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SECTION 1: CELL INJURY AND WOUND HEALING — QUESTIONS

For each question given below choose the ONE BEST option.

1.1 A 65-year-old man suffered a massive myocardial infarction that was complicated by shock and prolonged hypotension. On arrival in the emergency department he was found to have focal neurological signs in addition to features consistent with low-output cardiac failure. Despite the best efforts of the medical team he died the next day. At autopsy, the most likely change you would expect to see in a brain biopsy would be:

- A Acute haemorrhagic change
- B Coagulative necrosis
- C Granulomatous change
- D Lacunar infarct
- E Liquefactive necrosis

1.2 A 45-year-old woman with a chronic infective lesion on her leg underwent a full-thickness biopsy of the lesion. During histological examination of this lesion a rim of multinuclear giant cells is seen. The central region is most likely to show:

- A Caseous necrosis
- B Eosinophilic necrosis
- C Fibrinous necrosis
- D Foam cells
- E Pyogenic necrosis
1.3 A skin biopsy from an anorexic 16-year-old girl showed cellular atrophy. During atrophy:

- A The cell disappears
- B Cellular organelles swell
- C Cell size decreases
- D Cell size increases
- E Protein synthesis increases

1.4 A 35-year-old man is a habitual smoker. If a biopsy is taken from the respiratory tract in this man, the epithelium of respiratory tract is most likely to show:

- A Mucous hyperplasia
- B Smooth-muscle hyperplasia
- C Squamous cell anaplasia
- D Squamous cell hypertrophy
- E Stratified squamous metaplasia

1.5 Hypertrophy can be physiological or pathological and is caused by increased functional demand or by specific hormonal stimulation. Hypertrophy can be best described as:

- A Abnormal deposition in a cell
- B Change in cell morphology
- C Decrease in cell size
- D Increase in cell number
- E Increase in cell size and in its organelles
1.6 Apoptotic cells usually exhibit distinctive morphological features. Which one of the following morphological features is usually seen in pure apoptosis?

- A Cellular swelling
- B Chromatin condensation
- C Early disruption of the plasma membrane
- D Nuclear stabilisation
- E Phagocytosis of apoptotic bodies by neutrophils

1.7 A histopathologist reports fat necrosis after examining a slide. Fat necrosis might be found in which one of the following situations?

- A Brain injury
- B Muscle injury
- C Trauma to the abdomen
- D Trauma to the breast
- E Trauma to the bowel

1.8 A healthy 26-year-old man fractured his right tibia in a road traffic accident. His right leg was immobilised in a plaster cast. The cast was removed from his leg after 8 weeks of immobilisation. Which of the following changes is most likely to have taken place in his gastrocnemius muscle after this time?

- A Decrease in the number of muscle fibres
- B Decrease in the number of nerve fibres
- C Increase in the number of fast fibres
- D Increase in the mitochondrial content
- E Increase in the number of satellite cells
1.9  **A 21-year-old man sustained a severe soft-tissue injury following a road traffic accident. Which of the following metabolic effects is most likely to follow this injury?**

- A  Decreased aldosterone secretion
- B  Inhibition of gluconeogenesis
- C  Mobilisation of fat stores
- D  Protein anabolism
- E  Respiratory alkalosis

1.10  **A 32-year-old man, working in a power plant, was exposed to radioactive material. He is most likely to suffer radiation injury due to:**

- A  Decreased intracellular Na$^+$
- B  Decreased intracellular Ca$^{2+}$
- C  Free radical formation
- D  Increased adenosine triphosphate (ATP) production
- E  Inhibition of protein synthesis

1.11  **A 15-year-old girl with haemophilia A has had episodes of pain in her knees for the past 6 years. Over time, there has been an increase in size of her knee joints, with deformity. Laboratory studies show decreased levels of coagulation factor VIII activity. Which of the following is most likely to be seen within the joint space following episodes of pain?**

- A  Anthracotic pigment
- B  Cholesterol crystals
- C  Lipofuscin
- D  Neutrophils
- E  Russell bodies
1.12 A 42-year-old woman has complained of mild, burning, substernal or epigastric pain following meals for the past 3 years. Upper gastrointestinal endoscopy is performed and biopsies are taken of an erythematous area of the lower oesophageal mucosa 3 cm above the gastro-oesophageal junction. There is no mass lesion, no ulceration, and no haemorrhage is noted. The biopsies demonstrate the presence of columnar epithelium with goblet cells. Which of the following mucosal alterations is most likely to be represented by these findings?

- A Carcinoma
- B Dysplasia
- C Hyperplasia
- D Ischaemia
- E Metaplasia

1.13 A 62-year-old diabetic and hypertensive man suffered a stroke which affected his speech and movement in the right arm and leg. A cerebral angiogram revealed an occlusion of his left middle cerebral artery. Months later, a computed tomographic (CT) scan shows a large, 5-cm cystic area in his left parietal lobe cortex. This CT finding most likely demonstrates a lesion that is the consequence of resolution of which of the following events?

- A Apoptosis
- B Atrophy
- C Caseous necrosis
- D Coagulative necrosis
- E Liquefactive necrosis
1.14 A 25-year-old woman breastfed her first baby for almost 1 year with no difficulties and no complications. Which of the following cellular processes that occurred in the breast during pregnancy allowed her to nurse the infant for this period of time?

- A  Ductal epithelial metaplasia
- B  Epithelial dysplasia
- C  Lobular hyperplasia
- D  Stromal hypertrophy
- E  Steatocyte atrophy

1.15 An 80-year-old woman was found dead in her room in a nursing home one morning. An autopsy was carried out and her death was reported as being secondary to old age. At autopsy, her heart was small (250 g) and dark-brown in colour on section. Microscopically, there was light-brown perinuclear pigment seen after haematoxylin and eosin (H&E) staining of the cardiac muscle fibres. Which of the following substances is most likely to be increased in the myocardial fibres to produce this cardiac appearance?

- A  Calcium, following necrosis
- B  Cholesterol, as a consequence of atherosclerosis
- C  Glycogen, resulting from a storage disease
- D  Haemosiderin, resulting from iron overload
- E  Lipochrome, from ‘wear and tear’
1.16 A histopathologist examining a slide used a series of immunohistochemical stains to identify different cellular components. One particular stain identified the presence of intermediate filaments within cells. This cytokeratin stain is most likely to be useful for which of the following diagnostic purposes?

- A Confirmation of a history of chronic alcoholism
- B Confirmation that a neoplasm is a carcinoma
- C Determination of the contractile properties of cells
- D Visualisation of cytoskeletal alterations with impending cell death
- E Assessment of the degree of metaplasia or dysplasia

1.17 A 73-year-old woman with long-standing hypertension and aortic stenosis died suddenly one morning. An autopsy was performed on her body. At autopsy, her heart weighed 540 g. The size of her heart is most likely to be the result of which of the following processes involving the myocardial fibres?

- A Fatty degeneration
- B Fatty infiltration
- C Hyperplasia
- D Hypertrophy
- E Oedema
1.18 A 28-year-old woman developed a darker skin complexion after returning from a holiday trip to Goa. Her skin did not show warmth, erythema or tenderness. Her skin tone faded to its original appearance within 1 month. Which of the following substances contributes most to the biochemical process leading to these skin changes?

- A Glycogen
- B Haem
- C Homogentisic acid
- D Lipofuscin
- E Tyrosine

1.19 Metaplasia is a reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type. In which of the following situations is the process of epithelial metaplasia most likely to have occurred?

- A Acute myocardial infarction
- B Lactation following pregnancy
- C Tanning of the skin following sunlight exposure
- D Urinary obstruction due to an enlarged prostate
- E Vitamin A deficiency
1.20 A histopathologist reviewing a slide noticed a disease process which has led to scattered loss of individual cells, with the microscopic appearance of karyorrhexis and cell fragmentation. The overall tissue structure, however, has remained intact. This process is most typical of which of the following diseases?

☐ A Barbiturate overdose
☐ B Brown atrophy of the heart
☐ C Chronic alcoholic liver disease
☐ D Renal transplant rejection
☐ E Viral hepatitis

1.21 A 55-year-old woman with chronic atrial fibrillation suddenly developed an acute abdomen and was rushed to the emergency department. At emergency laparoscopy most of the small-bowel loops were dusky to purple-red in colour. Her mesenteric veins were patent. The most probable underlying pathological process is:

☐ A Coagulative necrosis
☐ B Dry gangrene
☐ C Gas gangrene
☐ D Liquefactive gangrene
☐ E Wet gangrene
SECTION 1: CELL INJURY AND WOUND HEALING — ANSWERS

1.1

Answer: E Liquefactive necrosis

Liquefactive necrosis is characteristic of focal bacterial or, occasionally, fungal infections, because microbes stimulate the accumulation of inflammatory cells. Hypoxic death of cells within the central nervous system often evokes liquefactive necrosis, though the reasons for this are obscure. Whatever the pathogenesis, liquefaction completely digests the dead cells. The end result is transformation of the tissue into a viscous liquid mass. If the process was initiated by acute inflammation the material is frequently creamy yellow in colour because of the presence of dead white cells and this is called ‘pus’.

1.2

Answer: A Caseous necrosis

Caseous necrosis, a distinctive form of coagulative necrosis, is encountered most often in foci of tuberculous infection. In this disease the characteristic lesion is called a ‘granuloma’ or a ‘tubercle’ and is classically characterised by the presence of central caseous necrosis. The term ‘caseous’ is derived from the cheesy white gross appearance of the area of necrosis. On microscopic examination, the necrotic focus appears as amorphous granular debris, seemingly composed of fragmented, coagulated cells and amorphous granular debris enclosed within a distinctive inflammatory border known as a ‘granulomatous reaction’. Unlike coagulative necrosis, the tissue architecture is completely obliterated. In a granuloma, macrophages are transformed into epithelium-like cells surrounded by a collar of mononuclear leukocytes, principally lymphocytes and occasionally plasma cells. In the usual haematoxylin and eosin-stained tissue...
sections, the epithelioid cells have a pale pink granular cytoplasm with indistinct cell boundaries, and often appear to merge into one another. The nucleus is less dense than that of a lymphocyte, is oval or elongated in shape, and can show folding of the nuclear membrane. Older granulomas develop an enclosing rim of fibroblasts and connective tissue. Epithelioid cells often fuse to form giant cells in the periphery or sometimes in the centre of granulomas. These giant cells can attain diameters of 40–50 µm. They have a large mass of cytoplasm containing 20 or more small nuclei arranged either peripherally (Langhans-type giant cell) or haphazardly (foreign body-type giant cell). There is no known functional difference between these two types of giant cells. The chronic infective lesion in this scenario is most probably a tuberculous granuloma.

1.3

Answer: C Cell size decreases

Atrophy is the shrinkage in the size of the cell due to loss of cell substance. It represents a form of adaptive response and can result in cell death. Involvement of a sufficient number of cells causes the entire tissue or organ to diminish in size or become atrophic. Atrophy can be physiological or pathological. Physiological atrophy is commonly seen during early development and is exemplified by atrophy of the notochord and the thyroglossal duct during foetal development. Another common example of physiological atrophy is the decrease in size of the uterus shortly after childbirth. Pathological atrophy can be local or generalised, depending on the underlying cause. The common causes of atrophy are the following:

- Ageing (senile atrophy). Ageing is associated with cell loss, typically seen in tissues containing permanent cells, particularly the brain and heart.

- Decreased workload (atrophy of disuse). This is best seen when a broken limb is immobilised in a plaster cast or when a patient is restricted to complete bed rest resulting in rapid skeletal muscle. The initial rapid decrease in cell size is reversible once activity is resumed. With more prolonged disuse, however, skeletal muscle fibres decrease in number as well
as in size, and this atrophy can be accompanied by increased bone resorption, leading to osteoporosis of disuse.

- **Diminished blood supply.** A decrease in blood supply (ischaemia) to a tissue occurring as a result of occlusive arterial disease results in atrophy of tissue because of progressive cell loss. An example of this is seen in late adult life as the brain undergoes progressive atrophy due to reduced blood supply secondary to atherosclerosis.

- **Inadequate nutrition.** In profound protein-calorie malnutrition (marasmus) skeletal muscle is used as a source of energy after other reserves such as adipose stores have been depleted. This results in marked muscle wasting (cachexia). Cachexia is also seen in patients with chronic inflammatory diseases or cancer. In the former, chronic overproduction of the inflammatory cytokine, tumour necrosis factor (TNF) is thought to be responsible for appetite suppression and muscle atrophy.

- **Loss of endocrine stimulation.** Many endocrine glands, the breast, and the reproductive organs are dependent on endocrine stimulation for normal metabolism and function. The loss of oestrogen stimulation after the menopause results in physiological atrophy of the endometrium, vaginal epithelium, and breast.

- **Loss of innervation (denervation atrophy).** Normal function of skeletal muscle depends on its nerve supply. Damage to the nerves leads to rapid atrophy of the muscle fibres supplied by those nerves.

- **Pressure.** Compression of tissues for any length of time can lead to atrophy. An enlarging benign tumour can cause atrophy in the surrounding compressed tissues. Atrophy in this setting is probably the result of ischaemic changes caused by compromise of the blood supply to the surrounding tissues by the expanding mass.
Atrophy is brought about by a reduction in the structural components of the cell with concomitant diminished function. For instance in atrophic muscle the cells contain fewer mitochondria and myofilaments and a reduced amount of endoplasmic reticulum. The fundamental cellular changes associated with atrophy are identical in all of the above settings and represent an adaptive response to ensure survival.

1.4

**Answer: E  Stratified squamous metaplasia**

Metaplasia is a reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type. It can represent an adaptive substitution of cells that are sensitive to stress by cell types better able to withstand the adverse environment. The most common type of epithelial metaplasia is columnar to squamous, as occurs in the respiratory tract in response to chronic irritation. In the habitual cigarette smoker, the normal ciliated columnar epithelial cells of the trachea and bronchi are often replaced focally or widely by stratified squamous epithelial cells.

The more rugged stratified squamous epithelium is able to survive under circumstances in which the more fragile, specialised columnar epithelium would have succumbed. Although the metaplastic squamous cells in the respiratory tract are capable of surviving this environment, an important protective mechanism — mucus secretion — is lost. Epithelial metaplasia is therefore a two-edged sword and, in most circumstances, represents an undesirable change. Moreover, the influences that predispose to metaplasia, if persistent, can induce malignant transformation in metaplastic epithelium. A common form of cancer in the respiratory tract is therefore composed of squamous cells, which arise in areas of metaplasia of normal columnar epithelium into squamous epithelium.
1.5

Answer: E Increase in cell size and in its organelles

Hypertrophy is caused by an increase in the size of cells, resulting in an increase in the size of the organ. The hypertrophied organ has no new cells, just larger cells. The increased size of the cells is due not to cellular swelling but to the synthesis of more structural components. Cells capable of division can respond to stress by undergoing both hyperplasia and hypertrophy, whereas in non-dividing cells (e.g., myocardial fibres), hypertrophy occurs. The nuclei in hypertrophied cells can have a higher DNA content than normal cells, probably because the cells arrest in the cell cycle without undergoing mitosis.

Hypertrophy can be physiological or pathological and is caused by increased functional demand or by specific hormonal stimulation. The striated muscle cells in both the heart and the skeletal muscles are capable of tremendous hypertrophy, perhaps because they cannot adapt adequately to increased metabolic demands by mitotic division and production of more cells to share the work. The most common stimulus for hypertrophy of muscle is increased workload. For example, the bulging muscles of bodybuilders engaged in ‘pumping iron’ result from an increase in size of the individual muscle fibres in response to increased demand. The workload is thus shared by a greater mass of cellular components, and each muscle fibre is spared excess work and so escapes injury. The enlarged muscle cell achieves a new equilibrium, permitting it to function at a higher level of activity. In the heart, the stimulus for hypertrophy is usually chronic haemodynamic overload, resulting from either hypertension or faulty valves. Synthesis of more proteins and filaments occurs, achieving a balance between the demand and the cell’s functional capacity. The greater number of myofilaments per cell permits an increased workload with a level of metabolic activity per unit volume of cell not different from that borne by the normal cell.

The massive physiological growth of the uterus that occurs during pregnancy is a good example of a hormone-induced increase in the size of an organ that results from both hypertrophy and hyperplasia. The cellular hypertrophy is stimulated by oestrogenic hormones acting on smooth-muscle oestrogen receptors, eventually resulting
in increased synthesis of smooth-muscle proteins and an increase in cell size. Similarly, prolactin and oestrogen cause hypertrophy of the breasts during lactation. These are examples of physiological hypertrophy induced by hormonal stimulation.

1.6

*Answer: B  Chromatin condensation*

Apoptosis is a pathway of cell death that is induced by a tightly regulated intracellular programme in which cells destined to die activate enzymes that degrade the cells’ own nuclear DNA and nuclear and cytoplasmic proteins. The cell’s plasma membrane remains intact, but its structure is altered in such a way that the apoptotic cell becomes an avid target for phagocytosis. The dead cell is rapidly cleared, before its contents have leaked out, and therefore cell death by this pathway does not elicit an inflammatory reaction in the host. Apoptosis is therefore fundamentally different from necrosis, which is characterised by loss of membrane integrity, enzymatic digestion of cells, and frequently a host reaction. However, apoptosis and necrosis sometimes coexist, and they can share some common features and mechanisms.

The following morphological features, some best seen with the electron microscope, characterise cells undergoing apoptosis:

- **Cell shrinkage.** The cell is smaller in size; the cytoplasm is dense; and the organelles, although relatively normal, are more tightly packed.

- **Chromatin condensation.** This is the most characteristic feature of apoptosis. The chromatin aggregates peripherally, under the nuclear membrane, into dense masses of various shapes and sizes. The nucleus itself can break up, producing two or more fragments.

- **Formation of cytoplasmic blebs and apoptotic bodies.** The apoptotic cell first shows extensive surface blebbing, then undergoes fragmentation into membrane-bound apoptotic bodies composed of cytoplasm and tightly packed organelles, with or without nuclear fragments.
• Phagocytosis of apoptotic cells or cell bodies, usually by macrophages. The apoptotic bodies are rapidly degraded within lysosomes, and the adjacent healthy cells migrate or proliferate to replace the space occupied by the now deleted apoptotic cell.

Plasma membranes are thought to remain intact during apoptosis, until the last stages, when they become permeable to solutes that are normally retained. This classic description is accurate with respect to apoptosis during physiological conditions such as embryogenesis and deletion of immune cells. However, forms of cell death with features of necrosis as well as of apoptosis are not uncommon in reaction to injurious stimuli. Under such conditions, the severity, rather than the specificity, of the stimulus determines the form in which death is expressed. If necrotic features are predominant, early plasma membrane damage occurs, and cell swelling, rather than shrinkage, is seen.

1.7

Answer: D  Trauma to the breast

Fat necrosis can be seen after trauma to the breast. It can present as a painless palpable mass, skin thickening or retraction, a mammographic density, or mammographic calcifications. The majority of women will give a history of trauma or prior surgery. The major clinical significance of the condition is its possible confusion with breast carcinoma when there is a palpable mass or mammographic calcifications.

Grossly, the lesion can consist of haemorrhage in the early stages and, later, central liquefactive necrosis of fat. Later still, it can appear as an ill-defined nodule of grey-white, firm tissue containing small foci of chalky-white or haemorrhagic debris. The central focus of necrotic fat cells is initially surrounded by macrophages and an intense neutrophilic infiltration. Then, during the next few days, progressive fibroblastic proliferation, increased vascularisation, and lymphocytic and histiocytic infiltration wall off the focus. Subsequently, foreign-body giant cells, calcifications, and haemosiderin make their appearance. Eventually, the focus is replaced by scar tissue or is encysted and walled off by collagenous tissue.
1.8

**Answer: A** Decrease in the number of muscle fibres

Shrinkage in the size of the cell by loss of cell substance is known as ‘atrophy’. It represents a form of adaptive response and can culminate in cell death. When a sufficient number of cells are involved, the entire tissue or organ diminishes in size, or becomes atrophic. When a broken limb is immobilised in a plaster cast or when a patient is restricted to complete bed rest, skeletal muscle atrophy rapidly ensues. The initial rapid decrease in cell size is reversible once activity is resumed. With more prolonged disuse, however, skeletal muscle fibres decrease in number as well as in size; this atrophy can be accompanied by increased bone resorption, leading to osteoporosis of disuse (see also Answer to 1.3).

1.9

**Answer: C** Mobilisation of fat stores

The metabolic response to injury is an important part of the stress reaction in that it improves the individual organism’s chances of surviving under adverse circumstances or when injured. The metabolic response to trauma includes:

- Acid–base disturbance — usually a metabolic alkalosis or acidosis
- Early reduced urine output and increased urine osmolality
- Early reduction in metabolic rate
- Gluconeogenesis via amino acid breakdown
- Hyponatraemia due to impaired sodium pump action
- Hypoxia and coagulopathy
- Immunosuppression
- Increased extracellular fluid volume volume and hypovolaemia
- Increased vascular permeability and oedema
• Late diuresis and increased sodium loss
• Late increased metabolism, negative nitrogen balance and weight loss
• Mobilisation of fat stores, lipolysis and ketosis
• Pyrexia in the absence of infection
• Reduced ‘free’ water clearance
• Reduced serum albumin.

1.10

Answer: C  Free radical formation

Cells generate energy by reducing molecular oxygen to water. During this process small amounts of partially reduced reactive oxygen forms are produced as an unavoidable byproduct of mitochondrial respiration. Some of these forms are free radicals that can damage lipids, proteins and nucleic acids. They are referred to as ‘reactive oxygen species’. Cells have defence systems for preventing injury caused by these products. An imbalance between free radical-generating and free radical-scavenging systems results in oxidative stress, a condition that has been associated with the cell injury seen in many pathological conditions. Free radical-mediated damage contributes to such varied processes as chemical and radiation injury, ischaemia-reperfusion injury (induced by restoration of blood flow in ischaemic tissue), cellular ageing and microbial killing by phagocytes.

1.11

Answer: B  Cholesterol crystals

In haemophiliac joints the lipid from the red cell membranes is broken down and cholesterol crystals form. Accumulation of lipofuscin is not a feature of haemorrhage. Russell bodies are intracellular accumulations of immunoglobulins in plasma cells. Neutrophils suggest acute inflammation. Anthracotic pigment is an exogenous carbon pigment from dusts in the air that accumulate in lung.
1.12

Answer: E   Metaplasia

Metaplasia is the substitution of one tissue type normally found at a site for another. The epithelium undergoes metaplasia in response to ongoing inflammation from reflux of gastric contents. It is common in the lower oesophagus with gastro-oesophageal reflux disease. The growth of the epithelial cells must become disordered in order to be dysplastic. Hyperplasia can occur with inflammation, as the number of cells increases, but hyperplasia does not explain the presence of the columnar cells. Carcinoma is characterised by cellular atypia with hyperchromatism and pleomorphism. Goblet cells would not be seen. Ischaemia would be unusual at this site and would be marked by coagulative necrosis.

1.13

Answer: E   Liquefactive necrosis

The brain undergoes liquefactive necrosis with infarction. As it resolves, a cystic area forms in the region of infarction. Atrophy would be a more generalised process, whereas a single cystic area in the brain suggests a remote infarction. Coagulative necrosis is more typical of parenchymal organs such as the kidney or spleen, which do not have as high a lipid content as the brain. Caseous necrosis is more typical of granulomatous inflammation with *Mycobacterium tuberculosis*. Apoptosis is single-cell necrosis that does not result in a grossly visible cystic area (see also Answer to 1.1).

1.14

Answer: C   Lobular hyperplasia

There is an increase in lobules under hormonal influence to provide for lactation. Lobular hyperplasia would allow this woman to nurse the infant. The stroma of the breast consists of connective tissue, which provides structural support but does not have cells that produce milk. Dysplasia in epithelia is a premalignant change and not a normal physiological event. With poor nutrition and weight
loss, steatocytes can decrease in size. Metaplasia is the exchange of normal epithelium for another type in response to chronic irritation. Metaplasia is not a normal physiological process.

1.15

Answer: E  Lipochrome, from ‘wear and tear’

Lipochrome is a very common finding in older people, but it has little effect on cardiac function. Lipochrome is also known as ‘lipofuscin’. Haemosiderosis is not a complication of ageing. Glycogen storage diseases are inherited conditions that appear early in life. Glycogen does not appear pigmented in haematoxylin and eosin-stained tissue sections. Cholesterol accumulates in atheromatous plaques in the arteries, not in the myocardium. Calcium deposits appear as irregular, dark-blue areas and are not associated with ageing of the myocardium.

1.16

Answer: B  Confirmation that a neoplasm is a carcinoma

Malignant tumours of diverse origin often resemble one another because they are poorly differentiated. These tumours are often quite difficult to distinguish on the basis of routine haematoxylin and eosin- (H&E-) stained tissue sections. For example, certain anaplastic carcinomas, malignant lymphomas, melanomas and sarcomas can look quite similar, but they must be accurately identified because their treatment and prognosis are different. Antibodies against intermediate filaments have proved to be of value in such cases because tumour cells often contain intermediate filaments characteristic of their cell of origin. For example, the presence of cytokeratins, detected immunohistochemically, points to an epithelial origin (carcinoma), whereas desmin is specific for neoplasms of muscle cell origin. Cytoskeletal alterations occur with ischaemia, but are not a useful marker for such an event. Many cell types contain intermediate filaments. Mallory’s alcoholic hyaline can be observed by H&E staining. However, it is not entirely specific for alcoholism. Metaplasia and dysplasia are assessed using their light-microscopic appearances after H&E staining.
1.17

Answer: D  Hypertrophy

In this patient the pressure load of hypertension led to myocardial fibre hypertrophy and a heart twice normal size. Fat in the heart does not increase in response to the increase in workload from hypertension. Myocardial fibres do not undergo hyperplasia. Fatty degeneration of the myocardium is typically the result of a toxic or hypoxic injury. Myocardial oedema is not a characteristic feature of myocardial injury or increased workload. However, heart failure could lead to peripheral oedema (see also Answer to 1.5).

1.18

Answer: E  Tyrosine

The tanning process in skin is stimulated by ultraviolet light exposure. Melanocytes have the enzyme tyrosinase to oxidize tyrosine to dihydroxyphenylalanine in the pathway for melanin production. Haem as part of haemosiderin from breakdown of red blood cells can impart a brownish colour, but this is typically local from trauma or more global as part of an iron storage disease such as haemochromatosis. Lipochrome (lipofuscin) is a ‘wear and tear’ pigment that imparts a golden-brown appearance to granules in cells (such as myocytes or hepatocytes), but this is not a feature of skin. Homogentisic acid can be part of the process of the rare disease alkaptonuria, in which a black pigment is deposited in connective tissues. Glycogen in sufficient quantity is starch-like and imparts a paler colour to organs in which it is stored in excess. It does not involve the skin.

1.19

Answer: E  Vitamin A deficiency

Vitamin A is necessary to maintain epithelia, and squamous metaplasia of the respiratory tract can occur if there is a deficiency. Tanning of the skin is a physiological event resulting from the accumulation of melanin pigment — there is no change of one cell type to another involved. Lactation following pregnancy is a form
of physiological hyperplasia of breast lobules that occurs as a result of hormonal influences. An acute myocardial infarction will lead to cardiac muscle fibre necrosis, which will heal with the production of fibrous scar tissue, but this is not a reversible metaplasia. The enlarged prostate represents primarily glandular hyperplasia.

**1.20**

*Answer: E  Viral hepatitis*

Viral infection leads to individual hepatocyte necrosis, which is characterised by the microscopic appearances of karyorrhexis and cell fragmentation. Brown atrophy of the heart results when there is marked lipofuscin deposition in the myocardium. Tissue destruction with transplant rejection is more widespread. Single cell necrosis is not evident in chronic alcoholic liver disease. Barbiturate overdose causes hypertrophy of smooth endoplasmic reticulum, not individual cell necrosis.

**1.21**

*Answer: E  Wet gangrene*

Small-intestinal infarction following sudden and total occlusion of mesenteric arterial blood flow can involve only a short segment, but more often involves a substantial portion. The splenic flexure of the colon is at greatest risk of ischaemic injury because it is the watershed between the distribution of the superior and inferior mesenteric arteries, but any portion of the colon can be affected. With mesenteric venous occlusion, anterograde and retrograde propagation of thrombus may lead to extensive involvement of the splanchnic bed. Regardless of whether the arterial or venous side is occluded, the infarction appears haemorrhagic because of blood reflow into the damaged area. In the early stages, the infarcted bowel appears intensely congested and dusky to purple-red, with foci of subserosal and submucosal ecchymotic discoloration. With time, the wall becomes oedematous, thickened, rubbery, and haemorrhagic. The lumen commonly contains sanguinous mucus or frank blood. In arterial occlusions the demarcation from normal bowel is usually sharply defined, but in venous occlusions the area
of dusky cyanosis fades gradually into the adjacent normal bowel, having no clear-cut definition between viable and non-viable bowel. Histologically, there is obvious oedema, interstitial haemorrhage, and sloughing necrosis of the mucosa. Normal features of the mural musculature, particularly cellular nuclei, become indistinct. Within 1–4 days, intestinal bacteria produce outright wet gangrene and sometimes perforation of the bowel. There may be little inflammatory response.

1.22

**Answer: C  Free radical injury**

Free radicals are chemical species that have a single unpaired electron in an outer orbit. Energy created by this unstable configuration is released through reactions with adjacent molecules, such as inorganic or organic chemicals (proteins, lipids, carbohydrates), particularly with key molecules in membranes and nucleic acids. Moreover, free radicals initiate autocatalytic reactions, whereby molecules with which they react are themselves converted into free radicals to propagate the chain of damage. Absorption of radiant energy such as ultraviolet rays in sunlight can hydrolyse water into hydroxyl (OH) and hydrogen (H) free radicals, which cause sunburn. The free radicals induce cell injury by the following mechanisms:

- **Lipid peroxidation of membranes:** free radicals in the presence of oxygen can cause peroxidation of lipids within plasma and organellar membranes. Oxidative damage is initiated when the double bonds in unsaturated fatty acids of membrane lipids are attacked by oxygen-derived free radicals, particularly by OH. The lipid-free radical interactions yield peroxides, which are themselves unstable and reactive, and an autocatalytic chain reaction ensues (called ‘propagation’), which can result in extensive membrane, organellar and cellular damage. Other more favorable termination options take place when the free radical is captured by a scavenger, such as vitamin E, embedded in the cell membrane.