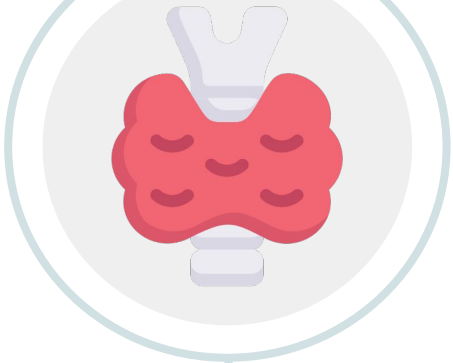
Practice file



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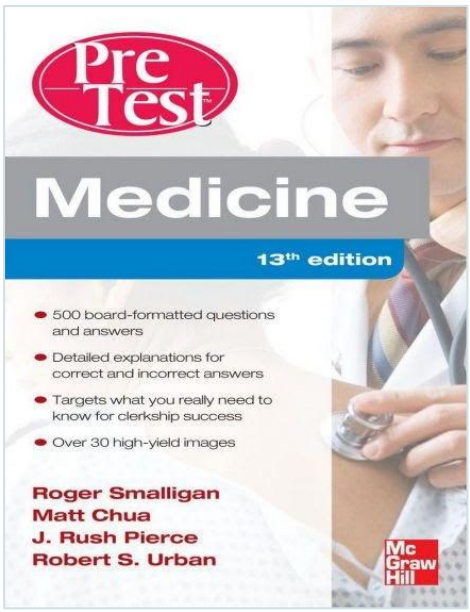

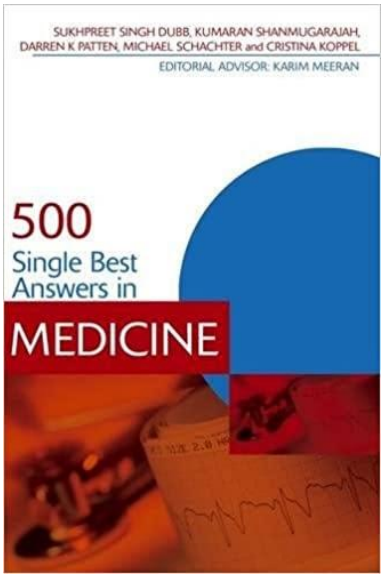

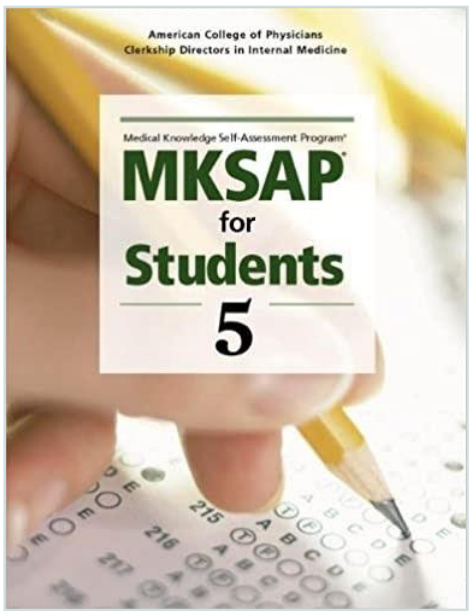

AMBOSS
medical knowledge distilled

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Pituitary disorders

Q1 (500Best): A 33-year-old man complains of a tingling sensation in his hands for several months which occasionally awakens him during sleep. The patient has noticed he has gained weight and no longer wears his wedding ring as it has become too tight. You notice the patient is sweating while speaking to you and has quite a large jaw, furrowed tongue and large hands. His blood pressure reading is 142/91 mmHg. The most appropriate investigation would be:

A. MRI scan of the pituitary
B. Glucose tolerance test
C. Growth hormone levels
D. Thyroid function tests
E. Serum prolactin levels

Explanation: **The glucose tolerance test (B) is diagnostic in patients with suspected acromegaly, many of whom will appear diabetic.** Growth hormone (GH) levels (C) can be raised during periods of stress and for most of the time remain <1mU/L. **A raised GH level is therefore not sufficient to diagnose acromegaly** though low or undetectable levels can exclude this diagnosis. An MRI scan (A) is the best modality to reveal a pituitary adenoma secreting GH, however this investigation should always follow an abnormal glucose tolerance test reading. Hyperprolactinaemia (E) is commonly associated in acromegaly patients as the pituitary adenoma often co-secretes GH and prolactin and is useful to measure in a confirmed diagnosis of acromegaly and especially if a patient presents with symptoms of elevated prolactin. Thyroid function tests (D) would not be correct in this case. Although the patient does show some symptoms of hypothyroidism, such as weight gain and carpal tunnel syndrome, patients tend not to have elevated blood pressure and increased sweating which would be a feature in hyperthyroidism.

Q2 (500Best): A 19-year-old woman presents with concerns about changes to her facial appearance, in particular her nose and jaw seem quite large, she is also quite sweaty and despite using antiperspirants is finding it difficult to control and is afraid of embarrassment at university. A glucose tolerance test is performed and found to be raised. The most appropriate management would be:

A. Trans-sphenoidal surgery
B. Octreotide
C. Bromocriptine
D. Pituitary radiotherapy
E. Pegvisomant

Explanation: Left untreated, acromegaly patients succumb to cardiovascular related morbidities, such as hypertension and heart failure, as well as an increased incidence of colon cancer. Trans-sphenoidal surgery (A) is first line therapy and is particularly effective against microadenomas. Pituitary radiotherapy (D) usually follows unsuccessful surgery, it is also more useful as an adjunct to other medical treatments as response to radiotherapy alone is often slow. Octreotide (B) is a somatostatin receptor agonist which is effective in reducing growth hormone levels and are often used for short-term treatment, but are not definitively used as first-line therapy. Bromocriptine (C) is a dopamine agonist and is primarily used to reduce the size of tumours before more definitive treatment such as surgery. This is useful since high GH levels are a poor prognostic markers prior to surgery. Pegvisomant (E) is a GH antagonist and is effective in lowering IGF-1 levels rather than GH or tumour size. They are used in patients refractory to surgical, radiotherapy and somatostatin therapy.

Q3 (500Best):A 49-year-old man presents with a history of difficulty sleeping. He reports feeling increasingly tired and general weakness which he attributes to his poor sleep pattern. Additionally, the patient has noticed he has gained weight and sweats very easily. On examination, the patient has coarse facial features. The most likely diagnosis is:

A. Hyperthyroidism
B. Cushing's disease
C. Acromegaly
D. Hypothyroidism
E. Diabetes

Explanation: Acromegaly (C) is most commonly due to a pituitary tumour usually identified on MRI scan, patients most frequently present with changes in appearance followed by visual defects and headaches. Sleep apnoea is often a common complaint among patients due to weight gain. Other manifestations include large hands and feet, hirsutism, prominent and coarse facial features, carpal tunnel syndrome, hypertension, diabetes and heart failure among others. The glucose tolerance test is diagnostic for suspected acromegaly, GH levels can be measured directly, although elevated findings are not sufficient for diagnosis. Hyperthryoidism (A) produces symptoms that are usually secondary to an elevation in metabolic rate, such symptoms include diarrhoea, goitre, sweating and intolerance to the temperature whereby the patient consistently feels hot irrespective of the true environmental temperature. Sleep apnoea is not usually a complaint among patients since they often lose weight despite an increased appetite. Cushing's disease (B) results from a pituitary tumour producing excess ACTH, the excess cortisol levels result in symptoms such as striae, bruising, thin skin, weight gain (particularly in the abdominal region) and often a dorsocervical fat pad (buffalo hump). Hypothyroidism (D) features include tiredness, depression, cold intolerance, constipation and weight gain. Patients do not tend to sweat more and the disease does not coarsen facial features. In diabetes (E), patients' symptoms often result in weight loss though in type 2 diabetes they may suffer from sleep apnoea due to their high BMI.

Answers: Q1: B | Q2: A | Q3: C

Pituitary disorders

Q4 (500Best): A 15-year-old girl complains of headaches which started 6 weeks ago. The headaches initially occurred 1–2 times a week but now occur up to five times a week, they are not associated with any neurological problems, visual disturbances, nausea or vomiting. The girl also reports a white discharge from both of her nipples. She has not started menstruating. The most appropriate investigation is:

A. Lateral skull x-ray
B. CT scan
C. MRI scan
D. Thyroid function tests
E. Serum prolactin measurement

Explanation: This patient is most likely suffering from hyperprolactinaemia, which is most commonly caused by a prolactinoma which is a pituitary adenoma causing stalk compression or hypothyroidism. Prolactin levels (E) must first be measured in order to confirm the diagnosis before more invasive tests are used to determine the cause. An MRI scan (C) is the most definitive investigation in this patient as the patient's complaint of headaches alongside the rest of the history point towards a pituitary tumour. Prolactin levels above 1000mU/L also strongly suggest this. A CT scan (B) is not able to reveal pituitary masses as readily as MRI scans can and also involve considerable radiation levels which are especially important in sensitive areas such as the brain. In large lesions, a lateral skull x-ray (A) can reveal fossa enlargement, lesions are often also discovered incidentally, however lateral skull x-rays are rarely used as definitive investigation. Thyroid function tests (D) are important to conduct as they can also cause hyperprolactinaemia; however, as the patient does not have features of thyroid disease they are not first line.

Q5 (500Best): A 37-year-old man presents with symptoms of an acute headache, vomiting, malaise and visual disturbance. A neurological examination reveals a bitemporal superior quadrantanopia. A CT scan shows a hyperdense area within the pituitary gland. The most likely diagnosis is:

A. Kallman syndrome
B. Septo-optic dysplasia
C. Sheehan's syndrome
D. Empty sella syndrome
E. Pituitary apoplexy

Explanation: Pituitary apoplexy (E) is characterized by a sudden headache, vomiting, visual disturbances and hormonal dysfunction. The cause is most commonly due to the abrupt growth of a pituitary adenoma or pituitary infarction. The headache in apoplexy is usually very abrupt and can be mistaken for a subarachnoid haemorrhage, although usually not as severe. The presentation can be unilateral or generalized. Visual defects are most commonly of the superior quadrant bitemporally. Visual disturbances, such as loss of vision and opthalmoplegia affecting cranial nerves III, IV and VI, help differentiate apoplexy from other intracranial pathology. Hypopituitarism can also follow an apoplexy although this is dependent on degree of damage and often patients present feeling very tired or nauseous. Kallman syndrome (A) is characterized by gonadotrophin deficiency and congenital anosmia. Septo-optic dysplasia (B) is a congenital disorder characterized by the triad of optic nerve hypoplasia, hypopituitarism and forebrain abnormalities. The empty sella syndrome (D) is the observation of absent pituitary tissue within the sella turcica observed on imaging, however pituitary function is normal due to ectopic or unusual position of pituitary tissue within the sella fossa. Sheehan syndrome (C) is also called postpartum hypopituitarism and is most commonly a rare complication of pregnancy. Patient's present with agalactorrhoea, amenorrhoea and hypothyroidism after pregnancy.

Q6 (500Best): A 38-year-old woman presents to clinic complaining of changes in her appearance and weight gain. She has recently been through a divorce and attributed her weight gain to this. However, despite going to the gym her clothes are still tight, especially around her waist, her face seems puffy and flushed. The most likely diagnosis is:

A. Hyperthyroidism
B. Cushing's disease
C. Acromegaly
D. Hypothyroidism
E. Diabetes

Explanation: Acromegaly (C) is most commonly due to a pituitary tumour, usually identified on MRI scan. Patients most frequently present with changes in appearance followed by visual defects and headaches. Sleep apnoea, due to weight gain, is often a common complaint among patients. Other manifestations include large hands and feet, hirsutism, prominent and coarse facial features, carpal tunnel syndrome, hypertension, diabetes and heart failure, among others. The glucose tolerance test is diagnostic for suspected acromegaly, GH levels can be measured directly, although elevated findings are not sufficient for diagnosis. Hyperthyroidism (A) produces symptoms that are usually secondary to an elevation in metabolic rate, such symptoms include diarrhoea, goitre, sweating and intolerance to the temperature, whereby the patient consistently feels hot irrespective of the true environmental temperature. Sleep apnoea is not usually a complaint among patients since they often lose weight despite an increased appetite. Cushing's disease (B) results from a pituitary tumour producing excess ACTH, excess cortisol levels result in symptoms such as striae, bruising, thin skin, weight gain, particularly abdominally, and often a dorsocervical fat pad (buffalo hump). Hypothyroidism (D) features include tiredness, depression, cold intolerance, constipation and weight gain. Patients do not tend to sweat more and the disease does not coarsen facial features. In diabetes (E) patients, symptoms often result in weight loss although in type 2 diabetes they may suffer from sleep apnoea due to their high BMI.

Answers: Q4: E | Q5: E | Q6: C

Pituitary disorders

Q7 (500Best): A 29-year-old man presents with a 4-week history of polyuria and extreme thirst. The patient denies difficulty voiding, hesitancy or haematuria, although the urine is very dilute. The patient does not believe he has lost any weight and maintains a good diet. No findings are found on urine dipstick. The most appropriate investigation is:

A. Serum osmolality
B. Fasting plasma glucose
C. Urinary electrolytes
D. Magnetic resonance imaging (MRI) scan of the head
E. Water deprivation test

Explanation: This patient is likely to be suffering from psychogenic polydipsia. The water deprivation test (E) is the most appropriate investigation to confirm this diagnosis. In a normal patient, the serum osmolality remains within the normal range (275–295 mOsm/kg), while the urine osmolality rises to >600 mOsm/kg as water is reabsorbed. In diabetes insipidus, the serum osmolality is elevated with no compensatory concentration of urine osmolality. If the patient responds to desmopressin, this confirms cranial DI rather than nephrogenic DI, hence a water deprivation test is the most appropriate answer. An MRI scan (D) is most appropriate for investigating a pituitary tumour. This commonly presents with visual field impairment and symptoms of elevated prolactin not seen in this patient. The fasting plasma glucose (B) would be appropriate for investigating a patient with suspected diabetes mellitus, however this is often accompanied by weight loss. Serum osmolality (A) would be useful in gauging how serious the patient's degree of dehydration is, but would not be diagnostic. Urinary electrolytes (C) and fasting plasma glucose would be useful in gauging the severity of the patient's clinical state, but would not confirm the diagnosis.

Q8 (500Best): A 69-year-old man presents with confusion. His carers state that over the last month he has become increasingly lethargic, irritable and confused. Despite maintaining a good appetite, he has lost 10kg in the last month. Blood results are as follows:
The most likely diagnosis is:

Sodium	125 mmol/L
Potassium	4 mmol/L
Urea	3
Glucose (fasting)	6 mmol/L
Urine osmolality	343 mmol/L

A. Hypothyroidism
B. Dilutional hyponatraemia
C. Addison's disease
D. Acute tubulointerstitial nephritis
E. Syndrome of inappropriate anti-diuretic hormone (SIADH)

Explanation:The syndrome of inappropriate anti-diuretic hormone (E) (SIADH) is due to inappropriately elevated levels of ADH which leads to the retention of water. The syndrome is therefore characterized by reduced serum sodium levels (hyponatraemia) and reduced serum osmolality, while urine osmolality and urine sodium levels are elevated. Patients are also euvolaemic without signs of oedema. In patients suffering from heart failure, liver failure or the nephrotic syndrome, the reduced circulatory volume acts as a stimulus for the ADH secretion. Despite the patient being in a hypo-osmolar state, ADH secretion is increased causing hyponatraemia, however such patients will be hypervolaemic as in dilutional hyponatraemia (B) due to fluid overload. The SIADH can arise from an inappropriate source of ADH such as tumours both in and out of the pituitary or failure in the feedback mechanism. Hypothyroidism (A) and Addison's disease (C) can also cause the SIADH, however the above patient does not exhibit any of the other signs of these diseases such as weight gain and hypotension, respectively. Acute tubulointerstitial nephritis (D) affects the tubules or interstitium of the kidney and most commonly arises due to hypersensitivity reactions from medications such as non-steroidal anti-inflammatory drugs (NSAIDs). Patients usually present with fever, arthralgia and renal failure.

Q9 (500Best): A 45-year-old Asian man is diagnosed with Cushing's disease in India. He undergoes a bilateral adrenalectomy and recovers well from the operation. On his return to the UK one year later, he complains of a constant dull headache, peripheral visual disturbances and increasing pigmentation of the skin creases of both hands. The most likely diagnosis is:

A. Ectopic ACTH secreting tumour
B. Prolactinoma
C. Nelson syndrome
D. Addison's disease
E. Side effects from iatrogenic steroid intake

Explanation: Nelson syndrome (C) occurs in patients who undergo bilateral adrenalectomies, the loss of negative feedback over time causes a macroadenoma to form in the pituitary which secretes adrenocorticotropin (ACTH). A spectrum of symptoms may arise due to the effects of serum ACTH, as well as the deficiency in other pituitary hormones. An ectopic tumour secreting ACTH (A) can produce similar symptoms, however they usually originate from oat cell of small cell lung carcinomas which are associated with weight loss rather than headaches and visual disturbances. Iatrogenic steroid side effects (E) would cause symptoms imitating cortisol excess such as striae, bruising, thin skin and weight gain. A prolactinoma (B) can cause some of the symptoms the patient complains of, such as headache and visual disturbances, due to impingement upon surrounding structures. However, symptoms in males does not involve hyperpigmentation and usually include loss of libido, impotence and gynaecomastia. Addison's disease (D) causes similar symptoms described in the question stem, however the cause of adrenal function loss is due to autoimmune action or infection.

Answers: Q7: E | Q8: E | Q9: C

Pituitary disorders

Q10 (MKSAP): A 34-year-old woman is seen for follow-up after results of laboratory studies confirm hypercortisolism. Adrenocorticotropic hormone Elevated. Urine free cortisol Elevated.
Cortisol (8 AM):
After 1 mg of dexamethasone the night before Elevated
After 8 mg of dexamethasone the night before Partial suppression
Which of the following is the most appropriate next diagnostic test?

(A) Adrenal CT
(B) Adrenal MRI
(C) Cosyntropin stimulation test
(D) Pituitary MRI

Explanation: The most appropriate next diagnostic test for this patient is pituitary MRI. She has biochemical features of adrenocorticotropic hormone (ACTH)-dependent Cushing syndrome (hypercortisolism and elevated ACTH). The cause of the ACTH hypersecretion is either a pituitary adenoma or an ectopic source, such as a carcinoid tumor. In this patient, partial suppression was achieved with high-dose dexamethasone, which suggests an ACTH-secreting pituitary microadenoma. High-dose dexamethasone is usually not successful in suppressing ACTH production from an ectopic source. However, there are exceptions, so caution must be exercised in interpretation. In such instances, expert consultation is highly recommended.
Adrenal imaging is indicated if the hypercortisolism is ACTH independent (hypercortisolism and normal or low ACTH level). In patients with hypercortisolism associated with suppressed ACTH secretion, a CT scan of the adrenal glands often shows a tumor (adenoma or carcinoma). However, this patient's ACTH level was elevated and adrenal imaging is not indicated with either a CT or MRI scan.
The cosyntropin stimulation test is used to determine the adrenal reserve by measuring the response to a standard dose of synthetic adrenocorticotropic hormone. The test does not detect Cushing syndrome but, rather, adrenal insufficiency and is therefore not indicated for this patient.

Answers: Q10: D

Thyroid disorders

Q1 (500Best): A 33-year-old obese woman complains of tiredness. She has recently given birth to a healthy baby boy and is enjoying being a mother. However, she is becoming more reliant on her partner for support as she always feels exhausted and often becomes depressed. The patient has a poor appetite and often does not finish her meals, despite this she has gained 5 kg in the last 2 weeks. The most likely diagnosis is:

A. Postpartum depression
B. Eating disorder
C. Hyperthyroidism
D. Hypothyroidism
E. Occult malignancy

Explanation: Hypothyroidism (D) is a common disease with a higher prevalence in females and is usually a primary disorder affecting the thyroid gland itself. Thyroid hormones control the metabolic rate in many tissues, underactivity produces symptoms which are often insidious. These include tiredness, depression, cold intolerance, constipation and weight gain. The main causes include iodine deficiency, autoimmune pathology such as Hashimoto's thyroiditis and, in females who have recently given birth, postpartum thyroiditis. Hyperthryoidism (C) results in an excess of thyroid hormones which inappropriately increases metabolic rate with symptoms such as weight loss, increased sweating, restlessness and palpitations. A goitre can occur in both hypo- and hyperthyroidism. Postpartum depression (A) is often accompanied by confusion and is characterized by low mood, anhedonia and anergia. Severely affected patients can have delusional thoughts about their newborn child, such as it being evil, and even progress to thoughts of harming the child or suicidal ideation. Eating disorders (B), such as bulimia or anorexia nervosa, often result in drastic changes in body weight resulting from psychological problems with self-image and include behaviours such as self-induced vomiting to avoid weight gain or binge eating. Most malignancies (E) result in considerable weight loss though this is dependent on the type of cancer and often symptoms provide clues as to the location, e.g. neurological problems.

Q2 (500Best): A 42-year-old woman presents with visual disturbances. She reports having double vision which was intermittent initially but has now become much more frequent. In addition, she becomes breathless very easily and experiences palpitations. On examination, raised, painless lesions are observed on the front of her shins and finger clubbing. The most likely diagnosis is:

A. De Quervain's thyroiditis
B. Thyroid storm
C. Phaeochromocytoma
D. Graves' disease
E. Plummer's disease

Explanation: Graves' disease (D) is the most common cause of hyperthyroidism. The condition is due to IgG antibodies binding to the TSH receptor, this in turn causes excess production of thyroid hormone. The antibodies also bind to other areas of the body such as the extraocular muscles leading to gaze abnormalities, the shins causing raised lesions known as 'pretibial myxoedema' and rarely the fingers causing clubbing known as 'thyroid acropachy'. These collective signs are only seen in Graves' disease, hence it is the only correct answer. De Quervain's thyroiditis (A) is a transient thyroid state most likely due to a viral infection. The patient usually complains of a fever and painful neck with some signs of hyperthyroidism, such as tachycardia, as well as raised ESR levels. A few weeks later, the patient suffers from transient hypothyroid symptoms before returning to a euthyroid state. Phaeochromocytomas (C) are malignancies of the sympathetic nervous system, 90 per cent arise in the adrenal medulla and produce excess catecholamines. The symptoms of a phaeochromocytoma are often similar to hyperthyroidism and include anxiety, palpitations and headache. However, these symptoms are usually intermittent and the main risk to patients is from cardiovascular compromise. Plummer's disease (E) is a solitary nodule in the thyroid gland producing excess thyroid hormones. It is usually refractory to antithyroid treatment. A thyroid storm or crisis (B) is a rapid deterioration in patients suffering from hyperthyroidism, often stimulated by a stressor such as infection. Patients present with acute-onset, severe tachycardia, distress and hyperpyrexia.

Q3 (500Best): A 16-year-old girl presents to her GP complaining of a swelling in her neck which she has noticed in the last 2 weeks. She has felt more irritable although this is often transient. On examination, a diffuse swelling is palpated with no bruit on auscultation. The most likely diagnosis is:

A. Hyperthyroidism
B. Simple goitre
C. Riedel's thyroiditis
D. Thyroid carcinoma
E. Thyroid cyst

Explanation: A simple goitre (B) is an idiopathic enlargement of the thyroid. Often the condition is associated with thyroid antibodies, but these do not cause any symptoms. Riedel's thyroiditis (C) is a rare inflammatory disease of the thyroid gland that is characterized by fibrosis of the thyroid gland and other structures in the neck. It is often stony or woody on palpation and patients are usually asymptomatic. The patient does not have any features of hyperthyroidism (A) in which a thyroid bruit can be present. A thyroid cyst or nodule (E) is usually harmless and is a fluid-filled swelling often presenting as a single compressible small lump rather than a diffuse swelling. A full history and examination should always be conducted with ultrasound and fine needle examination to exclude malignancy. Thyroid cancer (D) is a rare but important diagnosis, they often present as irregular thyroid nodules but can metastasize to the lung, brain, liver and bone. Papillary and follicular cancers usually have good prognoses compared to medullary and anaplastic cancers.

Answers: Q1: D | Q2: D | Q3: B

Thyroid disorders

Q4 (500Best): A 47-year-old woman is referred to the endocrine clinic complaining of a two- month history of tiredness. Despite wearing several items of clothing, the patient appears intolerant to the room temperature. She has noticed an increase in weight, particularly around her waist. The most appropriate investigation is:

A. Radioiodine scan
B. Thyroid stimulating hormone (TSH)
C. Total tetraiodothyronine level (T4)
D. Tri-iodothyronine level (T3)
E. Ultrasound scan of the neck

Explanation: This patient is suffering from hypothyroidism. The most appropriate firstline investigation is measurement of TSH (B) as this indicates if a primary disease affecting the thyroid is present. In a patient with symptoms of hypothyroidism due to a primary disorder of the thyroid, the TSH would be elevated. Similarly, in symptoms of hyperthyroidism due to a primary abnormality of the thyroid, the TSH would be depressed. The total tetraiodothyronine level (T4) (C) would be decreased hypothyroidism and elevated in hyperthyroidism, but this could be due to abnormalities of TSH secretion or a primary disorder of the thyroid. Hyperthyroidism due to elevated levels of tri-iodothyronine level (T3) (D) occurs much less commonly than T4 and hence is measured less often. A radioiodine scan (A) is useful for studying causes of hyperthyroidism, such as Plummer's disease. The patient in this question is suffering from symptoms of hypothyroidism. Ultrasound scan of the neck (E) is most useful for differentiating between solid and cystic nodules; these usually do not alter thyroid function.

Q5 (500Best): A 58-year-old woman presents with an acutely painful neck, the patient has a fever, blood pressure is 135/85 mmHg and heart rate 102 bpm. The patient explains the pain started 2 weeks ago and has gradually become worse. She also notes palpitations particularly and believes she has lost weight. The symptoms subside and the patient presents again complaining of intolerance to the cold temperatures. The most likely diagnosis is:

A. Thyroid papillary carcinoma
B. Plummer's disease
C. De Quervain's thyroiditis
D. Hyperthyroidism
E. Thyroid follicular carcinoma

Explanation: This patient is suffering from symptoms of hyperthyroidism (D) but with some atypical features that provide clues to the most accurate diagnosis. De Quervain's thyroiditis (C) causes a transient change in thyroid state usually due to a viral infection. The patient usually complains of a fever and painful neck with some signs of hyperthyroidism, such as tachycardia, as well as raised ESR levels. This is due to thyroid hormone release as viral organisms infect the thyroid cells. Patients will suffer hypothyroidism as thyroid hormone is depleted before becoming euthyroid again. Plummer's disease (B) usually presents with a solitary nodule in the thyroid gland producing excess thyroid hormones. Thyroid papillary (A) and follicular carcinoma (E) can present with all the features described in this case but are usually painless and less often associated with fever. Apart from De Quervain's thyroiditis, no other pathology swings from hyperthyroidism to hypothyroidism before returning to a euthyroid state.

Q6 (pretest): A 24-year-old woman presents 6 months after the delivery of her first child, a healthy girl, for evaluation of fatigue. She suspects that the fatigue is related to getting up at night to breastfeed her baby, but she has also noticed cold intolerance and mild constipation. She recalls having a tremor and mild palpitations for a few weeks, beginning 3 months after delivery. On examination, her BP is 126/84 and her pulse rate is 56. The thyroid gland is 2 times normal in size and nontender. The rest of the physical examination is normal. Laboratory studies reveal a free T4 level of 0.7 ng/ml (normal 0.9-2.4) and an elevated TSH at 22 microU/mL (normal 0.4-4). What is the likely course of her illness?

A. Permanent hypothyroidism requiring lifelong replacement therapy
B. Eventual hyperthyroidism requiring methimazole therapy
C. Recovery with euthyroidism
D. Infertility
E. Increased risk of thyroid cancer

Explanation: This patient has postpartum thyroiditis. Like other forms of destructive thyroiditis (including subacute or de Quervain thyroiditis), this illness is triphasic. Initially there is hyperthyroidism due to inflammation and release of preformed thyroid hormone from the inflamed follicles; this phase usually lasts 2 to 4 weeks. In subacute thyroiditis, the initial phase is usually noticed because of pain and tenderness over the thyroid gland, but in postpartum thyroiditis the thyroid is usually painless, and the hyperthyroid phase may be overlooked. This phase is then followed by transient hypothyroidism, usually lasting 1 to 3 months. The third phase is resolution and euthyroidism. Whereas Hashimoto thyroiditis usually leads to permanent autoimmune hypothyroidism, most patients with destructive thyroiditis have a full recovery. Some will be symptomatic enough to require thyroid supplementation for 1 to 3 months until the process resolves. Although the initial hyperthyroid phase can suggest Graves disease, in thyroiditis the absence of infiltrative ophthalmopathy and a suppressed radioiodine uptake will make the distinction. Antithyroid drug treatment of thyroiditis is ineffective and puts the patient at unnecessary risk of toxicity such as agranulocytosis. Although hypothyroidism can cause amenorrhea and hence impair fertility, the hypothyroid phase of postpartum thyroiditis is transient. Low-level radiation exposure, but not thyroiditis, increases the risk of subsequent development of thyroid cancer. Interestingly, therapeutic RAI, such as is given for Graves disease, does not increase the long-term risk of cancer, probably because the thyroid cells are destroyed.

Answers: Q4: B | Q5: C | Q6: C

Thyroid disorders

Q7 (MKSAP): A 55-year-old woman is evaluated for a 7-month history of worsening fatigue. She also reports that her hair is thinning and she has an unexplained weight gain of 4.1 kg (9lb) despite trying to limit food intake. She has no other medical problems and takes no medications. On physical examination, temperature is 36.7°C (98.0°F), blood pressure is 120/70 mm Hg, pulse rate is 60/min, and respiration rate is 12/min. BMI is 27. The thyroid is twice its normal size. Her voice is normal, and deep tendon reflexes are 2+ throughout. The remainder of the physical examination is normal. Laboratory evaluation reveals a serum thyroid-stimulating hormone (TSH) level of 14.1 U/mL (14.1 mU/L) and a free thyroxine level of 0.9 ng/dL. (12 pmol/L).
Which of the following tests are necessary before initiating therapy?

(A) Measurement of thyroid peroxidase (TO) antibody
(B) Radionuclide uptake scanning
(C) Measurement of thyroglobulin level
(D) No additional tests

Explanation: This patient requires no additional testing before levothyroxine therapy is initiated for her hypothyroidism. Hashimoto disease is the most common cause of hypothyroidism, and confirmation of this diagnosis with measurement of TP antibody is not necessary. Measurement of PO antibody levels may be helpful in patients with subclinical hypothyroidism (elevated thyroid-stimulating hormone [TSH] level but normal free thyroxine [Ta]). In these patients, increased titers of TPO antibody confer an increased risk of hypothyroidism (~4% per year), which escalates as TSH levels rise above the reference range.
The radioactive iodine uptake (RAIU) test measures thyroid gland iodine uptake over a timed period, usually 24 hours. Patients with thyrotoxicosis typically have an above- normal or high-normal RAIU, which is inappropriate in the context of a suppressed TSH level. In patients with thyroidit is or exposure to exogenous thyroid hormone, the RAIU will be below normal (<5% at 24 hours). Radionuclide uptake scanning has no role in the evaluation of hypothyroidism.
Thyroglobulin, a glycoprotein integral in follicular storage of thyroid hormone, can be detected in serum. Thyroglobulin levels can be elevated in hyperthyroidism and destructive thyroiditis. Intake of exogenous thyroid hormone generally suppresses thyroglobulin levels, which makes its measurement useful in patients with thyrotoxicosis due to surreptitious use of thyroid hormone. Thyroglobulin is also an effective tumor marker in patients with papillary or follicular thyroid cancer after thyroidectomy and radioactive iodine ablation therapy, because normal thyroid release of thyroglobulin should no longer be present. Measurement of thyroglobulin levels has no role in the evaluation of hypothyroidism.

Q8 (MKSAP): A 42-year-old woman is evaluated for an asymmetric enlargement of her thyroid. She is otherwise asymptomatic, and she has no risk factors for thyroid cancer. On physical examination, a possible thyroid nodule is palpated on the left side. A complete blood count, routine serum chemistry tests, and thyroid-stimulating hormone level (TSH) are normal. Ultrasound examination reveals a 2.2-cm left-sided solid nodule.
What is the appropriate next step in the evaluation of this patient?

(A) Fine-needle aspiration of the thyroid nodule
(B) Measurement of serum free thyroxine (Ta)
(C) Measurement of thyroglobulin level
(D) Thyroid scan and radioactive iodine uptake test
(E) Thyroidectomy

Explanation: The appropriate next step in the evaluation of this patient is a fine-needle aspiration of the thyroid nodule. The prevalence of palpable thyroid nodules is 4% to 7%. The cancer risk for a thyroid nodule is 5% to 10%. Factors associated with increased cancer risk include extremes of age (<20 or >60 years), male sex, a history of head or neck irradiation, a family history of thyroid cancer (especially medullary thyroid cancer), nodule size larger than 1 cm, rapid nodule growth, and hoarseness.
Fine-needle aspiration is a simple method of determining the presence of malignancy. Sensitivity is approximately 90% to 95%, with a false-negative rate of 1% to 11%. Guidelines recommend biopsy of any nodule greater than 1 cm in diameter, and biopsy of smaller nodules should be considered in patients with cancer risk factors.
Limited laboratory testing is typically required in the evaluation of a thyroid nodule. Beyond a routine complete blood count and serum chemistry panel, the serum thyroid-stimulating hormone (TSH) level should be measured, because the result will help guide the evaluation (autonomously functioning nodules and multinodular goiters that suppress TSH levels are rarely malignant). Concomitant measurement of the serum free thyroxine (Ta) level is also reasonable if patients have thyroid-related symptoms but unnecessary in an asymptomatic patient with a normal TSH level such as this patient.
Thyroglobulin, a glycoprotein integral in follicular storage of thyroid hormone, can be detected in serum of normal patients. Thyroglobulin levels can be elevated in hyperthyroidism and destructive thyroiditis and is an excellent thyroid cancer marker in patients who have undergone thyroidectomy or radioactive iodine ablation. In this patient with an intact thyroid gland, a thyroglobulin level measurement will not be helpful.
A thyroid scan and radioactive iodine uptake test are appropriate in the context of a suppressed serum TSH level because a toxic nodule or multinodular goiter may be present. Because such hyperfunctional nodules rarely harbor cancer (<1%), their evaluation and management are far different. This patient does not have a suppressed TSH, and a thyroid scan and radioactive iodine uptake test is not indicated.
Although surgery is sometimes considered for nodules larger than 4 cm in diameter, surgery has no role in this asymptomatic patient with a smaller nodule.

Answers: Q7: D | Q8: A

Thyroid disorders

Q9 (MKSAP): A 23-year-old woman comes to the office for follow-up. She has a 5-year history of hypothyroidism and has been on a stable dose of levothyroxine for the past 3 years. She is now 4 weeks pregnant with her first child. Physical examination findings are noncontributory. Results of laboratory studies 2 months ago showed a serum thyroid-stimulating hormone (TSH) level of 2.9 U/mL (2.9 mU/L) and a free thyroxine level of 1.4 ng/dL (18.1pmol/L).
Which of the following is the most appropriate management?

(A) Add iodine therapy
(B) Measure her free triiodothyronine (T3) level
(C) Recheck her serum TSH level
(D) Continue current management

Explanation: The most appropriate next step is to recheck this patient's serum thyroid-stimulating hormone (TSH) level. Because a fetus depends on maternal thyroid hormone for the first 10 to 12 weeks of gestation, the thyroid levels of pregnant women with hypothyroidism should be carefully monitored. Recent guidelines recommend that TSH and total thyroxine (T4) levels be monitored throughout pregnancy because standard free Ta levels are not as accurate in pregnant patients. The total T4 level should be kept stable at approximately 1.5 times the normal range, and the TSH level should be kept in the lower range of normal. This may require an increase in their levothyroxine dosage of approximately 35% to 50% as early as the first trimester. Because of estrogen elevation during pregnancy, thyroid-binding globulin (TBG) levels increase. However, without an increase in the dosage of levothyroxine, free Ta levels may decrease as more Ta becomes bound by TBG. After delivery, TBG levels decrease, as do thyroid hormone requirements.
Although maternal iodine replacement has been successfully used in countries with prevalent iodine deficiency, its use in patients who are iodine sufficient can be associated with catastrophic results, such as a fetal goiter (pharmacologic amounts of iodine blocks release of thyroid hormone). Because significant iodine deficiency in the United States is rare, iodine therapy in pregnant U.S. women is not indicated.
Measurement of the free triiodothyronine (T3) level is not useful in the evaluation of hypothyroidism because T levels typically remain within the reference range until the point of severe hypothyroidism. This pattern is unaltered by pregnancy.
Continuing the current management is inappropriate because undertreatment of maternal hypothyroidism can have a potentially negative effect on fetal neurocognitive development.

Q10 (MKSAP): An 18-year-old woman is evaluated for tachycardia, nervousness, decreased exercise tolerance, and weight loss of 6 months' duration. She has otherwise been healthy. Her sister has Graves disease. She takes no medications. On physical examination, blood pressure is 128/78 mm Hg, pulse rate is 124/min, respiration rate is 16/min, and BMI is 19. There is no proptosis. An examination of the neck reveals a smooth thyroid gland that is greater than 1.5 times the normal size. Cardiac examination reveals regular tachycardia. Her lungs are clear to auscultation. Human chorionic gonadotropin Negative. Thyroid-stimulating hormone <0.01 uU/mL (0.01 mU/L). Thyroxine (T4), free 5.5 ng/dL (71.0 pmol/L). Trirodothyronine (T3), free 9.1 ng/L (14.0 pmol/L)
Which of the following is the most appropriate treatment for this patient?

(A) Atenolol
(B) Atenolol and met himazole
(C) Methimazole
(D) Radioactive iodine and methimazole

Explanation: The most appropriate medical regimen for this patient with Graves disease is atenolol and methimazole. Graves disease can present with either subclinical or overt thyrotoxicosis. Physical examination may reveal tachycardia; an elevated systolic blood pressure with a widened pulse pressure; a palpable goiter, which is classically smooth; a thyrotoxic stare due to lid retraction; proptosis; and, infrequently, an infiltrative dermopathy. To control her tachycardia, a -blocker, such as atenolol, is indicated. Given the clinical and laboratory findings, this patient is also moderately hyperthyroid. To treat her hyperthyroidism, either methimazole or propylthiouracil can be used.
Methimazole, which generally has fewer side effects and results in quicker achievement of the euthyroid state than propylthiouracil, is preferred in most patients. Because of a presumed immunomodulatory effect, antithyroidal drugs result in drug-free remission rates of between 30% and 50% in patients with Graves disease who are treated for year.
Atenolol alone would only address this patient's adrenergic symptoms and not reduce her thyroid hormone levels, and methimazole alone would not immediately address her tachycardia.
Radioactive iodine therapy preceded or followed by adjunctive therapy with an antithyroidal drug is occasionally used to treat Graves disease. The drug is given in an attempt to decrease the risk of a transient worsening of the thyrotoxicosis after thyroid ablation. Because antithyroidal drugs render the thyroid radioresistant, they must be stopped for several days before and after giving the radioactive iodine. Although an occasional patient becomes euthyroid after radioactive iodine administration, the expected outcome is hypothyroidism, which typically occurs within 2 to 3 months of therapy, at which time thyroid hormone replacement therapy is begun

Answers: Q9: C | Q10: B

Thyroid disorders

Q11 (MKSAP): A 26-year-old woman is evaluated for a 2-week history of constipation, fatigue, and weight gain. Three months ago, she began experiencing nervousness, heat intolerance, and weight loss but says these symptoms abated after 6 weeks. The patient delivered a healthy infant 14 weeks ago. After thyroid function tests performed 8 weeks postpartum revealed a thyroid-stimulating hormone (TSH) level of 0.02 U/mL (0.02 mU/L) and a free thyroxine (Ta) level of 3.5 ng/dL (45.2 pmol/L), she was placed on atenolol, 25 mg/d. On physical examination, blood pressure is 115/70 mm Hg, pulse rate is 50/min, respiration rate is 14/min, and BMI is 23.3. No proptosis or inflammatory changes are noted on ocular examination. Examination of the neck reveals no tenderness or bruits; the thyroid gland cannot be palpated.
Which of the following is the best next step in management?

(A) Methimazole
(B) Repeat measurement of TSH and free Ta levels
(C) Thyroid scan and 24-hour radioactive iodine uptake test
(D) Thyroid ultrasonography

Explanation: The best next management step is repeat measurement of the thyroid-stimulating hormone (TSH) and free thyroxine (T.) levels. Postpartum thyroiditis, which occurs in approximately 5% of women in the United States within a few months of delivery, is a variant of painless thyroiditis. At presentation, patients may have transient thyrotoxicosis alone, transient hypothyroidism alone, or thyrotoxicosis that is followed by hypothyroidism and then by recovery. This patient most likely has postpartum thyroiditis that is now in the hypothyroid phase after a period of transient thyrotoxicosis. The hypothyroidism can be confirmed by remeasuring her TSH and free T4 levels.
In this patient, the absence of a goiter and eye disease points away from Graves disease, as does the recent development of symptoms associated with hypothyroidism Methimazole therapy is inappropriate for this patient because she most likely has hypothyroidism, not hyperthyroidism. If transient hypothyroidism is confirmed by a high TSH level and low free Ta level, thyroid hormone replacement, not methimazole, can be considered for bothersome symptoms.
With postpartum thyroiditis, results of thyroid scans and radioactive iodine uptake tests will be low during the thyrotoxic phase and then become elevated during the hypothyroid phase as the thyroid gland recovers and becomes very avid for iodine as stores are repleted. Before such testing can be advised, however, the results of current thyroid function tests are required to assess the patient's thyroid hormone status and determine if scan results suggest Graves disease or, what is more likely, recovery thyroiditis.
Ultrasound of the thyroid gland can be used to distinguish the high vascular flow of Graves disease from the low-flow pattern of autoimmune thyroiditis. A more direct test of this patient's thyroid function, however, is measurement of the TSH and free T4 levels, which can quantify thyroid function and provide a baseline with which to compare future thyroid function test results.

Answers: Q11: B

Parathyroid disorders

Q1 (500Best): A 54-year-old woman presents to her GP complaining of a change in her breathing sound. She first noticed numbness, particularly in her fingers and toes, three months ago but attributed this to the cold weather. Her partner now reports hearing a high pitched, harsh sound while she is sleeping. Her BMI is 27. While measuring blood pressure, you notice the patient's wrist flexing. The most likely diagnosis is:

A. Obstructive sleep apnoea
B. Hypocalcaemia
C. DiGeorge syndrome
D. Guillain–Barré syndrome
E. Raynaud's syndrome

Explanation: This patient exhibits many of the signs present in hypocalcaemia (B) including tingling in the fingers and toes and carpopedal spasm. In the latter, occlusion of the brachial artery, which occurs when measuring blood pressure, causes muscle spasming of the hand and forearm (Trosseau's sign). Other signs include facial muscle twitching when the facial nerve is tapped on the same side (Chvostek's sign), prolonged QT interval, hyperreflexia and stridor. Hypocalcaemia most commonly arises due to renal failure. DiGeorge syndrome (C) is a congenital condition that arises due to an abnormality at chromosome 22q11 causing malformation of the third and fourth pharyngeal arches. Patients present at a young age with cardiac abnormalities, abnormal facies, cleft palate and hypocalcaemia. Raynaud's syndrome (E) is characterized by triphasic changes in the peripheral digits, usually the fingers, stressors such as cold temperature causes arterial spasming which reduces the blood flow to the end arteries. Patients will notice their fingers turn white, blue and then red as the blood flow returns. In mild disease, this can be associated with mild tingling while severe disease can cause severe pain and even necrosis. Obstructive sleep apnoea (A) is a disorder of sleep that is characterized by loss of airway patency causing a significant reduction in airflow despite constant breathing effort. This can occur for a number of reasons such as obesity, asthma and hypothyroidism. However, there are not usually any underlying neurological signs. Guillain–Barré syndrome (D) is an immune-mediated disease which usually results following an infection such as cytomegalovirus (CMV) and campylobacter causing a polyneuropathy. The demyelination typically occurs in a symmetrical ascending pattern starting with the distal limbs. Paralysis of the respiratory muscles can occur, requiring emergency treatment, but there are no signs of hypocalcaemia as in the above patient.

Q2 (500Best): A 39-year-old man presents with a three-month history of depression. The patient recently lost a family member and around the same period began to feel unwell with constipation and a depressed mood. He has started taking analgesia for a sharp pain in his right lower back that often radiates towards his front. The most appropriate investigation is:

A. Serum parathyroid hormone
B. Serum thyroid stimulating hormone
C. Colonoscopy
D. Fasting serum calcium
E. MRI scan

Explanation: This patient appears to be suffering from symptoms of elevated calcium levels, these can include depression, constipation and renal stone formation causing abdominal pain. The normal calcium homeostatic pathway is controlled by parathyroid hormone (PTH). When calcium levels fall, as in malnutrition, PTH levels increase causing calcium reabsorption by the kidneys and the gastrointestinal system, while calcium stored in the bones is released. PTH malignancies are the most common cause of elevated calcium, however the diagnosis of hypercalcaemia itself is only confirmed by measuring the serum calcium itself (D). PTH (A) levels would then reveal whether the hypercalcaemia is due to hyperparathyroidism but are not appropriate before serum calcium measurements. Primary hyperparathyroidism occurs due to parathyroid adenomas producing excess PTH. Secondary hyperparathyroidism is a compensatory increase in PTH in renal failure or vitamin D deficiency. Tertiary hyperparathyroidism is autonomous PTH production after long-standing secondary hyperparathyroidism. An MRI scan (E) would not be appropriate without first measuring blood levels of PTH if a PTH tumour were suspected. Although hyperthyroidism can cause hypercalcaemia, TSH (B) is not measured before serum calcium or PTH. A colonoscopy (C) would be appropriate to investigate unexplained constipation, especially if a gastrointestinal (GI) malignancy were suspected alongside worrying symptoms such as significant weight loss. Less invasive investigations such as blood tests should always be considered before more invasive investigations.

Answers: Q1: B | Q2: D

Parathyroid disorders

Q3 (AMBOSS): A 71-year-old man comes to the emergency department because of a 2-month history of severe muscle cramps and back pain. He says that he is homeless and has not visited a physician in the past 20 years. He is 183 cm (6 ft 0 in) tall and weighs 62 kg (137 lb); BMI is 18.5 kg/m2. His blood pressure is 154/88 mm Hg. Physical examination shows pallor, multiple cutaneous excoriations, and decreased sensation over the lower extremities. Serum studies showed, An x-ray of the spine shows alternating sclerotic and radiolucent bands in the lumbar and thoracic vertebral bodies. Which of the following is the most likely explanation for these findings?

Calcium	7.2 mg/dL
Phosphorus	5.1 mg/dL
Glucose	221 mg/dL
Creatinine	4.5 mg/dL

A- Primary hypoparathyroidism
B- Pseudohypoparathyroidism
C- Secondary hyperparathyroidism
D- Tertiary hyperparathyroidism

Explanation: This patient presents with features of severe chronic kidney disease (CKD) such as high creatinine, cutaneous excoriations due to uremia, anemia (pallor), and a rugger-jersey spine. End-stage renal disease (ESRD) causes hyperphosphatemia due to decreased renal phosphate excretion and hypocalcemia due to decreased renal vitamin D activation. Hypocalcemia is responsible for the muscle cramps seen here. Hypocalcemia would also stimulate the parathyroid glands to secrete PTH (indicating secondary hyperparathyroidism), which results in bone pain with osteitis fibrosa cystica and a rugger-jersey spine (indicating renal osteodystrophy). ESRD is the most frequent cause of secondary hyperparathyroidism.

Q4 (AMBOSS): A 46-year-old woman comes to the physician for a routine health examination. She was last seen by a physician 3 years ago. She has been healthy aside from occasional mild flank pain. Her only medication is a multivitamin. Her blood pressure is 132/88 mm Hg. Physical examination shows no abnormalities. Serum studies showed, Subsequent serum studies show a repeat calcium of 11.2 mg/dL, parathyroid hormone concentration of 890 pg/mL, and 25-hydroxyvitamin D of 48 ng/mL (N = 25–80). Her 24-hour urine calcium excretion is elevated. An abdominal ultrasound shows several small calculi in bilateral kidneys. Further testing shows normal bone mineral density. Which of the following is the most appropriate next step in management?

Sodium	141 mEq/L
Potassium	3.7 mEq/L
Calcium	11.3 mg/dL
Phosphorus	2.3 mg/dL
Urea nitrogen	15 mg/dL
Creatinine	0.9 mg/dL
Albumin	3.6 g/dL

A- Refer to surgery for parathyroidectomy
B- Begin cinacalcet therapy
C- Recommend low-calcium diet
D- Order CT scan of the chest and abdomen

Explanation: The patient's elevated serum calcium level, confirmed by repeat measurement, together with her low phosphorus, elevated serum parathyroid hormone (PTH) level, and elevated 24-hour urine calcium excretion is diagnostic of primary hyperparathyroidism. Parathyroid gland adenomas are the most common cause of primary hyperparathyroidism and require surgical resection for definitive treatment. Surgery is indicated for patients with any of the following: age under 50; evidence of skeletal compromise (e.g., DEXA T-score < -2.5, vertebral fracture on radiograph); evidence of renal compromise (e.g., estimated GFR < 60 mL/min, > 400 mg/day 24-hour urine calcium excretion, presence of nephrolithiasis); serum calcium level > 1 mg/dL higher than the upper limit of normal or symptoms of hypercalcemia. This patient meets the criteria for surgery based on her age, nephrolithiasis, and elevated serum calcium. Prior to surgery, imaging (ultrasonography or nuclear imaging) is indicated to determine the exact location of the abnormal gland(s). Testing for MEN syndromes is generally not indicated in all patients with primary hyperparathyroidism and should be reserved for those with other suggestive features (e.g., family history of primary hyperparathyroidism or thyroid cancer, findings that raise concern for other tumors like pheochromocytoma).

Answers: Q3: C | Q4: A

Parathyroid disorders

Q5 (AMBOSS): A 44-year-old woman is brought to the physician by her friend, who is worried because the patient has recently appeared increasingly depressed. On questioning, the patient reports fatigue, constipation, and pain in her hands for the past few months. She has a history of peptic ulcer disease and recurrent nephrolithiasis. Current medications include esomeprazole. Her serum creatinine and urea nitrogen are within the reference range. An x-ray of her hands shows subperiosteal thinning of the phalanges and several well-defined, multiloculated cysts of the metacarpal bones bilaterally. Which of the following sets of serum parameters is most likely in this patient?

A- A
B- B
C- C
D- D
E- E
F- F

	Calcium	Phosphorus	Alkaline phosphatase	Parathyroid hormone
A	Increased	decreased	increased	increased
B	Decreased	decreased	increased	increased
C	Normal	normal	increased	normal
D	Increased	increased	normal	decreased
E	Normal	normal	normal	normal
F	Decreased	increased	increased	increased

Explanation: In primary hyperparathyroidism, high levels of PTH increase serum calcium levels by increasing bone turnover and by increasing renal calcium reabsorption from the distal convoluted tubule. Increased PTH would also cause hypophosphatemia by preventing phosphate reabsorption at the proximal convoluted tubule. Increased bone turnover would be evident in serum by increased alkaline phosphatase levels. In advanced osteitis fibrosa cystica, large, cystic, vascular cavities with a tumor-like appearance on x-ray and a brown color due to hemosiderin deposition ("brown tumors") can form in long bones. The most common cause of primary hyperparathyroidism is a parathyroid adenoma

Q6 (AMBOSS): A 68-year-old man comes to the physician for a follow-up examination. He has type 2 diabetes mellitus, hypertension, and chronic kidney disease. Medications include insulin, metoprolol, and atorvastatin. Physical examination shows pitting edema of both ankles. Serum creatinine concentration is 4.5 mg/dL. Which of the following sets of serum findings is most likely in this patient?

A- A
B- B
C- C
D- D
E- E

	Parathyroid hormone (PTH)	Vitamin D	Calcium	Phosphorus
A	Decreased	increased	increased	increased
B	Increased	decreased	decreased	increased
C	Increased	decreased	increased	decreased
D	Increased	decreased	decreased	decreased
E	Decreased	decreased	decreased	increased

Explanation: CKD is associated with vitamin D deficiency due to decreased 1-alpha hydroxylase activity. By reducing intestinal absorption of calcium, vitamin D deficiency also causes low calcium levels, which in turn stimulates the secretion of PTH, leading to secondary hyperparathyroidism. Although high levels of PTH normally stimulate renal reabsorption of calcium and excretion of phosphate, phosphate excretion is impaired in CKD, resulting instead in hyperphosphatemia. Other laboratory abnormalities in patients with CKD include hyperkalemia and metabolic acidosis.

Answers: Q5: A | Q6: C

Parathyroid disorders

Q7 (AMBOSS): Two hours after admission to the hospital for dialysis, a 63-year-old woman has severe pain in her lower back. The pain is 8 out of 10 in intensity and radiates down the legs. She underwent a laparoscopic cholecystectomy 4 years ago. She has hypertension, chronic kidney disease, type 2 diabetes mellitus, and major depressive disorder. She lives with her daughter and reports frequent fights with her at home. Her current medications include sertraline, insulin, enalapril, sodium bicarbonate, and sevelamer. She appears uncomfortable. Her temperature is 37.3°C (99.1°F), pulse is 102/min, respirations are 15/min, and blood pressure is 132/94 mm Hg. There is severe tenderness on palpation over the L2 vertebra; range of motion is limited. Neurologic examination shows no focal findings. Laboratory studies showed, An x-ray of the spine shows a wedge compression fracture of the L2 vertebra. Which of the following is the most likely explanation for these findings?

A- Tertiary hyperparathyroidism
B- Senile osteoporosis
C- Secondary hyperparathyroidism
D- Postmenopausal osteoporosis

Explanation: Chronic kidney disease (CKD), which this patient suffers from, is the most frequent cause of secondary hyperparathyroidism (sHPT). In sHPT due to CKD, decreased levels of serum calcium from impaired renal reabsorption and increased serum phosphate from impaired renal excretion cause reactive hyperplasia of the parathyroid glands, increasing PTH secretion. Furthermore, kidney disease decreases biosynthesis of vitamin D, causing hypocalcemia and a further reactive increase in PTH secretion. The lab values indicate that this patient has CKD and hypocalcemia, and likely also hyperphosphatemia given that she is taking sevelamer. Her CKD and low calcium levels predispose her to bony fractures, such as a compression fracture of the L2 vertebra. This decreased bone mass as a result of another medical condition is referred to as secondary osteoporosis.

Q8 (AMBOSS): A 65-year-old woman comes to the office for an annual health maintenance examination. She feels well. Her medical history is significant for vasospastic angina controlled with diltiazem. She has not had menses for 15 years. Her mother died of myocardial infarction at the age of 75 years. She has smoked one pack of cigarettes daily for 30 years and drinks alcohol occasionally. Her other medications are vitamin D and calcium supplements. The patient is 165 cm (5 ft 5 in) tall and weighs 52 kg (115 lb); BMI is 19 kg/m2. Physical examination shows no abnormalities. Results of laboratory studies, including serum calcium and creatinine concentrations, are within the reference ranges. Dual-energy x-ray absorptiometry scan shows a T-score of -2.7 SD. Which of the following is the most appropriate next step in pharmacotherapy?

A- Denosumab
B- Raloxifene
C- Teriparatide
D- Alendronate
E- No further pharmacotherapy is indicated at this time

Explanation: Oral bisphosphonates (e.g., alendronate, risedronate) are the preferred initial treatment in patients with osteoporosis because these drugs prevent bone resorption by inhibiting osteoclasts and can significantly decrease the risk of fracture. Bisphosphonates should be taken in the morning and evening at least 30 minutes before meals, with plenty of water, and the patient should maintain an upright position for at least 30 minutes following intake to prevent esophagitis. Other side effects are osteonecrosis of the jaw and hypocalcemia. Contraindications to bisphosphonates include hypocalcemia, esophageal abnormalities, and decreased glomerular filtration rate. In case of contraindications or unresponsiveness to bisphosphonates, medications such as parathyroid hormone analogs (teriparatide), selective estrogen receptor modulators (raloxifene), or RANKL inhibitors (denosumab) may be used.
Sufficient intake of calcium and vitamin D is recommended as primary prevention and adjunct therapy for osteoporosis. Lifestyle modifications, such as physical activity (e.g., strength and balance training) and avoidance of alcohol, tobacco, and glucocorticoids, should be encouraged.
Denosumab is indicated in patients with osteoporosis and impaired renal function or if the preferred initial treatment has failed. This patient's serum creatinine is normal; therefore, another initial treatment is indicated.
Raloxifene can be used in patients with osteoporosis who have contraindications and/or in those who are unresponsive to the preferred initial treatment. Raloxifene may also be used in patients with osteoporosis who require breast cancer prophylaxis. This patient has no family history of breast cancer. Furthermore, raloxifene increases the risk of thromboembolic events, which is already elevated in this patient who smokes.
Teriparatide can be used in patients with osteoporosis who have contraindications and/or are unresponsive to the preferred initial treatment. Moreover, teriparatide can be considered as an alternative for patients with osteoporosis and a high risk of fracture (e.g., T-score ≤ -3 SD, a history of severe and/or multiple fractures). However, this patient has no history of fractures and a T-score of -2.7 SD.

Answers: Q7: C | Q8: D

Parathyroid disorders

Q9 (AMBOSS): A 63-year-old man comes to the physician because of fatigue and muscle cramps for 6 weeks. He also noticed several episodes of tingling around the mouth and in the fingers and toes. He has osteoarthritis of his knees and hypertension. Current medications include ibuprofen and ramipril. He has smoked one pack of cigarettes daily for 35 years. Tapping over the facial nerve area in front of the ear elicits twitching of the facial muscles on the same side of the face. His serum alkaline phosphatase activity is 66 U/L, serum phosphorus is 5.2 mg/dL, and serum creatinine is 1.1 mg/dL. An ECG shows sinus rhythm with a prolonged QT interval. Which of the following is the most likely underlying cause of this patient's symptoms?

A- Vitamin D deficiency
B- Destruction of parathyroid glands
C- Ectopic hormone production
D- Medication side effect

Explanation: This patient presents with hypocalcemia due to hypoparathyroidism, as indicated by the elevated phosphorus, normal alkaline phosphatase, and symptoms of hypocalcemia in the setting of normal kidney function. Decreased parathyroid hormone (PTH) activity leads to decreased release of calcium and phosphorus from the bone, as well as decreased calcium reabsorption and phosphorus secretion at the kidney. The most common cause of hypoparathyroidism in adults is surgery (e.g., thyroidectomy, parathyroidectomy), which this patient has no history of. Instead, his hypoparathyroidism is most likely due to autoimmune destruction of parathyroid glands (the second most common cause in adults). Other less common causes of hypoparathyroidism are congenital (e.g., DiGeorge syndrome), infiltration of the parathyroid gland (e.g., hemochromatosis, granulomas), and radiation-induced destruction. Vitamin D deficiency can manifest with symptoms of hypocalcemia; however, additional symptoms such as pathological fractures, bone pain, and muscle weakness would be expected. Additionally, this patient's hyperphosphatemia shows that vitamin D-mediated absorption from the intestine remains intact. Moreover, the normal alkaline phosphatase indicates normal osteoblast activity, making metabolic bone disease such as osteomalacia unlikely. Finally, this patient does not have any risk factors for vitamin D deficiency, including low oral intake, malabsorption (e.g., chronic pancreatitis, celiac disease), or defective vitamin D metabolism (e.g., liver cirrhosis).

Q10 (AMBOSS): A 65-year-old woman comes to the physician because of a 4-month history of generalized bone pain. She has a 25-year history of Crohn disease with multiple hospitalizations for acute exacerbations, including a bowel obstruction last year. Current medications include mesalamine and bisoprolol. She is 165 cm (5 ft 6 in) tall and weighs 53 kg (117 lb); her BMI is 19.5 kg/m2. Examination shows a soft abdomen and pale conjunctivae. Neurological examination shows decreased vibratory sensation over her lower extremities. Muscle strength is 4/5 in the distal groups and 3/5 in proximal groups of the lower limbs. The pelvic bones are tender to palpation. An x-ray of the pelvis shows thin cortices and multiple radiolucent bands that are perpendicular to the cortex and surrounded by a thin sclerotic margin. Which of the following laboratory findings are most likely present in this patient?

A- A
B- B
C- C
D- D
E- E
F- F

	Calcium	Phosphate	Alkaline phosphatase	Parathyroid hormone
A	Normal	normal	normal	normal
B	Normal	normal	↑	normal
C	↓	↓	↑	↑
D	↑	↓	↑	↑
E	↓	↑	↑	↑
F	↑	↑	↑	↓
G	↓	↑	normal	↓

Explanation: Severe vitamin D deficiency can lead to hypocalcemia and hypophosphatemia by decreasing the amount of calcium and phosphate absorption in the intestine. As long as calcium levels are low, increased PTH secretion occurs in an attempt to maintain normal serum calcium levels (secondary hyperparathyroidism). PTH releases calcium stored in bone into serum by increasing bone turnover, which the elevated ALP levels (a marker of bone turnover) indicate here. Increased PTH levels also worsen hypophosphatemia by decreasing renal phosphate reabsorption.

Answers: Q9: B | Q10: C

Adrenal disorders

Q1 (500Best): A 28-year-old woman has noticed a change in her appearance; most notably her clothes do not fit properly and are especially tight around the waist. Her face appears flushed and more rounded than usual, despite exercising regularly and eating healthily her weight has steadily increased over the last 3 weeks. On visiting her GP, he notices her blood pressure has increased since her last visit and she has bruises on her arm. She is especially worried about a brain tumour. The most appropriate investigation would be:

A. Low-dose dexamethasone test
B. High-dose dexamethasone test
C. Urinary catecholamines
D. Computed tomography (CT) scan
E. Urinary free cortisol measurement

Explanation: The patient appears to be suffering from cushingoid symptoms. After a history to exclude causes such as high-dose steroid intake, the main differential diagnoses include an adrenal tumour, an ectopic tumour producing ACTH (Cushing's syndrome) or a pituitary tumour (Cushing's disease). Although a 24-hour urinary free cortisol level measurement (E) does not confirm the exact diagnosis, it does indicate if there is a pathological excess of cortisol (levels can vary up to 700 nmol/L in the morning to 280 nmol/L at midnight). A low dose (0.5 mg) dexamethasone test (A) involves measuring ACTH after dexamethasone administration. In Cushing's disease and syndrome, there is no suppression of ACTH. A highdose dexamethasone test (B) will differentiate between Cushing's disease and Cushing's syndrome since only in the former is there suppressed ACTH production after high-dose dexamethasone administration. A CT scan (D) can be used to identify a pituitary tumour if requiring surgical management. Urinary catecholamine (C) measurement is used in the diagnosis of a phaeochromocytoma, an adrenal tumour producing excess catecholamines measurable in the urine. Differentiating an adrenal tumour producing excess cortisol can be done by administering metyrapone, an 11-β hydroxysteroid dehydrogenase inhibitor, which effectively ceases adrenal cortisol production. If cortisol is still high it is due to an ectopic source, e.g. lung tumour.

Q2 (500Best): A 22-year-old woman complains of dizziness and feeling light-headed. She works in an office and most frequently experiences this when standing up to visit the toilet. She has never fainted. The patient has lost 5kg, but attributes this to eating more healthily. She has noticed a recent scar on the back of her hand which has started to turn very dark. The most appropriate investigation is:

A. Synacthen test
B. Low-dose dexamethasone test
C. Cortisol measurement
D. Urinary free cortisol measurement
E. Abdominal ultrasound (US) scan

Explanation: This patient has Addison's disease whereby the adrenal gland is destroyed, usually due to infection (TB) or autoimmunity. The reduced cortisol, aldosterone and sex steroids produce a myriad of signs and symptoms, most importantly postural hypotension due to reduced aldosterone and increased pigmentation often in palmar creases and newly formed scars. This latter sign is due to elevated melanocyte-stimulating hormone (MSH) which is derived from the POMC molecule which breaks down into MSH and ACTH. Other symptoms include weight loss, malaise and vitiligo. The synachten test (A) involves giving an infusion of ACTH which would be expected to cause an increase in measured cortisol. A short synacthen test confirms primary Addison's disease, whereas ACTH deficiency or suppression by steroids can be confirmed by doing a long synacthen test. Urinary free cortisol (D) and the low-dose dexamethasone test (B) is appropriate for investigating Cushing's syndrome and is not correct for this patient. A single cortisol measurement (C) is not very valuable for confirming diagnosis due to poor sensitivity and specificity, as well as the diurnal nature of cortisol. A random measurement below 100 nmol/L during the day is more suggestive of Addison's disease, while a value of >550 nmol/L makes the diagnosis less likely. An abdominal US scan (E) would not be appropriate until less invasive blood tests which can confirm Addison's had been conducted.

Q3 (500Best): A 47-year-old woman presents to clinic after being referred from her GP for consistently elevated blood pressure. Her last reading was 147/93. The female does not report any symptoms but recently lost her job and attributes the elevated reading to stress. Her blood tests are as follows:
The most appropriate investigation is:

Sodium	146
Potassium	3.4
Glucose (random)	7.7
Urea	4

A. CT scan
B. 24-hour ambulatory blood pressure
C. Abdominal ultrasound scan
D. Aldosterone–renin ratio
E. Glucose tolerance test

Explanation: The main differential in this patient is hyperaldosteronism arising from an adrenal tumour (Conn's syndrome). The excess aldosterone causes hypertension, elevated sodium reabsorption and potassium excretion. **However, given the patient history, the elevated blood pressure could easily be due to the stress of having blood pressure measured or the patient's personal situation. A 24-hour ambulatory blood pressure measurement (B) is therefore the most appropriate investigation** to eliminate essential hypertension. Since the blood results are only mildly deranged and essential hypertension has not been eliminated, an aldosterone–renin ratio (D), CT scan (A) or abdominal ultrasound (C) would not be the first-line investigations to consider. They would be useful to investigate Conn's syndrome if essential hypertension was excluded as a differential. A glucose tolerance test (E) is inappropriate in this case since the random glucose reading is not abnormal and the patient is not suffering from symptoms suggestive of diabetes.

Answers: Q1: E | Q2: A | Q3: B

Adrenal disorders

Q4 (500Best): A 65-year-old woman complains of panic attacks. She has recently retired as a school teacher, but 2–3 times a week she suffers extreme anxiety, becomes short of breath and sweats excessively. Elevated catecholamines are detected in the urine. The most appropriate medical treatment is:

A. Phenoxybenzamine alone
B. Prolopanolol alone
C. Phenoxybenzamine followed by propanolol
D. Sodium nitroprusside
E. Propanolol followed by phenoxybenzamine

Explanation: Phaeochromocytomas are malignancies of the sympathetic tract, most commonly arising as tumours of the adrenal medulla. The excess catecholamines put the patient at considerable risk of cardiovascular compromise, initial treatment must therefore protect against this with complete alpha and beta blockade (C). Phenoxybenzamine (A) is a nonreversible alpha antagonist which acts to protect against the effects of hypertension. Propanolol (B) is a non-selective beta-blocker which negates the increased heart contractility (inotropic effects) and heart rate (chronotropic effect). Alpha and beta blockade alone is not sufficient to protect the patient. The alpha blockade by phenoxybenzamine must be started first before propanolol to prevent exacerbating the hypertension (E). Sodium nitroprusside (D) is a potent vasodilator and is used during surgery when removing the adrenal tumour. Since severe hypertension can occur, sodium nitroprusside is used in this instance only.

Q5 (500Best): A 57-year-old woman, who has recently returned from a holiday in America, presents with dull grey-brown patches in her mouth and the palms of her hand which she has noticed in the last week. She has also noticed she gets very dizzy when rising from a seated position and is continually afraid of fainting. The most likely diagnosis is:

A. Addison's disease
B. SIADH
C. Conn's syndrome
D. Waterhouse–Friderichsen syndrome
E. 17-hydroxylase deficiency

Explanation: This patient is suffering from Addison's disease (A) whereby the adrenal gland is destroyed, usually due to infection (TB) or autoimmunity. The reduced cortisol, aldosterone and sex steroids produce a myriad of signs and symptoms: most importantly, postural hypotension due to reduced aldosterone and increased pigmentation often in palmar creases and newly formed scars. This latter sign is due to elevated MSH which is derived from the POMC molecule which breaks down into MSH and ACTH. Other symptoms include weight loss, malaise, postural hypotension and vitiligo. The SIADH is due to inappropriately elevated levels of ADH (B) which leads to the retention of water. The syndrome is therefore characterized by reduced serum sodium levels (hyponatraemia) and reduced serum osmolality, while urine osmolality and urine sodium levels are elevated. Patients are also euvolaemic without signs of oedema. In patients suffering from heart failure, liver failure or the nephrotic syndrome, the reduced circulatory volume acts as a stimulus for the ADH secretion. Conn's syndrome (C) causes a significantly elevated level of aldosterone secondary to an adrenal tumour. The Waterhouse–Friderichsen syndrome (D) is adrenal haemorrhage that most commonly occurs due to meningococcal infiltration. Patients tend to present with abdominal pain, although symptoms of hypoadrenalism do occur and include fatigue, weakness, dizziness and vomiting. Symptoms of the underlying disease process are also often present, such as fever. This condition tends to occur in younger patients and rarely affects adults. Patients therefore tend to be fluid overloaded resulting in elevated blood pressure. 17-hydroxylase deficiency (E) is usually recognized around puberty, patients present with hypertension, hypokalaemia and hypogonadism. The aldosterone synthesis pathway is overstimulated, while cortisol and sex steroid synthesis is reduced.

Q6 (pretest): A 58-year-old man is referred to your office after evaluation in the emergency room for abdominal pain. The patient was diagnosed with gastritis, but a CT scan with contrast performed during the workup of his pain revealed a 2-cm adrenal mass. The patient has no history of malignancy and denies erectile dysfunction. Physical examination reveals a BP of 122/78 with no gynecomastia or evidence of Cushing syndrome. His serum potassium is normal. What is the next step in determining whether this patient's adrenal mass should be resected?

A. Plasma aldosterone/renin ratio
B. Estradiol level
C. Plasma metanephrines and dexamethasone-suppressed cortisol level
D. Testosterone level
E. Repeat CT scan in 6 months

Explanation: This patient has what is commonly referred to as an adrenal incidentaloma. If the mass is greater than 1 cm, the first step is to determine whether it is a functioning or nonfunctioning tumor via measurement of serum metanephrines (pheochromocytoma) and dexamethasone suppressed cortisol (Cushing syndrome) levels. As the patient has no history of malignancy, a CT-guided fine-needle aspiration is not required. The patient has normal BP and potassium; therefore, plasma aldosterone/plasma renin ratio to evaluate primary hyperaldosteronism is not required. There are no signs of feminization or erectile dysfunction, so sex-steroid measurement is not indicated. Unenhanced CT would be required after appropriate serum workup to determine true size and characteristics (Hounsfield units [HU]). Malignant indicators include large-size (> 4-6 cm), irregular margins, soft tissue calcifications, tumor inhomogeneity, or high unenhanced CT attenuation values greater than 10 HU. CT scans should be performed in 6 months and again in 1 year to ensure stability of the adrenal mass, but only after a functioning tumor has been excluded.

Answers: Q4: C | Q5: A | Q6: C

Adrenal disorders

Q7 (MKSAP): A 51-year-old woman is evaluated in the office following an emergency department visit for abdominal pain. The pain spontaneously resolved. A CT scan in the emergency department revealed an incidentally discovered 1.4-cm left adrenal nodule with smooth borders and low attenuation and vascularity. She is otherwise healthy and takes no medications. On physical examination, temperature is 36.5°C (97.7°F), blood pressure is 120/80 mm Hg, pulse rate is 60/min, and respiration rate is 14/min. The remainder of the physical examination is normal. A comprehensive metabolic profile, including electrolytes, is normal.
Which of the following diagnostic tests should be done next?

(A) Aldosterone and renin levels and overnight suppression test
(B) Aldosterone and renin levels and dehydroepiandrosterone sulfate (DHEA-S) and testosterone levels
(C) Plasma metanephrine levels and overnight dexamethasone suppression test
(D) Plasma metanephrine levels, DHEA-S, and testosterone levels
(E) No additional tests

Explanation: Plasma-free metanephrine levels and overnight dexamethasone suppression test should be done next. The increasing use of imaging studies has revealed many previously unrecognized, often asymptomatic adrenal masses (adrenal incidentalomas). Initial assessment should include a careful history and physical examination to find any suggestion of malignant disease or clinical evidence of hormone hypersecretion. Most patients with metastatic cancer of the adrenal glands have clinical evidence of disease elsewhere.
Imaging characteristics of the mass (size, CT attenuation, vascularity) can provide important clues. The risk of primary or metastatic cancer is nearly 2% for tumors less than 4 cm in diameter but increases to 25% for tumors 6 cm or larger. Metastatic lesions to the adrenal glands tend to have a high CT attenuation (>20 Hounsfield units) and are often bilateral. Primary adrenocortical carcinoma tends to be large with irregular borders and may include areas of necrosis. Pheochromocytoma, adrenal carcinoma, and metastatic disease to the adrenal glands are often vascular, whereas benign adrenal adenomas are not highly vascular. Because overt clinical manifestations are typically scant, screening tests are often necessary to identify potentially functioning adrenal incidentalomas secreting cortisol, aldosterone, or catecholamines. Subclinical Cushing syndrome is the most common abnormality associated with adrenal incidentalomas. Because these patients have no symptoms or physical findings of Cushing syndrome, the possibility of autonomous hypersecretion of glucocorticoids should be evaluated with an overnight dexamethasone suppression test. Additionally, measurements of plasma catecholamines are reasonable screening tests to rule out pheochromocytoma, which can be asymptomatic or associated with intermittent symptoms.
Adrenal incidentalomas are unlikely to secrete aldosterone, but patients should be screened for that possibility if they have hypertension or hypokalemia, both of which are absent in this patient. Similarly, excess adrenal androgen production is rare, except when the mass represents adrenal cancer, and screening is not routinely performed in the absence of clinical signs or symptoms of feminization in men or hyperandrogenism in women, which is also absent in this patient.

Q8 (MKSAP): A 43-year-old man is evaluated for drug-resistant hypertension. Hypertension was diagnosed 1 year ago and has been difficult to control despite maximum dosages of lisinopril, metoprolol, and nifedipine. The patient reports feeling well. On physical examination, temperature is 36.5°C (97.7°F), blood pressure is 146/92 mm Hg, pulse rate is 88/min, respiration rate is 17/min, and BMI is 27. Results of the general physical examination and funduscopic examination are unremarkable.
Electrolytes: Sodium 143 meq/L (143 mmol/L). Potassium 3.3 meq/L (3.3 mmol/L).
Chloride 101 meq/L (101 mmol/L). Bicarbonate 33 meq/L (33 mmol/L). Creatinine 1.0 mg/dL (88.4 umol/L).
Spot urine potassium Inappropriately high
Urinalysis Normal
Which of the following is the most appropriate next diagnostic test?

(A) CT of the adrenal glands
(B) Determination of serum aldosterone to plasma renin activity ratio
(C) Digital subtraction renal angiography
(D) Measurement of plasma metanephrine and normetanephrine levels

Explanation: The most appropriate next diagnostic test is determination of the serum aldosterone to plasma renin activity ratio. This patient has drug-resistant hypertension (uncontrolled hypertension on three drugs, including a diuretic), unprovoked hypokalemia, and probable metabolic alkalosis; he also has an inappropriately high urine potassium level. In this setting, primary hyperaldosteronism is a very likely cause of his hypertension and hypokalemia, especially given his age. The best screening test for primary hyperaldosteronism is a determination of the ratio of serum aldosterone (in ng/dL) to plasma renin activity (in ng/mL/min). A ratio greater than 20, particularly when the serum aldosterone level is greater than 15 ng/dL (414 pmol/L), is consistent with the diagnosis of primary hyperaldosteronism.
After biochemical confirmation of hyperaldosteronism, localization procedures are appropriate to differentiate aldosterone-producing adenomas, which are amenable to surgical resection, from bilateral hyperplasia, which is medically treated. Given the high incidence of incidental adrenal lesions, however, imaging studies, such as CT of the adrenal glands, should not be performed before biochemical testing that confirms the presence of hyperaldosteronism.
This patient does not fit the demographic or clinical profile of a patient with renovascular hypertension, and thus evaluating the renal arteries with digital subtraction renal angiography is not indicated. Renovascular hypertension due to fibromuscular disease of the renal arteries usually presents in patients younger than 35 years, and azotemia is rarely present. Atherosclerotic renovascular hypertension is more common in patients older than 55 years and is frequently associated with vascular disease in other vessels; azotemia is often present. Other than sustained hypertension, this patient did not have any of other symptoms or signs suggestive of a pheochromocytoma (palpitations, headache, tremor, diaphoresis). Therefore, screening for a pheochromocytoma with measurement of the plasma metanephrine and normetanephrine levels is less likely to be helpful than is screening for hyperaldosteronism.

Answers: Q7: C | Q8: B

Adrenal disorders

Q9 (MKSAP): A 55-year-old woman is evaluated for a 6-month history of recurrent episodes of palpitations, sweating, and headaches. Medical history is otherwise unremarkable. She takes no medications. On physical examination, the patient appears anxious. Temperature is 36.9°C (98.4°F), blood pressure is 158/96 mm Hg, pulse rate is 88/min, respiration rate is 18/min, and BMI is 30. Findings from a general physical examination, including examination of the thyroid gland, are otherwise unremarkable.
Laboratory studies show elevated plasma epinephrine and norepinephrine levels.
Which of the following is the most appropriate next management step?

(A) Abdominal CT scan
(B) Adrenalectomy
(C) Bilateral adrenal vein sampling
(D) Metaiodobenzylguanidine (MIBG) scan

Explanation: The most appropriate next management step for this patient is an abdominal CT scan. She has the classic symptoms of pheochromocytoma--palpitations, sweating, headaches, and hypertension. Additionally, biochemical testing revealed increased plasma levels of catecholamines. Most pheochromocytomas are located in the adrenal medulla, although some are extra-adrenal in origin. CT has sensitivities of 93% to 100% in detecting adrenal pheochromocytoma and approximately 90% in detecting extra-adrenal catecholamine-secreting paragangliomas. MRI is as sensitive as CT in detecting adrenal pheochromocytomas and superior to CT in detecting extra-adrenal catecholamine-secreting paragangliomas.
An adrenalectomy is appropriate only when a tumor is confirmed. An adrenalectomy would not be indicated if the source of the catecholamines were confirmed to be extra-adrenal.
If an abdominal CT shows no masses, the next best localizing study would be a metaiodobenzylguanidine (MIBG) scan. MIBG scintigraphy is highly specific (99%) but less sensitive (80%) than CT techniques. MIBG scintigraphy is generally reserved for patients with equivocal CT results, extra-adrenal catecholamine-secreting tumors, or suspected malignancy.
Adrenal vein sampling is a technically difficult and hazardous procedure, especially in a patient with a pheochromocytoma. The availability of the highly specific and sensitive MIBG scan should take precedence over this more hazardous procedure.

Q10 (MKSAP): A 65-year-old woman is evaluated for a 3-week history of fatigue, nausea, and poor appetite. In the week before symptom onset, she had acute bronchitis with productive cough and fever. The patient has a 2-year history of osteoarthritis of the knees that requires intra-articular corticosteroid injections every 3 to 4 months; her last injection was 3 months ago. Her only other medication is acetaminophen. On physical examination, the patient looks tired. Temperature is 37.5°C (99.5°F), blood pressure is 112/58 mm Hg, pulse rate is 92/min, respiration rate is 17/min, and BMI is 32. The patient has cushingoid features and central obesity. There are multiple ecchymoses on the upper and lower extremities. Decreased axillary and pubic hair is noted. There is bony hypertrophy and small effusions of the knees bilaterally but no evidence of warmth or erythema.
Adrenocorticotropic hormone (AM) Low normal
Cortisol (8 AM):
Initial measurement Low.
After cosyntropin stimulation Low normal.
Which of the following is the most likely cause of this patient's recent symptoms?

(A) Adrenal adenoma
(B) Exogenous corticosteroids
(C) Pituitary microadenoma
(D) Primary adrenal insufficiency

Explanation: This patient has central adrenal insufficiency secondary to exogenous corticosteroid use. Systemic corticosteroids are the most common cause of central adrenal insufficiency, with supraphysiologic doses of exogenous corticosteroids causing disruption of hypothalamic/pituitary adrenocorticotropic hormone (ACTH) production. Consequently, the adrenal cortex atrophies. When subsequently challenged by stress, the hypothalamus and pituitary gland are unable to stimulate adequate adrenal production of cortisol. This central effect of exogenous corticosteroids can occur after only 3 weeks of suppressive therapy. The patient appears to have developed Cushing syndrome as a result of chronic systemic exposure to the intra-articular injections of corticosteroids. Despite her cushingoid features, however, she has clinical and biochemical evidence of adrenal insufficiency. Her low-normal serum ACTH level and her partial response to cosyntropin stimulation indicate that she has central (secondary) adrenal insufficiency. Patients with adrenal insufficiency often decompensate during concurrent illnesses.
An adrenal adenoma could cause a suppressed ACTH level, cushingoid features, and central obesity, but her symptoms also suggest glucocorticoid deficiency. Furthermore, an adrenal adenoma would cause an elevated, not suppressed, cortisol level.
A functioning pituitary adenoma might produce excessive ACTH, but in that case both the ACTH and cortisol levels would be elevated, not suppressed as they are in this patient. A nonfunctioning pituitary adenoma might cause suppressed levels of ACTH and cortisol but there would be no signs of hypercortisolism, as seen in this patient.
Primary adrenal insufficiency (Addison disease) is typically associated with low cortisol production and elevated ACTH levels.

Answers: Q9: A | Q10: B

Obesity

Q1 (AMBOSS): A 57-year-old man comes to the physician two weeks after a blood pressure of 160/92 mm Hg was measured at a routine health maintenance examination. Subsequent home blood pressure measurements since the last visit have been: 159/98 mm Hg, 161/102 mm Hg, and 152/95 mm Hg. Over the past 3 years, the patient has had a 10-kg (22-lb) weight gain. He has type 2 diabetes mellitus. He does not follow any specific diet; he usually eats sandwiches at work and fried chicken or burger for dinner. He says that he has been struggling with a stressful project at work recently. His mother was diagnosed with hypertension at the age of 45. The patient's only medication is metformin. His pulse is 82/min, and blood pressure now is 158/98 mm Hg. The patient is 178 cm (5 ft 10 in) tall and weighs 133 kg (293 lb); BMI is 42 kg/m2. Physical examination shows no other abnormalities except for significant central obesity. Fasting serum studies show: (Total cholesterol;260 mg/dL) (HDL-cholesterol;25 mg/dL) (Triglycerides;230 mg/dL) (Glucose;120 mg/dL). Which of the following is the most important factor in the development of this patient's condition?

A- Accumulation of fat in visceral tissue
B- Resistance to insulin
C- Elevation of blood lipids
D- Genetic predisposition
E- Increased dietary salt intake

Explanation: Metabolic syndrome is caused by resistance to insulin. This condition increases the risk for several health problems including cardiovascular disease and fatty liver. Weight gain leads to accumulation of body fat that requires more insulin in order to take up glucose from the bloodstream. In the initial stages of the disease, the pancreas is able to compensate by increased insulin secretion. However, as insulin resistance progresses and more insulin is necessary, the pancreas is not able to compensate, leading to hyperglycemia.

Q2 (AMBOSS): A 42-year-old woman comes to the physician for a routine health maintenance examination. She has generalized fatigue and has had difficulties doing her household chores for the past 3 months. She has eczema and gastroesophageal reflux disease. She has a history of using intravenous methamphetamine in her youth but has not used illicit drugs in 23 years. Her medications include topical clobetasol and pantoprazole. She is 160 cm (5 ft 3 in) tall and weighs 105 kg (231 lb); BMI is 42 kg/m2. Her temperature is 37°C (98.6°F), pulse is 95/min, and blood pressure is 145/90 mm Hg. The lungs are clear to auscultation. Cardiac examination shows no abnormalities. Pelvic examination shows a normal vagina and cervix. Laboratory studies show:

Hemoglobin	13.1 g/dL
Leukocyte count	7800/mm^3
Platelet count	312,000/mm^3
Serum	
Na+	141 mEq/L
K+	4.6 mEq/L
Cl-	98 mEq/L
Urea nitrogen	12 mg/dL
Fasting glucose	115 mg/dL
Creatinine	0.8 mg/dL
Total cholesterol	280 mg/dL
HDL-cholesterol	55 mg/dL
LDL-cholesterol	175 mg/dL
Triglycerides	250 mg/dL

Urinalysis is within normal limits. An x-ray of the chest shows no abnormalities. She has not lost any weight over the past year despite following supervised weight loss programs, including various diets and exercise regimens. Which of the following is the most appropriate next step in the management of this patient?

A- Metformin and statin therapy and follow-up in 3 months
B- Bariatric surgery
C- Behavioral therapy
D- Phentermine and topiramate therapy and follow-up in 3 months
E- Liposuction

Explanation: Abdominal obesity is the greatest contributing factor to the development of metabolic syndrome.
The main therapeutic goal in the treatment of this condition is therefore weight loss, which will typically lead to resolution or improvement of the other constituent conditions of metabolic syndrome. Lifestyle modification, including diet and exercise programs, is the preferred method for weight loss, but since this patient has already attempted supervised lifestyle changes for a year now and continues to be morbidly obese, bariatric surgery is recommended to ensure weight loss for the best outcome

Answers: Q1: B | Q2: B

Obesity

Q3 (AMBOSS): A 57-year-old woman comes to the physician for a routine health maintenance examination. She has well-controlled type 2 diabetes mellitus, for which she takes metformin. Four years ago, she underwent cholecystectomy for recurrent cholecystitis. She is 163 cm (5 ft 4 in) tall and weighs 84 kg (185 lb); BMI is 32 kg/m2. Her blood pressure is 140/92 mm Hg. Physical examination shows central obesity, with a waist circumference of 94 cm. Serum studies show:

Fasting glucose	112 mg/dL
Total cholesterol	200 mg/dL
HDL-cholesterol	36 mg/dL
Triglycerides	170 mg/dL

Without treatment, this patient is at greatest risk for which of the following conditions?

A- Central sleep apnea
B- Osteoporosis
C- Steatohepatitis
D- Subarachnoid hemorrhage
E- Rheumatoid arthritis

Explanation: The most common complications of metabolic syndrome include cardiovascular disease, type 2 diabetes mellitus, and nonalcoholic steatohepatitis (NASH). NASH arises independently of alcohol use and occurs due to fatty infiltration of hepatocytes, hepatocyte necrosis, and, eventually, fibrosis of the liver. This patient is at high risk of NASH due to her metabolic syndrome and, therefore, at increased risk of developing liver cirrhosis and hepatocellular carcinoma..

Q4 (AMBOSS): A 43-year-old woman comes to the physician for an annual health maintenance examination. On questioning, she has had excessive fatigue for the last month. A few weeks ago, she was diagnosed with carpal tunnel syndrome for which she received a padded cast. She has mild persistent asthma and anxiety disorder. She drinks 2–3 glasses of red wine per night and has smoked one pack of cigarettes daily for 16 years. She is sexually active with her husband of 19 years. Menses occur at regular 28-day intervals and last 4–6 days. Her last menstrual period was 2 weeks ago. She works a desk job in accounting and has recently been working long hours due to an upcoming company merger. Her father has a history of a brain tumor. Current medications include alprazolam and a fluticasone-formoterol inhaler. She is 160 cm (5 ft 3 in) tall and weighs 81.6 kg (180 lb); her BMI is 32 kg/m2. Her temperature is 37.2°C (99° F), pulse is 92/min, and blood pressure is 128/80 mm Hg. Examination shows no abnormalities. Fasting laboratory studies show:

Hemoglobin	13 g/dL
Serum	
Na+	137 mEq/L
K+	4.6 mEq/L
Cl-	105 mEq/L
HCO_3-	22 mEq/L
Urea nitrogen	17 mg/dL
Glucose	160 mg/dL
Creatinine	0.9 mg/dL

Which of the following is the most likely underlying mechanism behind this patient's hyperglycemia?

A- Adverse effect of medication
B- Stress
C- Hypersecretion of ACTH
D- Insulin resistance
E- Increased serum IGF-1 concentration

Explanation: Insulin resistance and subsequent pancreatic β-cell dysfunction are the major pathophysiological mechanisms of type 2 diabetes mellitus. This patient meets the criteria for obesity, a cardinal risk factor for type 2 diabetes mellitus. A fasting glucose level of ≥ 126 mg/dL is diagnostic of diabetes mellitus.

Answers: Q3: C | Q4: D

Obesity

Q5 (pretest): A 42-year-old man sees you because of obesity. He played football in high school and at age 18 weighed 250 lb. He has gradually gained weight since. Many previous attempts at dieting have resulted in transient weight loss of 10 to 15 lb, which he then rapidly regains. He has been attending weight watchers for the last 3 months and has successfully lost 4 lb. Recent attempts at exercise have been limited because of bilateral knee pain and swelling. On examination height is 6 ft 0 in, weight 340 lb, BMI 46. Blood pressure with a large cuff is 150/95. Baseline laboratory studies including CBC, biochemical profile, thyroid-stimulating hormone, and lipids are normal with the exception of fasting serum glucose, which is 145 mg/dL. What is the best next step?

A. Discuss bariatric surgery with the patient.
B. Refer to a commercial weight-loss program.
C. Recommend a 1000-calorie per day diet.
D. Prescribe phentermine.
E. Recommend a low-fat diet.

Explanation: This patient has morbid obesity (BMI over 40) and has comorbidities of hypertension, diabetes, and osteoarthritis of the knees. Two large meta-analyses have established that bariatric surgery is more effective than nonsurgical therapy for achieving sustained weight loss and controlling comorbid conditions for patients with morbid obesity. Surgical mortality is low (< 1%) and surgery is associated with long-term sustained weight loss of 45 to 65 lb. Several professional organizations, including the American College of Physicians, now recommend bariatric surgery as the treatment of choice for patients with morbid obesity, especially if they have comorbid conditions and have failed dietary therapy. Controlled trials have established that caloric restriction and physical activity can achieve modest weight reduction, usually on the order of 2% to 8%. A review of commercial weight-loss programs demonstrated that Weight Watchers was the most effective with a sustained weight reduction of 3% at 2 years. Medications such as orlistat and phentermine are FDA approved for weight reduction but have demonstrated only modest effectiveness. Sibutramine has been removed from the U.S. market due to increased risk of cardiovascular events. This patient has morbid obesity with comorbid conditions and has failed dietary therapy and exercise program. Therefore his physician should discuss the possibility of bariatric surgery for treatment of his obesity.

Answers: Q5: A

Hyperlipidemia

Q1 (MKSAP): A 50-year-old man is evaluated during a routine physical examination. He is asymptomatic, has no medical problems, and takes no medications. He is a nonsmoker and drinks two alcoholic beverages daily. His father, uncle, and a brother had myocardial infarctions bet ween the ages of 55 and 60 years. On physical examination, vital signs are normal. BMI is 28. On the skin examination, he has soft, nontender, yellow plaques measuring between 0.5 and 1 cm on his upper eyelids. The remainder of the physical examination results are normal.
Which of the diagnostic studies should be done next?

(A) Aminotransferase and alkaline phosphatase
(B) Serum ferritin
(C) Serum glucose and hemoglobin A1c
(D) Serum lipids
(E) Thyroid-stimulating hormone

Explanation: The patient's skin lesions are xanthelasmas, which are the most common type of xanthomas. Xanthomas are the characteristic skin conditions associated with primary (due to genetic defects) or secondary hyperlipidemias. Xanthomas are yellow, orange, reddish, or yellow-brown papules, plaques, or nodules. If the infiltration is deep, the xanthoma may be nodular and have normal-appearing overlying skin. The type of xanthoma closely correlates with the type of lipoprotein that is elevated. Xanthelasma is a type of xanthoma characterized by soft, nontender, nonpruritic plaques localized to the eyelids. Xanthelasma can occur without hyperlipidemia, but is often associated with familial dyslipidemias. Other types of xanthomas include eruptive xanthomas, which present as clusters of erythematous papules typically on the extensor surfaces. They are most often associated with extremely high (greater than 3000 mg/dL [33.9 mmol/L]) serum triglyceride levels. Eruptive xanthomas regress with treatment of hypertriglyceridemia. Plane xanthomas are yellow-to-red plaques found in skin folds of the neck and trunk. They can be associated with familial dyslipidemias and a variety of hematologic malignancies.
Tendon xanthomas are subcutaneous nodules occurring on the extensor tendons. They are associated with familial hypercholesterolemia.
Hypothyroidism is associated with elevated lipid levels and can be a cause of secondarv hyperlipidemias. However, hypothyroidism is not directly associated with the formation of xanthomas and usually does not result in lipid levels high enough to cause xanthomas. An elevated serum ferritin suggests the diagnosis of hemochromatosis, but hemochromatosis is not associated with xanthomas. Although liver chemistry tests may be abnormal in patients with extremely elevated lipid levels and are important to monitor during lipid therapy with statins, they are not associated with xanthoma formation. Type 2 diabetes is often seen in association with dyslipidemias, but abnormal glucose levels are not directly related to xanthoma formation.

Q2 (MKSAP): A 41-year-old man is evaluated for follow-up of a lipid profile obtained a month ago. He is a smoker with a 15 pack-year history. He works in an office and does not regularly exercise. He does not have hypertension and does not have a family history of premature coronary heart disease. On physical examination, vital signs are normal. BMI is 38. His waist circumference is 94 cm (43 in). The remainder of his physical examination results are normal. Serum glucose (fasting) 98 mg/dL (5.4 mmol/L).
Total cholesterol 188 mg/dL (4.8 mmol/L). HDL cholesterol 31 mg/dL (0.8 mmol/L).
LDL cholesterol 128 mg/dL (3.3 mmol/L). Triglycerides 145 mg/dL (1.6 mmol/L).
Which of the following is the most appropriate next management step?

(A) Initiate fibrate therapy
(B) Initiate lifestyle modifications
(C) Initiate statin therapy
(D) Ultrasonography to measure carotid artery intimal thickness

Explanation: The most appropriate next management step is to recommend lifestyle modifications. In evaluating and managing low HDL cholesterol, it is important to remember the primary target of therapy is LDL cholesterol. After LDL cholesterol has been evaluated and managed, non-HDL cholesterol is evaluated as a secondary target in patients with elevated triglycerides. This patient has isolated low HDL cholesterol. Because of insufficient evidence of risk reduction from controlled trials, ATP III has not set a specific goal for raising HDL cholesterol. In patients in whom the HDL cholesterol remains low despite use of stat ins or fibrates to treat high LDL or non-HDL cholesterol, or in patients with isolated low HDL cholesterol such as this patient, the first management step is institution of lifestyle interventions, including exercise, tobacco cessation, and weight management, because these interventions are capable of increasing the HDL cholesterol level.
The patient does not meet criteria for stat in therapy because his LDL cholesterol goal is 130 mg/dL (3.4 mmol/L) and his measured LDL cholesterol is 128 mg/dL (3.3 mmol/L). His LDL cholesterol goal is based on the presence of two cardiovascular risk factors: smoking and low HDL cholesterol. Fibrate therapy is not indicated to treat his triglycerides because his non-HDL cholesterol, measured as total cholesterol-HDL cholesterol, is 157 mg/dL (4.0 mmol/L) and is below his target of 160 mg/dL (4.1 mmol/L)
The non-HDL cholesterol goal is calculated as 30 mg/dL (0.8 mmol/L) above the patient's LDL cholesterol goal. Fibrate therapy would be indicated if the patient had a coronary heart disease equivalent such as diabetes or peripheral vascular disease, because fibrate therapy in this setting results in reduced mortality. Ultrasonography is not needed to determine carotid intimal thickness, because such information will not modify therapeutic decisions.

Answers: Q1: D | Q2: B

Hyperlipidemia

Q3 (MKSAP): A 38-year-old man is evaluated during a follow-up visit. A fasting lipid panel was performed 3 weeks ago. The patient does not use tobacco and has no history of heart disease, stroke, transient ischemic attack, diabetes mellitus, or renal, liver, or thyroid disease. His father has hypertension.
He takes no medications and has no allergies. Vital signs are normal; BMI is 32. Physical examination is unremarkable. Fasting lipid levels are as follows: total cholesterol, 234 mg/dL (6.1 mmol/L); HDL-cholesterol, 48mg/dL (1.2 mmol/L); LDL-cholesterol, 158 mg/dL (4.1 mmol/L); triglycerides: 142 mg/dL (1.6 mol/L). All other laboratory findings are within normal limits.
Which of the following is the most appropriate management option for this patient?

(A) Begin therapy with a fibrate
(B) Begin therapy with a statin
(C) Obtain lipoprotein(a) level
(D) Repeat lipid screening in 1 to 2 years

Explanation: The best management for this patient is to repeat a fasting lipid level in the future. This patient has hyperlipidemia, defined by a total cholesterol level above 200 mg/dL (5.2mmol/L). The LDL-cholesterol goal varies depending on the presence or absence of five major cardiovascular risk factors: cigarette smoking, hypertension, older age (men≥45 years; women ≥55 years), low HDL-cholesterol level (<40 mg/dL [1.0 mmol/L]), and a family history of coronary artery disease (first degree male relative <55 years;female relative <65 years).
In patients with zero or one risk factor, the LDL-cholesterol goal is below 160 mg/dL (4.1 mmol/L). This patient has no major risk factors. Because his current LDL-cholesterol level is below 160 mg/dL (4.1 mmolL), no therapy is indicated. The U.S. Preventive Services Task Force (USPSTF) concluded that the optimal interval for repeat screening is uncertain. It would be reasonable to repeat screening every 5 years, as recommended by the National Cholesterol Education Program, or select a shorter interval if the lipid levels are close to the threshold for treatment, as in this patient.
Fibrate therapy would be indicated for hypertriglyceridemia (>200 mg/dL [2.3 mmol/L]) in the setting of elevated non-HDL-cholesterol levels, which is not present in this patient.
Statin therapy would be appropriate for this patient with no risk factors if his LDL-cholesterol level were above 190 mg/dL (5.0 mmol/L) and would be optional if the level were between 160 mg/dL and 190 mg/dL (4.1 and 5.0 mmol/L).
Lipoprotein(a) [Lp(a)] level determination is not recommended for routine practice. Lp(a) is associated with increased risk for CAD but does not appear to be an independent predictor of risk of CAD

Q4 (MKSAP): A 60-year-old man with type 2 diabetes mellitus and hypertension visits the office to establish medical care. His daily medications are metformin, lisinopril, amlodipine, and aspirin. On physical examinat ion, blood pressure is 128/65 mm Hg and pulse is 76/min; BMI is 26. T he remaining physical examinat ion findings are normal.
Cholesterol Total 215 mg/dL (5.6 mmol/L). HDL 39 mg/dL (1.0 mmol/L). LDL 145 mg/dL (3.8 mmol/L). Triglycerides 185 mg/dL (2.1 mmol/L). Hemoglobin A1c 6.5%
Which of the following drugs should be initiated?

(A) Colestipol
(B) Ezetimibe
(C) Niacin
(D) Simvastat in

Explanation: The most appropriate therapy is initiation of a stat in, such as simvastatin. This patient has multiple risk factors for coronary artery disease, including diabetes mellitus, hypertension, and hypercholesterolemia. Diabetes is a coronary artery disease equivalent risk factor, and patients with diabetes have the same LDL-cholesterol goal as patients who have had a myocardial infarction, namely, below 100 mg/dL (2.6 mmol/L). A stat in is the first-line treatment for cholesterol reduction. A 40-mg daily dose of simvast at in would likely reduce the LDL-cholesterol level by 30% and achieve the target goal.
Colestipol interrupts bile acid reabsorption and reduces LDL-cholesterol levels by 10% to 15%. It is often used as a second-line drug with statins because it acts synergistically to induce LDL receptors. However, colestipol can interfere with the absorption of this patient's other medications and, for this reason, is not the best initial management of his hyperlipidemia.
Although ezetimibe reduces LDL-cholesterol levels by reducing cholesterol absorption from the intestine, there are presently no clinical trial results showing that this medication reduces cardiovascular disease events, in contrast to statins. Therefore, ezetimibe should be reserved as an adjunct to other cholesterol-lowering medications if goal level is not achieved or for patients intolerant or allergic to other proven medications.
Niacin is an effective medication for modestly lowering LDL-cholesterol levels and increasing HDL-cholesterol levels but is often not tolerated because of its adverse effects (nausea and flushing), particularly at the dosage needed to achieve adequate reduction of the LDL-cholesterol level. Niacin would be a poor choice for this patient because it can cause glucose intolerance, potentially worsening his glucose control.

Answers: Q3: D | Q4: D

Hyperlipidemia

Q5 (AMBOSS): A 16-year-old girl is brought to the physician by her parents because they are worried about her weight. They have repeatedly tried to make her lose weight over the past year by encouraging her to exercise and eat healthy without any success. She feels well, and her medical history is unremarkable. Her father has hypercholesterolemia and coronary artery disease and her mother has type 2 diabetes mellitus and hypertension. She is 164 cm (5 ft 5 in) tall and weighs 83 kg (183 lb); BMI is 31 kg/m2. Her blood pressure is 127/81 mm Hg. She is at the > 90th percentile for waist circumference. Physical examination shows multiple yellow-pink papules around her elbows and on the back of her thighs. Serum studies showed, Which of the following is the most appropriate initial pharmacotherapy?

(A) Atorvastatin
(B) Orlistat
(C) Fenofibrate
(D) Ezetimibe

Explanation: While management of children and adolescents with hypertriglyceridemia mainly focuses on lifestyle modification (i.e., promoting a healthy diet, physical activity, and weight loss), pharmacotherapy to reduce the risk of acute pancreatitis should be initiated in patients with triglyceride serum levels >1000 mg/dL and can be considered for patients with serum levels of 400–1000 mg/dL. Fibrates, such as fenofibrate, are the most effective drug for lowering triglyceride serum levels and therefore are the treatment of choice.

Causes of dyslipidemia in children and adolescents include an unhealthy diet (e.g., high in saturated fats), an underlying condition (e.g., obesity, type 2 diabetes mellitus), and genetic defects. This patient's presentation with severe hypertriglyceridemia and a family history of dyslipidemia suggests a genetic disorder (e.g., familial hypertriglyceridemia). While hypertriglyceridemia itself is not a strong risk factor for cardiovascular disease, affected patients commonly have other cardiovascular risk factors (e.g., diabetes mellitus, obesity).

Q6 (AMBOSS): A 35-year-old man comes to the physician because of several episodes of crushing substernal chest pain on exertion over the past 6 weeks. The pain occurs when he goes for his morning run and disappears if he slows down to a walk. The patient is concerned because two of his uncles died of myocardial infarction in their early 50s. Physical examination shows yellow plaques on both the palms. Serum lipid studies showed, An ECG shows no abnormalities. Which of the following is the most likely cause of this patient's symptoms?

(A) Defective apolipoprotein B-100
(B) Defective apolipoprotein E
(C) Decreased apolipoprotein C-II
(D) Decreased apolipoprotein B-48

Total cholesterol	650 mg/dL
HDL cholesterol	40 mg/dL
VLDL cholesterol	185 mg/dL
Triglycerides	800 mg/dL
Chylomicron remnants	elevated

Explanation: Type III familial hyperlipidemia (remnant hyperlipidemia) is caused by an autosomal recessive defect in apolipoprotein E (ApoE). ApoE normally mediates the uptake of VLDL and chylomicron remnants into liver cells. Defective ApoE results in the reduced uptake of these lipids, which then causes hyperlipidemia and chylomicronemia. Premature coronary artery disease and peripheral vascular disease due to accelerated atherosclerosis are common complications in such patients.

Q7 (AMBOSS): A 13-month-old boy is brought to the physician for a well-child examination. Physical examination shows hepatosplenomegaly. A venous blood sample obtained for routine screening tests is milky. After refrigeration, a creamy supernatant layer appears on top of the sample. Genetic analysis shows a mutation in the apolipoprotein C-II gene (APOC2) on chromosome 19. This patient is at greatest risk for developing which of the following complications?

(A) Tendinous xanthomas
(B) Myocardial infarction
(C) Acute pancreatitis
(D) Cholesterol embolization syndrome

Explanation: Patients with familial hyperchylomicronemia (type I dyslipidemia) have an increased risk of developing recurrent episodes of acute pancreatitis. These patients typically have serum triglyceride concentrations > 880 mg/dL; the breakdown of these triglycerides by pancreatic lipases creates free fatty acids that directly injure the pancreas and cause an autoinflammatory response. Additional manifestations of familial hyperchylomicronemia that can develop during childhood include eruptive xanthomas, lipemia retinalis, and hepatosplenomegaly (due to chylomicron accumulation).

Answers: Q5: C | Q6: B | Q7: C

Hyperlipidemia

Q8 (AMBOSS): A previously healthy 16-year-old boy comes to the physician because of a 5-day history of pain at the back of his left ankle. His mother had a myocardial infarction at 54 years. His BMI is 23 kg/m2. There is tenderness above the left posterior calcaneus and a firm, 3-cm, skin-colored nodule that moves with the left Achilles tendon. Serum studies in this patient are most likely to show increased levels of which of the following?

(A) Low-density lipoprotein
(B) Triglycerides
(C) Uric acid
(D) Rheumatoid factor

Explanation: Tendinous xanthomas indicate particularly high levels of LDL and are commonly associated with familial hypercholesterolemia, in which extremely elevated circulating LDL occurs due to impaired LDL receptor signaling and breakdown. Other cutaneous manifestations of hyperlipidemia include xanthelasma, arcus lipoides corneae, and non-tendinous xanthoma. Familial hypercholesterolemia is associated with premature complications of atherosclerosis, as illustrated by this patient's maternal history of MI at an early age, and intensive lipid-lowering therapy with statins is vital in preventing cardiovascular complications.
Hereditary causes of hypertriglyceridemia include type I hyperlipidemia (hyperchylomicronemia), type III hyperlipoproteinemia, and type IV hyperlipidemia (hypertriglyceridemia), none of which are associated with Achilles tendon xanthomas. Type I hyperlipidemia may present with eruptive xanthomas but would not explain the premature atherosclerosis seen in this patient's mother. Type III hyperlipoproteinemia is associated with early atherosclerosis but the xanthomas are more commonly found in the palmar creases, rather than the Achilles tendon xanthoma seen in this patient.

Q9 (AMBOSS): A 50-year-old man comes to the physician for his annual health maintenance examination. The patient feels well. He has a history of hypertension, for which he currently takes lisinopril. He has smoked a pack of cigarettes daily for 20 years. He drinks five to six beers on weekends. He is 181 cm tall (5 ft 11 in) and weighs 80 kg (176 lb); BMI is 25 kg/m2. His pulse is 75/min, respirations are 18/min, and blood pressure is 140/85 mm Hg. Physical examination is unremarkable. Laboratory studies showed, In addition to dietary and lifestyle modification, administration of which of the following agents is the most appropriate next step in management?

(A) Cholesterol absorption inhibitor
(B) HMG-CoA reductase inhibitor
(C) Peroxisome proliferator-activated receptor alpha activator
(D) Bile acid resins

Total cholesterol	263 mg/dL
High-density lipoprotein cholesterol	36 mg/dL
Triglycerides	180 mg/dL

Explanation: HMG-CoA reductase inhibitors, more commonly referred to as statins, are the first-line treatment for dyslipidemia. According to the 2018 AHA/ACC guidelines, adults ≤ 75 years of age should be started on statin therapy if they have concomitant clinical ASCVD, an LDL-cholesterol concentration ≥ 190 mg/dL, and/or an estimated 10-year ASCVD risk ≥ 7.5%; adults age 40–75 with diabetes mellitus should also be started on statin therapy. This patient has a calculated LDL level of 191 mg/dL, which is an indication for statin therapy. Statins are the most effective drug for reducing LDL levels and also improving HDL and triglyceride levels. The treatment goal should be an LDL level < 130 mg/dL.

Q10 (pretest): A 32-year-old, overweight, diabetic woman is found to have a triglyceride level greater than 1000 mg/dL. Family history is positive for diabetes, pancreatitis, and premature coronary artery disease. TSH is normal. You advise the patient to follow a low-fat diabetic diet, to exercise regularly and to avoid alcohol. What medication would be most appropriate to start at this time?

A. High-dose rosuvastatin
B. Nicotinic acid
C. Low-dose atorvastatin
D. High-dose fenofibrate
E. Over-the-counter fish oil

Explanation: A normal triglyceride (TG) level is below 150 mg/dL. A moderate to high triglyceride level is between 150 to 499 mg/dL, and over 500 is considered very high. Obesity increases TG levels by causing increased hepatic VLDL production. In diabetes, insulin insufficiency leads to decreased lipoprotein lipase activity and impairment of VLDL catabolism. In addition, this patient may have familial hypertriglyceridemia or familial combined hyperlipidemia. All such patients should be advised to follow a low-fat diet. Because of the risk of acute pancreatitis with such high levels of TG, medication should be instituted as well. Patients with levels over 500 should be started on a fibrate such as fenofibrate or gemfibrozil.
While potent statins such as rosuvastatin and atorvastatin decrease TG modestly, they are second-line agents in this situation. Nicotinic acid also reduces TG levels but often elevates the blood glucose level in diabetics. Fish oil in high doses can lower the TG level but not as effectively as fenofibrate or gemfibrozil.

Answers: Q8: A | Q9: B | Q10: D

Diabetes type 1

Q1 (500Best): A 29-year-old woman is referred to a diabetic clinic for poor diabetes management. She was diagnosed with type 1 diabetes at the age of 12 and prescribed actrapid insulin injections. Recently, the patient has been suffering fluctuations in her plasma glucose levels and her previously well-controlled glycated haemoglobin has risen to 8.1 per cent. The patient admits she has recently been avoiding using her injections. On examination, the patient has a raised, smooth lump that is firm on palpation at the lower abdomen. The most likely diagnosis is:

A. Worsening of diabetes
B. Lipohypertrophy
C. Injection scarring
D. Lipoma
E. Injection abscess

Explanation: Management of diabetes care should always involve explaining the risks of treatment, especially in young children who are using insulin injections. Shallow injections should be avoided as they are painful and can lead to scarring (C). Allergic responses may occasionally occur, but are usually mild and resolve spontaneously. Importantly, patients should be encouraged to alternate injection sites between the thighs, abdomen and shoulder to prevent build up of adipose tissue creating smooth, firm lumps known as lipohypertrophy (B). This is not dissimilar to a lipoma (D) which are benign masses consisting of fatty tissue enclosed by a fibrous capsule. They are usually mobile, painless and soft on palpation. Worsening diabetes (A) does not cause lipohypertrophy, but would likely worsen symptoms of diabetes such as weight loss and osmotic diuresis. Patients also increase their risk of diabetic complications such as retinopathy, neuropathy and nephropathy. An injection abscess (E) can occur in any situation where needles are being used in poor sanitary conditions; the presentation, however, is usually of a pus-filled cavity that is painful and erythematous.

Q2 (500Best): A 29-year-old man presents to his GP complaining of being constantly thirsty, tired and visiting the toilet more often than usual during the last 4 days. He has noticed his clothes have become more baggy and he now needs to tighten his belt. His parents both have diabetes requiring insulin therapy. A fasting plasma glucose result is most likely to be:

A. 9.0 mmol/L
B. 6.0 mmol/L
C. 16.3 mmol/L
D. 5.0 mmol/L
E. 3.0 mmol/L

Explanation: Diabetes symptoms with polyuria, polydipsia and weight loss occur due to the osmotic diuresis that results from elevated blood glucose. In symptomatic patients, a single abnormal glucose reading is adequate and this may be a fasting plasma glucose ≥7.0 mmol/L or a random plasma glucose of ≥11.1 mmol/L, hence the most appropriate answer is (A) while answer (C) is most likely to occur in a patient with significant symptoms with a random plasma glucose measurement. Asymptomatic patients require two abnormal readings, such as two fasting or two random plasma glucose measurements ≥7.0 mmol/L. Answer (D) is within the normal fasting plasma glucose range (3.9–5.5 mmol/L), while answer (E) is hypoglycaemia. Answer (B) is mildly impaired fasting plasma glucose which is unlikely in a patient who is symptomatic.

Q3 (MKSAP): A 20-year-old woman is brought to the emergency department by her college roommate. The patient is lethargic with rapid respirations. Her roommate reports that the patient has had a cough, fever, and chills for the 3 days. She has a 12-year history of type 1 diabetes mellitus. During the previous 24 hours, the patient has had poor oral intake and has not taken her insulin. Today she developed abdominal pain, nausea, and vomiting. On physical examination, the patient is lethargic but arousable. Temperature is 35.5°C (96.0°F), blood pressure is 90/68 mm Hg, pulse rate is 120/min, and respiration rate is 28/min and deep. The cardiopulmonary examination is normal. Bowel sounds are diminished but present. Palpation elicits generalized tenderness, but no peritoneal signs are present. Other than lethargy, the neurologic examination is normal.
Which the following tests will establish the diagnosis?

(A) Serum glucose and electrolytes and urine ketones
(B) Serum glucose and potassium, complete blood count, and urinalysis
(C) Serum glucose, electrolytes, and ketones and arterial blood gases
(D) Serum glucose, phosphate, and potassium and arterial blood gases
(E) Serum ketones and carbon dioxide, complete blood count, and urine ketones

Explanation: This patient has diabetic ketoacidosis (DKA), and the tests to establish the diagnosis are serum glucose, electrolytes, and ketones and arterial blood gases. The most life-threatening acute complication of diabetes is DKA, which mostly affects patients with type 1 diabetes and is sometimes its presenting manifestation. At presentation, patients with DKA usually report a several-day history of polyuria, polydipsia, and blurred vision, culminating in nausea, vomiting, abdominal pain, dyspnea, and altered mental status. Physical examination typically reveals deep, labored breathing (Kussmaul respirations), a fruity odor to the breath (from acetone), poor skin turgor, tachycardia, and hypotension. This complication can occur as a result of precipitating acute stresses such as infections (influenza, pneumonia, or gastroenteritis) or acute myocardial infarction; in patients with insulin pumps, when a technical interruption of insulin infusion occurs; and in patients who are nonadherent to their medication regimen. In almost all instances, DKA is entirely preventable if patients practice regular glucose monitoring and understand the need for increased insulin doses during acute stress events. The diagnosis of DKA is based on a blood glucose level less than 250 mg/dL (13.9 mmolL), anion gap metabolic acidosis (arterial pH <7.30), a serum carbon dioxide level less than 15 meg/L (15 mmol/L), and positive serum or urine ketone concentrations.

Answers: Q1: B | Q2: A | Q3: C

Diabetes type 1

Q4 (AMBOSS): A 12-year-old boy is brought to the physician because of increased frequency of micturition over the past month. He has also been waking up frequently during the night to urinate. Over the past 2 months, he has had a 3.2-kg (7-lb) weight loss. There is no personal or family history of serious illness. He is at 40th percentile for height and weight. Vital signs are within normal limits. Physical examination shows no abnormalities. Serum concentrations of electrolytes, creatinine, and osmolality are within the reference range. Urine studies show:

Blood	negative
Protein	negative
Glucose	1+
Leukocyte esterase	negative
Osmolality	620 mOsmol/kg H_2O

Which of the following is the most likely cause of these findings?

A. Insulin resistance
B. Insulin deficiency
C. Elevated thyroxine levels
D. Inadequate ADH secretion
E. Inadequate ADH secretion

Explanation: Absolute insulin deficiency is the underlying pathology of type 1 diabetes mellitus, caused by an autoimmune-mediated destruction of pancreatic β cells. The resulting elevation of blood glucose levels lead to a range of symptoms, typically including polyuria, nocturia, polydipsia, and increased appetite. Nonspecific symptoms of fatigue, weight loss, and an increased tendency to infections (e.g., skin infections, UTIs) are also common. The symptoms usually develop within days to a few weeks, or manifest suddenly with diabetic ketoacidosis. While glucosuria detected via urine dipstick is suggestive of diabetes mellitus, the diagnosis is confirmed through an oral glucose tolerance test or a random blood glucose level ≥ 200 mg/dL.

Q5 (AMBOSS): A 22-year-old woman with type 1 diabetes mellitus and mild asthma comes to the physician for a follow-up examination. She has had several episodes of sweating, dizziness, and nausea in the past 2 months that occur during the day and always resolve after she drinks orange juice. She is adherent to her diet and insulin regimen. The physician recommends lowering her insulin dose in certain situations. This recommendation is most important in which of the following situations?

A. During a viral infection
B. After large meals
C. Before exercise
D. Before using an albuterol inhaler
E. During pregnancy

Explanation: This patient should be advised to lower her insulin dose before exercise because exertion can cause hypoglycemia by increasing insulin sensitivity (resulting in a reduced need for exogenous insulin) and by increasing insulin-independent glucose uptake. Higher sensitivity to insulin increases glycolysis and reduces gluconeogenesis. The patient should also be advised to closely monitor her blood glucose before, during, and after exercise to watch out for symptoms of hypoglycemia.

Q6 (AMBOSS): A 19-year-old woman comes to the physician for a follow-up examination. She has a history of type 1 diabetes mellitus and is adherent with her medications. After reviewing the patient's recent blood sugar levels, the physician changes the patient's antidiabetic regimen by changing the dosage of an insulin that does not produce an observable peak in serum insulin concentration. The dosage of which of the following types of insulin was most likely changed in this patient's medication regimen?

A. Insulin glargine
B. Insulin glulisine
C. Regular insulin
D. Insulin lispro
E. NPH insulin

Explanation: Insulin glargine is a basal, long-acting, peakless insulin that is nearly identical to human insulin. It can be used in basal-bolus insulin regimens and as basal supported oral therapy. After subcutaneous administration, glargine precipitates in the tissue and forms hexamers, which delay absorption and prolongs the duration of action. Long-acting insulins are usually administered once daily.

Answers: Q4: B | Q5: C | Q6: A

Diabetes type 1

Q7 (MKSAP): A 23-year-old woman with type 1 diabetes mellitus is admitted to the hospital with a diagnosis of community-acquired pneumonia and lethargy. Before admission, her insulin pump therapy was discontinued because of confused mentation. On physical examination, temperature is 37.5°C (99.5° F), blood pressure is 108/70 mm Hg, pulse rate is 100/min, and respiration rate is 24 min. There are decreased breath sounds in the posterior right lower lung. Neurologic examination reveals altered consciousness. Blood urea nitrogen 38 mg/dL. (13.6 mmol/L). Creatinine 1.4 mg/dI. (123.8 umol/L)
Electrolytes: Sodium 130 meg/L (130 mmol/L). Potassium 5.0 meg/L (5.0 mmol/L).
Chloride 100 meq/L (100 mmol/L). Bicarbonate 14 meq/L (14 mmol/L). Glucose 262 mg/dL. (14.5 mmol/L).
Urine ketones Positive. Rapid infusion of normal saline is initiated.
Which of the following is the most appropriate next management step?

(A) Add insulin glargine
(B) Add neutral protamine Hagedorn (NPH) insulin
(C) Implement a sliding scale for regular insulin
(D) Start an insulin drip

Explanation: This patient should be started on an insulin drip. Discontinuation of insulin pump therapy resulted in inadequate insulin coverage; as a result, the patient developed diabetic ketoacidosis, as evidenced by the plasma glucose level of 262 mg/dL (14.5 mmol/L), the positive urine ketones, and an anion gap. It is imperative to recognize that patients with insulin-deficient diabetes mellitus can develop ketoacidosis with only moderate glucose elevations. This patient should now be started on an insulin drip in a monitored setting. Intravenous insulin infusion is usually the preferred met hod of insulin delivery in an emergency because dehydration may be severe (which decreases subcutaneous absorption) and rapid titration of insulin may be required. Her plasma glucose level should be measured every 1 to 2 hours and adjustments made to the insulin infusion, as required, to gradually normalize her glucose level and reverse the ketoacidosis. After the metabolic abnormalities have been corrected and the patient is ready to be transferred to subcutaneous administration of insulin (usually when the patient starts eating), intravenous and subcutaneous insulin administration need to be overlapped to avoid rebound ketoacidosis. Short-acting or rapid-acting insulins should be given for 1 to 2 hours or more intermediate or long-acting insulins for 2 to 3 hours before terminating the insulin infusion to ensure adequate overlap.
Insulin glargine and neutral protamine Hagedorn (NPH) insulin are long-acting preparations that do not provide the flexibility needed to aggressively treat diabetic ketoacidosis. The use of sliding scale insulin will not allow for adequate insulin coverage, and the ketoacidosis can be expected to progress.

Q8 (AMBOSS): A 25-year-old man comes to the physician for a 2-month history of abdominal discomfort, fatigue, and increased urinary frequency, especially at night. He has also noticed that despite eating more often he has lost 14-lbs (6-kg). He has a congenital solitary kidney and a history of Hashimoto thyroiditis, for which he takes levothyroxine. He has smoked two packs of cigarettes daily for 10 years. BMI is 18 kg/m2. His temperature is 36.7°C (98.1°F), pulse is 80/min, and blood pressure is 110/60 mm Hg. Physical examination is unremarkable. Serum studies show an osmolality of 305 mOsm/L and bicarbonate of 17 mEq/L. Urinalysis shows clear-colored urine with no organisms. Which of the following is most likely to be helpful in establishing the diagnosis?

A. Ultrasonography of the thyroid gland
B. Serum glucose
C. Water deprivation test
D. Serum creatinine
E. Digital rectal examination

Explanation: A single random serum glucose level of ≥ 200 mg/dL is sufficient for the diagnosis of diabetes mellitus in a patient with other classic signs of the disease (e.g., polyuria, dehydration, weight loss). Alternatively, a fasting plasma glucose ≥ 126 mg/dL, oral glucose tolerance test ≥ 200 mg/dL, or hemoglobin A1C ≥ 6.5 % are also diagnostic of diabetes mellitus. This patient's young age, history of autoimmune disease, evidence of acidosis, and weight loss are suggestive of type 1 diabetes mellitus, which is caused by autoimmune destruction of pancreatic beta cells.

Q9 (AMBOSS): A previously healthy 15-year-old girl is brought to the physician by her parents for lethargy, increased thirst, and urinary frequency for 10 days. She is 173 cm (5 ft 8 in) tall and weighs 54 kg (120 lb); BMI is 18 kg/m2. Physical examination shows no abnormalities. Her serum glucose concentration is 224 mg/dL. A urine dipstick is positive for ketone bodies. Which of the following is most likely involved in the pathogenesis of this patient's condition?

A. Expression of human leukocyte antigen subtype A3
B. Complement-mediated destruction of insulin receptors
C. Pancreatic islet amyloid polypeptide deposition
D. T-cell infiltration of pancreatic islets

Explanation: In patients with type 1 diabetes mellitus, infiltration of autoreactive CD4 and CD8 positive T cells into the pancreatic islets leads to the progressive destruction of insulin-producing β cells, which ultimately results in insulin deficiency. The immune system is thought to be activated by one or more environmental triggers (e.g., a viral infection, dietary factors) in genetically susceptible individuals. The loss of functioning β cells continues over months to years; symptoms usually manifest once 80–90% of β cells have been destroyed.

Answers: Q7: D | Q8: B | Q9: D

Diabetes type 2

Q1 (500Best): A 60-year-old man visits his GP complaining of tiredness. He has noticed weight loss over the last six months and irritation of the tip of his penis which appears inflamed on examination. He mentions he has been visiting the toilet more often than usual and feeling thirsty. The most appropriate investigation would be:

A. Oral glucose tolerance test
B. Measurement of glycated haemoglobin
C. Random plasma glucose test
D. Water deprivation test
E. Measurement of triglyceride levels

Explanation: Type 2 diabetes symptoms are usually well recognized, as in this patient, with polyuria and weight loss occurring due to the osmotic diuresis that results from elevated blood glucose. In subacute presentations, more subtle signs include lethargy and opportunistic infections, such as Candida, causing pruritus vulvae in females or penile inflammation (balantis) in males. The criteria for diabetes diagnosis depends on the clinical presentation. In symptomatic patients, a single abnormal glucose reading is adequate and this may be a fasting plasma glucose ≥7.0 mmol/L or as in this case a random plasma glucose (C) of ≥11.1 mmol/L. In asymptomatic presentations, two abnormal readings are required, e.g. two fasting plasma glucose ≥7.0 mmol/L or two random plasma values ≥11.1 mmol/L. Water deprivation (D) is useful in investigating polydipsia for conditions such as diabetes insipidus. An oral glucose tolerance test (A) is only used for borderline cases or diagnosis of gestational diabetes. Other investigations, such as triglyceride (E), cholesterol and glycated haemoglobin (B), can be conducted after diagnosis to monitor the progress of the condition and used as potential risk factors for other conditions.

Q2 (500best): A 50-year-old Asian man is referred to the diabetes clinic after presenting with polyuria and polydipsia. He has a BMI of 30, a blood pressure measurement of 137/88 and a fasting plasma glucose of 7.7 mmol/L. The most appropriate first-line treatment is:

A. Dietary advice and exercise
B. Sulphonylurea
C. Exenatide
D. Thiazolidinediones
E. Metformin

Explanation: The initial management of type 2 diabetes (T2DM) should begin with lifestyle changes (A) which involve obtaining a dietary history, physical exercise per week and other factors such as a smoking history. Expert clinical advice may then be offered with the help of a registered dietician, regular exercise encouraged and smoking cessation encouraged. The aim should be to normalize blood glucose, blood pressure and lipid levels. Unfortunately, T2DM becomes progressively worse with time until eventually exogenous insulin replacement is required. Metformin (E) is particularly proficient in lowering serum glucose and should be used in overweight/obese patients with particular difficulty in controlling glucose levels. Insulin secretagogues (B) (sulphonylureas and rapid-acting insulin secretagogues, such as nateglinide and repaglinide) are particularly effective in controlling HbA1 c levels and improving cardiovascular outcomes. They should be used as first-line treatment if patients are not overweight and require rapid glucose control due to hyperglycaemic symptoms. Patients unable to maintain or achieve adequate glucose control may use sulphonylureas as second-line therapy. Exenatide (C) and thiazolidinediones (D) tend to be considered following lifestyle, metformin and sulphonylurea action to control HbA1 c levels.

Q3 (500Best): A 49-year-old man has recently been diagnosed with type 2 diabetes and is being carefully monitored. He has been advised to maintain a healthier diet and lifestyle, he attends a follow-up clinic and claims to have been following the diet stringently since his last appointment three months ago. The most appropriate investigation is:

A. Random plasma glucose
B. Fasting plasma glucose
C. Urine dipstick
D. Glycated haemoglobin
E. Weight measurement

Explanation: Glycated haemoglobin (D) reflects the level of blood glucose due to glucose attachment to red blood cells non-enzymatically. Since red blood cells have a half-life of 120 days, they will reflect the glucose level of the patient for approximately three months. Measuring the random plasma glucose (A) and fasting glucose (B) will show the state of glucose control at the instant of measurement, but provides no information about the degree of control the patient has over a longer period of time. Patients may therefore fast closer to the date of their appointments despite poor compliance. Similarly, urine dipstick (C) can only reflect the control of glucose homeostasis at the instance of measurement, it is also only appropriate as a screening measurement and must be quantified with blood tests. Weight measurement (E) would be useful to measure to record the change in BMI over time; however, it provides no information to the state of diabetes control.

Answers: Q1: C | Q2: A | Q3: D

Diabetes type 2

Q4 (500Best): A 41-year-old man has been recently diagnosed with type 2 diabetes and has been following a plan of lifestyle measures to improve his diet and increase his level of exercise. On returning to clinic, his BMI is 23, fasting plasma glucose 9.0mmol/L, blood pressure 133/84mmHg and HbA1c of 7.1 per cent. The most appropriate treatment option is:

A. Metformin
B. Sulphonylurea
C. Insulin
D. Exenatide
E. Further diet and exercise

Explanation: If after a trial of lifestyle measures aimed at improving diet content and increasing exercise fails to control blood glucose levels and HbA1c , patients may be started on medical therapy. Diet and exercise (E) should continue to be employed alongside medical therapy, but since adequate control has not been achieved following this measure it is not appropriate to continue without medical adjuncts. Sulphonylureas (B) can be considered as first-line medical treatment if the patient is not overweight or if their blood glucose levels are particularly elevated, as in this patient. If neither of these factors exist, as in most patients, metformin (A) is used as firstline treatment. HbA1 c values are used to monitor patient progress and, in the case of improvement, patients are monitored for side effects. If patients on metformin fail to improve their HbA1 c (this can be taken as <6.5 per cent, but patients and clinicians usually agree on a target value) sulphonylureas can be used together to augment therapy. Insulin therapy (C) is usually started after a trial of lifestyle measures, metformin and sulphonylurea has failed to control blood glucose and HbA1 c values (>7.5 per cent or on a target value agreed upon by patient and clinician). Exenatide (D) may also be considered at this juncture instead of insulin if body weight is a particular issue in the patient's management. (Kumar: Metformin is the best-validated treatment for type 2 diabetes and appears as the first-line pharmacological agent in all type 2 diabetes guidelines, sulphonylureas can be used as an alternative first-line agent where metformin is contraindicated (renal impairment, cardiac failure and hepatic failure))

Q5 (pretest): A 50-year-old woman is 5 ft 7 in tall and weighs 185 lb. There is a family history of diabetes mellitus. Fasting blood glucose (FBG) is 160 mg/dL and 155 mg/dL on two occasions. HgA1c is 7.8%. You educate the patient on medical nutrition therapy. She returns for reevaluation in 8 weeks. She states she has followed diet and exercise recommendations, but her FBG remains between 130 and 140 and HgA1C is 7.3%. She is asymptomatic, and physical examination shows no abnormalities. Which of the following is the treatment of choice?

A. Thiazolidinediones such as pioglitazone
B. Encourage compliance with medical nutrition therapy
C. Insulin glargine at bedtime
D. Metformin
E. Glipizide

Explanation: The classification of diabetes mellitus has changed to emphasize the process that leads to hyperglycemia. Type 2 DM is a group of heterogeneous disorders characterized by insulin resistance, impaired secretion of insulin, and increased glucose production. In this type 2 patient, the first intervention, medical nutrition therapy, failed to achieve the goal HgA1c of less than 7.0%. Medical nutrition therapy (MNT) is a term now used to describe the best possible coordination of calorie intake, weight loss, and exercise. It emphasizes modification of risk factors for hypertension and hyperlipidemia, not just weight loss and calorie restriction. Blood glucose control should be evaluated after 4 to 6 weeks and additional therapy should be added; therefore, continued observation is not the best option. Metformin is considered first-line therapy in that it promotes mild weight loss, has known efficacy and side-effect profile, and is available as a generic with very low cost. Thiazolidinediones ("glitazones"), sulfonylureas, and insulin are considered second-line or add-on therapy for most patients with type 2 DM.

Q6 (MKSAP): A 48-year-old man comes to the office for a routine physical examination. The patient is asymptomatic but overweight. Although he has no pertinent personal medical history, he has a strong family history of diabetes mellitus. He currently takes no medications. Results of physical examination are normal, except for a BMI of 29. Results of routine laboratory studies show a fasting plasma glucose level of 158 mg/dL (8.8 mmol/L). These results are confirmed 2 days later.
Which of the following terms best describes his current glycemic status?

A. Impaired fasting glucose
B. Impaired glucose tolerance
C. Metabolic syndrome
D. Type 2 diabetes mellitus

Explanation: This patient has type 2 diabetes mellit us. The diagnosis of diabetes mellit us can be established by a fasting plasma glucose level of at least 126 mg/dL (7.0 mmol/L), a random plasma glucose level of at least 200 mg/dL (11.1 mmol/L) and symptoms of hyperglycemia (for example, polyuria, polydipsia, or blurred vision), or a 2-hour oral glucose tolerance test (OGTT) result of at least 200 mg/dL (11.1 mmol/L). In 2010, the American Diabetes Association endorsed a hemoglobin A1 value of 6.5% of greater as diagnostic of diabetes.Impaired fasting glucose, impaired glucose tolerance, or both mark the transition from normal glucose tolerance to type 2 diabetes mellitus. Impaired fasting glucose is diagnosed when the fasting plasma glucose level is in the range of 100 to 125 mg/dL (5.6 to 6.9 mmolL), and impaired glucose tolerance an analogous prediabetic state--iS diagnosed when the plasma glucose level at the 2-hour mark of an OGTT is 140 to 199 mg/dL (7.8 to 11.0 mmol/L). For a diagnosis of the metabolic syndrome to be made, information about the patient's blood pressure (≥130/85 mm Hg), lipid levels (triglyceride level ≥150 mg/dL [1.7 mmol/L]; HDL-cholesterol <40 mg/dL in men [1.0 mmol/L]), fasting plasma glucose level (≥110 mg/dL [6.1 mmol/L]), and waist circumference (>40 in [>102 cm] in men) is necessary. Insufficient data have been provided for this diagnosis.

Answers: Q4: B (A according to Kumar) | Q5: D | Q6: D

Diabetes type 2

Q7 (MKSAP): A 68-year-old woman is re-evaluated after laboratory studies show a fasting plasma glucose level of 113 mg/dL (6.3 mmol/L). She has a family history of type 2 diabetes mellitus. On physical examination, blood pressure is 142/88 mm Hg and BMI is 29. Other vital signs and examination findings are normal. She undergoes an oral glucose tolerance test, during which her 2-hour plasma glucose level increases to 135 mg/dL. (7.5 mmol/L).
Which of the following is the most appropriate treatment recommendation?

A. Acarbose
B. Metformin
C. Ramipril
D. Rosiglitazone
E. Diet and exercise

Explanation: The most appropriate treatment for this patient is diet and exercise. She has impaired fasting glucose (IFG), defined as a fasting plasma glucose level in the range of 100 to 125 mg/dL (5.6 to 6.9 mmol/L), and should begin a program of intensive lifestyle change, including 30 minutes of exercise most days of the week and a calorie-restricted diet. to achieve weight reduction on the order of 7% of body weight.
Diet and exercise is the recommended approach for patients with either IFG or impaired glucose tolerance (IGT), the prediabetic states. The relative risk reduction (RRR) in the incidence of diabetes in patients with IGT associated with intensive lifestyle change is 58%.
Pharmacologic therapy with glucose-lowering drugs is not indicated for this patient with isolated IFG. In pharmacologic studies of diabetes prevention, acarbose therapy resulted in only a 25% RRR, which is inferior to that obtained with diet and exercise.
Met formin therapy is associated with an RRR of 31%, which is also inferior to the 58% RRR obtained with diet and exercise. Met formin therapy may be considered in patients with both IFG and IGT, who constitute a higher risk group. This patient does not have IGT (fasting plasma glucose level of 140 to 199 mg/dL [7.7 to 11.0 mmol/L] at the 2-hour mark of an oral glucose tolerance test) and so should not receive met formin.
Modulators of the renin-angiotensin axis, such as ramipril and other angiotensin-converting enzyme inhibitors, do not contribute to diabetes prevention
Rosiglitazone and pioglitazone have been associated with 62% and 81% RRRs, respectively, in the incidence of diabetes. These agents, however, are not endorsed for rout < pharmacologic use in patients with prediabetes because of their costs and adverse effects, including edema, increased fracture risk in women, and possible increased cardiovascular morbidity.

Q8 (MKSAP): An obese 44-year-old woman is evaluated for persistent hyperglycemia. For the past 3 months, she has followed a strict regimen of diet and exercise in an attempt to control her hyperglycemia. Home blood glucose monitoring has shown preprandial levels between 120 and 160 mg/dL (6.7 and 8.9 mmol/L) and occasional postprandial levels exceeding 200 mg/dL (11.1 mmol/L). She takes no medications. Vital signs and physical examination findings are normal, except for a BMI of 30. Laboratory studies show a serum creatinine level of 0.8 mg/dL (70.7 umol/L); the urine is negative for microalbuminuria.
Which of the following is the most appropriate treatment?

A. Begin exenatide
B. Begin glimepiride
C. Begin metformin
D. Begin pioglitazone
E. Continue the diet and exercise for an additional 3 months

Explanation: The most appropriate treatment for this patient is to begin metformin. Various oral and injectable agents are available for the initial management of type 2 diabetes, most of which reduce hyperglycemia to a similar degree. Because of its low cost, effectiveness, good tolerability, relative safety, favorable effects on body weight, and absence of hypoglycemia as a side effect, met formin remains the best first-line agent available. Metformin is contraindicated in patients with renal insufficiency (serum creatinine level >1.4 mg/dL [123.8 umol/L] for women and >1.5 mg/dL [132.6 umol/L] for men. For this patient, ongoing attempts at lifestyle change are unlikely to reduce her blood glucose level further. Therefore, initiation of met formin therapy is most likely to improve her glycemic control.
Exenatide, an injectable agent, is only approved for use in combination regimens with oral agents and is inappropriate in most circumstances as monotherapy.
Glimepiride could be used but is associated with weight gain and the risk of hypoglycemia. Overall, it remains a less attractive choice than met formin in most patients, including this one.
Pioglitazone is also available for monotherapy, but its side effects of weight gain, edema, increased peripheral bone fracture rates in women, and high cost make it less attractive than met formin as a first-line therapy.

Answers: Q7: E | Q8: C

Diabetes type 2

Q9 (AMBOSS): A 41-year-old woman comes to the office as a new patient. She recently moved to the area. She feels well. She has dyslipidemia treated with pravastatin. Her past three Pap smears have shown no abnormalities; the most recent Pap smear was 2 years ago. Her maternal aunt was diagnosed with breast cancer at the age of 56 years, and her brother died of a ruptured abdominal aortic aneurysm at the age of 51 years. The patient smoked one-half pack of cigarettes daily for 20 years but quit 10 years ago. She is sexually active with one male partner and uses condoms consistently. She is 155 cm (5 ft 1 in) tall and weighs 70 kg (154 lb); BMI is 29 kg/m2. Her pulse is 68/min, and blood pressure is 129/78 mm Hg. Physical examination shows no abnormalities. Which of the following is the most appropriate health maintenance recommendation at this time?

A. Measure fasting blood glucose concentration
B. Perform abdominal ultrasonography
C. Obtain low-dose CT scan of the chest
D. Perform breast ultrasonography
E. Obtain Pap smear

Explanation: Measurement of fasting blood glucose (FBG) concentration is routinely used to screen for diabetes mellitus. Although screening recommendations for diabetes mellitus differ among expert groups, this 41-year-old patient with dyslipidemia and a BMI of 29 kg/m2 meets the screening criteria of both the United States Preventive Services Task Force (USPSTF) and the American Diabetes Association (ADA). The USPSTF recommends screening individuals 35–70 years of age with a BMI ≥ 25 kg/m2. The ADA recommends screening individuals with a BMI ≥ 25 kg/m2 who have at least one additional risk factor (e.g., physical inactivity, hypertension, dyslipidemia, a first-degree relative with diabetes) and individuals ≥ 45 years of age who have no risk factors. Besides FBG, other tests used to screen for diabetes mellitus include hemoglobin A1C (HbA1c) and the oral glucose tolerance test (OGTT). Each of the following findings can be used to establish a diagnosis of diabetes mellitus: FBG ≥ 126 mg/dL, HbA1c ≥ 6.5%, and a 2-hour plasma glucose ≥ 200 mg/dL during an OGTT.

Q10 (AMBOSS): An 81-year-old man is admitted to the hospital due to acute decompensated heart failure. He has type 2 diabetes mellitus, hypertension, coronary artery disease, and congestive heart failure. Current medications include lisinopril, metformin, and low-dose aspirin. He has smoked one pack of cigarettes daily for 45 years. His temperature is 37.6°C (99.7°F), pulse is 105/min and regular, respirations are 21/min, and blood pressure is 103/64 mm Hg.

A. Begin hydrochlorothiazide therapy
B. Discontinue aspirin therapy
C. Discontinue metformin therapy
D. Begin norepinephrine therapy
E. Begin nitroprusside therapy

Explanation: Metformin is associated with an increased risk of life-threatening lactic acidosis in patients with predisposing conditions that reduce lactic acid clearance (i.e., renal and/or hepatic insufficiency), increased lactic acid production (e.g., sepsis), or a combination of both (e.g., heart failure with low cardiac output). This patient's renal insufficiency and heart failure with decreased cardiac output are both contraindications to metformin therapy, which should therefore be discontinued immediately. Insulin should instead be used for inpatient glycemic control.

Q11 (AMBOSS): A 69-year-old man with type 2 diabetes mellitus comes to the physician for a follow-up examination. His only medication is metformin. He has tried to lose weight for several years without success. He is 168 cm (5 ft 6 in) tall and weighs 110 kg (243 lb); BMI is 39 kg/m2. His hemoglobin A1c is 8.5%. Which of the following is the most appropriate antidiabetic drug to address both this patient's glucose control and weight?

A. Liraglutide
B. Sitagliptin
C. Glipizide
D. Miglitol
E. Rosiglitazone

Explanation: Liraglutide, which is a GLP-1 agonist, can facilitate weight loss and control hyperglycemia. Incretin-based therapeutic agents such as GLP-1 agonists also have the additional benefit of carrying only a low risk of medication-induced hypoglycemia. Besides metformin and GLP-1 agonists, other drugs that can be used for weight loss in diabetic patients include SGLT-2 inhibitors (e.g., dapagliflozin), orlistat, and pramlintide. However, orlistat does not cause glycemic control, which is desired in this patient, and pramlintide is only used in combination with insulin therapy.

Answers: Q9: A | Q10: C | Q11: A

Diabetes complications

Q1 (500Best): A 55-year-old diabetic woman presents with altered sensations in her hands and feet. She finds it difficult to turn pages of books and discriminating between different coins. When walking, the floor feels different and she likens the sensation to walking on cotton wool. The most likely diagnosis is:

A. Autonomic neuropathy
B. Diabetic amyotrophy
C. Acute painful neuropathy
D. Symmetrical sensory neuropathy
E. Diabetic mononeuropathy

Explanation: Diabetic neuropathy is likely to occur through various pathways, occlusion of the vasa nervorum may explain mononeuropathies (E) that occur in isolation and not symmetrically as in this patient. Diffuse symmetrical neuropathies produce more variable presentations and are likely to be due to metabolic damage. The build up of sorbitol and fructose in Schwann cells due to hyperglycaemia is a popular theory. Symmetrical sensory neuropathy (D) is characterized by early loss of vibration, pain and temperature sense in a glove and stocking pattern. In advanced disease, patients often lose their balance and complain of altered sensations. Painful neuropathies (C) are less common and patients typically present with burning sensations or painful parasthesia of their feet, shins or thighs. Diabetic amyotrophy (B) is characterized by painful wasting of the patients' quadriceps muscles and is usually asymmetrical. Control of glucose levels over time usually resolves the condition. Autonomic neuropathy (A) is rarely symptomatic, but can present with a number of different problems of the sympathetic and parasympathetic system. This includes vagal neuropathy causing tachycardia at rest, gastroparesis which rarely can lead to vomiting, erectile dysfunction and atonic bladder.

Q2 (500Best): A 6-year-old girl presents to accident and emergency with severe abdominal pain, nausea and vomiting. On examination, the patient is tachypnoeic, capillary refill is 3 seconds and she has a dry tongue. While listening to the patient's lungs, you detect a sweet odour from her breath. The most likely diagnosis is:

A. Diabetic ketoacidosis
B. Non-ketotic hyperosmolar state
C. Gastroenteritis
D. Pancreatitis
E. Adrenal crisis

Explanation: In diabetic ketoacidosis (A), the body enters a catabolic state as it perceives a lack of energy stores. Ketones are produced from the breakdown of fat which causes an acidotic state in the body. Patients commonly present with nausea, vomiting, dehydration and abdominal pain. The acidosis is partially compensated by hyperventilation (Kussmaul respiration) and the sweet breath is acetone as the body tries to equilibrate the serum pH. A non-ketotic hyperosmolar state (B) usually occurs in type 2 diabetes whereby the hyperglycaemic state causes a hyperosmolar state causing polyuria and dehydration which exacerbate the elevated glucose concentration. Ketones are not responsible as there is a small presence of insulin inhibiting lipolysis. In an adrenal crisis (E), the adrenal gland is destroyed, usually due to infection (TB) or autoimmunity. The reduced cortisol, aldosterone and sex steroids produce a myriad of signs and symptoms, most importantly postural hypotension due to reduced aldosterone and increased pigmentation often in palmar creases and newly formed scars. This latter sign is due to elevated melanocyte-stimulating hormone (MSH) which is derived from the POMC molecule which breaks down into MSH and ACTH. Other symptoms include weight loss, malaise and vitiligo. Gastroenteritis (C) and pancreatitis (D) have more prominent symptoms of abdominal pain and do not usually feature acetone breath.

Q3 (500Best): A 29-year-old woman is found unconscious by her partner and rushed to accident and emergency. She is a type 1 diabetic and has maintained excellent glucose control using insulin injections. Blood biochemistry results demonstrate a moderately raised level of insulin, no detectable C-peptide and very low blood glucose. Her partner mentions she is a lawyer and has been working particularly hard in the last week, eating quick meals and occasionally missing meals. The most likely diagnosis is:

A. Hyperosmolar coma
B. Diabetic ketoacidosis
C. Insulin overdose
D. Hypoglycaemic coma
E. Autonomic neuropathy

Explanation: In this case, the most likely answer is a hypoglycaemic coma (D). The history indicates that the patient has been missing meals but adheres to her insulin regime. The raised insulin level and absent C-peptide indicates no endogenous insulin production (which would produce insulin and C-peptide) but exogenous insulin. The patient has therefore not eaten sufficiently to maintain an adequate glucose level despite taking a recommended dose of insulin. This differs from an insulin overdose (C) where an excess level of insulin is injected causing an abnormally low glucose level. A diabetic ketoacidosis (B) occurs due to the body's attempt to compensate for the perceived lack of glycogen stores due to insulin deficiency. Therefore, by definition, serum insulin levels would be low or absent. A hyperosmolar coma (A) affects type 2 diabetics whereby the hyperglycaemic state causes hyperosmolarity causing polyuria and dehydration. The glucose, however, is low in this case. Diabetic neuropathy can cause a myriad of symptoms due to autonomic dysfunction (E) including urinary incontinence, constipation and postural hypotension. However, there is usually a collection of such symptoms rather than an isolated event. Patients affected also tend to have poor diabetic control.

Answers: Q1: D | Q2: A | Q3: D

Diabetes complications

Q4 (500Best): A 22-year-old woman is found unconscious in her room by her boyfriend and brought into accident and emergency. A urine dipstick is positive for glucose and ketones and blood analysis shows the following results. The most likely anion gap is:

pH	6.9
PCO_2	3.0 kPa
PO_2	13 kPa
Sodium	144 mmol/L
Potassium	5.0 mmol/L
Urea	11
Glucose	20
Chloride	100
Bicarbonate	2.9

A. 180
B. 118
C. 139.2
D. 46.1
E. 28

Explanation: This patient is suffering from an episode of diabetic ketoacidosis; the accumulation of ketones causes a metabolic acid. Calculating the anion gap is useful, narrowing the number of differentials that can cause a metabolic acidosis by showing whether it is due to the retention of H + and Cl − or due to other acids which can help support the suspected diagnosis. The pH balance in the body is maintained by cations such as Na+ , K + and anions such as Cl− , HCO 3 − (there are other cations and anions, but these are the main ones used in anion gap calculations). The anion gap is therefore calculated by ([Na+] + [K+]) − ([HCO3 −] + [Cl−]). The anion gap calculation in this case is ([144]) + ([5]) − ([2.9]) − ([100]) giving 46.1 mmol/L (D). A normal anion gap is 10–18 mmol/L. A normal anion gap in an acidotic patient suggests the retention of H+ /Cl − or the loss of Na+ /HCO3 − . This can be due to diarrhoea, renal tubular acidosis or hyperparathyroidism, among other causes. In a metabolic acidosis with an elevated anion gap, as in this case, an unmeasured anion is present in increased quantities, such as lactate or ketones. Causes include lactic acidosis, ketoacidosis and excess salicylates.

Q5 (MKSAP): A 48-year-old man is evaluated for mild blurring of his central vision bilaterally. He has had type 1 diabetes mellitus for 24 years. The patient is referred for an immediate retinal examination, which reveals macular edema and new neovascularization.
Which of the following is the most appropriate next management step?

A. Addition of aspirin
B. Addition of atorvastatin
C. Decrease in the insulin dosage
D. Retinal photocoagulation

Explanation: Panretinal photocoagulation is the most appropriate next step in management. Diabetic retinopathy is a well-recognized microvascular complication of type 1 diabetes mellitus and is one of the leading causes of visual loss in adults in the United States. Diabetic retinopathy is classified as nonproliferative (with hard exudates, microaneurysms, and minor hemorrhages), which is not associated with visual decline, and proliferative (with "cotton-wool spots" and neovascularization), which is associated with loss of vision. Changes in retinal blood flow occur after several years of diabetes. These changes cause retinal ischemia, which in turn promotes growth factors that stimulate proliferation of new blood vessels. This process leads to scarring and fibrosis. Fibrous tissue can put traction on the retina, which can cause retinal detachment with resultant vision loss. New vessels can also become more permeable and leak serum, which causes macular edema. Tight glycemic control has been shown to decrease the incidence and progression of retinopathy. Blood pressure reduction appears to exert as great a beneficial effect on retinopathy as glycemic control. Once proliferative retinopathy or macular edema is established, vision can be preserved by appropriately timed laser photocoagulation.
Randomized clinical trials have detected no beneficial effect of aspirin on the incidence or progression of proliferative retinopathy or visual loss. At the same time, other studies have not demonstrated harm to the optic system of patients who must take aspirin for cardiovascular protection.
Although lipid-lowering drugs, such as atorvastatin, have been associated in some studies with reduced rates of retinopathy, they cannot alter the course of established retinopathy and are not indicated in this patient.
Abrupt rapid improvement in glycemic control has been associated with modest worsening of diabetic retinopathy in early studies, but there is no evidence that allowing control to deteriorate by reducing the intake of insulin will improve retinopathy. This patient's glycemic control has been stable, so his insulin regimen should not be changed.

Answers: Q4: D | Q5: D

Diabetes complications

Q6 (AMBOSS): A 62-year-old woman with type 2 diabetes mellitus comes to the physician because of a 3-month history of fatigue and weakness. Her hemoglobin A1c concentration was 13.5% 12 weeks ago. Her blood pressure is 152/92 mm Hg. Examination shows lower extremity edema. Serum studies show:
Which of the following is the most appropriate parameter for early detection of this patient's renal condition?

K^+	5.1 mEq/L
Phosphorus	5.0 mg/dL
Ca^{2+}	7.8 mg/dL
Urea nitrogen	60 mg/dL
Creatinine	2.2 mg/dL

A- Urinary red blood cell casts
B- Serum total protein
C- Urinary albumin
D- Serum creatinine

Explanation: Microalbuminuria is the earliest diagnostic sign of diabetic nephropathy. Progression of glomerular damage (nodular glomerulosclerosis) leads to increased urinary loss of albumin, which can manifest as nephrotic syndrome. The extent of albuminuria in patients with diabetic nephropathy also correlates with the risk of future cardiovascular events. ACE inhibitors can prevent the progression of albuminuria in patients with diabetic nephropathy.

Q7 (AMBOSS): A 53-year-old woman comes to the physician because of pain in her ankle. She twisted her right ankle inward when walking on uneven ground the previous day. She describes the pain as 6 out of 10 in intensity. She is able to bear weight on the ankle and ambulate. Three weeks ago, she had an episode of gastroenteritis that lasted for two days and resolved spontaneously. She has type 2 diabetes mellitus, hypertension, and hyperlipidemia. Her father has type 2 diabetes mellitus and chronic renal failure. Her mother has hypothyroidism and a history of alcohol abuse. The patient drinks 8–10 beers each week and does not smoke or use illicit drugs. She adheres to a strict vegetarian diet. Current medications include metformin, atorvastatin, and lisinopril. Her temperature is 36.9°C (98.4°F), heart rate is 84/min, and blood pressure is 132/80 mm Hg. Examination of the right ankle shows edema along the lateral aspect. She has pain with eversion and tenderness to palpation on the lateral malleolus. The foot is warm to touch and has dry skin. Pedal pulses are palpable. She has decreased sensation to light touch on the plantar and dorsal aspects of the big toe. She has full range of motion with 5/5 strength in flexion and extension of the big toe. Laboratory studies show:
Which of the following is the most likely cause of the decreased sensation in this patient?

Hemoglobin	15.1 g/dL
Hemoglobin A1c	8.1%
Leukocyte count	7,200/mm^3
Mean corpuscular volume	82 μm^3
Serum	
Na^+	136 mEq/L
K^+	4.0 mEq/L
Cl^-	101 mEq/L
Urea nitrogen	24 mg/dL
Creatinine	1.3 mg/dL
Thyroid-stimulating hormone	1.2 µU/mL

A- Microvascular damage
B- Vitamin B12 deficiency
C- Acute inflammatory demyelinating polyradiculopathy
D- Medication side effect

Explanation: This patient has a personal and family history of type 2 diabetes mellitus, as well as a hemoglobin A1c > 8%, which suggests that she has not received adequate treatment for her condition. One of the major complications of long-standing undertreated diabetes mellitus is microvascular damage, which typically arises 5–10 years after disease onset and may manifest as diabetic nephropathy, retinopathy, or neuropathy. Diabetic sensory neuropathy presents with a progressive symmetric loss of sensation in the peripheral nerves of the distal extremities, typically in a "stocking-glove" distribution. Patients may also report a burning sensation (dysesthesia) in the affected areas. This patient's loss of sensation on the dorsal and plantar aspects of her right big toe are consistent with diabetic sensory neuropathy. Furthermore, the preservation of motor function is also consistent with the diagnosis, as motor neuropathy is very rare in diabetes..

Answers: Q6: C | Q7: A

Diabetes complications

Q8 (AMBOSS): A 56-year-old woman comes to the physician because of frequent urination. For the past year, she has had to urinate multiple times every hour. She has been thirstier and hungrier than usual. She has not had any pain with urination. She has no time to exercise because she works as an accountant. Her diet mostly consists of pizza and cheeseburgers. Her vital signs are within normal limits. Physical examination shows no abnormalities. Today, her blood glucose level is 200 mg/dL and her hemoglobin A1c is 7.4%. Urinalysis shows microalbuminuria. Which of the following is the most likely cause of this patient's proteinuria?

A- Increased glomerular filtration
B- Diffuse nodular glomerulosclerosis
C- Continuous activation of complement factor C3
D- Renal papillary necrosis

Explanation: Non-enzymatic glycosylation (NEG) is the process driving increased glomerular filtration and progressive loss of glomerular function. This chronic degenerative process can be monitored by measuring urine albumin levels. NEG of the glomerular membrane causes increased permeability and thickening. At the same time, NEG makes the efferent glomerular arterioles more rigid, which further accelerates hyperfiltration and mesangial expansion. Intracellular sorbitol accumulation causes osmotic cell damage.

Q9 (AMBOSS): A 61-year-old man comes to the physician because of progressively worsening swelling of his ankles. He says he has felt exhausted lately. Over the past 3 months, he has gained 5 kg (11 lb). He has smoked one pack of cigarettes daily for 30 years. His pulse is 75/min and his blood pressure is 140/90 mm Hg. Examination shows 2+ pitting edema in the lower extremities. Neurologic examination shows diminished two-point discrimination in the fingers and toes. Laboratory studies show a hemoglobin A1c concentration of 7.9% and a serum creatinine concentration of 1.9 mg/dL. A urine sample is noted to be foamy. A biopsy specimen of the kidney is most likely to show which of the following?

A- Interstitial inflammation
B- Wire looping of capillaries
C- Nodular glomerulosclerosis
D- Immune complex deposition

Explanation: Nodular glomerulosclerosis with Kimmelstiel-Wilson nodules is pathognomonic of diabetic nephropathy, even though diffuse glomerulosclerosis is the most common finding. Early antihypertensive treatment, e.g., with ACE inhibitors, can delay the progression of diabetic nephropathy. Antihyperglycemic therapy for this patient should include lifestyle changes (i.e., weight reduction, increased physical activity, medical nutrition therapy), as well as monotherapy with metformin or insulin therapy to target a hemoglobin A1c < 7%...

Q10 (AMBOSS): A 63-year-old woman comes to the emergency department because of a 1-day history of progressive blurring and darkening of her vision in the right eye. Upon waking up in the morning, she suddenly started seeing multiple dark streaks. She has migraines and type 2 diabetes mellitus diagnosed at her last health maintenance examination 20 years ago. She has smoked one pack of cigarettes daily for 40 years. Her only medication is sumatriptan. Her vitals are within normal limits. Ophthalmologic examination shows visual acuity of 20/40 in the left eye and 20/100 in the right eye. The fundus is obscured and difficult to visualize on fundoscopic examination of the right eye. The red reflex is diminished on the right. Which of the following is the most likely diagnosis?

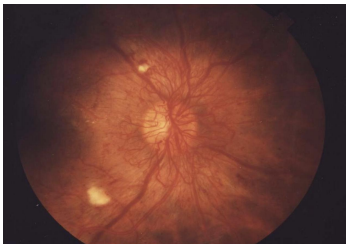
A- Cataract
B- Retinal detachment
C- Vitreous hemorrhage
D- Central retinal artery occlusion

Explanation: Vitreous hemorrhage may occur secondary to proliferative diabetic retinopathy in which friable vessels in areas of neovascularization bleed, resulting in sudden, painless loss of vision or visual obscuration with haze or floaters. This patient's fundus is difficult to visualize and examination demonstrates no red reflex in the right eye, which is consistent with opacifying blood in the vitreous.

Answers: Q8: A | Q9: C | Q10: C

Diabetes complications

Q11 (AMBOSS): A 55-year-old woman comes to the physician because of increased blurring of vision in both eyes for the past 4 months. She has tried using over-the-counter reading glasses, but they have not helped. She has a history of hypertension, type 2 diabetes mellitus, and chronic obstructive pulmonary disease. Current medications include lisinopril, insulin, metformin, and a fluticasone-vilanterol inhaler. Vital signs are within normal limits. Examination shows visual acuity of 20/70 in each eye. A photograph of the fundoscopic examination of the right eye is shown. Which of the following is the most appropriate next step in management?



A- Intravenous acetazolamide therapy
B- Topical timolol therapy
C- Laser photocoagulation
D- Oral ganciclovir therapy

Explanation: Non-enzymatic glycosylation (NEG) is the process driving increased glomerular filtration and progressive loss of glomerular function. This chronic degenerative process can be monitored by measuring urine albumin levels. NEG of the glomerular membrane causes increased permeability and thickening. At the same time, NEG makes the efferent glomerular arterioles more rigid, which further accelerates hyperfiltration and mesangial expansion. Intracellular sorbitol accumulation causes osmotic cell damage.

Q12 (AMBOSS): A 45-year-old woman comes to the physician because of early satiety and intermittent nausea for 3 months. During this period she has also felt uncomfortably full after meals and has vomited occasionally. She has not had retrosternal or epigastric pain. She has longstanding type 1 diabetes mellitus, diabetic nephropathy, and generalized anxiety disorder. Current medications include insulin, ramipril, and escitalopram. Vital signs are within normal limits. Examination shows dry mucous membranes and mild epigastric tenderness. Her hemoglobin A1C concentration was 12.2% 3 weeks ago. Which of the following drugs is most appropriate to treat this patient's current condition?

A- Omeprazole
B- Exenatide
C- Clarithromycin
D- Metoclopramide

Explanation: Metoclopramide therapy would benefit this diabetic patient with gastroparesis by inducing gastric contractions, promoting peristalsis, and increasing the tone of the fundus. In addition, metoclopramide has antiemetic properties, making it the preferred first-line treatment for gastroparesis. Patients should be started on the lowest possible dose and monitored closely for extrapyramidal side effects (e.g., acute dystonia). In addition, patients with diabetic gastroparesis should be maintained on strict glycemic control to prevent further complications, and they should be advised to avoid eating large fatty meals and raw vegetables. Other drugs used to treat gastroparesis include domperidone and erythromycin.

Answers: Q11: C | Q12: D

General endocrinology

Q1 (pretest): A 65-year-old diabetic patient is hospitalized because of acute cholecystitis. His diabetes is normally controlled with metformin 850 mg twice daily; a recent hemoglobin A1C level was 6.4. Cholecystectomy is performed, but is complicated by postoperative pneumonia and septic shock. The patient requires endotracheal intubation and ICU care. Blood cultures grow gram-negative rods, and vasopressors are required to maintain peripheral perfusion. What is the best method of controlling blood sugars in this patient?

a. Continue metformin via nasogastric tube.
b. IV insulin infusion to maintain blood glucose 140 to 180 mg/dL.
c. Sliding scale regular insulin to maintain blood glucose 80 to 120 mg/dL.
d. IV insulin infusion to maintain blood glucose below 100 mg/dL.
e. Contact endocrinology for subcutaneous insulin pump and continuous glucose monitoring.

Explanation: The best way to maintain glucose control in the critically ill patient is to use continuous glucose infusion with frequent fingerstick blood glucose measurements and dosage adjustments. Although initial studies suggested the benefit of "tight" glucose control (especially in septic or postoperative patients), subsequent trials showed that a more modest target (140-180) leads to better outcomes and prevents complications (especially adverse cardiac events and severe hypoglycemia). Once stabilized and taking enteral nutrition, the patient can often be easily transitioned to a basal-bolus regimen (ie, a long-acting insulin supplemented by pre-meal boluses of a short-acting insulin). Although metformin is usually the initial oral agent chosen for the outpatient management of type 2 diabetes, it should not be used in the setting of critical illness, where fluctuations in renal perfusion and GFR increase the risk of lactic acidosis. Metformin should be withheld around the time of surgery and radiographic procedures involving the use of IV contrast agents for the same reason. "Sliding scale" insulin has fallen out of favor in this setting as well; it is reactive rather than proactive and often leads to wide fluctuations and inadequate glucose control. Although continuous insulin infusion using a subcutaneous pump may be employed as an outpatient for tight glucose control, its use in the critical care setting has not been well studied and is probably inferior to IV insulin.

Q2 (pretest): A 25-year-old woman is admitted for hypertensive crisis. The patient's urine drug screen is negative. In the hospital, blood pressure is labile and responds poorly to antihypertensive therapy. The patient complains of palpitations and apprehension. Her past medical history shows that she developed hypertension during an operation for appendicitis at age 23. Hct: 49% (normal range 37%-48%) WBC: 11,000/mm3 (4.3-10.8) Plasma glucose: 160 mg/dL (75-115) Plasma calcium: 11 mg/dL (9-10.5) Which of the following is the most likely diagnosis?

a. Panic attack
b. Renal artery stenosis
c. Essential hypertension
d. Type 1 diabetes mellitus
e. Pheochromocytoma

Explanation: The patient has excessive growth of soft tissue that has resulted in coarsening of facial features, prognathism, and frontal bossing—all characteristic of acromegaly. This growth hormone–secreting pituitary tumor will result in bitemporal hemianopsia when the tumor impinges on the optic chiasm, which lies just above the sella turcica. Growth hormone– secreting tumors are the second commonest functioning pituitary tumors (second to prolactinomas). Serum IGF-1 (insulin-like growth factor-1) level will be elevated and is usually the first diagnostic test. Since 40% of GH-producing tumors also produce prolactin, a prolactin level should be obtained as well. Growth hormone secretion is pulsatile and a single GH level is often equivocal; the GH level must be suppressed (usually with glucose) to diagnose autonomous overproduction.Dexamethasone suppression is used in the evaluation of Cushing syndrome, with partial suppressibility suggesting a pituitary cause, but this patient's presentation strongly suggests acromegaly, not Cushing syndrome. Once GH overproduction is documented, an MRI scan of the pituitary will show the size and extent of the tumor (most are macroadenomas > 1 cm). The lateral skull film is insufficiently sensitive for this purpose. Growth hormone stimulation tests (insulin-induced hypoglycemia, arginine plus GHRH) may be used to diagnose growth hormone deficiency, but would not be useful to diagnose GH overproduction, where a suppression test should be used.

Answers: Q1: B | Q2: E

General endocrinology

Q3 (pretest): A 23-year-old man complains of persistent headache. He has noticed gradual increase in his ring size and his shoe size over the years. On physical examination, he has a peculiar deep, hollow-sounding voice and a prognathic jaw. Bedside visual field testing suggests bitemporal hemianopsia. What initial studies are indicated?

A. Serum insulin-like growth factor 1(IGF-1) and prolactin levels
B. Morning growth hormone levels
C. Overnight dexamethasone-suppressed cortisol level
D. Lateral skull film to assess sella turcica size
E. GHRH-stimulated growth hormone level

Explanation: The patient has excessive growth of soft tissue that has resulted in coarsening of facial features, prognathism, and frontal bossing—all characteristic of acromegaly. This growth hormone–secreting pituitary tumor will result in bitemporal hemianopsia when the tumor impinges on the optic chiasm, which lies just above the sella turcica. Growth hormone– secreting tumors are the second commonest functioning pituitary tumors (second to prolactinomas). Serum IGF-1 (insulin-like growth factor-1) level will be elevated and is usually the first diagnostic test. Since 40% of GH-producing tumors also produce prolactin, a prolactin level should be obtained as well. Growth hormone secretion is pulsatile and a single GH level is often equivocal; the GH level must be suppressed (usually with glucose) to diagnose autonomous overproduction.Dexamethasone suppression is used in the evaluation of Cushing syndrome, with partial suppressibility suggesting a pituitary cause, but this patient's presentation strongly suggests acromegaly, not Cushing syndrome. Once GH overproduction is documented, an MRI scan of the pituitary will show the size and extent of the tumor (most are macroadenomas > 1 cm). The lateral skull film is insufficiently sensitive for this purpose. Growth hormone stimulation tests (insulin-induced hypoglycemia, arginine plus GHRH) may be used to diagnose growth hormone deficiency, but would not be useful to diagnose GH overproduction, where a suppression test should be used.

Q4 (pretest): A 52-year-old man complains of impotence. On physical examination, he has an elevated jugular venous pressure, S3 gallop, and hepatomegaly. He also appears tanned, with pigmentation along joint folds. His left knee is swollen and tender. The plasma glucose is 250 mg/dL, and liver enzymes are elevated. Which of the following studies will help establish the diagnosis?

A. Detection of nocturnal penile tumescence
B. Determination of iron saturation
C. Determination of serum copper
D. Detection of hepatitis B surface antigen
E. Echocardiography

Explanation: Iron overload should be considered among patients who present with any one or a combination of the following: hepatomegaly, weakness, hyperpigmentation, atypical arthritis, diabetes, impotence, unexplained chronic abdominal pain, or cardiomyopathy. Diagnostic suspicion should be particularly high when the family history is positive for similar clinical findings. The most frequent cause of iron overload is the common genetic disorder, idiopathic hemochromatosis. Secondary iron storage problems can occur after multiple transfusions in a variety of anemias. The most practical screening test is the determination of serum iron, transferrin saturation, and ferritin. Transferrin saturation greater than 50% in males or 45% in females suggests increased iron stores. Substantially elevated serum ferritin levels confirm total body iron overload. Genetic screening is now used to assess which patients are at risk for severe fibrosis of the liver. Definitive diagnosis can be established by liver biopsy. Determination of serum copper is needed when Wilson disease is the probable cause of hepatic abnormalities. Wilson disease does not cause hypogonadism, heart failure, diabetes, or arthropathy. Chronic liver disease caused by hepatitis B would not account for the heart failure, hyperpigmentation, or diabetes. Nocturnal penile tumescence and echocardiogram can confirm clinical findings but will not establish the underlying diagnosis.

Answers: Q3: A | Q4: B

General endocrinology

Q5 (pretest): A 30-year-old man is evaluated for a thyroid nodule. The patient reports that his father died from thyroid cancer and that a brother had a history of recurrent renal stones. Blood calcitonin concentration is 2000 pg/mL (normal is < 100); serum calcium and phosphate levels are normal. The patient is referred to a thyroid surgeon. Which of the following studies should also be obtained?

A. Obtain a liver scan.
B. Measure parathormone level.
C. Measure urinary catecholamines.
D. Administer suppressive doses of thyroxine and measure levels of thyroid-stimulating hormone.
E. Treat the patient with radioactive iodine.

Explanation: For the patient described, the markedly increased calcitonin level indicates the diagnosis of medullary carcinoma of the thyroid. In view of the family history, the patient most likely has multiple endocrine neoplasia (MEN) type 2A, which includes medullary carcinoma of the thyroid gland, pheochromocytoma, and parathyroid hyperplasia. Pheochromocytoma may exist without sustained hypertension, as indicated by excessive urinary catecholamines. Before thyroid surgery is performed on this patient, a pheochromocytoma must be ruled out through urinary catecholamine determinations; the presence of such a tumor might expose him to a hypertensive crisis during surgery. The serum calcium serves as a screening test for hyperparathyroidism. At surgery, the entire thyroid gland must be removed because foci of parafollicular cell hyperplasia, a premalignant lesion, may be scattered throughout the gland. Successful removal of the medullary. carcinoma can be monitored with serum calcitonin levels. Medullary carcinoma of the thyroid rarely metastases to the liver, so a liver scan would be unnecessary if liver enzymes are normal. Thyroxine will be needed after surgery, but MEN type 2 is not associated with hypothyroidism. Radioactive iodine can be used to treat malignancies that arise from the follicular cells of the thyroid; parafollicular cells, however, do not take up iodine and do not respond to radioactive iodine. Hyperparathyroidism, while unlikely in this eucalcemic patient, is probably present in his brother.

Q6 (pretest): A 55-year-old woman with a history of severe depression and radical mastectomy for carcinoma of the breast 1 year previously develops polyuria, nocturia, and excessive thirst. Laboratory values are as follows:
Serum electrolytes: Na+ 149 mEq/L; K+ 3.6 mEq/L Serum calcium: 9.5 mg/dL
Blood glucose: 110 mg/dL
Blood urea nitrogen: 30 mg/dL
Urine osmolality: 150 mOsm/L
Which of the following is the most likely diagnosis?

A. Psychogenic polydipsia
B. Renal glycosuria
C. Hypercalciuria
D. Diabetes insipidus
E. Inappropriate antidiuretic hormone syndrome

Explanation: Metastatic tumors rarely cause diabetes insipidus, but of the tumors that cause it, carcinoma of the breast is by far the most common. In this patient, the diagnosis of diabetes insipidus is suggested by hypernatremia and low-urine osmolality. To distinguish between central (ADH deficiency) and nephrogenic (peripheral resistance to ADH action) diabetes insipidus, vasopressin (ADH by another name) is administered. If the urine osmolality rises and the urine output falls, the diagnosis is central DI. There will be little response to vasopressin in nephrogenic DI.Psychogenic polydipsia is an unlikely diagnosis since serum sodium is usually mildly reduced in this condition. Renal glycosuria would be expected to induce higher-urine osmolality than this patient has because of the osmotic effect of glucose. While nephrocalcinosis secondary to hyper-calcemia may produce polyuria, hypercalciuria does not. Finally, the findings in inappropriate antidiuretic hormone syndrome are the opposite of those observed in diabetes insipidus and thus are incompatible with the clinical picture in this patient.

Answers: Q5: C | Q6: D