

Complications of Diabetes Mellitus: Review Questions

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QUESTIONS

Choose the single best answer for each question.

Questions 1 and 2 refer to the following case.

A 22-year-old pregnant woman with a 15-year history of type 1 diabetes mellitus presents to the clinic at 11 weeks' gestation. Although the patient's diabetes was well-controlled as a child, her glycemic control has progressively worsened over the past few years. One month prior to her pregnancy, the patient's hemoglobin A_{1c} (HbA_{1c}) level was 8.8% and serum creatinine was 0.5 mg/dL. Since learning of the pregnancy, the patient no longer misses doses of basal or prandial insulin and she checks her blood glucose level regularly. She reports that fasting and postprandial blood glucose levels are always less than 100 and 180 mg/dL, respectively, with an occasional low blood glucose level less than 70 mg/dL. Recent laboratory testing reveals an HbA_{1c} level of 6.7% and a urine microalbumin/creatinine ratio of 50 mg/g.

1. With this patient's recent history of improved glycemic control during the first trimester of pregnancy, she is at increased risk for which of the following complications?

- (A) Coronary vasospasm
- (B) Fetal malformations and miscarriage
- (C) Progression of diabetic nephropathy
- (D) Progression of diabetic retinopathy

2. The patient presents to the ophthalmologist as part of routine health maintenance. She has never undergone laser therapy. Fundoscopic examination reveals several hemorrhages and some hard and soft exudates in the left eye (Figure). No proliferative changes are noted. How should this patient be managed?



Figure. Nonproliferative diabetic retinopathy of the left eye. (Image courtesy of Manju Subramaniam, MD, Boston University Eye Associates, Boston, MA.)

- (A) Arrange follow-up once the patient has delivered the baby
 - (B) Close follow-up with frequent fundoscopic examinations throughout the pregnancy
 - (C) Less strict glycemic control
 - (D) Prophylactic laser therapy
3. A 28-year-old man with no past medical history presents to the emergency department with a nonhealing, painful, erythematous perianal abscess. Incision and drainage of the abscess reveals copious purulent fluid. He also has an erythematous papular rash with satellite lesions in his groin and a hyperpigmented velvety discoloration in the creases of the neck and bilateral axilla. The patient reports a 1-day history of severe nausea and vomiting. He is obese with a body mass index of 42 kg/m². Laboratory testing reveals blood glucose, 580 mg/dL; sodium, 125 mEq/L; chloride, 98 mEq/L; potassium, 5.1 mEq/L; carbon dioxide, 10.4 mEq/L; blood urea nitrogen, 34 mg/dL; and serum creatinine, 1.2 mg/dL. He is admitted to the intensive care unit and receives intravenous antibiotics, hydration, and treatment for diabetic

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ketoacidosis (DKA). HbA_{1c} is found to be 12%. He is treated with intravenous insulin and is transitioned to subcutaneous insulin. Screening for glutamic acid decarboxylase antibodies and islet cell antibodies is negative. Other than encouraging diet and lifestyle changes, what is the most appropriate discharge regimen for this patient?

- (A) Insulin glargine and glyburide
- (B) Insulin glargine and insulin lispro
- (C) Metformin and glyburide
- (D) Metformin, glyburide, and pioglitazone

4. An 85-year-old woman with a long history of type 2 diabetes and progressive diabetic nephropathy presents to the clinic with her daughter. The daughter reports frequent spells in which the patient is confused and “out of her mind.” One month ago, the patient’s serum creatinine level was 2.2 mg/dL and HbA_{1c} level was 5.8%. Over the past 5 years, her HbA_{1c} level has been improving, but renal function has been worsening. She checks her blood glucose level 1 to 2 times per week. The patient only eats once or twice daily. Her diabetes has been treated with glyburide 5 mg twice daily. The patient was previously on metformin, but it was discontinued when her kidney function deteriorated. During the interview, the patient seems distant, and a random blood glucose test in the clinic is 40 mg/dL. The patient also complains of swelling in her feet. How should this patient’s diabetes be managed at this time?

- (A) Change glyburide to metformin to reduce the risk of hypoglycemia
- (B) Change glyburide to pioglitazone
- (C) Start basal/bolus insulin based on weight
- (D) Stop glyburide, recommend regular blood glucose monitoring, and reassess in 1 week

5. A 16-year-old girl with a 6-year history of type 1 diabetes presents to her physician because her mother is concerned about her weight. She has no other medical problems. She has always been and still is a good eater; however, she has lost enough weight that she is now wearing smaller-sized clothes. The patient denies bingeing or purging behaviors. She has managed her diabetes independently for the past few years. Two months ago, her HbA_{1c} level was 12%. The patient appears very thin, with a body mass index of 18 kg/m². She reports feeling well, is satisfied with her current weight, and does not understand why her mother is worried. The patient reports that she gains weight when she takes her insulin as recommended. She admits to missing some insulin doses when she

gets too busy or is out with friends. Her mother notes that the patient urinates frequently at night. The patient denies excessive sweating, palpitations, or heat intolerance. Family history is notable for Hashimoto’s thyroiditis in the mother treated with thyroid hormone replacement. What is a likely cause of this patient’s weight loss?

- (A) Diuretic use
- (B) Healthy weight loss
- (C) Intentional omission of insulin
- (D) Surreptitious use of thyroid hormone

ANSWERS AND EXPLANATIONS

1. (D) **Progression of diabetic retinopathy.** Retinopathy occurs via a variety of mechanisms, including disruption of the autoregulation of retinal blood flow, accumulation of sorbitol in the retina, and accumulation of advanced glycosylation end products in extracellular fluid. Advanced retinopathy, including neovascularization and proliferative changes, may be mediated by growth factors such as insulin growth factor 1 or vascular endothelial growth factor. Both pregnancy and intensive insulin therapy have been associated with advancing diabetic retinopathy.^{1,2} Factors that affect progression of retinopathy during pregnancy include the severity of retinopathy prior to pregnancy, duration of diabetes, use of more intensive therapy to decrease the rate of maternal and fetal complications of hyperglycemia, smoking, and presence of hypertension, hyperlipidemia, or hypoglycemia.³ Increased, not decreased, HbA_{1c} values during the first trimester are associated with a high risk of major congenital malformations and miscarriage.⁴ Coronary vasospasm is not associated with improvements in glycemic control. Pregnancy and improved glycemic control will not accelerate the progression of diabetic nephropathy in women with mild renal dysfunction.¹

2. (B) **Close follow-up with frequent fundoscopic examinations throughout the pregnancy.** Women with diabetes should be screened for retinopathy during the first trimester and then every 3 months thereafter while pregnant. Even in patients with no history of retinopathy prior to pregnancy, retinopathy can develop progressively throughout pregnancy. Nonproliferative diabetic retinopathy produces increased capillary permeability, microaneurysms, hemorrhages, and exudates. It can be treated with focal laser therapy when clinically significant macular edema develops. Both laser therapy and vitreous surgery can be performed safely during pregnancy.

Women should be advised that despite the short-term exacerbation during pregnancy, the long-term risk of progressive retinopathy remains unchanged. Thus, glycemic control should remain a priority during pregnancy. Of note, women who develop gestational diabetes are not at risk for retinopathy.

3. (B) Insulin glargine and insulin lispro. This patient with no prior history of diabetes presents with DKA. Physical examination is consistent with insulin resistance as evidenced by his obesity and significant acanthosis nigricans. The very high HbA_{1c} level indicates that the patient has been extremely hyperglycemic for some time. Based on current guidelines, patients with diabetes who are naive to therapy with an HbA_{1c} level greater than 10% should be started primarily on insulin therapy.⁵ The most effective means of treating hyperglycemia in an insulin-deficient patient recovering from DKA is to start both basal and prandial insulin to mimic physiologic insulin release. Overestimating the patient's basal or prandial insulin requirements can result in hypoglycemia. Many patients with severe insulin resistance also benefit from an insulin sensitizer such as metformin or pioglitazone. However, these therapies would not be sufficient to treat this patient's extreme glucose toxicity. Metformin is a well-tolerated insulin sensitizer, but its use is limited by renal insufficiency and the risk of lactic acidosis and should be avoided during recovery from DKA. Glyburide has little role in treating this patient at this time. Although DKA is commonly seen in patients with type 1 diabetes, this patient most likely has type 2 diabetes given that he has a phenotype consistent with insulin resistance and negative titers of glutamic acid decarboxylase and islet cell antibodies.

4. (D) Stop glyburide, recommend regular blood glucose monitoring, and reassess in 1 week. This patient's HbA_{1c} level likely reflects significant hypoglycemia on the current treatment regimen. Diminishing renal function can predispose patients with diabetes to hypoglycemia. The kidneys contribute to gluconeogenesis, and with declining renal function, this protective mechanism is lost. In end-stage renal disease, insulin is the safest therapeutic option; however, the pharmacodynamics of insulin is altered with renal dysfunction. Metformin is contraindicated in men and women with a serum creatinine level greater than 1.5 and 1.4 mg/dL, respectively. Although thiazolidinediones are hepatically metabolized and do not require dose adjustment for renal impairment, their use is limited by adverse effects such as fluid retention

and potential heart failure. Sulfonylureas have a prolonged duration of action and may precipitate severe hypoglycemia in elderly individuals, especially in those with underlying renal disease. The meglitinides are also insulin secretagogues but are safer in the setting of compromised renal function.⁶ Insulin is likely the safest way to treat diabetes in patients with significant renal failure; however, it is important to accurately assess glycemic control prior to starting insulin therapy.

5. (C) Intentional omission of insulin. This patient has poor glycemic control with significant nocturia as a result of osmotic diuresis associated with hyperglycemia. Long-standing hyperglycemia leads to glucosuria and resultant weight loss.⁷ This patient is likely skipping insulin doses to prevent weight gain. Insulin omission has been observed in approximately 30% of young women with type 1 diabetes as a means of preventing weight gain.⁸ Insulin noncompliance promotes a catabolic state and can lead to both short- and long-term consequences, including potentially fatal episodes of DKA in individuals with type 1 diabetes. Poor glycemic control can also hasten the devastating vascular consequences of diabetes. It is important to address healthy lifestyles and good glycemic control in all patients with diabetes. Eating disorders are more common in young women with type 1 diabetes than in nondiabetic women.⁹ This patient's symptoms are not consistent with hyperthyroidism, and therefore she is not likely taking her mother's thyroid medication.

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