا ال gel

isoelectric charge : net charge of protein at specific PH = zero
 با اتم ال 20 بيفترنا ال isoelectric point لفرقة واحد 5 دواحد 6 بيفترنا 5
 اذا ال PH = 5 الي ال isoelectric عا 5 طه حثرك لانه هين ما عليه لحنة
 سب ال 6 يح حثرك لانه عليه +ve

Ketones

الKetone bodies يتبين سببها إذا الواحد هيام الأياع بعين 16 ساعة هيام ما بين

- They increase in case of DM, starvation/fasting, high-fat diet, prolonged vomiting and glycogen storage disease

severe diarrhea

- Measurement of ketones:

- Nitroprusside: with acetoacetic acid and alkaline pH gives purple colour

- Enzymatic: NADH + acetoacetic acid $\xrightarrow[\text{B-HBD}]{\text{B-hydroxybutyrate dehydrogenase}}$ $\text{NAD}^+ + \text{B-hydroxybutyrate}$

enzyme is specific to acetic acid

ال ketone bodies يدي اكتف عنها لأنه يدي
اشتون اذا عنو ketonosis او ك

ال Abs تقي رقبية على 340nm
قوة ال NADH هو إلى ال Abs
بالتالي ال blank به يقين مع
ورقنية على reagent فبطني Abs
نعبن حقه بعينها مع reagent
ح بطني Abs اول
الذق بال Abs بتغير تركيز ال Aceto Acetate

Laboratory tests to prevent and delay complications of diabetes

People with diabetes usually die from macrovascular complications of their diabetes; namely cardiovascular disease. This is influenced by all of the commonly recognised risk factors for cardiovascular disease as well as glycaemic control. Fasting lipid levels are measured three monthly until stable and then 6 - 12 monthly thereafter.

Stable: 6-12 mths
unstable: 3 mths

It is important that management should be individualised

يخضع الشخص إلى هذه كل
ال risk factors نسبة ال HbA_{1c}
اقل من 6 من اقل من 7
إذا مرتبه السكري صحت نافعة مع الأورج
بجوله على الأسترويت

حتى تقلل من مضاعفات السكري لأن
ال lipid نسبة طبيعي وال HbA_{1c} نسبة
طبيعي كان حتى اقل من CVD كان
لأنه أكبر مشكلة عند حصول المرضه انهم
بجولته من الصلابة سواء عالجها او عالجها

Parameter	Optimal value
Total cholesterol	< 4 mmol/L
LDL cholesterol	< 2.5 mmol/L
HDL cholesterol	> 1 mmol/L
TC:HDL ratio	< 4.5
Triglycerides	< 1.7 mmol/L
HbA _{1c}	< 7 %

Diabetic renal disease

The best way of testing for diabetic renal disease is by urinary albumin:creatinine ratio (ACR) and serum creatinine with estimated glomerular filtration rate (eGFR). These tests are performed on everyone with diabetes at diagnosis and repeated at least annually – more frequently if there is proteinuria, microalbuminuria or reduced eGFR.

Albumin:creatinine ratio Urine sample

- ACR provides an estimate of daily urinary albumin excretion.
- Microalbuminuria cannot be detected on a conventional urinary protein dip stick.
- Microalbuminuria is urinary albumin excretion between 30 and 300 mg/day; above 300mg/day represents proteinuria.
- ACR is best measured in the laboratory using a first morning urine sample where possible when the patient is well.
- An abnormal initial test requires confirmation by testing on two further occasions. If at least one of these tests is positive microalbuminuria has been confirmed.

Renal testing in diabetes

ACR mg/mmol (confirmed)	eGFR mL/min/ 1.73 ²	Risk	Management
men < 2.5 women < 3.5	and > 60 Stage 1-2	2 - 4% per year progress to microalbuminuria.	Annual ACR and eGFR. Good diabetes & BP management.
men ≥ 2.5 women ≥ 3.5	or < 60	One third progress to overt nephropathy. CVD risk doubled.	Review ACR and eGFR at each visit. Intensive management of glycaemia and CVD risk factors. Use ACE inhibitor and low-dose aspirin. Avoid nephrotoxic drugs. Investigate if suspicious of causes other than diabetes*
> 30	or < 30	Almost all proceed to end stage renal disease or die prematurely of CVD.	Overt nephropathy Refer specialist Dialysis

المستوى ACR المستر
مستوى ال level عشان
ال muscle إن يكون
Cr بكرة أقل بالتالي إن
Cr إنك يكون بالبروتين يكون أقل

أكثر فور
مستوى

فحص سنوي

إذا الأدوية مش كلتيه متخوله علاج ندرلين

عشان اقل كاسترول ال BP
عشان عمل مشكلة ال kidneys
baby Aspirin

مزمعة انه يفسر عندهم جيلان كمارت
أعلى بالهنتف

secondary UTI
Kidney stones
متألمون

*Non-diabetic renal disease is suspected when there is absence of diabetic retinopathy in a person with renal disease, there are urinary abnormalities such as haematuria or casts, or when there is renal disease without microalbuminuria or proteinuria.

Other tests

Testing of LFTs is recommended for people with diabetes:

- at diagnosis,
- at the start of antidiabetic drug therapy, and
- at any other time indicated by clinical judgement

liver function tests
Check for fatty liver or jaundice

Check liver enzymes

Other laboratory tests

In patients with type 1 diabetes, intermittent checks for other autoimmune conditions may be useful. This could include testing for thyroid dysfunction or coeliac disease.

CASE STUDY 13-1

An 18-year-old, male high school student who had a 4-year history of diabetes mellitus was brought to the emergency department because of excessive drowsiness, vomiting, and diarrhea. His diabetes had been well controlled with 40 units of NPH insulin daily until several days ago, when he developed excessive thirst and polyuria. For the past 3 days, he has also had headaches, myalgia, and a low-grade fever. Diarrhea and vomiting began 1 day ago.

Questions

1. What is the probable diagnosis of this patient based on the data presented?
2. What laboratory test(s) should be performed to follow this patient and aid in adjusting insulin levels?
3. Why are the urine ketones positive?
4. What methods are used to quantitate urine ketones? Which ketone(s) do they detect?

URINALYSIS RESULTS

Specific gravity	1.012
pH	5.0
Glucose	4+
Ketone	Large

CHEMISTRY TEST RESULTS

Sodium	126 mEq/L
Potassium	6.1 mEq/L
Chloride	87 mEq/L
Bicarbonate	6 mEq/L
Plasma glucose	600 mg/dL
BUN	48 mg/dL
Creatinine	2.0 mg/dL
Serum ketones	4+

CASE STUDY 13-2

A 58-year-old, obese man with frequent urination is seen by his primary care physician. The following laboratory work was performed, and the following results were obtained:

CASUAL PLASMA GLUCOSE		225 mg/dL	
URINALYSIS RESULTS			
Color and appearance	Pale/clear	Blood	Negative
pH	6.0	Bilirubin	Negative
Specific Gravity	1.025	Urobilinogen	Negative
Glucose	2+	Nitrites	Negative
Ketones	Negative	Leukocyte esterase	Negative

Questions

1. What is the probable diagnosis of this patient?
2. What other test(s) should be performed to confirm this? Which is the preferred test?
3. After diagnosis, what test(s) should be performed to monitor his condition?

CASE STUDY 13-3

A 14-year-old, male student was seen by his physician. His chief complaints were fatigue, weight loss, and increases in appetite, thirst, and frequency of urination. For the past 3 to 4 weeks, he had been excessively thirsty and had to urinate every few hours. He began to get up 3 to 4 times a night to urinate. The patient has a family history of diabetes mellitus.

LABORATORY DATA

Fasting plasma glucose	160 mg/dL	
Urinalysis	Specific gravity	1.040
	Glucose	4+
	Ketones	Moderate

Questions

1. Based on the preceding information, can this patient be diagnosed with diabetes?
2. What further tests might be performed to confirm the diagnosis?
3. According to the American Diabetes Association, what criteria are required for the diagnosis of diabetes?
4. Assuming this patient has diabetes, which type would be diagnosed?

CASE STUDY 13-4

A 13-year-old girl collapsed on a playground at school. When her mother was contacted, she mentioned that her daughter had been losing weight and making frequent trips to the bathroom in the night. The emergency squad noticed a fruity breath. On entrance to the emergency department, her vital signs were as follows:

Blood pressure	98/50 mm Hg
Respirations	Rapid
Temperature	99°F

Stat lab results included:

RANDOM URINE		SERUM CHEMISTRIES	
pH	5.5	Glucose	500 mg/dL
Protein	Negative	Ketones	Positive
Glucose	4+	BUN	6 mg/dL
Ketones	Moderate	Creatinine	0.4 mg/dL
Blood	Negative		

Questions

1. Identify this patient's most likely type of diabetes.
2. Based on your identification, circle the common characteristics associated with that type of diabetes in the case study above.
3. What is the cause of the fruity breath?

CASE STUDY 13-5

A 28-year-old woman delivered a 9.5-lb infant. The infant was above the 95th percentile for weight and length. The mother's history was incomplete; she claimed to have had no medical care through her pregnancy. Shortly after birth, the infant became lethargic and flaccid. A whole blood glucose and ionized calcium were performed in the nursery with the following results:

Whole blood glucose	25 mg/dL
Ionized calcium	4.9 mg/dL
Plasma glucose was drawn and analyzed in the main laboratory to confirm the whole blood findings.	
Plasma glucose	33 mg/dL
An intravenous glucose solution was started and whole blood glucose was measured hourly.	

Questions

1. Give the possible explanation for the infant's large birth weight and size.
2. If the mother was a gestational diabetic, why was her baby hypoglycemic?
3. Why was there a discrepancy between the whole blood glucose concentration and the plasma glucose concentration?
4. If the mother had been monitored during pregnancy, what laboratory tests should have been performed and what criteria would have indicated that she had gestational diabetes?

CASE STUDY 13-6

Laboratory tests were performed on a 50-year-old lean white woman during an annual physical examination. She has no family history of diabetes or any history of elevated glucose levels during pregnancy.

LABORATORY RESULTS

Fasting blood glucose	90 mg/dL
Cholesterol	140 mg/dL
HDL	40 mg/dL
Triglycerides	90 mg/dL

Questions

1. What is the probable diagnosis of this patient?
2. Describe the proper follow-up for this patient.
3. What is the preferred screening test for diabetes in nonpregnant adults?
4. What are the risk factors that would indicate a potential of this patient's developing diabetes?

CASE STUDY 13-7

For 3 consecutive months, a fasting glucose and glycosylated hemoglobin were performed on a patient. The results are as follows:

	QUARTER 1	QUARTER 2	QUARTER 3
Plasma glucose, fasting	280 mg/dL	85 mg/dL	91 mg/dL (FPG)
Glycosylated hemoglobin	7.8%	15.3%	8.5%

Questions

1. In which quarter was the patient's glucose the best controlled? The least controlled?
2. Do the fasting plasma glucose and glycosylated hemoglobin match? Why or why not?
3. What methods are used to measure glycosylated hemoglobin?
4. What potential conditions might cause erroneous results?

CASE STUDY 13-8

A 25-year-old, healthy, female patient complains of dizziness and shaking 1 hour after eating a large, heavy-carbohydrate meal. The result of a random glucose test performed via fingerstick was 60 mg/dL.

Questions

1. Identify the characteristics of hypoglycemia in this case study.
2. What test(s) should be performed next to determine this young woman's problem?
3. To which category of hypoglycemia would this individual belong?
4. What criteria would be used to diagnose a potential insulinoma?

CASE STUDY 13-9

A nurse caring for patients with diabetes performed a fingerstick glucose test on the Accu-Chek glucose monitor and obtained a value of 200 mg/dL. A plasma sample, collected at the same time by a phlebotomist and performed by the laboratory, resulted in a glucose value of 225 mg/dL.

Questions

1. Are these two results significantly different?
2. Explain.