Self assessment/CPD answers

Below, you can find the answers to the self-assessment questions published in this chapter.

Answers

What is diabetes?

Question 1

Correct answer: A. As per American Diabetes Association guidelines, if a patient has discordant results on two different tests for diabetes, the test that has produced a result above the diagnostic cut-off point should be repeated, and the diagnosis made on the outcome. In this case, the fasting glucose is in the prediabetes range but the HbA_{1c} is in the diabetes range. In this scenario the HbA_{1c} should be repeated. An oral glucose tolerance test (C) and fasting glucose and insulin (D) are unnecessary. It is appropriate to clarify the diagnosis before treatment, and therefore it is incorrect to give metformin (B). Although there is a family history of diabetes, there is no evidence to suggest a diagnosis other than type 2 diabetes mellitis (T2DM) (so E is incorrect).

Question 2

Correct answer: D. Women should be tested after delivery to ensure that the diabetes has resolved. In this setting, HbA_{1c} (B) is not reliable as it gives an estimate of prevailing plasma glucose over a 2–3-month period; therefore an oral glucose tolerance test (D) is required. Metformin (A) and daily capillary glucose monitoring (C) are not indicated before testing for persistent diabetes. The first-trimester HbA_{1c} was normal and there is no suggestion of type 1 diabetes mellitis (T1DM), so testing for autoimmune markers of T1DM (E) is unnecessary.

Question 3

Correct answer: D. A random plasma glucose concentration has been shown to be $\geq$11.1 mmol/litre in the presence of classical symptoms of hyperglycemia, which meets the criteria for a diagnosis of diabetes. In the absence of symptoms, confirmatory testing would be required (A), but the patient has symptoms. For the same reason, an HbA_{1c} (B), fasting plasma glucose (C) and oral glucose tolerance test (E) are incorrect next steps. Furthermore, the diagnosis is consistent with recent-onset corticosteroid-induced diabetes, so HbA_{1c} measurement is unhelpful as this reflects the prevailing glucose over the previous 2–3 months.

What is type 1 diabetes?

Question 1

Correct answer: C. Positive glutamic acid decarboxylase (GAD) autoantibodies would suggest an insidious presentation of adult-onset T1DM. Raised HbA_{1c} (A) will indicate diabetes, but does not help to differentiate between type 1 and type 2 diabetes. C-peptide (B) is unlikely to be helpful here. In new-onset type 1 diabetes, patients continue to have some residual C-peptide, and therefore a 'normal' value does not necessarily exclude a diagnosis of type 1 diabetes. Genetic susceptibility alleles (D) can be helpful, however this would not be the next test. Insulin autoantibodies (E) are associated with acute-onset type 1 diabetes in children.

Question 2

Correct answer: C. Migrants adopt the type 1 diabetes risk of their host population within one generation. The monozygotic twin concordance rate is not 100% (A). Migration cannot explain the rapid increase in prevalence (B). The epidemic increase in type 1 diabetes cannot be explained by relatively slow changes in the gene pool (D). Type 1 diabetes most commonly presents in the under-20 age group (E).

Question 3

Correct answer: E. The likely diagnosis here is type 1 diabetes, as suggested by ketosis, rapid weight loss, family history of autoimmunity and positive glutamic acid decarboxylase (GAD) autoantibodies. Subcutaneous insulin is the most appropriate treatment. Liraglutide (A), pioglitazone (C) and sitagliptin (D) are used in type 2 diabetes, not type 1 diabetes. Intravenous insulin (B) is not indicated as this patient does not have diabetic ketoacidosis.

What is type 2 diabetes?

Question 1

Correct answer: B. Based on his clinical presentation and strong family history, there is a high suspicion for type 2 diabetes in this patient. The next best step is to confirm the diagnosis by ordering repeat fasting plasma glucose and/or an HbA_{1c} (B). Although this patient will require further management recommendations when the diagnosis is confirmed, recommending weight loss and physical activity (A), metformin (B) or insulin therapy (D) are not appropriate at this time. Although he may benefit from bariatric surgery (E) a referral is not appropriate at this time.

Question 2

Correct answer: A. Given her clinical presentation, this patient has classic features of cortisol excess (A).

Question 3

Correct answer: D. The only medication known to cause type 2 diabetes among the options is olanzapine, an antipsychotic

medication. Antipsychotic medications are commonly used, and clinicians should be aware of this possible adverse effect.

Monogenic diabetes

Question 1

Correct answer: B. This presentation would fit well for maturity-onset diabetes of the young (MODY) due to an *HNF1A* mutation (HNF1A-MODY) as well as a number of other monogenic cause (although not GCK-MODY, as the glucose and glycated haemoglobin (HbA_{1c}) concentrations are a bit too high for this). As the patient is presenting sub-acutely it is acceptable to check β-cell antibodies – if positive the diagnosis of type 1 diabetes can be made and insulin commenced. The patient should be asked to perform blood glucose and ketone monitoring and to seek help urgently if ketones become detectable as this would be suggestive of type 1 diabetes requiring insulin treatment.

So long as the patient remains well, a decision on insulin (**A**) can be delayed until β-cell antibodies are back. Metformin (**C**) and gliclazide (**D**) treatment are the correct treatments for Type 2 diabetes and some forms of MODY respectively, but more clarity on the correct aetiology should be sought initially. As he has a significantly raised HbA_{1c} some treatment will be required so (**E**) is incorrect. If β-cell antibodies are negative, low-dose gliclazide could be trialled if the patient remained symptomatic but without very high blood glucose (e.g. >12 mmol/litre) and absence of ketonaemia whilst genetic testing was arranged.

The history of gestational diabetes in the patient's mother may be relevant as many women with MODY (not just GCK-MODY) report previous gestational diabetes, whereas in incipient type 1 diabetes a 4-year gap before re-presentation would be unusual.

Question 2

Correct answer: C. The combination of young-onset type 2 diabetes mellitus and deafness in a lean young person provides high suspicion of mitochondrial diabetes, and the mother's cardiomyopathy could be a further manifestation of mitochondrial disease. If mitochondrial disease is confirmed, genetic counselling is advisable before pregnancy is contemplated because the mitochondrial mutation is likely to be passed on to all offspring of a female patient and can have a very variable phenotypic outcome in the offspring, ranging from normal to severe disability. In some severe mitochondrial conditions, fertility treatment using nuclear transfer to a donated oocyte with normal mitochondria is offered.

A lean person with apparent young-onset type 2 diabetes might have HNF4A-MODY (**A**) or a K_{ATP} channel mutation (in *KCNJ11* or *ABCC8*) arising in adult life (**E**), but deafness is not typical.

Wolfram syndrome (**B**) typically presents with insulin-requiring diabetes in childhood and sensorineural deafness also starts in childhood, but the other prominent features of Wolfram syndrome are not present in this case (visual loss due to optic atrophy, diabetes insipidus, neurological features and bladder dysfunction). Type 1 diabetes (**D**) in young adults would typically progress to insulin requirement within 2 years.

Question 3

Correct answer: D. This is a classic presentation of an insulin receptor mutation as hyperandrogenism in a young woman. The key aspect differentiating it from other forms of insulin resistance is that the lipid profile and liver enzymes are normal despite highly raised insulin levels. If they could be measured, adiponectin levels would also be raised, which is unusual in insulin resistance. High testosterone levels sometimes warrant investigation for virilizing tumour (**C**) but this is less likely. *PPARG* mutations (**E**) tend to present with partial lipodystrophy and severe hypertension in young adults, and insulin resistance is not generally seen in maturity-onset diabetes of the young (**B**). She does have polycystic ovarian syndrome (**A**), but this is a consequence of the insulin receptor mutation.

Epidemiology of diabetes

Question 1

Correct answer: B. (A) Urinalysis is not a diagnostic test recommended for diagnosis; (B) is correct because she can be offered any of the three tests, but if she tests positive, the key issue will be to repeat the same test in order to confirm the diagnosis; (C) – there is no reason to do both tests, but if she tests positive on either, the key issue will be to repeat the same test to confirm the diagnosis; (D) – there is no basis to avoid using the glycated haemoglobin test in specific ethnic groups. The interpretation of an HbA_{1c} result may be affected by anaemia or a haemoglobinopathy, neither of which she has; (E) – there is no reason that only an oral glucose tolerance test is appropriate; see answer as in B above.

Question 2

Correct answer: E. (A repeat test as a confirmatory test should always be done, regardless of which method of diagnosis is used (ie, fasting glucose, oral glucose tolerance test or glycated haemoglobin concentration). Also, regardless of whether a diagnosis of diabetes is confirmed or not, he should be given specific individually-tailored lifestyle advice about losing weight through improved diet and physical activity, and he should be reviewed again in approximately 3 months.)

(A) – An elevated HbA_{1c} concentration above the diagnostic threshold (>48 mmol/mol or >6.5%) is indicative of a diagnosis of diabetes, but a single test is not sufficient, and must be repeated to confirm or reject a diagnosis. (the same would apply if a glucose-based test was done). (B) – There is no reason to additionally do an oral glucose tolerance test. Any one of the diagnostic tests can be used, including fasting glucose, oral glucose tolerance test or glycated haemoglobin concentration. (C) – There is no need to immediately start medication, especially as the diagnosis should first be

confirmed with a repeat test. He should be offered weight loss advice, and to improve his diet quality and increase physical activity in the first instance as there is strong evidence for lifestyle management in the management of type 2 diabetes. (D) – Correct to repeat the test to confirm diagnosis (as in answer A above). Some would argue that after confirmation of diagnosis, a trial of lifestyle behavioural advice should first be given before starting antidiabetic medication, but some would want to start therapy together with lifestyle advice. However, if medication is started, a sulfonylurea is not the recommended first line therapy, and metformin would be more appropriate. (see also answer C above).
(E) is correct. Always confirm a diagnosis by repeat testing, and the appropriate management will be to offer advice of lifestyle behaviour change to aim for weight loss, and review again.

Question 3

Correct answer: C. Genetic susceptibility is important but not sufficient in the causation of type 1 diabetes. Several environmental factors have been linked, but are not proven to be causally related, with the onset of type 1 diabetes, including early social mixing, viral infections, vaccinations, drugs, toxins, intrauterine factors, and dietary and nutritional factors such as exclusive breastfeeding and delayed introduction of cows' milk, vitamin D deficiency and omega-3 fatty acids. The incidence of type 1 diabetes has been rising in most populations (A), with average increases of around 3% per year worldwide.

In those aged over 35, it is not known if the rates are stable, on the rise or declining in this group (B). Incidence rates can vary substantially within a country (D) as well as between countries.
Diabetes is well recognized to be diagnosed more commonly in the winter (E)

Modern strategies for management of glycaemia in type 1 diabetes

Question 1

Correct answer: C. The HbA_{1c} value suggests that there may be major issues with how she currently uses insulin, and basic facts such as missing doses, injection sites, etc. should be diplomatically explored. She is using fixed doses of insulin, and structured education may give her the skills to adjust her insulin as needed for different foods, activities, etc. Although insulin pump therapy (B) and continuous glucose monitoring (E) may be future options for her, there are many things to address first. It is also worth asking whether pregnancy is being planned in the near future as this may increase the urgency with which changes are needed.

Question 2

Correct answer: E. He has now had two severe episodes requiring rescue in an 8-week period, and this needs careful review, probably back in a specialist diabetes service. He does not need to be admitted to hospital (A) if he has recovered and there are no medical reasons. The other strategies (B, C, D) are inadequate. Probable specialist strategies when he is reviewed include revisiting his current insulin-dosing skills and assessing whether he would be better using technology such as continuous glucose monitoring with alarms and/or insulin pump therapy. If the event 8 weeks ago was not a nocturnal one (i.e. occurring during sleep), he should be informed that he needs to stop driving and contact the Driver and Vehicle Licensing Agency (DVLA) to self-notify these events. Document this carefully. It is also worth checking whether he has been prescribed glucagon in case his partner has to rescue him again at home. Buccal glucose should not be used if patients are semi-conscious or unconscious as airway protection may be impaired.

Question 3

Correct answer: C. The management clearly depends on how the woman looks and feels, but the problem here is likely to be an interruption in insulin delivery related to the change of infusion set. Standard instructions for those using pumps say not to change infusion sets at the end of the day, and that if the glucose (and ketones) rise after a set change, to change the set and give a 'manual' subcutaneous bolus. If the woman is not better after a couple of hours, she should be admitted to hospital for intravenous fluids and variable rate intravenous insulin (B) to ensure insulin replacement.

Glycaemic management of type 2 diabetes

Question 1

Correct answer: E. Because of the presence of CKD 3B, it may be advisable not to increase the dose of metformin because of associated precautions. Insulin, although an option, may not be needed at this stage and, because of the social circumstances, may have compliance issues. Sodium glucose co-transporter 2 (SGLT-2) inhibitors are not licensed to be commenced at this level of CKD. Sitagliptin is an option, but it needs to be commenced at a lower dose of 50 mg daily because of the present estimated glomerular filtration rate (eGFR). Because the patient has failed to attend multiple reviews and because of the difficulty in monitoring the eGFR, linaglitptin is the most appropriate option because a single 5 mg daily dose can be commenced irrespective of renal function.

Question 2

Correct answer: C. Most of the other medications are options for optimizing glycaemia. However, with a BMI >35 kg/m^2, a glucagon-like peptide 1 (GLP-1) agonist would be the most appropriate choice, with the associated benefit of weight reduction. SGLT-2 inhibitors are also accompanied by weight loss, but the reductions in weight and glycated haemoglobin (HbA_{1c}) are less than are seen with GLP-1 agonists. A target HbA_{1c} of 54 mmol/mmol (7%)or less is an ideal for a young, health-conscious patient.

Question 3

Correct answer: B. Gliclazide is also an option, but even with the maximum dose the expected reduction in HbA_{1c} is only to around 85 mmol/mol (9.9%), which is unsatisfactory for

elective surgery. Sodium glucose co-transporter 1 (SGLT2i) drugs carry a relative risk of exacerbating lower urinary tract infection and provide a drop of only 20 mmol/mmol in HbA_{1c}. Glucagon-like peptide 1 (GLP-1) agonists are relatively contraindicated with a history of obstructive jaundice that has not been evaluated. Both these drug groups can be used once these medical problems have been addressed.

Glycaemic management in patients with diabetes in hospital

Question 1

Correct answer: D. Patients with moderate to poorly controlled diabetes as indicated by the glycated haemoglobin (HbA_{1c}) concentration have a higher risk of bacteraemia and consequent septicaemia as a result of cellulitis. Hence in this scenario, despite the stable clinical status, it is recommended to stop the empagliflozin temporarily (European Medicines Agency [EMA] guidelines due to risk of ketosis (A, C). It is safe to continue metformin. Because the patient appears clinically stable and capillary blood glucose levels between 7 and 11 mmol/litre are acceptable, intravenous insulin (B) is not indicated. Blood glucose levels as an inpatient should be repeated 4–6-hourly and the dose of isophane insulin should initially be titrated accordingly. Failing this, other forms of insulin therapy, including a change of regimen (E), should be considered.

Question 2

Correct answer: C. In this scenario, this patient had developed diabetic ketoacidosis (DKA) because of the use of potent corticosteroids. Owing to the ketonaemia, she was vomiting, and hence oral medications should be discontinued (A) and initially replaced by a fixed variable-rate intravenous insulin infusion as per local diabetes management guidelines. It has already been before that subcutaneous 'sliding scale regimens' should be abandoned due to lack of efficacy and high glucose variability (B). Variable-rate intravenous insulin infusions (D, E) are generally started when there is evidence of ketone clearance.[3]

Question 3

Correct answer: D. It is preferable to use a variable-rate intravenous insulin infusion for patients who are being given either enteral or parenteral nutrition. In such scenarios, subcutaneous insulin regimens (A, B) are associated with high glucose variability and hence are not recommended. Rather than stopping all subcutaneous insulins, the basal insulin should be continued since it helps transition to stable regimes later on (C). Insulin pumps with glucose sensors (E) are new developments that could be efficacious, but there is as yet little evidence to recommend their usage for diabetes management in inpatients.

Diabetic ketoacidosis and hyperosmolar crisis in adults

Question 1

Correct answer: A. The woman has two risk factors – pregnancy and being on a SGLT-2 inhibitor. Although most people with diabetic ketoacidosis (DKA) present with glucose concentrations >5.0 mmol/litre, a lower glucose does not exclude DKA: remember the diagnostic criteria – either a glucose >11.1 mmol/litre or a history of diabetes.

Hyperemesis is a possibility, given the urine ketones, pregnancy and hypotension. However, in this context the most important test is the venous blood gas to exclude euglycaemic acidosis associated with SGLT-2 use. Thyrotoxicosis is unlikely but needs to be considered when someone is unwell, tachycardic and confused. Placental abruption is unlikely here, but should be in the differential of pregnancy, unwell, hypotension. Pre-eclampsia is usually associated with hypertension and thus is not the correct answer here.

Question 2

Correct answer: E. This is hyperosmolar, hyperglycaemic state (HHS), and the initial treatment is intravenous sodium chloride 0.9% solution. Once the glucose concentration has stopped decreasing with fluid resuscitation, insulin should be added at 0.05 U/kg per hour.

The treatment here is 0.9% saline first and then only add insulin once the glucose has stopped dropping with fluid resuscitation alone.
0.45% sodium chloride solution should only be substituted if the osmolality is no longer declining despite adequate fluid replacement with 0.9% sodium chloride solution AND an adequate rate of fall of plasma glucose is not being achieved.

Question 3

Correct answer: D. Hyperchloraemic metabolic acidosis is frequently seen after aggressive fluid resuscitation with intravenous sodium chloride 0.9% solution. It needs no treatment, and is likely to resolve on its own within 24–36 hours if renal function is normal. If glucose concentration is normal and ketones are negative, a chloride measurement is necessary to make this diagnosis.

Aspirin overdose is associated with a high anion gap metabolic acidosis, however, after 24 hours this should have resolved.
If his urine ketones were undetectable, it would be highly unusual to have plasma ketones detectable.
Alcoholic ketoacidosis is associated with a variety of acid base disturbances. The anion gap may be high, but with a relatively high bicarbonate, because of the concomitant metabolic alkalosis. The anion gap may also be normal because of urinary bicarbonate losses.

Hypoglycaemia in diabetes

Question 1

Correct answer: All the answers are acceptable to some degree but C is the best choice. According to the novel classification of hypoglycaemia, she had an episode of level 1, hypoglycaemia alert and should respond to this. She treated her hypoglycaemic episode appropriately and should be commended for this. But as it is an 'alert' she should check she is not developing impaired awareness.

Insulin is best adjusted by reflecting on the weekly glucose profile.

Question 2

Correct answer: D. He has a degree of Impaired awareness of hypoglycaemia (IAH) as at this blood glucose concentration, one would expect him to be symptomatic if his awareness was intact. A. is not the ideal treatment approach. Current guidelines suggest treating all blood glucose readings <4 mmol/litre as hypoglycaemia with 15–20 g of fast-acting carbohydrates. B. HbA_{1c} readings <48 mmol/mol (6.5%) should always raise a suspicion of frequent/unrecognized hypoglycaemia. This does not have to be always the case, but this possibility should be explored and doing more blood glucose tests does not deal with the underlying cause. C and E are drastic approaches to reduced awareness which are rarely needed.

At first instance a careful history should be taken especially in relation to previous severe hypoglycaemia (SH) at work in particular, in particular the concentration of glucose at which he develops symptoms. Glucose levels <3 mmol/litre indicate impaired awareness of hypoglycaemia. His lifestyle, insulin type, dosing and timing of injections should be reviewed. Strict avoidance of hypoglycaemia for a couple of weeks might be everything that is required to re-gain his hypoglycaemia awareness. He should also undertake a structured education programme if not done before.

Question 3

Correct answer: All responses are correct to some degree but the best response is B. She had an episode of SH while on sulfonylurea derivate (gliclazide). She was found to have impaired renal function which is the most likely precipitating factor that cause the SH. She should be admitted to hospital and her blood glucose monitored for approximately 24 hours. A. not ideal and although it may be sufficient, admission and reducing the dose is probably the correct approach. Current recommendations suggest monitoring blood glucose readings for 24 hours because of the danger of late hypoglycaemia caused by impaired renal excretion of gliclazide. C may be true but doing nothing is a risky option as this may occur again. There is no information given about this lady's metabolic control. SH can occur in any patient with diabetes who is on hypoglycaemia-causing agents, independently of metabolic control. D is good advice but does not deal with the underlying problem. E. It is wise to reduce or stop metformin if renal function is impaired but this will not deal with the hypoglycaemia.