ACCESS TO SURGERY: 500 SINGLE BEST ANSWER QUESTIONS IN GENERAL & SYSTEMIC PHYSIOLOGY

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SECTION 1: GENERAL PHYSIOLOGY – QUESTIONS

For each question given below choose the ONE BEST option.

1.1 A fluorescent dye that cannot cross cell membranes is used to label several contiguous cells. One cell in the middle is experimentally bleached with light that destroys the dye, but the cell soon recovers dye fluorescence. This recovery is best explained by the presence of which of the following structures between the bleached cell and its fluorescent neighbours?

- A Basal lamina
- B Desmosomes
- C Gap junctions
- D Glycosaminoglycans
- E Tight junctions

1.2 During pregnancy the uterus increases considerably in size. After delivery, the regression of uterine size is brought about by which of the following cellular organelles?

- A Endoplasmic reticulum
- B Golgi apparatus
- C Mitochondria
- D Lysosomes
- E Nucleus

1.3 During an experiment a poison is injected into the cell that specifically destroyed the rough endoplasmic reticulum. This will result in no:

- A Synthesis of glycogen
- B Synthesis of proteins
- C Glycosylation of protein and carbohydrate moieties
- D Synthesis of lipids
- E Autolysis of proteins

1.4 Myoglobin is released from damaged muscle tissue (rhabdomyolysis), which has very high concentrations of myoglobin. In a skeletal muscle, myoglobin:

- A Acts like haemoglobin and binds with O_2
- B Is found in fast fibres only
- C Releases O_2 only at high $p(O_2)$
- D Forms sigmoid dissociation curve (similar to haemoglobin)
- E Is devoid of iron

1.5 A person standing in the upright position begins to lean to one side. The postural muscles that are closely connected to the vertebral column on the side will stretch. Because of this, stretch receptors in those muscles contract to correct posture. Which of the following statements regarding the stretch reflex is CORRECT?

- A It is monosynaptic
- B It is polysynaptic
- C It is initiated by stimulation of Golgi tendon organ
- D It involves type II fibres
- E It involves higher centres

1.6 An organelle is a discrete structure of a cell having specialised functions. There are many types of organelles, particularly in the eukaryotic cells of higher organisms. What is the organelle that regenerates and replicates spontaneously?

- A Golgi apparatus
- B Mitochondrion
- C Smooth endoplasmic reticulum
- D Rough endoplasmic reticulum
- E Vacuole

1.7 Atractyloside is an inhibitor of the electron transport chain. It would be expected to have little or no effect on the functioning of which of the following cell types?

- A Cardiac muscle cells
- B Parietal cells of the stomach
- C Parotid duct cells
- D Proximal convoluted tubule cells
- E Red blood cells

1.8 Action potentials can be created by many types of cells, but are used most extensively by the nervous system for communication between neurones and to transmit information from neurones to other body tissues such as muscles and glands. During the activation of a nerve cell membrane:

- A Chloride ions flow outward
- B Potassium ions flow inward
- C Potassium ions flow outward
- D Sodium ions flow inward
- E Sodium ions flow outward

1.9 Skeletal muscle fibres can be divided into two basic types, type I (slow-twitch fibres) and type II (fast-twitch fibres). Fast muscle fibres:

- A Use anaerobic metabolism
- B Have lots of myoglobin
- C Are shorter for great strength of contraction
- D Have relatively high endurance
- E Have numerous mitochondria

1.10 A patient developed a stitch granuloma following surgery. Which leukocyte in the peripheral blood will become an activated macrophage in this granuloma?

- A Basophil
- B Eosinophil
- C Lymphocyte
- D Monocyte
- E Neutrophil

1.11 A 36-year-old man with end-stage renal disease who is undergoing haemodialysis has normocytic normochromic anaemia. Which of the following is the most appropriate therapy?

- A Erythropoietin
- B Ferrous sulphate
- C Folate
- D Vitamin B_6
- E Vitamin B_{12}

1.12 A blood sample taken from the umbilical artery of a newborn was subjected to electrophoresis to detect antibodies (immunoglobulins). Which of the following antibodies will have the highest percentage in a newborn?

- ○ A IgA
- ○ B IgD
- ○ C IgE
- ○ D IgG
- ○ E IgM

1.13 A 58-year-old male patient needed a blood transfusion after repair of an abdominal aortic aneurysm. His blood was sent to the laboratory. The technician, while checking for this patient's blood group, said that the patient's blood agglutinates with antisera anti-A and anti-D, while the patient's serum agglutinates cells of blood group B. What is the blood group of this patient?

- ○ A A positive
- ○ B B positive
- ○ C A negative
- ○ D B negative
- ○ E O positive

1.14 In humans there are five types of antibody: IgA, IgD, IgE, IgG and IgM. Which of the following statements regarding IgM is CORRECT?

- ○ A It binds to allergens
- ○ B It functions mainly as an antigen receptor on B cells
- ○ C It is the largest immunoglobulin molecule
- ○ D It is the most abundant immunoglobulin
- ○ E It is a tetramer of four subunits

1.15 The lack of normal factor VIII causes haemophilia A, an inherited bleeding disorder. Factor VIII is synthesised predominantly in:

- A Hepatocytes
- B Histiocytes
- C Kupffer cells
- D Platelets
- E Vascular endothelium

1.16 A 45-year-old woman, with a past history of easy bruising and heavy menstrual periods, was admitted for elective cholecystectomy and was diagnosed with von Willebrand's disease on routine preoperative investigations. von Willebrand's disease is:

- A Autosomal dominant
- B Characterised by decreased bleeding time
- C Characterised by decreased factor VII
- D Characterised by decreased platelets
- E X-linked

1.17 A 68-year-old woman complaining of easy fatigability and shortness of breath after abdominal aortic aneurysm repair was diagnosed with iron-deficiency anaemia and prescribed an oral iron preparation. Which of the following statements about iron metabolism is CORRECT?

- A Ferritin is a plasma protein that transports iron in the blood
- B Haemosiderin is a product of haemoglobin degradation
- C Iron is more efficiently absorbed in the ferrous state (Fe^{2+}) than in the ferric state (Fe^{3+})
- D Most iron in the body is stored as haemosiderin
- E The gastrointestinal rate of iron absorption is extremely high

1.18 A 45-year-old man on warfarin for a mechanical mitral valve was admitted in the Accident and Emergency Department with persistent bleeding following dental extraction. He was told that his coagulation was deranged. Which of the following statements about blood coagulation is CORRECT?

- ○ A Absence of Ca^{2+} promotes blood coagulation
- ○ B Disseminated intravascular coagulation (DIC) results in depletion of fibrin split products
- ○ C Patients with haemophilia A usually have a normal bleeding time
- ○ D von Willebrand factor suppresses platelet adhesion
- ○ E von Willebrand factor suppresses blood coagulation

1.19 Nerve gas (organophosphate) is a weapon of chemical warfare that kills by causing respiratory and cardiovascular failure. The expected effect of organophosphate poisoning on the heart would be:

- ○ A Decrease the force of myocardial contractions by potentiating the vagal tone to the ventricular muscle
- ○ B Decrease the rate of rhythmicity of the sinoatrial (SA) node by inducing hyperpolarisation
- ○ C Depolarise cells of the SA node by closing potassium channels under the control of the muscarinic acetylcholine receptor
- ○ D Increase the rate of rhythmicity of the SA node by increasing the upward drift in membrane potential caused by sodium leakage
- ○ E Increase conductivity at the atrioventricular (AV) junction by inducing depolarisation

1.20 The resting membrane potential of a neuronal cell body is −60 mV. Opening chloride channels in the neuronal membrane will most likely cause:

- A Depolarisation to about −30 mV
- B Depolarisation to about +30 mV
- C Hyperpolarisation to about −70 mV
- D Initiation of an action potential
- E No change in membrane potential

1.21 Chloride ions are associated with changes in neuronal membrane potential. Which of the following statements most accurately describes the response of a neurone to a decrease in the conductance of the cell membrane to chloride ions?

- A The cell will depolarise if its membrane potential is positive with respect to the equilibrium potential for chloride ions
- B The cell will hyperpolarise if its membrane potential is positive with respect to the equilibrium potential for chloride ions
- C The cell will hyperpolarise if the external chloride concentration is greater than the internal chloride concentration
- D The cell will hyperpolarise if the external chloride concentration is less than the internal chloride concentration
- E No change in membrane potential will occur if the external and internal chloride ion concentrations are equal

SECTION 1: GENERAL PHYSIOLOGY – ANSWERS

1.1

Answer: C Gap junctions

A gap junction is a junction between certain animal cell types that allows different molecules and ions to pass freely between cells. The junction connects the cytoplasm of cells. One gap junction is composed of two connexons (or hemichannels), which connect across the intercellular space. They are analogous to the plasmodesmata that join plant cells. In vertebrates, gap-junction hemichannels are primarily homo- or hetero-hexamers of connexin proteins. Invertebrate gap junctions comprise proteins from the hypothetical innexin family. However, the recently characterised pannexin family, functionally similar but genetically distinct from connexins and expressed in both vertebrates and invertebrates, probably encompasses the innexins. Gap junctions formed from two identical hemichannels are called homotypic, while those with differing hemichannels are heterotypic. In turn, hemichannels of uniform connexin composition are called homomeric, while those with differing connexins are heteromeric. Channel composition is thought to influence the function of gap-junction channels but it is not yet known how.

Gap junctions:

- allow for direct electrical transmission between cells
- allow for chemical transmission between cells, through the transmission of small second messengers, such as IP_3 and Ca^{2+}
- allow any molecule smaller than 1 kDa to pass through.

1.2

Answer: D Lysosomes

Lysosomes are organelles that contain digestive enzymes (acid hydrolases) to digest macromolecules. They are found in both animal and plant cells but they are rare in plant cells. They are built in the Golgi apparatus. The name comes from the Greek words 'lysis', which means dissolution or destruction and 'soma', which means body. They are frequently nicknamed 'suicide-bags' by cell biologists due to their role in autolysis. Lysosomes were discovered by the Belgian cytologist Christian de Duve in the 1949. The lysosomes are used for the digestion of macromolecules from phagocytosis (ingestion of cells), from the cell's own recycling process (where old components such as worn out mitochondria are continuously destroyed and replaced by new ones and receptor proteins are recycled) and for autophagic cell death, a form of programmed self-destruction or autolysis, of the cell, which means that the cell is digesting itself. Other functions include digesting foreign bacteria that invade a cell and helping repair damage to the plasma membrane by serving as a membrane patch, sealing the wound. Lysosomes also do much of the cellular digestion required to digest tails of tadpoles and to remove the web from the fingers of a 3–6-month-old fetus. This process of programmed cell death is called apoptosis.

1.3

Answer: B Synthesis of proteins

The rough endoplasmic reticulum (ER) contains protein-manufacturing ribosomes (the ribosomes on its surface are responsible for its being named 'rough') and transports proteins destined for membranes and secretion. Rough ER is connected to the nuclear envelope as well as linked to the cis cisternae of the Golgi complex by vesicles that shuttle between the two compartments. The rough ER works in concert with the Golgi apparatus to target new proteins to their proper destinations.

1.4

Answer: A Acts like haemoglobin and binds with O_2

Myoglobin is a single-chain globular protein of 153 amino acids, containing a haem (iron-containing porphyrin) prosthetic group in the centre around which the remaining apoprotein folds. With a molecular weight of 16 kDa, it is the primary oxygen-carrying pigment of muscle tissues. Unlike the blood-borne haemoglobin, to which it is structurally related, this protein does not exhibit co-operative binding of oxygen, since positive co-operativity is a property reserved for multimeric proteins. Instead, the binding of oxygen by myoglobin is unaffected by the oxygen pressure in the surrounding tissue. Myoglobin is often cited as having an 'instant binding tenacity' to oxygen given its hyperbolic oxygen dissociation curve. In 1958, John Kendrew and associates successfully determined the structure of myoglobin by high-resolution X-ray crystallography. For this discovery, John Kendrew shared the 1962 Nobel Prize in chemistry with Max Perutz.

1.5

Answer: A It is monosynaptic

A stretch reflex is a muscle contraction in response to stretching within that muscle. It is a monosynaptic reflex that provides automatic regulation of skeletal muscle length. Muscle spindles are sense organs sensitive to stretch of the muscle in which they lie. The patellar (knee-jerk) reflex is an example. Another example is the group 1a fibres in the calf muscle, which synapse with motor neurones supplying muscle fibres in the same muscle. A sudden stretch, such as tapping the Achilles' tendon, causes a reflex contraction in the muscle as the spindles sense the stretch and send an action potential to the motor neurones, which then cause the muscle to contract; this particular reflex causes a contraction in the soleus–gastrocnemius group of muscles. This reflex can be enhanced by the Jendrassik manoeuvre. Jendrassik's manoeuvre (Erno Jendrassik, Hungarian physician, 1858–1921) is a medical manoeuvre wherein the patient flexes both sets of fingers into a hook-like form and interlocks those sets of fingers together. The tendon below the patient's knee is then hit with a reflex hammer. The elicited response is compared with the reflex

result of the same action when the manoeuvre is not in use. Often a larger reflex response will be observed when the patient is occupied with the manoeuvre, as the manoeuvre may prevent the patient from consciously inhibiting or influencing his or her response to the hammer. This manoeuvre is particularly useful in that, even if the patient is aware that the interlocking of fingers is just a distraction to elicit a larger reflex response, it still functions properly.

1.6

Answer: B Mitochondrion

A mitochondrion (plural mitochondria) is a membrane-enclosed organelle, found in most eukaryotic cells. Mitochondria are sometimes described as 'cellular power plants', because they convert food molecules into energy in the form of ATP via the process of oxidative phosphorylation. A typical eukaryotic cell contains about 2000 mitochondria, which occupy roughly one-fifth of its total volume. Mitochondria contain DNA that is independent of the DNA located in the cell nucleus. They have the ability to regenerate and replicate spontaneously.

1.7

Answer: E Red blood cells

An electron transport chain (also called electron transport system or electron transfer chain) is a series of membrane-associated electron carriers mediating biochemical reactions that produce ATP, which is the energy currency of life. Only two sources of energy are available to living organisms: oxidation–reduction (redox) reactions and sunlight (photosynthesis). Organisms that use redox reactions to produce ATP are called chemotrophs. Organisms that use sunlight are called phototrophs. Both chemotrophs and phototrophs utilise electron transport chains to convert energy into ATP. The overall purpose of the electron transport chain is to create ATP using energy contained in high-energy electrons.

This is achieved through a three-step process:

- Gradually sap energy from a high-energy electron in a series of individual steps.
- Use that energy to forcibly unbalance the proton concentration across the membrane.
- Use the proton concentration's drive to rebalance itself as a means of producing ATP.

Electron transport chains are present in the mitochondria. Energy sources such as glucose are initially metabolised in the cytoplasm. The products are imported into mitochondria. Mitochondria continue the process of catabolism using metabolic pathways including the Krebs cycle, fatty acid oxidation and amino acid oxidation.

The end-result of these pathways is the production of two energy-rich electron donors, NADH and $FADH_2$. Electrons from these donors are passed through an electron transport chain to oxygen, which is reduced to water. This is a multi-step redox process that occurs on the mitochondrial inner membrane. The enzymes that catalyse these reactions have the remarkable ability to simultaneously create a proton gradient across the membrane, producing a thermodynamically unlikely high-energy state with the potential to do work. Although electron transport occurs with great efficiency, a small percentage of electrons are prematurely leaked to oxygen, resulting in the formation of the toxic free radical, superoxide.

Four membrane-bound complexes have been identified in mitochondria. Each is an extremely complex transmembrane structure that is embedded in the inner membrane. Three of them are proton pumps. The structures are electrically connected by lipid-soluble electron carriers and water-soluble electron carriers. The overall electron transport chain is:

NADH $\rightarrow$ Complex I $\rightarrow$ Q $\rightarrow$ Complex III $\rightarrow$ Cytochrome c $\rightarrow$ Complex IV $\rightarrow$ O_2

$\uparrow$

Complex II

Much of our knowledge of mitochondrial function results from the study of toxic compounds. Specific inhibitors were used to distinguish the electron transport system from the phosphorylation system and helped to define the sequence of redox carriers along the respiratory chain. If the chain is blocked then all the intermediates on the substrate side of the block become more reduced, while all those on the oxygen side become more oxidised. It is easy to see what has happened, because the oxidised and reduced carriers often differ in their spectral properties. If a variety of different inhibitors are available then many of the respiratory carriers can be placed in the correct order. Atractyloside transport inhibitor blocks the adenine nucleotide porter by binding to the outward-facing conformation (contrast with bongkrekic acid). It has no effect on submitochondrial particles, which re-seal spontaneously after sonication with the membranes inside-out. This ATP/ADP transport inhibitor resembles oligomycin when used with intact mitochondria. Of all the options given in this question, red blood cells are the only cell type that do not have mitochondria and hence will not be affected by electron transport chain inhibitor, atractyloside.

1.8

Answer: D Sodium ions flow inward

A local membrane depolarisation caused by an excitatory stimulus causes some voltage-gated sodium channels in the neurone cell-surface membrane to open and therefore sodium ions diffuse in through the channels along their electrochemical gradient. Being positively charged, they begin a reversal in the potential difference across the membrane from negative-inside to positive-inside. Initially, the inward movement of sodium ions is also favoured by the negative-inside membrane potential. Overall, the ions are under the influence of the *driving force,* the difference between the membrane potential and the equilibrium potential of sodium.

1.9

Answer: A Use anaerobic metabolism

Skeletal muscle fibres can be divided into two basic types, type I (slow-twitch fibres) and type II (fast-twitch fibres). Type I muscle fibres (slow-oxidative fibres) use primarily cellular respiration and, as a result, have relatively high endurance. To support their high-oxidative metabolism, these muscle fibres typically have lots of mitochondria and myoglobin and so appear red or what is typically termed 'dark' meat in poultry. Type I muscle fibres are typically found in muscles of animals that require endurance, such as chicken leg muscles or the wing muscles of migrating birds (eg, geese). Type II muscle fibres use primarily anaerobic metabolism and have relatively low endurance. These muscle fibres are typically used during tasks requiring short bursts of strength, such as sprints or weightlifting. Type II muscle fibres cannot sustain contractions for significant lengths of time and are typically found in the 'white' meat (eg, the breast) of chicken.

There are two subclasses of type II muscle fibres, type IIa (fast-oxidative) and IIb (fast-glycolytic). The Type IIa fast-oxidative fibres actually also appear red, due to their high content of myoglobin and mitochondria. Type IIb (fast-glycolytic) tire the fastest and are the prevalent type in sedentary individuals. These fibres appear white histologically, due to their low oxidative demand, manifested by the lack of myoglobulin and mitochondria (relative to the type I and type IIa fibres). Some research suggests that these subtypes can switch with training to some degree. The biochemical difference between the three types of muscle fibres is in their myosin heavy chains.

1.10

Answer: D Monocyte

A monocyte is a leukocyte, part of the human body's immune system that protects against blood-borne pathogens and moves quickly (approx. 8–12 hours) to sites of infection in the tissues. Monocytes are usually identified in stained smears by their large bilobed nucleus. They are produced by the bone marrow from haemopoietic stem cell precursors called monoblasts. Monocytes circulate in the bloodstream for about one to three days and then typically move

into tissues throughout the body. They consist of between 3 and 8% of the leukocytes in the blood. In the tissues, monocytes mature into different types of macrophages at different anatomical locations. Monocytes are responsible for phagocytosis (ingestion) of foreign substances in the body. Monocytes can perform phagocytosis using intermediary (opsonising) proteins such as antibodies or complement that coat the pathogen, as well as by binding to the microbe directly via pattern-recognition receptors that recognise pathogens. Monocytes are also capable of killing infected host cells via antibody, termed antibody-mediated cellular cytotoxicity. Vacuolisation may be present in a cell that has phagocytosed foreign matter.

Monocytes that migrate from the bloodstream to other tissues are called macrophages. Macrophages are responsible for protecting tissues from foreign substances, but are also suspected to be the predominant cells involved in triggering atherosclerosis. They are cells that possess a large smooth nucleus, a large area of cytoplasm and many internal vesicles for processing foreign material.

A *monocyte count* is part of a complete blood count and is expressed either as a ratio of monocytes to the total number of white blood cells counted or by absolute numbers. Both may be useful in determining or refuting a possible diagnosis. Monocytosis is the state of excess monocytes in the peripheral blood. It may be indicative of various disease states. Examples of processes that can increase a monocyte count include:

- chronic inflammation
- stress response
- hyperadrenocorticism
- immune-mediated disease
- pyogranulomatous disease
- necrosis
- red cell regeneration.

1.11

Answer: A Erythropoietin

Erythropoietin, or EPO, is a glycoprotein hormone that is a cytokine for erythrocyte (red blood cells) precursors in the bone marrow. Also called haematopoietin or haemopoietin, it is produced by the kidney and is the hormone regulating red blood cell production. Erythropoietin is available as a therapeutic agent produced by recombinant DNA technology in mammalian cell culture. It is used in treating anaemia resulting from chronic renal failure or from cancer chemotherapy. Its use is also believed to be common as a doping agent in endurance sports such as bicycle racing, triathlons and marathon running.

1.12

Answer: D IgG

IgG is a monomeric immunoglobulin, built of two heavy chains γ and two light chains. Each molecule has two antigen-binding sites. This is the most abundant immunoglobulin and is approximately equally distributed in blood and in tissue liquids, constituting 75% of serum immunoglobulins in humans. This is the only isotype that can pass through the placenta, thereby providing protection to the newborn in its first weeks of life before its own immune system has developed. It can bind to many kinds of pathogens, for example viruses, bacteria and fungi, and protects the body against them by complement activation (classic pathway), opsonisation or phagocytosis and neutralisation of their toxins. There are four subclasses: IgG1 (66%), IgG2 (23%), IgG3 (7%) and IgG4 (4%):

- IgG1, IgG3 and IgG4 cross the placenta easily
- IgG3 is the most effective complement activator, followed by IgG1 and then IgG2
- IgG4 does not activate complement
- IgG1 and IgG3 bind with high affinity to Fc receptors on phagocytic cells
- IgG4 has intermediate affinity and IgG2 affinity is extremely low.

1.13

Answer: A A positive

According to the ABO blood typing system there are four different kinds of blood types: A, B, AB or O.

- Blood group A - If you belong to the blood group A, you have A antigens on the surface of your red blood cells and B antibodies in your blood plasma.
- Blood group B - If you belong to the blood group B, you have B antigens on the surface of your red blood cells and A antibodies in your blood plasma.
- Blood group AB - If you belong to the blood group AB, you have both A and B antigens on the surface of your red blood cells and no A or B antibodies at all in your blood plasma.
- Blood group O - If you belong to the blood group O, you have neither A nor B antigens on the surface of your red blood cells but you have both A and B antibodies in your blood plasma.

Many people also have a so-called Rh factor on the red blood cell's surface. This is also an antigen and those who have it are called Rh+. Those who have not are called Rh–. A person with Rh– blood does not have Rh antibodies naturally in the blood plasma (as one can have A or B antibodies, for instance) but they can develop Rh antibodies in the blood plasma if they receive blood from a person with Rh+ blood, whose Rh antigens can trigger the production of Rh antibodies. A person with Rh+ blood can receive blood from a person with Rh– blood without any problems. So, in this vignette the patient's blood group is A positive as he has antigen A, antibody B and Rh antigens.

1.14

Answer: C It is the largest immunoglobin molecule

IgM forms polymers where multiple immunoglobulins are covalently linked together with disulphide bonds, normally as a pentamer or occasionally as a hexamer. It has a large molecular mass of approximately 900 kDa (in its pentamer form). The J chain is attached to most pentamers, while hexamers do not possess the J chain due to space constraints in the complex. Because each monomer has two antigen binding sites, an IgM has 10 of them; however, it cannot bind 10 antigens at the same time because they hinder each other. Because it is a large molecule, it cannot diffuse well and is found in the interstitium only in very low quantities. IgM is primarily found in serum; however, because of the J chain, it is also important as a secretory immunoglobulin.

Due to its polymeric nature, IgM possesses high avidity and is particularly effective at complement activation. It is sometimes called a 'natural antibody', but it is likely that the antibodies arise due to sensitisation in the very young to antigens that are naturally occurring in nature. For example anti-A and anti-B IgM antibodies can be formed in early life as a result of exposure to anti-A- and anti-B-like substances that are present on bacteria or perhaps also on plant materials. In germ-line cells, the gene segment encoding the μ constant region of the heavy chain is positioned first among other constant-region gene segments. For this reason, IgM is the first immunoglobulin expressed by mature B cells.

IgM is also by far the physically largest antibody in the circulation. IgM antibodies are mainly responsible for the clumping (agglutination) of red blood cells if the recipient of a blood transfusion receives blood that is not compatible with his/her blood type. IgM antibodies appear early in the course of an infection and usually do not reappear after further exposure. IgM antibodies do not pass across the human placenta. These two biological properties of IgM make it useful in the diagnosis of infectious diseases. Demonstrating IgM antibodies in a patient's serum indicates recent infection or, in serum from a neonate, indicates intrauterine infection such as congenital rubella.

1.15

Answer: E Vascular endothelium

Factor VIII (FVIII) is an essential clotting factor. The lack of normal FVIII causes haemophilia A, an inherited bleeding disorder. The gene for Factor VIII is located on the X chromosome (Xq28). FVIII is a glycoprotein pro-cofactor. Factor VIII is synthesised predominantly in the vascular endothelium and is not affected by liver disease. In fact, levels usually are elevated in such instances. It is also synthesised and released into the bloodstream by the liver. In the circulating blood, it is mainly bound to von Willebrand factor (vWF, also known as factor VIII-related antigen) to form a stable complex. Upon activation by thrombin or factor Xa, it dissociates from the complex to interact with factor IXa in the coagulation cascade. It is a co-factor to factor IXa in the activation of factor X, which, in turn, with its co-factor factor Va, activates more thrombin. Thrombin cleaves fibrinogen into fibrin, which polymerises and crosslinks (using factor XIII) into a blood clot. No longer protected by vWF, activated FVIII is proteolytically inactivated in the process (most prominently by activated protein C and factor IXa) and quickly cleared from the bloodstream. FVIII concentrated from donated blood plasma or alternatively recombinant FVIII can be given to haemophiliacs to restore haemostasis. So, FVIII is also known as antihaemophilic factor. The transfer of a plasma by-product into the bloodstream of a patient with haemophilia often led to the transmission of diseases such as HIV and hepatitis before purification methods were improved. In the early 1990s, pharmaceutical companies began to produce recombinant synthesised factor products, which now prevent nearly all forms of disease transmission during replacement therapy.

1.16

Answer: A Autosomal dominant

von Willebrand's disease (vWD) is the most common hereditary coagulation abnormality described in humans, although it can also be acquired as a result of other medical conditions. It arises from a qualitative or quantitative deficiency of von Willebrand factor (vWF), a multimeric protein that is required for platelet adhesion. It

is known to affect humans and, in veterinary medicine, dogs. There are three types of hereditary vWD, but other factors such as ABO blood group may also play a part in the cause of the condition. The various types of vWD present with varying degrees of bleeding tendency. Severe internal or joint bleeding is rare (only in type 3 vWD); bruising, nosebleeds, heavy menstrual periods (in women) and blood loss during childbirth (rare) may occur. Death may occur

The *vWF* gene is located on chromosome 12 (12p13.2). It has 52 exons spanning 178 kbp. Types 1 and 2 are inherited as autosomal dominant traits and type 3 is inherited as autosomal recessive. Occasionally type 2 also inherits recessively. In humans, the incidence of vWD is roughly about 1 in 100 individuals. Because most forms are rather mild, they are detected more often in women, whose bleeding tendency shows during menstruation. The actual abnormality (which does not necessarily lead to disease) occurs in 0.9–3% of the population. It may be more severe or apparent in people with blood group O. Acquired vWD can occur in patients with autoantibodies. In this case the function of vWF is not inhibited but the vWF–antibody complex is rapidly cleared from the circulation. A form of vWD occurs in patients with aortic valve stenosis, leading to gastrointestinal bleeding (Heyde's syndrome). This form of acquired vWD may be more prevalent than is presently thought. Acquired vWF has also been described in the following disorders: Wilms' tumour, hypothyroidism and mesenchymal dysplasias.

Patients with vWD normally require no regular treatment, although they are always at increased risk for bleeding. Prophylactic treatment is sometimes given for patients with vWD who are scheduled for surgery. They can be treated with human-derived medium purity factor VIII concentrates. Mild cases of vWD can be trialled on desmopressin (1-desamino-8-D-arginine vasopressin, DDAVP) (antihaemophilic factor, more commonly known as humate-P), which works by raising the patient's own plasma levels of vWF by inducing release of vWF stored in the Weibel–Palade bodies in the endothelial cells.

1.17

Answer: C Iron is more efficiently absorbed in the ferrous state (Fe^{4}) than in the ferric state (Fe^{3+})

The absorption of non-haem iron in any food is strongly affected by the composition of the meals. Iron is more efficiently absorbed in the ferrous state (Fe^{2+}) than in the ferric state (Fe^{3+}) and commercial iron preparations often contain vitamin C to prevent oxidation of Fe^{2+} to Fe^{3+}. Still, only 3–6% of the ingested daily iron is actually absorbed in the upper gastrointestinal tract. Seventy per cent of the total body iron is used for haemoglobin and myoglobin; the remainder is stored as readily exchangeable ferritin and some is stored in less easily mobilised haemosiderin. When old red blood cells are destroyed by the tissue macrophage system, haem is separated from globin and degraded to biliverdin. Iron in the plasma is bound to the iron-transporting protein transferrin. Transferrin level (total iron-binding capacity) and saturation are clinically important indicators of iron-deficiency anaemia.

1.18

Answer: C Patients with haemophilia A usually have a normal bleeding time

Prolonged bleeding time is characteristic of platelet disorders, eg, thrombocytopaenia. Patients with haemophilia A or B (ie absence of factor VIII or IX, respectively) have a prolonged partial thromboplastin time (PTT), but do not have a prolonged bleeding time. Ca^{2+} is a necessary co-factor for blood coagulation, and chelation of Ca^{2+} ions by citrate inhibits coagulation. Von Willebrand factor is part of the factor VIII complex and also promotes platelet adherence to the vascular subendothelium. Patients who lack this factor (von Willebrand's disease) have both a prolonged PTT and a prolonged bleeding time. Disseminated intravascular coagulation results in depletion of coagulation factors and accumulation of fibrin split products.

1.19

Answer: B Decrease the rate of rhythmicity of the sinoatrial (SA) node by inducing hyperpolarisation

The toxic effects of nerve gas derive from its ability to inhibit the enzyme cholinesterase. The inhibition of this naturally occurring degradative enzyme engenders a massive accumulation of acetylcholine evoking an overstimulation of the acetylcholine receptors throughout the body. In the heart, specifically, acetylcholine released by the vagal nerve stimulates muscarinic receptors in the cells of the sinoatrial (SA) node. This results in the opening of potassium channels and hyperpolarisation of the SA node. It therefore takes longer for sodium leakage to cause the membrane potentials of these cells to reach the threshold required for an action potential. The rate of rhythmicity is so decreased. A similar hyperpolarisation of the fibres at the atrioventricular (AV) junction decreases conduction velocity of atrial impulses to the ventricle. The force of ventricular contractions is not affected by the vagus nerve.

1.20

Answer: C Hyperpolarisation to about -70mV

Increasing the membrane's conductance to chloride will result in chloride influx and the membrane potential approaching the value dictated by the chloride equilibrium potential (calculated from the Nernst equation), which is about –70 mV for neurones. A value of –30 mV is near the Nernst potential for Cl^- ions in smooth muscle cells, but not in neurones; +30 mV is near the Nernst potential for Na^+ ions. The membrane potential would remain unchanged only if the cell resting membrane potential is already at the Nernst potential of the ion channels that were opened. Action potentials occur if the cell membrane is depolarised above threshold.

1.21

Answer: A The cell will depolarise if its membrane potential is positive with respect to the equilibrium potential for chloride ions

Although electrogenic pumps may contribute to the membrane potential of certain cells, the major determinants of membrane potential are the external and internal concentrations of permeant ions and their relative permeabilities in the membrane. Decreasing the conductance causes the membrane potential to move away from the equilibrium potential for that ion. So, a decrease in the conductance of a membrane to chloride ions causes the cells to depolarise – that is, become more positive – if the membrane potential is positive with respect to the chloride equilibrium potential. Conversely, increasing the conductance for an ion causes the membrane potential to approach the equilibrium potential for that ion. External and internal ion chloride concentrations are needed to calculate the Nernst potential for this ion, but a simple comparison of these two values does not allow predictions about the change in membrane potential.

1.22

Answer: E Reflex inhibition of motor neurones

The stimulation of receptors in the Golgi tendon organs leads to the inverse stretch reflex. This reflex is responsible for the relaxation that is observed when a muscle is subjected to a strong stretch. Impulses from the organs travel in type Ib fibres to the spinal cord, where they activate inhibitory interneurones. These in turn suppress the activity of motor neurones and therefore lead to relaxation of the extrafusal muscle fibres attached to the tendons. The state of contraction of intrafusal fibres, the gamma-efferent discharge rate and the activity in group II afferent fibres control the stretch reflex, which, distinct from the inverse stretch reflex, is mediated by the Golgi tendon organs.