BITSAT Biology Sample Paper – 20

Duration: 60 Minutes **Maximum Marks: 120**

Instructions

- This paper contains **40** Multiple Choice Questions (Single Correct Answer).
- Each correct answer carries **+3 marks**. Each incorrect answer carries **−1** mark. Unattempted questions carry **0** marks.
- Only **one** option is correct. Choose carefully.
- Use of mobile phones, calculators, or electronic gadgets is strictly prohibited.

Q1. The cell-cell junction in vertebrate epithelia (e.g. between intestinal absorptive cells) that creates a leak-proof seal preventing molecules from passing between adjacent cells is the:

(A) Gap junction

(B) Tight junction — formed by claudin and occludin transmembrane proteins arranged in a continuous belt at apical regions of epithelial cells; seal the paracellular space; create the apical-basolateral polarity of the epithelium; selectivity for ions varies with claudin type (the “leaky” vs “tight” epithelia distinction)

(C) Desmosome

(D) Hemidesmosome

Q2. The button-like spot welds between adjacent epithelial cells, connecting intermediate filament networks across the gap and providing mechanical resistance to shear stress (especially abundant in skin and cardiac muscle), are:

(A) Desmosomes (maculae adherentes) — linked by cadherin proteins (desmogleins, desmocollins) extending into intercellular space; cy-

toplasmic plaque proteins (plakoglobin, desmoplakin) anchor keratin intermediate filaments; pemphigus and pemphigoid are autoimmune blistering diseases targeting these proteins

(B) Tight junctions

(C) Gap junctions

(D) Plasmodesmata

Q3. Specialised peroxisomes in plant cells (germinating fatty seeds) that contain the glyoxylate cycle enzymes for converting stored fats to sucrose are called:

(A) Lysosomes

(B) Spherosomes

(C) Oleosomes

(D) Glyoxysomes — bound by a single membrane; contain the glyoxylate cycle (isocitrate lyase, malate synthase) plus β-oxidation enzymes; allow plants to net synthesise sugars from acetyl-CoA (bypassing the two CO_2-releasing steps of TCA); essential during seedling growth before photosynthesis is established; especially prominent in oilseed cotyledons (castor, sunflower)

Q4. Membrane microdomains enriched in cholesterol and sphingolipids that organise GPI-anchored proteins, signalling molecules, and platforms for receptor clustering are called:

(A) Caveolae (these are flask-shaped invaginations rich in caveolin)

(B) Clathrin-coated pits

(C) Lipid rafts — the cholesterol + sphingolipid clusters segregate from the more fluid phospholipid bilayer; concentrate GPI-anchored proteins, src-family kinases, certain receptors; serve as signalling platforms for FcR, TCR, BCR clustering; exploited by some pathogens (HIV, influenza, prions) for cell entry/exit

(D) Adherens junctions

Q5. Molecular chaperones (a class of proteins assisting folding of nascent polypeptides and refolding of denatured proteins under stress) include the famous family of:

(A) Heat shock proteins (HSPs) — HSP70 (Hsp70/DnaK), HSP60 (chaperonin, the GroEL/GroES barrel that gives substrate a sequestered folding chamber), HSP90 (folds steroid receptors and many kinases), small HSPs; expression strongly induced by heat shock and other proteotoxic stresses; help proteins fold correctly and prevent aggregation; clients include cancer-driving oncoproteins, making HSP90 a drug target

(B) Microtubules

(C) Cytoskeletal motors

(D) Lysosomal hydrolases

Q6. Within cells, the two nicotinamide nucleotides NAD^+ and $NADP^+$ have distinct roles:

(A) They are interchangeable

(B) NAD^+ supplies electrons for reductive biosynthesis only

(C) $NADP^+$ is the principal acceptor in catabolic oxidations only

(D) NAD^+ (mostly oxidised form in cells) is the principal electron acceptor in catabolic oxidations (glycolysis, TCA, β-oxidation); NADH so generated is oxidised at Complex I of the electron transport chain. $NADP^+$ differs only by a $2'$-phosphate; mostly maintained in the REDUCED form (NADPH) in cells; supplies reducing power for anabolic reactions (fatty acid synthesis, nucleotide synthesis, cholesterol synthesis) and for antioxidant defence (regenerates reduced glutathione). NADPH is generated by the pentose phosphate pathway and by the malic enzyme

Q7. The secondary structure of proteins (α-helix, β-sheet, turns) is held together principally by:

(A) Disulfide bridges between cysteine residues

(B) Ionic bonds (salt bridges) between charged side chains

(C) Hydrogen bonds — between backbone carbonyl C=O of one residue and the backbone N–H of another, 4 residues ahead in an α-helix (i and i+4), or between adjacent extended strands in a β-sheet. The H-bond is individually weak (~ 5 kcal/mol) but collective cooperativity makes secondary structure stable. Linus Pauling deduced both structures from precise model-building (1951). Disulfide and ionic interactions stabilise tertiary, not secondary, structure

(D) Hydrophobic interactions

Q8. In eukaryotic chromosomes, DNA replication during S phase initiates simultaneously at many sites called:

(A) Telomeres (the chromosome ends)

(B) Origins of replication (Ori) — pre-replication complexes (preRCs) assemble at thousands of origins during G_1 (ORC, Cdc6, Cdt1, MCM helicase loaded); origins fire (helicase activated, replication forks formed) in S phase under CDK and DDK control; each origin licensed only once per cell cycle (preventing re-replication); $\sim 30{,}000$–$50{,}000$ origins in mammalian genome

(C) Centromeres

(D) Nucleoli

Q9. The principal enzyme of dietary fat digestion in the human small intestine, secreted by the pancreas and acting on emulsified triglyceride droplets formed by bile salts, is:

(A) Pepsin

(B) Amylase

(C) Phospholipase A_2

(D) Pancreatic lipase — hydrolyses triglycerides at the 1- and 3-positions, releasing 2 free fatty acids + 1 2-monoacylglycerol; requires coli-

pase (a small accessory protein) to overcome bile-salt inhibition at the lipid-water interface; products incorporated into mixed micelles for absorption by enterocytes. Orlistat (anti-obesity drug) inhibits pancreatic lipase, reducing fat absorption

Q10. Of the total oxygen carried by arterial blood at sea level (normal Hb $15\,\text{g/dL}$, 98% saturated), the percentage carried bound to haemoglobin (vs dissolved in plasma) is approximately:

(A) $\sim 50\%$

(B) $\sim 70\%$

(C) $\sim 98\%$ bound to Hb (each gram of Hb carries $1.34\,\text{mL}$ O_2 when fully saturated; arterial blood carries $\sim 20\,\text{mL}$ O_2/dL total, of which only $\sim 0.3\,\text{mL}$ is dissolved in plasma per $100\,\text{mL}$); the dissolved fraction follows Henry's Law and is proportional to pO_2 — importantly, this dissolved O_2 creates the gradient that loads Hb

(D) Equal contributions from both

Q11. The capillary fluid that filters out into tissues (interstitial fluid) but is not reabsorbed at the venous end (small excess) is returned to the bloodstream via the:

(A) Hepatic portal vein

(B) Lymphatic system — blind-ended lymphatic capillaries in tissues pick up interstitial fluid; lymph flows through lymph nodes (filtration, immune surveillance) via collecting vessels; finally returned to the venous system at the junctions of internal jugular and subclavian veins (right lymphatic duct, thoracic duct); also absorbs dietary fats from intestinal lacteals (the chyle); flow driven by skeletal muscle pumping, smooth muscle in vessel walls, one-way valves; obstruction $\rightarrow$ lymphoedema (e.g. in lymphatic filariasis)

(C) Coronary sinus

(D) Vena cava directly

Q12. Venous blood draining the small intestine, large intestine (most), pancreas, and spleen reaches the liver through:

(A) The hepatic portal vein — carries nutrient-rich, partly deoxygenated blood from the GI tract to the liver before it enters the systemic circulation; allows the liver to process absorbed nutrients (first-pass metabolism), detoxify ingested substances, and synthesise plasma proteins; about 75% of liver blood supply; the hepatic artery supplies the remaining 25% (oxygen-rich)

(B) The renal vein

(C) The pulmonary vein

(D) The hepatic artery only

Q13. Of the special senses, the one that uses chemoreceptors located on the tongue (responding to molecules dissolved in saliva, encoding the basic tastes sweet/sour/salty/bitter/umami) is:

(A) Olfaction (smell) — detects volatile molecules in the air via olfactory receptors in the nasal epithelium

(B) Hearing

(C) Gustation (taste) — five basic tastes encoded by taste receptor cells in taste buds on tongue papillae; sweet/umami/bitter via T1R and T2R GPCRs, sour via H^+/proton channels, salty via Na^+ channels (ENaC); signal travels via cranial nerves VII (chorda tympani) and IX to the nucleus of solitary tract $\rightarrow$ thalamus $\rightarrow$ insular cortex

(D) Vision

Q14. The hormone calcitonin, which lowers plasma calcium by inhibiting osteoclast bone resorption, is secreted by the:

(A) Parathyroid glands (these secrete parathyroid hormone, PTH, which RAISES calcium)

(B) Parafollicular C cells of the thyroid — these neuroendocrine cells lie between the thyroid follicles; secrete calcitonin in response to high

plasma Ca^{2+}; calcitonin opposes PTH but is much less important in adult humans (thyroidectomy doesn't cause major Ca disturbance). Medullary thyroid carcinoma arises from C cells and produces calcitonin (a useful tumour marker)

(C) Adrenal cortex

(D) Pancreatic islets

Q15. The chemical potential of water in a plant cell or its environment, the principal determinant of water movement in plants, is expressed as:

(A) Water potential (Ψ_w) = solute potential (Ψ_s, negative due to dissolved solutes) + pressure potential (Ψ_p, positive in turgid cells, can be negative under tension in xylem); water flows spontaneously from high (less negative) Ψ_w to low (more negative) Ψ_w. Pure water at 1 atm has $\Psi_w = 0$; all other values relative

(B) Vapour pressure deficit alone

(C) Atmospheric pressure alone

(D) Hydrostatic pressure alone

Q16. In the linear (non-cyclic) photosynthetic electron transport chain of the chloroplast thylakoid membrane, the electron acceptor immediately after Photosystem I, which then delivers electrons to $NADP^+$ reductase, is:

(A) Plastoquinone (PQ)

(B) Cytochrome b_6f complex

(C) Plastocyanin (PC)

(D) Ferredoxin (Fd) — a small iron-sulfur protein; receives electrons from PSI ($P700^*$) via internal acceptors; transfers them to ferredoxin-$NADP^+$ reductase (FNR), which reduces $NADP^+$ to NADPH. The complete linear flow: $H_2O \rightarrow$ PSII $\rightarrow$ PQ $\rightarrow$ Cyt b_6f $\rightarrow$ PC $\rightarrow$ PSI $\rightarrow$ Fd $\rightarrow$ FNR $\rightarrow$ NADPH. Ferredoxin also branches to cyclic flow around PSI (producing extra ATP without NADPH)

Q17. In the MN blood group system in humans, individuals can be homozygous M (genotype $L^M L^M$, blood type M) or N ($L^N L^N$, type N), or heterozygous ($L^M L^N$, type MN, showing both M and N antigens on RBCs). This is an example of:

(A) Codominance — both alleles produce their full phenotypic effect in the heterozygote (BOTH antigens expressed); contrasts with incomplete dominance (where the heterozygote phenotype is intermediate). ABO blood group I^A/I^B pair is also codominant

(B) Incomplete dominance (would give an intermediate antigen, not both)

(C) Complete dominance

(D) Epistasis

Q18. In female mammalian somatic cells, one of the two X chromosomes is randomly inactivated early in embryonic development, observable cytologically as a heterochromatic Barr body. The phenomenon is called:

(A) Genomic imprinting

(B) Maternal effect inheritance

(C) Polyploidy

(D) X-inactivation (lyonisation) — proposed by Mary Lyon (1961); achieves dosage compensation between XX females and XY males; the X-inactive specific transcript (XIST) lncRNA coats the chromosome to be inactivated and recruits epigenetic silencing machinery; the choice is random (paternal or maternal X) in each cell at ~ 100-cell embryo stage, but is then clonally maintained; explains tortoiseshell calico cats (heterozygous X-linked coat colour) and patchy expression of X-linked diseases in carrier females (e.g. DMD muscle, haemophilia A)

Q19. Most adult somatic cells lack telomerase activity. Consequently, with each cell division, their telomeres:

(A) Lengthen progressively

(B) Remain constant

(C) Shorten progressively (the end-replication problem; lagging-strand DNA polymerase cannot replicate the very end after primer removal) by $\sim$ 50–200 bp per division; when telomeres reach a critical short length, cells exit the cycle and enter replicative senescence (the Hayflick limit, $\sim$ 40–60 divisions in human fibroblasts); contributes to organismal ageing; bypassed in $\sim$ 85% of cancers by telomerase reactivation

(D) Circularise into rings

Q20. The hypothesis that the earliest self-replicating life forms used RNA both as genetic material AND as catalysts (before DNA and proteins took over their respective roles) is called:

(A) Protein-first hypothesis

(B) RNA world hypothesis — proposed by Walter Gilbert (1986); supported by the discovery of ribozymes (catalytic RNAs) by Cech and Altman (Nobel 1989), the catalytic RNA core of the ribosome (peptidyl transferase is rRNA), the riboswitches in bacteria, and the central role of RNA in many information-processing tasks (splicing, RNAi, telomerase); Miller-Urey-style chemistry plus newer prebiotic synthesis routes can generate ribonucleotides under early Earth conditions

(C) DNA-first hypothesis

(D) Panspermia

Q21. Among hominin fossils, the genus that lived in eastern and southern Africa $\sim$ 4–2 million years ago, walked bipedally, had a brain size of $\sim$ 400–500 cm^3 (chimpanzee-sized), and includes "Lucy" (*A. afarensis*) is:

(A) *Homo sapiens*

(B) *Homo erectus*

(C) *Homo habilis*

(D) *Australopithecus* — includes *A. afarensis* (Lucy, ~ 3.2 Mya; Donald Johanson, 1974, Ethiopia), *A. africanus* (Taung child, Raymond Dart 1924), and others. Bipedal locomotion was established (footprint trails at Laetoli, 3.6 Mya); brain was still small. The genus *Homo* (larger brain, stone tools) emerged from an Australopithecine ancestor ~ 2.5–2.0 Mya. *Paranthropus* (the "robust" australopithecines) was a side branch

Q22. A relatively common sex chromosome aneuploidy: a phenotypic male with 47 chromosomes (XXY), characterised by tall stature, small testes, infertility, gynecomastia, and reduced facial/body hair:

(A) Turner syndrome (45,X — this is a female with only one X chromosome)

(B) Down syndrome (trisomy 21)

(C) Klinefelter syndrome (47,XXY) — ~ 1 in 600 male births; arises from non-disjunction at meiosis (either parent); presence of Y $\rightarrow$ male phenotype but extra X $\rightarrow$ impaired testicular development; testosterone supplementation in adolescence aids secondary sexual characteristics; most are infertile (azoospermia) but ICSI occasionally successful

(D) Triple-X (47,XXX) syndrome

Q23. The release of mature spermatozoa from Sertoli cells into the lumen of the seminiferous tubule is called:

(A) Spermatogenesis (the entire process of sperm production from spermatogonia)

(B) Spermiation — the final step of spermatogenesis where mature sperm are released from their Sertoli cell embrace into the seminiferous tubule lumen; from there they pass to the rete testis and epididymis

where they mature further (acquire motility) and are stored. Spermatogenesis = the whole process; spermiogenesis = the morphological transformation of round spermatids into streamlined spermatozoa (acrosome formation, flagellum, nuclear condensation); spermiation = the release step

(C) Spermiogenesis (the morphological transformation of spermatid into spermatozoon)

(D) Capacitation (occurs in female reproductive tract)

Q24. The peptide hormone released from the posterior pituitary that triggers uterine contraction during parturition and the milk-ejection reflex during breastfeeding is:

(A) Oxytocin — a 9-amino-acid peptide; synthesised by paraventricular and supraoptic nuclei of hypothalamus, transported down axons to the posterior pituitary, released into blood; binds oxytocin receptors on uterine smooth muscle (which proliferate in late pregnancy) $\rightarrow$ contractions; binds myoepithelial cells of mammary alveoli $\rightarrow$ milk let-down. Positive-feedback loop with cervical/nipple stretch during labour and suckling. Synthetic oxytocin (Pitocin) used to induce/augment labour

(B) Prolactin (anterior pituitary; promotes milk PRODUCTION, not ejection)

(C) Vasopressin (ADH)

(D) Progesterone (maintains pregnancy; falls before labour)

Q25. In India's Reproductive and Child Health (RCH) programme, the public-health initiative for safe delivery and reduced maternal/infant mortality emphasises:

(A) Compulsory caesarean section

(B) Home delivery without medical supervision

(C) Skilled birth attendance — antenatal check-ups, delivery by trained personnel (skilled birth attendants, ANMs, doctors, midwives) at

health facilities (Janani Suraksha Yojana provides cash incentives for institutional delivery), tetanus immunisation, iron-folic acid supplementation, postnatal visits, infant immunisation, breastfeeding promotion. Has substantially reduced maternal mortality ratio (from ~ 437 in 1990s to ~ 97 per $100{,}000$ in recent years)

(D) Restriction of maternal health information

Q26. An older sub-dermal contraceptive implant releasing levonorgestrel slowly over 5 years from 6 small Silastic capsules placed under the arm skin (largely replaced now by single-rod implants like Implanon/Nexplanon) was called:

(A) Copper-T IUD

(B) Norplant — the first long-acting reversible contraceptive (LARC) implant, approved 1990 in the US; 6 capsules releasing levonorgestrel; very effective but removal sometimes difficult; withdrawn from US market 2002 for marketing reasons; succeeded by simpler one-rod (Norplant-2/Jadelle, Implanon, Nexplanon) systems

(C) Mifepristone (an abortifacient, not contraceptive)

(D) Combined oral contraceptive

Q27. In a mature angiosperm seed, the outer protective layer (the seed coat) develops from:

(A) The integuments of the ovule — when the ovule matures into a seed after fertilisation, the integuments harden into the seed coat (testa, the outer layer; tegmen, an inner layer if two integuments are present). The micropyle of the ovule remains as a tiny opening in the testa, useful for water uptake during germination. The funicle (stalk attaching ovule to placenta) leaves a scar called the hilum on the seed

(B) The pericarp (this becomes the fruit wall, not seed coat)

(C) The endosperm

(D) The embryo

Q28. In many *Citrus* species (orange, lemon) and *Mangifera indica* (mango), a single seed often contains multiple embryos, mostly genetically identical to the maternal plant, arising not from the fertilised egg but from somatic cells of the:

(A) Synergids

(B) Antipodal cells

(C) Pollen grain

(D) Nucellus — nucellar embryony (a form of apomixis): nucellar cells (sporophytic tissue surrounding the embryo sac, of maternal origin) develop directly into embryos within the same ovule; explains polyembryony; products are clones of the maternal plant; useful in horticulture (rootstocks of consistent quality from seed); naturally maintains desirable cultivar characteristics

Q29. A class of plant steroid hormones (first isolated from *Brassica napus* pollen, 1979) that promote cell elongation and division, stress tolerance, and senescence-related responses is:

(A) Auxins

(B) Brassinosteroids — the only true plant steroid hormones; perceived by BRI1 receptor kinase at the plasma membrane (unlike intracellular animal steroid receptors); regulate cell elongation, vascular differentiation, stomatal development, stress tolerance; deficient mutants are dwarfs

(C) Cytokinins

(D) Gibberellins

Q30. The directional growth response of plant tendrils (in peas, cucumber, grapevine) coiling around a support upon contact is called:

(A) Thigmotropism — directional growth in response to touch (contact stimulus); contact triggers differential growth on the touched vs untouched side (slower on touched), causing the tendril to coil around the support; mediated by changes in cell-wall extensibility and in some cases auxin redistribution; allows climbing plants to exploit support structures without dedicating tissue to thick stems

(B) Chemotropism (response to chemicals)

(C) Geotropism (response to gravity)

(D) Skototropism (a rare response to shade direction; in some tropical vines)

Q31. The unconventional infectious agent causing spongiform encephalopathies (CJD, kuru, BSE, scrapie) consists of:

(A) DNA + protein capsid

(B) RNA only (like viroid)

(C) Circular DNA

(D) A misfolded form of a normal cellular protein (PrP^{Sc}, the scrapie form, derived from normal PrP^{C}) — the misfolded form converts the normal form into more misfolded copies, propagating without any nucleic acid. The protein-only "infectious" agent. Stanley Prusiner coined "prion" (proteinaceous infectious particle); 1997 Medicine Nobel. Prion diseases: long incubation, progressive neurological deterioration, fatal; spongiform vacuolation and amyloid plaques of PrP^{Sc} in brain

Q32. Phylum Chordata is diagnosed by the presence (at some stage of life) of four key features. One of these, a flexible rod-like structure dorsal to the gut, providing skeletal support and a developmental signalling axis, is the:

(A) Coelom

(B) Hydrostatic skeleton

(C) Notochord — a flexible rod of vacuolated cells with a fibrous sheath, dorsal to the gut, ventral to the neural tube; present in all chordate embryos. In adult cephalochordates (*Amphioxus*) and tunicate larvae, the notochord persists. In vertebrates, it is largely replaced by the vertebral column during development, but remnants persist as the nucleus pulposus of intervertebral discs. The other three chordate features: dorsal hollow nerve cord (gives rise to spinal cord and brain in vertebrates), pharyngeal slits (gills in fish; modified into Eustachian tube, tonsils in mammals), post-anal tail

(D) Aboral skeleton

Q33. The marine deuterostome phylum exclusively, with adult radial (pentaradial) symmetry, a unique water vascular system with tube feet, and a calcareous endoskeleton, is:

(A) Echinodermata — $\sim$ 7000 species (sea stars, sea urchins, sea cucumbers, brittle stars, sea lilies); larvae are bilateral (revealing their bilaterian ancestry); secondarily evolved pentaradial symmetry in adults; **water vascular system**: a unique hydraulic network of canals filled with sea water; ends in tube feet (podia) that act as suckers for locomotion, feeding, gas exchange; calcareous ossicles forming the endoskeleton (often visible as spines); regeneration is remarkable

(B) Cnidaria

(C) Annelida

(D) Mollusca

Q34. Lymphatic filariasis (elephantiasis), with chronic disfiguring oedema of legs and genitals, is caused in most cases worldwide by:

(A) *Ascaris lumbricoides*

(B) *Plasmodium falciparum*

(C) *Trypanosoma cruzi*

(D) *Wuchereria bancrofti* (and to a lesser extent *Brugia malayi*, *B. timori*) — a thread-like nematode; adult worms live in human lymphatic

vessels; release microfilariae into blood with strong nocturnal periodicity (matching peak biting time of *Culex* mosquito vector). Adult worms block lymphatic flow $\rightarrow$ chronic lymphoedema. Microfilariae ingested by mosquito, develop, transmitted to next human bite. WHO-led global programme to eliminate lymphatic filariasis uses mass drug administration with albendazole + DEC or ivermectin

Q35. Systemic lupus erythematosus (SLE) is the prototypical multi-system autoimmune disease, characterised by:

(A) Selective destruction of pancreatic β-cells (this describes type 1 diabetes)

(B) Demyelination of CNS neurons (multiple sclerosis)

(C) Production of autoantibodies (anti-nuclear antibodies including anti-dsDNA, anti-Smith, anti-Ro, anti-La) against many self-antigens, leading to immune-complex deposition in multiple organs: skin (malar "butterfly" rash, discoid rash, photosensitivity), joints (non-erosive arthritis), kidneys (lupus nephritis), serous membranes (pleurisy, pericarditis), CNS, blood (cytopenias). Strongly female-predominant ($\sim$ 9:1); peak onset in childbearing years; complement consumption; flare-and-remit course. Treated with hydroxychloroquine, corticosteroids, immunosuppressants (mycophenolate, azathioprine), biologics (belimumab)

(D) IgE-mediated mast cell degranulation

Q36. The illicit psychostimulant derived from leaves of the South American coca plant (*Erythroxylum coca*), acting in the brain by blocking dopamine, noradrenaline, and serotonin reuptake at presynaptic terminals (leading to intense but short-lived euphoria, tachycardia, hypertension, vasoconstriction, addiction), is:

(A) Cannabis

(B) Cocaine — blocks the dopamine transporter (DAT) primarily; massive synaptic dopamine accumulation in nucleus accumbens reward

circuitry $\rightarrow$ addiction; also blocks NA and serotonin transporters. Acute effects: euphoria, alertness, restlessness; sympathomimetic (HR, BP increase). Toxicity: arrhythmias, MI (vasospasm), stroke, seizures, hyperthermia. Chronic use $\rightarrow$ nasal septum perforation (snorted), endocarditis (injected), cognitive decline, depression. Mortality particularly high when combined with alcohol (forms cocaethylene). "Crack" is the free-base form, smokable, more rapid and severe addiction

(C) Heroin (an opioid)

(D) LSD (a hallucinogen)

Q37. The trapping of long-wave (infrared) radiation re-emitted by Earth's surface, by atmospheric water vapour, carbon dioxide, methane, nitrous oxide, and ozone, raising surface temperatures above what they would be otherwise, is called:

(A) Ozone depletion

(B) Acid rain

(C) Eutrophication

(D) The greenhouse effect — a natural and necessary phenomenon (without it Earth's mean surface temperature would be $\sim -18\,^{\circ}\mathrm{C}$ instead of $\sim 15\,^{\circ}\mathrm{C}$). The problem is the ENHANCED greenhouse effect from anthropogenic emissions: industrial-era CO_2 has risen from ~ 280 to > 420 ppm; methane has more than doubled. Causes global warming, climate change, sea-level rise, ocean acidification, polar ice melt, more extreme weather. Mitigated by reducing fossil fuel use, deforestation, agricultural emissions (Paris Agreement, 2015)

Q38. Large-scale clearing of forested land for agriculture, urbanisation, logging, or mining, with consequences including loss of biodiversity, soil erosion, altered hydrology, and reduced carbon sequestration, is called:

(A) Eutrophication

(B) Biomagnification

(C) Deforestation — globally, forests have lost $\sim 30\%$ of their original cover; current rate ~ 10 million hectares/year, mostly in tropical regions (Amazon, Southeast Asia, Congo basin). Causes: cattle ranching, soy and oil-palm cultivation, logging, fuelwood demand. Consequences: species extinction (rainforests contain $\sim 50\%$ of terrestrial biodiversity), $\sim 10\%$ of anthropogenic CO_2 emissions, hydrological disruption, displacement of indigenous peoples. Mitigation: REDD+ programmes (Reducing Emissions from Deforestation and Forest Degradation), agroforestry, sustainable land-use policy, reforestation

(D) Biological oxygen demand

Q39. The first successful human gene therapy (1990, NIH; Ashanti DeSilva, 4-year-old girl) treated which inherited single-gene deficiency by infusing the patient's own T-lymphocytes engineered to carry a functional copy of the missing gene?

(A) Sickle cell disease

(B) ADA-SCID — Adenosine Deaminase deficiency Severe Combined Immunodeficiency. Loss of ADA enzyme causes accumulation of deoxyadenosine, which is toxic to lymphocytes $\rightarrow$ severe combined immunodeficiency ("bubble baby" disease). Gene therapy by retroviral vector delivery of functional ADA cDNA into the patient's own T cells, then reinfused. Ashanti DeSilva and other children showed lasting improvement. Field had setbacks (insertional mutagenesis-induced leukaemia in some X-SCID trials) before resurging with safer lentiviral vectors and now CRISPR; Strimvelis (the first commercial ex vivo gene therapy, 2016, for ADA-SCID) and many others since

(C) Cystic fibrosis

(D) Phenylketonuria

Q40. A laboratory mouse in which a specific gene has been deliberately inactivated ("knocked out") by homologous recombination in embryonic stem

cells (Capecchi-Smithies-Evans, Nobel 2007), used to investigate gene function, is called a:

(A) Knockout mouse — the standard reverse-genetics tool in mammalian biology; gene targeting in mouse ESCs, then chimeric mouse, then germline-transmitting offspring, then homozygous knockout. Has elucidated function of thousands of genes; underlies most modern understanding of mammalian gene function. Now complemented by conditional/tissue-specific knockouts (Cre-loxP) and rapid CRISPR-based gene editing (no ESC step required)

(B) Transgenic mouse (this usually refers to a mouse carrying an ADDED gene; the term is sometimes used broadly to include knockouts, but the question's emphasis on gene inactivation by homologous recombination specifies knockout)

(C) Cloned mouse

(D) Chimeric mouse (an intermediate stage, not the final knockout)

Detailed Solutions

Q1.

Solution

Concept — Tight junctions (zonula occludens): The seal between epithelial cells; defines the paracellular permeability of the epithelium and maintains apical-basolateral polarity.

Step 1 — Structure:

- Continuous belt encircling the apical region of each epithelial cell.
- Transmembrane proteins of two main families: **claudins** (a ~ 24-member family; primary determinants of selectivity) and **occludin**.
- Cytoplasmic scaffolding proteins (ZO-1, ZO-2, ZO-3) link claudins to the actin cytoskeleton.
- In freeze-fracture EM, appear as ridges of intramembrane particles forming a network of strands.

Step 2 — Function:

- Seal the paracellular space; force molecules to go transcellularly via regulated transporters.
- Maintain apical-basolateral polarity: prevent membrane proteins of apical and basolateral membranes from mixing by lateral diffusion (the "fence" function).
- Selectivity depends on claudin composition: "leaky" epithelia (proximal tubule, small intestine) vs "tight" epithelia (blood-brain barrier, distal nephron, urinary bladder).

Step 3 — Specific claudins:

- Claudin-1: skin barrier; mutation $\rightarrow$ neonatal ichthyosis with sclerosing cholangitis.
- Claudin-16: paracellular Mg^{2+} reabsorption in thick ascending limb; mutation $\rightarrow$ familial hypomagnesaemia.
- Claudin-5: blood-brain barrier; defects implicated in CNS oedema.
- Claudin-14: outer hair cells; mutation $\rightarrow$ deafness.

Step 4 — Pathology:

- *Clostridium perfringens* enterotoxin binds claudin-3, 4 $\rightarrow$ disrupts barrier $\rightarrow$ food poisoning.

- *Helicobacter pylori* disrupts gastric tight junctions.
- "Leaky gut" is implicated in inflammatory bowel disease, coeliac disease, food allergies.
- Many viruses (HCV, dengue) hijack tight junction components for cell entry.

Step 5 — Other epithelial junctions:

- Adherens junctions (zonula adherens): E-cadherin links across cells; catenins link to actin; tissue cohesion.
- Desmosomes: spot welds; intermediate filaments; mechanical resistance.
- Gap junctions: communication channels.
- Hemidesmosomes: cell-to-matrix; integrins link to laminin.
- Junctional complex (apical-to-basal order in intestinal epithelium): tight junction $\rightarrow$ adherens junction $\rightarrow$ desmosomes.

Final Answer: Tight junctions (claudin/occludin) $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q1

Q2.

Solution

Concept — Desmosomes (maculae adherentes): "Spot welds" that hold cells together against mechanical shear. Especially abundant in tissues that experience high mechanical stress.

Step 1 — Structure:

- Disc-shaped junctions ($\sim 0.2\,\mu$m diameter).
- Transmembrane: desmosomal cadherins — desmogleins (Dsg1-4) and desmocollins (Dsc1-3).
- Cytoplasmic plaque: plakoglobin, plakophilin, desmoplakin (the major linker to intermediate filaments).
- The intermediate filaments (keratins in epithelia; desmin in cardiac muscle) attach to the plaque, forming a continuous network across cells through the tissue.

Step 2 — Where prominent:

- Skin epidermis: numerous; resist abrasion.
- Cardiac muscle intercalated discs: hold cardiomyocytes mechanically as they contract.

- Bladder, uterus, oesophagus.
- Hair, nails.

Step 3 — Diseases of desmosomes:

- **Pemphigus vulgaris:** autoimmune; IgG autoantibodies against desmoglein 3 (skin and mucous membranes) $\rightarrow$ loss of cell-cell adhesion $\rightarrow$ intra-epidermal blisters; potentially life-threatening. Treated with corticosteroids, rituximab (anti-CD20).
- Pemphigus foliaceus: autoantibodies against desmoglein 1 (skin only).
- **Bullous pemphigoid:** autoantibodies against hemidesmosomal antigens (BP180, BP230) $\rightarrow$ subepidermal blisters.
- **Arrhythmogenic right ventricular cardiomyopathy (ARVC):** mutations in desmosomal genes (plakophilin-2, desmoplakin, etc.) $\rightarrow$ progressive replacement of myocardium with fibrofatty tissue $\rightarrow$ ventricular arrhythmias, sudden cardiac death; common in athletes.
- Skin fragility syndromes: desmoplakin mutations.

Step 4 — Bacterial exploitation: *Staphylococcus aureus* exfoliative toxin cleaves desmoglein 1 $\rightarrow$ scalded skin syndrome (similar histology to pemphigus foliaceus).

Step 5 — Hemidesmosomes: A related structure connecting basal epithelial cells to the basement membrane (cell-to-matrix, not cell-to-cell); use integrins ($\alpha_6\beta_4$) instead of cadherins; anchor keratin filaments to the basal lamina.

Final Answer: Desmosomes $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q2

Q3.

Solution

Concept — Glyoxysomes — specialised peroxisomes in plants: Allow plant seedlings to net synthesise sugar from stored fats during germination, before photosynthesis is established. Crucial for oilseed crops.

Step 1 — The fundamental problem: The TCA cycle generates 2 CO_2 from each acetyl-CoA. Animals (and most cells) therefore CANNOT make net glucose from acetyl-CoA (the lipid-to-sugar pathway is blocked). But germinating oilseeds need to do exactly this — convert stored oil to sugars to fuel embryonic growth.

Step 2 — The glyoxylate cycle solution: A modified TCA cycle that BYPASSES the two CO_2-losing steps (isocitrate dehydrogenase and α-ketoglutarate dehydro-

genase). Two unique enzymes:

- **Isocitrate lyase:** cleaves isocitrate $\rightarrow$ succinate + glyoxylate.
- **Malate synthase:** condenses glyoxylate + a second acetyl-CoA $\rightarrow$ malate.

Net for two acetyl-CoA: succinate + malate (both 4C). Succinate exits to mitochondria, malate to cytosol; cytosolic malate oxidised to oxaloacetate, which then enters gluconeogenesis to make sucrose.

Step 3 — Glyoxysome:

- A specialised peroxisome found in oilseed cotyledons (and endosperm of some seeds) during germination.
- Single membrane; contains β-oxidation enzymes AND the unique glyoxylate cycle enzymes.
- Fatty acids from stored oil bodies are taken up; β-oxidised to acetyl-CoA within the glyoxysome; acetyl-CoA enters the glyoxylate cycle; products feed gluconeogenesis.
- As cotyledons green and start to photosynthesise, glyoxysomes transition to leaf-type peroxisomes (gain photorespiratory enzymes, lose glyoxylate cycle).

Step 4 — Other plant peroxisome types:

- Leaf peroxisomes: photorespiration (oxidation of glycolate to glyoxylate to glycine).
- Root nodule peroxisomes: ureide synthesis in legumes.
- Unspecialised peroxisomes: H_2O_2-handling.

Step 5 — Bacteria and the glyoxylate cycle: The glyoxylate cycle also operates in bacteria (*E. coli* on acetate as sole carbon source) and fungi. Allows growth on 2-carbon compounds. Absent in animals.

Step 6 — Application: Oilseed crops are economically critical. Understanding glyoxysome biology is key to manipulating seed energy storage; soybean, canola, sunflower, palm oil are major examples.

Final Answer: Glyoxysomes $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q3

Q4.

Solution

Concept — Lipid rafts: Dynamic, nanoscale membrane microdomains enriched in cholesterol and sphingolipids. The concept evolved through the 1990s (Simons & Ikonen, 1997) and remains a focus of active research.

Step 1 — Composition:

- Cholesterol-rich.
- Sphingolipids (sphingomyelin, glycosphingolipids): saturated long-chain acyl groups that pack tightly with cholesterol.
- Phase: liquid-ordered (Lo) microdomains, denser than the surrounding liquid-disordered (Ld) bilayer of unsaturated glycerophospholipids.
- Size: nanoscale (10–200 nm), transient unless stabilised by protein interactions.

Step 2 — Resident protein types:

- GPI-anchored proteins (CD59, DAF, alkaline phosphatase, PrP, prion protein).
- Doubly acylated proteins (Src-family kinases like Fyn, Lck, Lyn; Gα subunits).
- Some transmembrane proteins: T-cell receptor, B-cell receptor, IgE high-affinity receptor (FcϵRI), insulin receptor (some forms), adhesion molecules.

Step 3 — Functions:

- Signalling platforms: receptor clustering at rafts triggers downstream signalling cascades.
- T-cell activation: TCR engagement recruits raft-resident Lck and other components into the immunological synapse.
- Mast-cell activation: FcϵRI clustering on rafts.
- Membrane trafficking: apical sorting in polarised epithelia.
- Cell-cell adhesion.

Step 4 — Pathogen exploitation:

- HIV uses CD4 + chemokine receptor (raft-resident) for entry; HIV buds from raft regions.
- Influenza haemagglutinin is sorted to apical rafts; budding from rafts.
- Cholera toxin binds GM1 ganglioside (raft component).

- Prion conversion (PrP^{C} to PrP^{Sc}) occurs at rafts.
- Pathogenic mycobacteria use rafts for entry.

Step 5 — Caveolae — a specialised raft type:

- Flask-shaped invaginations (50–100 nm).
- Coated cytoplasmically with caveolin protein.
- Especially abundant in endothelium, adipocytes, smooth muscle.
- Roles in: endocytosis, signal transduction, lipid trafficking, mechanosensing.

Step 6 — Methods of study:

- Detergent-resistant membrane (DRM) extraction: rafts are resistant to cold non-ionic detergents (Triton X-100 at $4\,^{\circ}C$).
- Cholesterol depletion (MβCD): disrupts rafts.
- Super-resolution microscopy.
- Single-particle tracking.

Final Answer: Lipid rafts $\Rightarrow$ C

Answer: (C) Go Back to Q4

Q5.

Solution

Concept — Molecular chaperones and the proteostasis network: Proteins that assist correct folding of other proteins. Discovered through heat-shock response studies in the 1970s-80s (Ritossa, Lindquist, others).

Step 1 — The folding problem:

- Newly synthesised polypeptides must fold into precise three-dimensional structures.
- The cell interior is crowded ($\sim$ 300 mg/mL protein); risk of misfolding and aggregation.
- Hydrophobic patches can stick together with other proteins before folding finishes.
- Chaperones bind to exposed hydrophobic regions, shield them, and allow proper folding.

Step 2 — Major chaperone families:

- **HSP60 family (chaperonins):**

  - Large barrel-shaped complexes: bacterial GroEL/GroES; eukaryotic Hsp60/Hsp10 (mitochondrial); TRiC/CCT (cytosolic, eukaryotic).
  - Substrate enters the central chamber, lid closes (Hsp10/GroES), folding occurs in isolation from cytosol; ATP-driven cycle releases folded product.

- **HSP70 family:**
  - Bacterial DnaK + DnaJ (co-chaperone) + GrpE (nucleotide exchange factor).
  - Eukaryotic Hsp70 + Hsp40 (J-protein) + nucleotide exchange factors (BAG, HspBP1).
  - Bind to short hydrophobic segments in unfolded chains; ATP-cycle binds and releases substrate iteratively.
  - Many substrate-specific J-proteins target Hsp70 to different clients.
  - Roles: co-translational folding, organelle import (ER/mitochondrial precursors), disaggregation, refolding of denatured proteins.
- **HSP90 family:**
  - Cytosolic Hsp90 (and mitochondrial TRAP1, ER-resident GRP94).
  - Dimeric ATPase; folds a specific clientele: steroid hormone receptors, kinases ($\sim 60\%$ of human kinases are Hsp90 clients), telomerase, p53, nitric oxide synthase, etc.
  - Many oncoproteins depend on Hsp90 $\rightarrow$ Hsp90 inhibitors (geldanamycin, 17-AAG) tested as anticancer drugs.
- **Small HSPs (sHsps):**
  - Hsp27, α-crystallin (the major lens protein), HspB1-10.
  - Form oligomers; bind unfolded substrates to prevent aggregation; ATP-independent "holdases".
  - Crystallins maintain lens transparency; mutations cause cataracts.
- **Hsp100 family (Clp, Hsp104):**
  - Disaggregases; threading machines that can pull apart protein aggregates; some link to proteasomal degradation.

Step 3 — Heat shock response:

- Stress (heat, oxidative, etc.) increases misfolded protein burden.
- Heat shock factor 1 (HSF1) is normally bound by Hsp90 and kept inactive.
- Misfolded proteins titrate Hsp90 away; HSF1 trimerises, enters nucleus, binds heat shock elements (HSEs) $\rightarrow$ massive transcriptional induction of Hsp genes.

- Restores proteostasis.
- Some sHsps are constitutively expressed; others (like Hsp70, Hsp90) are strongly stress-induced.

Step 4 — Disease and ageing:

- Neurodegenerative diseases involve protein misfolding/aggregation: Alzheimer's (β-amyloid, tau), Parkinson's (α-synuclein), Huntington's (polyQ huntingtin), ALS (SOD1, TDP-43, FUS), prion diseases (PrP).
- Chaperone capacity declines with age $\rightarrow$ proteostasis collapse.
- Many drugs target the proteostasis network (HSP90 inhibitors in cancer; pharmacological chaperones for cystic fibrosis ΔF508 CFTR; tafamidis for transthyretin amyloidosis).

Step 5 — The unfolded protein response (UPR): ER-specific stress response to accumulation of misfolded proteins in the ER lumen; three branches (PERK, IRE1, ATF6); upregulates ER chaperones (BiP/GRP78, calnexin), expands ER capacity, and if sustained, triggers apoptosis. Important in diabetes, ischaemia, cancer.

Final Answer: Heat shock proteins (HSPs) $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q5

Q6.

Solution

Concept — The two nicotinamide nucleotide carriers — specialised division of labour: NAD^+ and $NADP^+$ differ by a single phosphate group on the $2'$-OH of adenine ribose, yet are used in fundamentally different metabolic compartments.

Step 1 — Structure:

- Both have nicotinamide-ribose-(P-P)-ribose-adenine backbone.
- The nicotinamide ring accepts/donates electrons (hydride ion, H^-) at its 4-position.
- NADP differs from NAD only in carrying an extra phosphate on the $2'$-OH of the adenosine ribose.
- This small structural difference allows enzymes to discriminate the two coenzymes with high selectivity.

Step 2 — Cellular pools and redox states:

- NAD pool: total NAD^+ + NADH; maintained in the OXIDISED state

($[NAD^+]/[NADH]$ ratio ~ 700 in cytosol).
- NADP pool: total $NADP^+$ + NADPH; maintained in the REDUCED state ($[NADPH]/[NADP^+]$ ratio ~ 100 in cytosol).
- This thermodynamic separation enables NAD^+ to readily accept electrons (oxidations) and NADPH to readily donate electrons (reductions).

Step 3 — NAD^+/NADH — catabolism: NAD^+ is the principal electron acceptor in oxidations:

- Glycolysis: glyceraldehyde-3-phosphate dehydrogenase.
- Pyruvate dehydrogenase complex.
- TCA cycle: isocitrate DH, α-KG DH, malate DH.
- Fatty acid β-oxidation: 3-hydroxyacyl-CoA dehydrogenase.
- Amino acid catabolism: many oxidative steps.

NADH so generated feeds Complex I of the electron transport chain; oxidative phosphorylation harvests the energy as ATP. NAD^+ is regenerated and the cycle continues.

Step 4 — NADPH/$NADP^+$ — anabolism and antioxidant defence:

- Reductive biosynthesis: fatty acid synthesis (each two-carbon addition uses 2 NADPH), cholesterol synthesis (many NADPH), steroid hormone synthesis, deoxyribonucleotide synthesis (ribonucleotide reductase).
- Antioxidant defence: regenerates reduced glutathione (GSH) via glutathione reductase; GSH detoxifies H_2O_2 and lipid peroxides.
- Phagocyte respiratory burst: NADPH oxidase (NOX2) uses NADPH to generate superoxide for microbial killing.
- Cytochrome P450 drug metabolism uses NADPH.

Step 5 — Sources of NADPH:

- Pentose phosphate pathway (HMP shunt): G6PD and 6PGD generate NADPH.
- Malic enzyme: malate $\rightarrow$ pyruvate.
- Isocitrate dehydrogenase (NADP-dependent isoform).

Step 6 — Clinical relevance:

- G6PD deficiency: X-linked; reduced NADPH in RBCs; oxidative stress (fava beans, primaquine, sulfa drugs, infection) causes haemolysis. Most common human enzyme deficiency.

- Chronic granulomatous disease (CGD): defective NADPH oxidase in phagocytes; recurrent bacterial/fungal infections.
- Nicotinic acid (niacin, vitamin B_3) deficiency: pellagra (the "3 D's": dermatitis, diarrhoea, dementia).
- NAD^+ supplements (nicotinamide riboside, NMN) are studied for metabolic and ageing effects.

Step 7 — NAD^+ as substrate (not just coenzyme):

- PARPs (poly-ADP-ribose polymerases): use NAD^+ in DNA damage response.
- Sirtuins: NAD^+-dependent deacylases; longevity-related.
- NAD^+ levels decline with age; supplementation increases lifespan in some model organisms.

Final Answer: NAD^+ in catabolism; NADPH in anabolism + antioxidant defence $\Rightarrow$ D

Answer: (D) Go Back to Q6

Q7.

Solution

Concept — Hydrogen bonds and protein secondary structure: Linus Pauling's deduction of α-helix and β-sheet (1951) from precise model-building is one of the great triumphs of structural biology.

Step 1 — Levels of protein structure:

- Primary: linear amino acid sequence (peptide bonds).
- Secondary: local repeated patterns (α-helix, β-sheet, turns); held by backbone H-bonds.
- Tertiary: overall 3D fold of a single polypeptide; held by side-chain interactions (hydrophobic core, ionic, H-bond between side chains, disulfide bridges).
- Quaternary: arrangement of multiple subunits in oligomeric proteins.

Step 2 — The α-helix:

- Right-handed helix; 3.6 residues per turn; 5.4 Å rise per turn (1.5 Å per residue).
- H-bonds between carbonyl O of residue i and N-H of residue $i+4$; nearly straight and aligned along helix axis.

- Side chains project outward.
- Stable but flexible; common building block.
- Proline disrupts α-helices (its N is in a ring; no N-H to donate).
- Examples: myoglobin/haemoglobin, transmembrane domains, coiled-coils (keratin, myosin).

Step 3 — The β-sheet:

- Extended polypeptide strands (β-strands); each residue contributes one H-bond donor and one acceptor.
- Strands run parallel (same N-to-C direction) or antiparallel (alternating direction); antiparallel H-bonds are straighter and stronger.
- Side chains alternate above and below the sheet plane.
- Pleated appearance.
- Examples: silk fibroin, immunoglobulin domains, β-barrels (outer membrane porins), β-amyloid fibrils.

Step 4 — Turns and loops: Reverse turns (especially β-turns: 4 residues with $1 \rightarrow 4$ H-bond) reverse chain direction; often glycine or proline (the only residues that easily fit into the unusual conformation). Connect secondary structure elements.

Step 5 — H-bond properties:

- Energy: ~ 5 kcal/mol (much weaker than a covalent bond at ~ 80–100 kcal/mol, but stronger than van der Waals).
- Directional (linear H-bonds are strongest).
- Distance ~ 2.5–3.5 Å between donor and acceptor atoms.
- Cooperative: many backbone H-bonds together stabilise the structure.
- Strength depends on environment: shielded from water (e.g. in protein interior) are stronger than exposed.

Step 6 — Other forces in protein structure:

- Hydrophobic effect: largest contributor to tertiary fold stability; nonpolar side chains cluster in protein interior, away from water; entropic driving force.
- Disulfide bonds: cysteine-cysteine S-S covalent links; especially in secreted/extracellular proteins (insulin, antibodies, ECM proteins).
- Ionic (salt) bridges: between oppositely charged side chains (Lys-Glu, Arg-Asp); often at protein surfaces.
- Van der Waals contacts: weak but numerous; cumulative effect.

Final Answer: Backbone hydrogen bonds stabilise secondary structure $\Rightarrow$ C

Answer: (C) Go Back to Q7

Q8.

Solution

Concept — Origins of replication — launch sites for DNA synthesis: DNA replication initiates at specific sites; in prokaryotes one origin per genome (*oriC*), in eukaryotes thousands of origins per chromosome to complete replication in reasonable time.

Step 1 — Bacterial origin (*E. coli oriC*):

- ~ 245 bp; contains AT-rich 13-mer repeats and DnaA boxes (9-mer).
- DnaA protein binds, melts AT-rich region.
- DnaB helicase loaded by DnaC; unwinds DNA bidirectionally.
- DNA polymerase III holoenzyme assembles; replisome formed.
- Replication proceeds bidirectionally around the circular chromosome.

Step 2 — Eukaryotic origins:

- Thousands of origins distributed across chromosomes ($\sim$ 30,000–50,000 in mammals).
- Spaced every 30–300 kb (variable).
- Yeast (*Saccharomyces cerevisiae*) has well-defined ARS (autonomously replicating sequences) with ~ 100 bp specific elements.
- In metazoans, origin specification is more flexible; depends on chromatin context (DNase-hypersensitive sites, transcriptional state) more than DNA sequence per se.

Step 3 — Licensing in G_1:

- Origin Recognition Complex (ORC) binds origin throughout cell cycle.
- In G_1: Cdc6 and Cdt1 recruited; load MCM2-7 helicase as inactive "double hexamer" encircling DNA $\rightarrow$ pre-replication complex (preRC).
- Origins now "licensed" but inactive.

Step 4 — Firing in S phase:

- CDK and DDK kinases activated at G_1/S transition.

- Phosphorylate MCMs and recruit accessory factors (CDC45, GINS) $\rightarrow$ CMG helicase complex active.
- Helicase unwinds DNA bidirectionally; replication forks established.
- DNA polymerases (Pol α for primers, Pol δ for lagging strand, Pol ϵ for leading strand) take over.

Step 5 — Once-per-cell-cycle control: A central feature: each origin must fire ONCE and only once per S phase. Mechanisms:

- After firing, MCM helicases travel with forks; original origins no longer have MCMs.
- CDK activity (high in S, G_2, M) prevents new MCM loading; only in G_1 (low CDK) can preRCs reassemble.
- Geminin: an inhibitor of Cdt1 in S/G_2/M.
- Failure of this control $\rightarrow$ re-replication $\rightarrow$ genomic instability, gene amplification, cancer.

Step 6 — Temporal program of firing: Origins fire in a defined temporal order; early-firing regions are typically gene-rich, transcriptionally active, GC-rich (euchromatic). Late-firing are heterochromatic, gene-poor. "Dormant origins" are licensed but rarely fire unless replication forks stall (back-up function for completing replication).

Step 7 — Telomeres and centromeres:

- Telomeres: chromosome ends; present the end-replication problem; need telomerase.
- Centromeres: kinetochore assembly point for mitotic spindle attachment; rich in repetitive DNA; epigenetically marked by histone variant CENP-A.
- Nucleolus: rRNA transcription factory.

Final Answer: Origins of replication $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q8

Q9.

Solution

Concept — Digestion of dietary fats: A multi-step process involving emulsification, hydrolysis, micelle formation, and enterocyte uptake.

Step 1 — Lipid digestion pre-pancreatic:

- Mouth: minor; lingual lipase (acid-stable).
- Stomach: gastric lipase (acid-stable); accounts for ~ 10–15% of triglyceride hydrolysis (especially short/medium-chain).
- Mechanical churning helps disperse fat into smaller droplets.

Step 2 — Bile-mediated emulsification (duodenum):

- CCK from I cells of duodenum (stimulated by fat) $\rightarrow$ gallbladder contraction $\rightarrow$ bile released into duodenum.
- Bile salts (sodium glycocholate, sodium taurocholate, etc.) are amphipathic; coat fat droplets, reducing surface tension; emulsify large fat globules into many small droplets ($\sim 1\,\mu$m).
- Emulsification dramatically increases the surface area for lipase action.

Step 3 — Pancreatic lipase action:

- Secreted by pancreatic acinar cells along with other digestive enzymes; CCK stimulates secretion.
- Hydrolyses triglycerides at the sn-1 and sn-3 positions $\rightarrow$ produces $2\times$ free fatty acid (FFA) $+1 \times$ 2-monoacylglycerol (the sn-2 ester remains intact).
- Requires **colipase** (a $10\,$kDa cofactor secreted by pancreas as procolipase, activated by trypsin) which anchors lipase to the lipid-water interface despite the bile-salt coating that would otherwise sterically exclude the enzyme.
- Optimal at duodenal pH ($\sim$ 7–8).

Step 4 — Other pancreatic lipases:

- Phospholipase A_2: hydrolyses phospholipids at sn-2 position $\rightarrow$ FFA + lysophospholipid.
- Cholesterol esterase: hydrolyses dietary cholesterol esters.

Step 5 — Mixed micelle formation:

- Bile salts together with FFA, monoacylglycerol, cholesterol, lysophospholipids form mixed micelles (~ 4–$8\,$nm).

- These deliver hydrophobic lipid molecules to the apical brush border of enterocytes.
- At the brush border, the lipid components dissociate from the micelle (bile salts stay outside) and diffuse/transport into the enterocyte.

Step 6 — Within the enterocyte:

- FFA and monoacylglycerol resynthesised into triglyceride in the smooth ER.
- TGs + cholesterol + apoprotein B-48 + phospholipids assembled into **chylomicrons**.
- Chylomicrons released by exocytosis at the basolateral surface; too large for blood capillaries; enter the lacteals (lymphatic capillaries) and flow through the lymphatic system, eventually emptying into the venous blood at the thoracic duct.

Step 7 — Bile-salt recycling: After their function in the small intestine, $> 95\%$ of bile salts are reabsorbed in the terminal ileum (via ASBT transporter) and return to the liver via the portal vein — the enterohepatic circulation. Cycles ~ 6 times per meal. Loss of terminal ileum (e.g. Crohn's disease, resection) $\rightarrow$ bile-salt malabsorption $\rightarrow$ fat malabsorption.

Step 8 — Pharmacology and pathology:

- Orlistat: reversible inhibitor of pancreatic and gastric lipases; reduces dietary fat absorption by $\sim 30\%$; used for obesity treatment.
- Pancreatic insufficiency (cystic fibrosis, chronic pancreatitis): reduced lipase $\rightarrow$ steatorrhoea (oily, foul-smelling, floating stools), fat-soluble vitamin (A, D, E, K) deficiency.
- Obstructive jaundice (bile duct blockage): no bile reaches duodenum $\rightarrow$ fat malabsorption.

Final Answer: Pancreatic lipase (with colipase) $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q9

Q10.

Solution

Concept — Oxygen carriage in blood: The vast majority of arterial O_2 is carried bound to haemoglobin within RBCs; only a small fraction is dissolved in plasma.

Step 1 — Quantifying total arterial O_2 content: For a typical healthy adult at sea level:

- Hb concentration: $15\,\text{g/dL}$.
- Each gram of fully saturated Hb carries: $1.34\,\text{mL } O_2$ (Hufner's constant).
- Arterial SaO_2: $\sim 98\%$.
- Hb-bound O_2: $15 \times 1.34 \times 0.98 \approx 19.7\,\text{mL } O_2$ per dL.

Step 2 — Dissolved O_2:

- Henry's Law: $C_{\text{diss}} = \alpha \cdot P_{O_2}$, where $\alpha = 0.003\,\text{mL/dL/mmHg}$.
- Arterial $pO_2 \approx 100\,\text{mmHg}$.
- Dissolved $O_2 = 0.003 \times 100 = 0.3\,\text{mL } O_2$ per dL.

Step 3 — Total and fractions:

- Total $\sim 20.0\,\text{mL } O_2\text{/dL}$ arterial blood.
- Hb-bound: $19.7/20 \approx 98.5\%$ ($\sim 98\%$).
- Dissolved: $0.3/20 \approx 1.5\%$.

The Hb-bound fraction is overwhelmingly dominant.

Step 4 — But the dissolved fraction is critical: The dissolved O_2 creates the partial pressure gradient that drives:

- O_2 loading onto Hb in pulmonary capillaries.
- O_2 unloading from Hb in tissue capillaries.
- Diffusion across capillary wall and into tissue cells.

Hb-bound O_2 does not contribute to partial pressure — it is a "reservoir" that buffers the dissolved pool.

Step 5 — Hyperbaric oxygen therapy: In a hyperbaric chamber at 2–3 atm 100% O_2, dissolved O_2 rises substantially ($\alpha \times P_{O_2}$). At 3 atm, dissolved O_2 can reach $\sim 6\,\text{mL/dL}$ — enough alone to meet basal metabolic demand even without Hb! Useful in:

- Carbon monoxide poisoning (CO occupies Hb's O_2 sites; hyperbaric O_2 accelerates CO dissociation and provides dissolved O_2).

- Decompression sickness.
- Anaerobic infections (gas gangrene).
- Selected chronic wounds, radiation tissue injury.

Step 6 — Anaemia and tissue oxygenation:

- Halve the Hb (severe anaemia, $7.5\,\text{g/dL}$): arterial O_2 content drops to $\sim 10\,\text{mL/dL}$.
- Compensations: increased cardiac output, increased $2{,}3$-BPG (right-shifts O_2-Hb curve), more efficient O_2 extraction (lower venous saturation).
- If demand exceeds delivery $\rightarrow$ tissue hypoxia, anaerobic metabolism, lactic acidosis.

Step 7 — Pulse oximetry: Non-invasive measurement of SpO_2 (peripheral arterial saturation) using two wavelengths of light (red, $660\,\text{nm}$; infrared, $940\,\text{nm}$) that distinguish oxy- from deoxy-Hb spectroscopically. Normal $\geq 95\%$. Limitations: doesn't detect anaemia (saturation can be normal but content low), CO poisoning (carboxyHb absorbs like oxyHb), methaemoglobinaemia. Crucial monitor in anaesthesia, ICU, sleep medicine, and during the COVID-19 pandemic.

Final Answer: $\sim 98\%$ bound to Hb $\Rightarrow \boxed{\text{C}}$

Answer: (C) Go Back to Q10

Q11.

Solution

Concept — The lymphatic system: A one-way drainage network that complements the cardiovascular system; essential for fluid balance, lipid absorption, and immune function.

Step 1 — Capillary fluid balance — the Starling forces:

- At arteriolar end of capillary: hydrostatic pressure ($\sim 35\,\text{mmHg}$) $>$ oncotic pressure ($\sim 25\,\text{mmHg}$) $\rightarrow$ net outward filtration of fluid into interstitium.
- At venular end: hydrostatic pressure has fallen ($\sim 15\,\text{mmHg}$) $<$ oncotic pressure $\rightarrow$ net reabsorption.
- Filtration and reabsorption are nearly balanced, but slight net filtration occurs (~ 2–$4\,\text{L/day}$ excess).
- This excess interstitial fluid must be returned; otherwise interstitial space would accumulate fluid (oedema).

Step 2 — Lymphatic capillary structure:

- Blind-ended capillaries in interstitial tissue.
- Endothelium overlapping like “flap valves” that open when interstitial pressure rises.
- No basement membrane; allow easy entry of fluid, macromolecules (including escaped plasma proteins), and cells.
- Anchored to surrounding ECM by filaments that pull the flaps open when tissue swells.

Step 3 — Onward flow:

- Capillaries → collecting lymphatics (smooth muscle, valves) → lymph nodes → lymphatic trunks → two major ducts:
  - Thoracic duct (the major one): drains lower body and left upper body; empties into left subclavian/internal jugular junction.
  - Right lymphatic duct: drains right upper body; empties into right subclavian/internal jugular junction.
- Flow is propelled by: skeletal muscle pump, respiratory pressure changes, smooth muscle contractions of lymphatic walls, one-way valves preventing backflow.
- Lymph composition resembles plasma but with lower protein, with added lymphocytes from nodes, and with added chylomicrons from intestinal lacteals.

Step 4 — Lymph nodes — immune surveillance:

- Hundreds of small bean-shaped organs distributed along lymphatics.
- Highly organised cortex (B-cell follicles), paracortex (T-cell zones), medulla.
- Antigen-presenting dendritic cells arrive from peripheral tissues carrying antigens; present to T cells.
- Site of clonal expansion of antigen-specific T and B cells.
- Swollen tender lymph nodes are common signs of regional infection.
- Sentinel lymph node biopsy: in breast cancer, melanoma — the first node draining the tumour predicts metastatic spread.

Step 5 — Intestinal lacteals — lipid absorption:

- Lymphatic capillaries within each intestinal villus.
- Absorb chylomicrons (too large for blood capillaries) packed with dietary triglycerides.
- Lacteal lymph (“chyle”) has a milky appearance after a fatty meal.

- Chyle flows up the thoracic duct to enter blood at neck.

Step 6 — Pathology:

- Lymphoedema: lymphatic obstruction or insufficiency → tissue swelling, especially limbs.
  - Primary: congenital (Milroy disease, FOXC2, VEGF-C/VEGFR-3 mutations).
  - Secondary: post-surgery (e.g. after axillary lymph node dissection for breast cancer), radiation, infection.
- Filariasis: tropical lymphoedema from *Wuchereria bancrofti*, adult worms living in lymphatics → elephantiasis.
- Lymphangitis: inflammation/infection of lymphatic vessels, often visible as red streaks toward regional nodes.
- Lymphoma: malignancy of lymph nodes (Hodgkin or non-Hodgkin).
- Metastatic spread: cancers often spread via lymphatics.

Step 7 — Other lymphoid organs: Spleen (filters blood; immune; RBC turnover), tonsils, Peyer's patches (intestinal), thymus (T-cell maturation), bone marrow (lymphocyte production).

Final Answer: Lymphatic system ⇒ B

Answer: (B) Go Back to Q11

Q12.

Solution

Concept — The hepatic portal circulation: A "portal system" is a venous arrangement where blood passes through TWO capillary beds in series. The hepatic portal system is the most prominent in the body.

Step 1 — Anatomy:

- GI tract capillaries (small intestine, large intestine, stomach, pancreas, spleen) drain via:
- Mesenteric and splenic veins → join behind the pancreas → **hepatic portal vein**.
- Portal vein carries blood to the liver; ramifies into sinusoidal capillaries (second capillary bed) intermingled with hepatocytes.
- Sinusoidal blood drained by hepatic veins → inferior vena cava → right atrium → general circulation.

Step 2 — Liver blood supply:

- About 75% from hepatic portal vein (low O_2, nutrient-rich).
- About 25% from hepatic artery (oxygen-rich).
- Both mix in sinusoids.
- Total liver blood flow: ~ 1.5 L/min ($\sim 25\%$ of cardiac output) — a remarkably high perfusion.

Step 3 — Physiological rationale — first-pass metabolism: The liver intercepts everything absorbed from the GI tract BEFORE it reaches general circulation:

- Absorbed sugars (glucose, fructose, galactose) $\rightarrow$ glycogen storage, gluconeogenesis regulation, blood glucose buffering.
- Absorbed amino acids $\rightarrow$ urea cycle (disposal of N), plasma protein synthesis (albumin, clotting factors), gluconeogenesis.
- Vitamins and minerals $\rightarrow$ storage or processing (iron, copper, vitamin A, B_{12}).
- Drugs $\rightarrow$ Phase I (CYP450 oxidation) and Phase II (conjugation with glucuronate, sulfate, glutathione, etc.) metabolism; products often excreted in bile.
- Toxins (ammonia, ingested poisons): detoxified.
- Lipids: chylomicrons enter via thoracic duct (not portal); but after first round, lipid metabolism centres in liver.

Step 4 — First-pass effect (pharmacology):

- Many orally administered drugs are extensively metabolised on first passage through the liver $\rightarrow$ much smaller fraction reaches systemic circulation.
- Examples: lidocaine (almost completely cleared on first pass; useless orally), propranolol (high first-pass), morphine (active metabolites), nitroglycerin.
- Bypassed by sublingual, rectal, parenteral, transdermal, inhaled routes.

Step 5 — Portal hypertension: Pathological elevation of portal vein pressure (> 10 mmHg, normally ~ 5–10 mmHg). Causes:

- Cirrhosis (most common): scar tissue distorts sinusoids, increases resistance.
- Portal vein thrombosis.
- Hepatic schistosomiasis (developing-world).
- Budd-Chiari syndrome (hepatic vein thrombosis, post-hepatic).

Consequences:

- Porto-systemic anastomoses dilate: oesophageal varices (life-threatening bleeding), caput medusae (around umbilicus), haemorrhoids.
- Splenomegaly with hypersplenism (cytopenias).
- Ascites (combined with hypoalbuminaemia).
- Hepatic encephalopathy: ammonia and other gut-derived toxins bypass liver, reach brain $\rightarrow$ confusion, asterixis, coma.

Treatment: β-blockers (propranolol) reduce portal pressure; transjugular intrahepatic portosystemic shunt (TIPS) procedure for severe cases; liver transplant.

Step 6 — Other portal systems in the body:

- Hypothalamic-pituitary portal: hypothalamic releasing factors $\rightarrow$ anterior pituitary.
- Renal portal (in some lower vertebrates; absent in mammals).

Final Answer: Hepatic portal vein $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q12

Q13.

Solution

Concept — Gustation (taste) — the lingual chemoreception system: A specialised chemosensory modality detecting dissolved molecules; partners with olfaction to give flavour perception.

Step 1 — Five basic tastes:

- **Sweet:** sugars (glucose, sucrose, fructose), some amino acids, artificial sweeteners. Sensed by T1R2+T1R3 GPCR heterodimer.
- **Bitter:** alkaloids (caffeine, nicotine, quinine, many toxins). Sensed by ~ 25 T2R GPCRs (broad specificity for diverse toxic compounds; evolutionary protective).
- **Salty:** Na^+. Sensed via amiloride-sensitive ENaC channels on taste receptor cells.
- **Sour:** H^+ (acidic). Sensed via proton channels (OTOP1) on sour-taste receptor cells.
- **Umami** ("savoury"): L-glutamate (and synergistically with 5′-IMP, 5′-GMP). Sensed by T1R1+T1R3 GPCR heterodimer. Discovered 1908 by Ikeda; led to commercial MSG.

Other proposed tastes: fat (CD36, GPR120 receptors for free fatty acids), calcium,

kokumi (mouthfeel).

Step 2 — Taste buds:

- Embedded in fungiform, foliate, and circumvallate papillae on the tongue (also palate, epiglottis).
- Onion-shaped clusters of ~ 50–100 taste receptor cells, surrounded by support cells.
- Apical microvilli of receptor cells project into taste pore $\rightarrow$ exposed to saliva.
- Type II cells: sweet, bitter, umami sensors (GPCR-based).
- Type III cells: sour sensors.
- Salt sensing: distinct cell population.

Step 3 — Signal transduction:

- Sweet/bitter/umami: GPCR $\rightarrow$ gustducin (a G-protein) $\rightarrow$ PLCβ_2 $\rightarrow$ IP_3 $\rightarrow$ Ca^{2+} release $\rightarrow$ TRPM5 channel opens $\rightarrow$ depolarisation $\rightarrow$ ATP released as neurotransmitter via CALHM channels.
- Sour: H^+ enters cell through OTOP1 or blocks K^+ channels $\rightarrow$ depolarisation.
- Salty: Na^+ enters through ENaC $\rightarrow$ depolarisation.
- Released ATP activates afferent gustatory neurons.

Step 4 — Central pathway:

- Afferent nerves: chorda tympani branch of facial nerve (CN VII; anterior $2/3$ of tongue), glossopharyngeal (CN IX; posterior $1/3$), vagus (CN X; epiglottis).
- First synapse: nucleus of the solitary tract (medulla).
- Then: ventral posteromedial nucleus of thalamus.
- Then: gustatory cortex (insula and frontal operculum) for conscious perception.
- Hypothalamus and amygdala connections for hedonic and reward aspects.

Step 5 — Genetic variation in taste:

- PTC (phenylthiocarbamide) taster vs non-taster phenotype: famous case of population polymorphism (TAS2R38 gene).
- Bitter receptor diversity affects perception of cruciferous vegetables, beer, coffee, etc.
- Some pathological deletions affect overall taste sensitivity.

Step 6 — Flavour vs taste:

- Flavour: taste + olfaction (retronasal smell during chewing) + texture + temperature + pungency (capsaicin, mustard) + chemesthesis (TRP channels).
- Most "taste" perception is actually smell: blocking the nose with a cold or pinch reveals foods to be much blander.
- Capsaicin (chili): activates TRPV1 heat/pain receptor, not a taste receptor; produces "hot" burning sensation.
- Menthol: activates TRPM8 cold receptor.

Final Answer: Gustation (taste) $\Rightarrow$ C

Answer: (C) Go Back to Q13

Q14.

Solution

Concept — Calcium homeostasis: Plasma Ca^{2+} is tightly regulated (normal $\sim$ 8.5–10.5 mg/dL) by three hormones acting on three target organs (bone, kidney, gut).

Step 1 — Calcitonin:

- Peptide hormone, 32 amino acids.
- Secreted by **parafollicular C cells** of the thyroid gland (also called "clear cells"; lie between thyroid follicles).
- Stimulus: high plasma Ca^{2+}.
- Mechanism: directly inhibits osteoclast activity (osteoclast has receptors for calcitonin; high cAMP, then loss of ruffled border, then apoptosis) $\rightarrow$ reduces bone resorption $\rightarrow$ less Ca^{2+} released to plasma.
- Also slightly increases renal Ca^{2+} excretion.
- Net: lowers plasma Ca^{2+}.

Step 2 — PTH (parathyroid hormone):

- 84-amino-acid peptide; secreted by chief cells of parathyroid glands (4 small glands behind thyroid).
- Stimulus: LOW plasma Ca^{2+} (sensed by Ca-sensing receptor, CaSR, on parathyroid chief cells).
- Actions:
  - Bone: increases osteoclast activity (indirectly via RANKL on osteoblasts) $\rightarrow$ Ca^{2+} and phosphate released.

  - Kidney: increases Ca^{2+} reabsorption in distal tubule; decreases phosphate reabsorption (phosphaturic); stimulates 1α-hydroxylase $\rightarrow$ active vitamin D.
  - Gut: indirect via vitamin D activation $\rightarrow$ increased Ca^{2+} and phosphate absorption.
- Net: raises plasma Ca^{2+}.

Step 3 — Vitamin D (calcitriol):

- Steroid hormone; from cholesterol via 7-dehydrocholesterol; activated by sequential hydroxylation: 25-OH in liver, 1α-OH in kidney (PTH-stimulated) $\rightarrow 1,25(OH)_2D_3$ (calcitriol).
- Acts on gut epithelium: increases Ca^{2+} and phosphate absorption (by inducing calbindin, TRPV6 channel).
- Also acts on bone, kidney, immune cells.
- Deficiency: rickets (children), osteomalacia (adults). UVB sunlight or dietary supplementation needed.

Step 4 — Importance of calcitonin in humans:

- Less critical than PTH in adults; complete thyroidectomy doesn't cause major Ca disturbance.
- Likely more important in pregnancy and lactation (protects maternal skeleton from excessive resorption).
- More important in some other vertebrates (fish, amphibians).
- Therapeutic uses: salmon calcitonin (more potent than human) for postmenopausal osteoporosis, Paget's disease, hypercalcaemia of malignancy (short-term).

Step 5 — Medullary thyroid carcinoma:

- Cancer of C cells.
- Secretes calcitonin (used as a tumour marker).
- Sporadic (75%) or familial as part of MEN 2A/2B (multiple endocrine neoplasia type 2; RET proto-oncogene mutations).
- RET-targeted therapy (vandetanib, selpercatinib).

Step 6 — Disorders of Ca homeostasis:

- Hypercalcaemia: primary hyperparathyroidism (parathyroid adenoma), malignancy (PTHrP from tumour, bone metastases), vitamin D toxicity, sarcoidosis.

- Hypocalcaemia: hypoparathyroidism (post-thyroid/parathyroid surgery, autoimmune), vitamin D deficiency, hypomagnesaemia, hyperphosphataemia (CKD), pancreatitis.
- Symptoms of hypocalcaemia: neuromuscular irritability (Chvostek's sign, Trousseau's sign), tetany, seizures, paraesthesias, prolonged QT.
- Symptoms of hypercalcaemia: "stones, bones, abdominal groans, psychiatric moans" (kidney stones, bone pain, GI symptoms, confusion).

Final Answer: Parafollicular C cells of thyroid $\Rightarrow$ B

Answer: (B) Go Back to Q14

Q15.

Solution

Concept — Water potential (Ψ_w) — the master variable in plant water relations: The chemical potential of water (free energy per unit volume) in a system, relative to pure water at standard conditions. Determines the direction of water flow.

Step 1 — The equation:

$$\Psi_w = \Psi_s + \Psi_p + \Psi_g + \Psi_m$$

- Ψ_s (solute or osmotic potential): always negative; depends on solute concentration ($\Psi_s = -i\,c\,R\,T$ where i = ionisation factor, c = molarity, R = gas constant, T = temperature). Pure water has $\Psi_s = 0$.
- Ψ_p (pressure potential): can be positive (turgid cell with positive turgor pressure) or negative (xylem under tension).
- Ψ_g (gravitational potential): typically small except in tall trees.
- Ψ_m (matric potential): negative; due to interaction with surfaces (especially in soil, seeds).
- Pure water at $1\,\text{atm}$, $25\,^\circ\text{C}$ has $\Psi_w = 0$. Other systems have negative Ψ_w.

Step 2 — Water flows from high to low Ψ_w: This is the universal rule. Water moves spontaneously from less negative (more positive) to more negative water potential.

- Soil ($\Psi_w \sim -0.3\,\text{MPa}$, moist) $\rightarrow$ root ($\sim -0.6\,\text{MPa}$) $\rightarrow$ stem ($\sim -0.8\,\text{MPa}$) $\rightarrow$ leaf ($\sim -1.0\,\text{MPa}$) $\rightarrow$ atmosphere (-30 to $-100\,\text{MPa}$, depending on humidity).
- This gradient drives the transpiration stream.

Step 3 — Soil water and field capacity:

- Field capacity: water held by soil after gravitational drainage; $\Psi_w \sim -0.03\,\text{MPa}$.
- Permanent wilting point: plants cannot extract water; $\Psi_w \sim -1.5\,\text{MPa}$ for most crop species.
- Available water: between field capacity and PWP.

Step 4 — Cell turgor:

- Turgid cell: $\Psi_w = 0$ (at equilibrium with pure water); Ψ_s very negative; Ψ_p equally positive. Cell is fully expanded against the cell wall.
- Flaccid cell: $\Psi_p = 0$, $\Psi_w = \Psi_s$.
- Plasmolysed cell: cell loses water, plasma membrane retracts from wall, Ψ_p can become negative.

Step 5 — Stomatal regulation:

- Guard cells uptake K^+ (and other solutes) $\rightarrow$ Ψ_s becomes more negative $\rightarrow$ water enters $\rightarrow$ turgor rises $\rightarrow$ stoma opens.
- Solute efflux reverses the process; stomata close.
- ABA in water-stressed plants signals stomatal closure to conserve water.

Step 6 — Cohesion-tension theory of xylem ascent:

- Transpiration from leaves creates negative pressure (tension) in xylem.
- Water columns held intact by COHESION (H-bonds between water molecules) and ADHESION to xylem walls.
- Negative pressure (high tension) pulls water up from roots; transmitted to roots, which then take up more water from soil.
- Tensions of -1 to $-3\,\text{MPa}$ typical; up to $-10\,\text{MPa}$ in tall trees and water-stressed plants.
- Cavitation (air bubble breaks the column) can occur under extreme tension or after freezing; repaired by root pressure overnight or by structural mechanisms.

Step 7 — Aquaporins:

- Membrane water channels; allow rapid water flow.
- Regulated by phosphorylation (open/closed), allowing plants to control membrane water permeability dynamically.

- Especially important in root water uptake (PIPs and TIPs in different membranes).
- Discovery: Agre, Nobel 2003.

Final Answer: Water potential ($\Psi_s + \Psi_p$) $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q15

Q16.

Solution

Concept — The Z scheme of photosynthetic electron transport: Light energy drives electrons from water (high potential, hard to oxidise) through two photosystems in series, generating NADPH and an H^+ gradient.

Step 1 — Linear electron flow (overview):

$$H_2O \rightarrow \text{PSII} \rightarrow \text{PQ} \rightarrow \text{Cyt } b_6f \rightarrow \text{PC} \rightarrow \text{PSI} \rightarrow \text{Fd} \rightarrow \text{FNR} \rightarrow \text{NADPH}$$

Step 2 — PSII (P680):

- Reaction centre absorbs 680 nm light; P680* ejects electron.
- Oxygen evolving complex (Mn_4Ca cluster) splits water: $2H_2O \rightarrow O_2 + 4H^+ + 4e^-$.
- Source of Earth's atmospheric O_2.

Step 3 — Intermediate carriers:

- Plastoquinone (PQ): lipid-soluble; carries $2e^- + 2H^+$ across thylakoid membrane.
- Cytochrome b_6f: pumps H^+ into lumen via Q-cycle (analogous to mitochondrial Complex III).
- Plastocyanin (PC): Cu-containing soluble lumenal protein; delivers electrons to PSI.

Step 4 — PSI (P700) and ferredoxin:

- Reaction centre absorbs 700 nm; second photon "re-boost" raises electron to most negative potential of any biological reductant.
- Internal acceptors (A_0, A_1, F_X, F_A, F_B, iron-sulfur clusters) shuttle the electron.

- Soluble **ferredoxin (Fd)** in stroma is the first stable acceptor outside PSI; a [2Fe-2S] protein.
- Fd transfers electrons to ferredoxin-$NADP^+$ reductase (FNR), which produces NADPH.

Step 5 — Ferredoxin branch points:

- $NADP^+$ reduction (main path, linear flow).
- Cyclic flow back to cyt b_6f (extra ATP, no NADPH).
- Nitrite reductase, sulfite reductase, thioredoxin — many reductive metabolism endpoints depend on reduced Fd.

Step 6 — ATP synthesis: The H^+ gradient (lumen pH ~ 5, stroma ~ 8) drives ATP synthase on the stromal side; products ATP and NADPH then power the Calvin cycle.

Step 7 — Cyclic photophosphorylation: PSI alone; electrons from Fd return to cyt b_6f to plastocyanin and back to PSI; pumps H^+ without making NADPH or O_2. Adjusts ATP:NADPH ratio for Calvin cycle.

Final Answer: Ferredoxin (Fd) $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q16

Q17.

Solution

Concept — Codominance vs incomplete dominance: Two different "non-Mendelian" allele relationships, often confused.

Step 1 — Codominance:

- Both alleles fully expressed in the heterozygote.
- Both phenotypes simultaneously visible (not blended).
- Example: MN blood group — L^ML^N heterozygotes have BOTH M and N antigens on RBCs.
- Example: ABO blood group — I^AI^B individuals have both A and B antigens (blood type AB).
- Example: roan cattle — heterozygote has both red and white hairs interspersed (not pink).

Step 2 — Incomplete dominance:

- Heterozygote shows INTERMEDIATE phenotype.
- Example: *Mirabilis jalapa* — red (RR) $\times$ white (rr) $\rightarrow$ pink (Rr).
- Example: sickle cell trait — heterozygotes (Aa) have intermediate severity (mostly asymptomatic but RBCs can sickle at low O_2).
- Example: familial hypercholesterolaemia.

Step 3 — MN blood group specifics:

- Landsteiner and Levine (1927).
- Glycophorin A (GYPA) gene; two alleles differing by amino acid substitutions.
- Three genotypes/phenotypes: $L^M L^M$ (M), $L^M L^N$ (MN), $L^N L^N$ (N).
- Allele frequency: $\sim 0.55\, L^M / 0.45\, L^N$ in Europeans; varies by population.
- Clinically less important than ABO or Rh (antibodies are weak); useful in paternity and forensic studies.

Step 4 — Multiple alleles: More than two alleles exist in the population, although any individual has only two. ABO has I^A, I^B, i alleles; HLA loci have hundreds of alleles each.

Step 5 — ABO blood group — a mix of relationships:

- I^A and I^B: codominant to each other (AB type).
- I^A and i: I^A completely dominant (A type).
- I^B and i: I^B completely dominant (B type).
- i and i: blood type O.

Final Answer: Codominance (both antigens expressed) $\Rightarrow$ A

Answer: (A) Go Back to Q17

Q18.

Solution

Concept — X-inactivation (lyonisation): Mammalian dosage compensation between XX females and XY males. Proposed by Mary Lyon (1961).

Step 1 — The dosage problem:

- Females have two X chromosomes (~ 800 genes each); males have one.
- Without compensation, females would have double the dose of X-linked proteins.

- Solution in mammals: silence one X in each female somatic cell.

Step 2 — Mechanism — XIST lncRNA:

- XIST gene (X-inactive specific transcript) at the X-inactivation centre (XIC).
- Expressed ONLY from the X to be inactivated.
- XIST RNA (~ 17 kb non-coding) coats the chromosome IN CIS.
- Recruits Polycomb repressive complex (PRC2) $\rightarrow$ H3K27me3 heterochromatin mark.
- Triggers DNA methylation, histone deacetylation, late replication timing.
- TSIX (antisense lncRNA) regulates the choice.

Step 3 — Random and clonal:

- Choice of paternal or maternal X is random in each cell at ~ 100-cell embryo stage.
- All descendant cells inherit the same inactive X (clonal maintenance).
- Females are mosaics of two cell populations.

Step 4 — The Barr body:

- The inactivated X appears as a dense heterochromatic body at the nuclear periphery in interphase.
- Counted in buccal smears in classical cytogenetics: $N_{\text{Barr}} = N_{\text{X}} - 1$.
- 46,XX: 1 Barr body. 46,XY: 0. 47,XXY: 1. 47,XXX: 2. 45,X: 0.

Step 5 — Mosaicism — visible examples:

- Calico/tortoiseshell cats: X-linked orange (O) and black (o) coat alleles. Heterozygous Oo females show patches of orange (cells with active O allele) and black (cells with o active). Calico spots come from a separate white-spotting gene. Male tortoiseshells are rare ($\sim 1/3000$) and usually 47,XXY.
- Female carriers of Duchenne muscular dystrophy: random patches of dystrophin-positive and -negative muscle fibres; usually asymptomatic.
- Female carriers of haemophilia: factor VIII or IX levels intermediate.
- Anhidrotic ectodermal dysplasia: female carriers have patches of hairless/sweat-gland-less skin.

Step 6 — Genes escaping X-inactivation:

- About 15–25% of X-linked genes escape silencing.

- Especially in pseudoautosomal regions (PARs) at chromosome tips.
- Higher dose in females contributes to phenotypic differences and to Turner (45,X) and Klinefelter (47,XXY) syndromes.

Final Answer: X-inactivation (lyonisation) $\Rightarrow$ D

Answer: (D) Go Back to Q18

Q19.

Solution

Concept — The end-replication problem: A fundamental consequence of how DNA polymerases work; explains why somatic cells age replicatively.

Step 1 — Why telomeres shorten:

- DNA polymerases work only $5' \to 3'$ and need a primer.
- Leading strand: synthesised continuously to the end; OK.
- Lagging strand: synthesised in Okazaki fragments, each needing a primer.
- The final RNA primer at the very $3'$ end of the lagging strand cannot be replaced by DNA — nothing upstream for polymerase to extend from.
- Net loss per division: ~ 50–200 bp at each chromosome end.

Step 2 — Telomere structure:

- Tandem TTAGGG repeats (vertebrates), ~ 5–15 kb at each chromosome end.
- Coated by shelterin complex (TRF1, TRF2, POT1, TIN2, TPP1, RAP1).
- Shelterin distinguishes telomere from a DNA break; prevents NHEJ chromosome fusion.
- $3'$ overhang invades the duplex, forming a protective T-loop.

Step 3 — Telomerase — the only known solution:

- Reverse transcriptase with integral RNA template.
- TERT: catalytic protein.
- TERC: RNA template ("CCCAAUC" templates TTAGGG synthesis).
- Extends the $3'$ overhang; lagging strand fills in.
- Active in germline, embryonic and some adult stem cells; SILENCED in most somatic cells.

Step 4 — The Hayflick limit:

- Leonard Hayflick (1961): cultured human fibroblasts divide $\sim$ 40–60 times then stop.
- Cause: critically short telomeres trigger DNA-damage response $\rightarrow$ p53-mediated permanent G_1 arrest (replicative senescence).
- Senescent cells stop dividing but stay metabolically active; secrete SASP factors (pro-inflammatory).

Step 5 — Disease relevance:

- Telomere biology disorders (dyskeratosis congenita, aplastic anaemia, IPF): mutations in telomerase or shelterin $\rightarrow$ critically short telomeres $\rightarrow$ stem cell exhaustion.
- Cancer: $\sim 85\%$ reactivate telomerase (often via TERT promoter mutations); the rest use ALT (alternative lengthening of telomeres).
- Aging: telomere shortening correlates with biological age but the causal direction is complex.

Final Answer: Shorten progressively (end-replication problem) $\Rightarrow$ C

Answer: (C) Go Back to Q19

Q20.

Solution

Concept — The RNA world hypothesis: A leading model for the origin of life. Proposed by Walter Gilbert (1986); echoes earlier ideas by Crick, Orgel, Woese.

Step 1 — The chicken-and-egg problem:

- Modern cells: DNA stores info $\rightarrow$ RNA $\rightarrow$ proteins do chemistry.
- DNA replication needs proteins; protein synthesis needs DNA. Which came first?
- RNA does BOTH — stores info AND catalyses chemistry. Plausible solution: an early "RNA world" where RNA performed both functions.

Step 2 — Evidence for ribozymes (catalytic RNAs):

- Cech (1981): self-splicing Group I intron in *Tetrahymena* pre-rRNA.
- Altman (1980s): RNase P catalytic RNA subunit.
- Cech and Altman: Nobel 1989.
- The ribosome itself is a ribozyme — peptidyl transferase activity is in the 23S rRNA, not protein (proven by atomic-resolution structures; Ramakrishnan, Steitz, Yonath, Nobel 2009).

- Spliceosome catalytic core: RNA (snRNAs).
- Many viroids are ribozymes.

Step 3 — In vitro evolution shows RNA's versatility: Starting from random RNA pools, selection in the lab can produce ribozymes for almost any chemistry: RNA polymerisation, peptide bond formation, aminoacylation, Diels-Alder reactions, etc. Demonstrates RNA's catalytic potential.

Step 4 — Prebiotic chemistry:

- Miller-Urey (1953): simulated atmosphere $\rightarrow$ amino acids.
- Subsequent work: nucleobases, sugars, simple peptides.
- Sutherland (2009): UV-driven prebiotic route to pyrimidine ribonucleotides.
- Hydrothermal vents, mineral surfaces, warm ponds: candidate environments.

Step 5 — Vestiges in modern biology:

- Ribose in coenzymes (NAD, FAD, CoA, SAM) — could be "molecular fossils" from when these were attached to ribozymes.
- ATP/GTP as energy currencies and substrates: maybe relics.
- Riboswitches in bacteria: RNAs that directly sense metabolites.

Step 6 — Transition out of the RNA world:

- Peptides took over most catalysis (more diverse chemistry with 20 amino acids vs 4 nucleotides).
- DNA evolved as more stable storage (T instead of U, 2′-deoxy resists hydrolysis).
- Reverse transcriptase-like enzymes bridged RNA $\rightarrow$ DNA.

Final Answer: RNA world hypothesis $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q20

Q21.

Solution

Concept — Australopithecines — early bipedal hominins: The genus that bridges ape-like ancestors and early *Homo*; bipedal but small-brained.

Step 1 — The hominin lineage:

- Hominini = human-line after split from chimps (~ 6–7 Mya).
- Earliest pre-australopithecines: *Sahelanthropus* (~ 7 Mya), *Orrorin* (~ 6 Mya), *Ardipithecus* (~ 4.4 Mya).
- Australopithecines: ~ 4–2 Mya in eastern and southern Africa.

Step 2 — *Australopithecus afarensis*:

- ~ 3.9–2.9 Mya, East Africa.
- **"Lucy"** (AL 288-1): $\sim 40\%$ complete skeleton, 3.2 Mya, Hadar, Ethiopia.
- Discovered by Donald Johanson (1974).
- Adult height ~ 1.0–1.5 m; weight 30–45 kg.
- Brain ~ 400–$500\,\text{cm}^3$ (chimp-sized).
- Clearly bipedal: pelvis, knee, foot structure.
- Laetoli footprints (Tanzania, 3.6 Mya): two bipedal individuals walked through wet volcanic ash — direct evidence of bipedalism.

Step 3 — Other Australopithecus species:

- *A. anamensis* (~ 4.2–3.9 Mya, Kenya).
- *A. africanus* (~ 3.0–2.0 Mya, South Africa). Taung Child (1924, Raymond Dart): first proof of African human origins.
- *A. sediba* (~ 2 Mya, South Africa): mosaic features; possible bridge to *Homo*.

Step 4 — *Paranthropus* (robust australopithecines):

- *P. aethiopicus*, *P. boisei*, *P. robustus*.
- Massive jaws, large molars, sagittal crest (anchor for jaw muscles).
- Adapted for chewing tough plant material.
- Side branch; extinct ~ 1.2 Mya.

Step 5 — Genus *Homo* (emerging from australopithecines):

- *H. habilis* (~ 2.4–1.4 Mya): first stone tools (Oldowan); brain ~ 600–$750\,\text{cm}^3$.
- *H. erectus* (~ 2.0–0.1 Mya): first hominin out of Africa; brain 850–$1100\,\text{cm}^3$; controlled fire; Acheulean hand-axes.

- *H. heidelbergensis* ($\sim$ 700–200 kya): possible ancestor of Neanderthals and modern humans.
- *H. neanderthalensis* ($\sim$ 400–40 kya): Europe/west Asia; brain $\sim$ 1500 cm^3 (large!); interbred with *H. sapiens* (1–4% Neanderthal DNA in non-Africans).
- *H. denisovan*: discovered 2010 from finger bone in Denisova cave, Siberia; interbred with humans.
- *H. sapiens* (modern humans): emerged in Africa $\sim$ 300 kya.

Step 6 — Brain size in hominin evolution: 400 (*Australopithecus*) $\rightarrow$ 750 (*H. habilis*) $\rightarrow$ 1000 (*H. erectus*) $\rightarrow$ 1500 (Neanderthal) $\rightarrow$ 1350 cm^3 (modern *H. sapiens*). Threefold expansion — among the fastest in mammalian evolution.

Step 7 — Bipedalism — the hallmark adaptation:

- Predates large brain by $\sim$ 2 My.
- Skeletal changes: shorter broader pelvis; knee angle (carrying angle); foot with arch and aligned big toe; spinal S-curve; foramen magnum below skull.
- Selective advantages: freed hands (carrying, tool use); savanna thermoregulation; energy efficiency in long-distance walking.

Final Answer: *Australopithecus* $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q21

Q22.

Solution

Concept — Klinefelter syndrome (47,XXY): The most common sex chromosome aneuploidy in males.

Step 1 — Karyotype and origin:

- 47,XXY (most common); also mosaics (46,XY/47,XXY); rarer higher-grade (48,XXXY; 49,XXXXY, more severe).
- Incidence: $\sim$ 1 in 600–1000 male births.
- Arises from non-disjunction at meiosis (in either parent):
  - $\sim$ 50% from maternal meiosis I.
  - $\sim$ 30% from paternal meiosis I.
  - $\sim$ 20% from maternal meiosis II.
- Risk rises with advanced maternal age.

Step 2 — Phenotype:

- Male (because Y chromosome carries SRY).
- Tall stature (legs disproportionately long).
- Small firm testes (< 5 mL each).
- Azoospermia or severe oligospermia; usually infertile.
- Low testosterone (primary hypogonadism) with elevated FSH and LH.
- Gynecomastia in $\sim 50\%$.
- Reduced facial and body hair, sparse pubic hair (female pattern).
- Broad hips, narrow shoulders.
- Reduced muscle mass and strength.
- Mild reduction in verbal IQ in some.

Step 3 — Diagnosis:

- Often delayed: presents at adolescence (failure of normal puberty) or adulthood (infertility evaluation).
- Karyotype confirms.
- Buccal smear: 1 Barr body (like normal female).
- Many cases undiagnosed lifelong.

Step 4 — Health risks:

- Osteoporosis (low testosterone).
- Breast cancer (much higher risk than in normal males).
- Type 2 diabetes, metabolic syndrome.
- Autoimmune disorders (lupus, RA).
- Mediastinal germ cell tumours.
- Mildly increased mortality.

Step 5 — Treatment:

- Testosterone replacement (from puberty): improves secondary sexual development, bone density, muscle mass, mood, libido.
- Speech therapy if needed for language delays.
- Fertility: testicular sperm extraction (TESE) + ICSI sometimes successful in younger patients (sperm preservation in adolescence).

Step 6 — Other sex chromosome aneuploidies (compare):

- Turner (45,X): phenotypic female; short stature, streak gonads, no puberty without estrogen; webbed neck; cardiovascular anomalies.

- Triple X (47,XXX): phenotypic female, tall, usually fertile, mild learning differences.
- XYY (47,XYY): phenotypic male, tall, usually fertile; cognition mostly normal (older association with criminality is unjustified by current evidence).

Final Answer: Klinefelter syndrome (47,XXY) $\Rightarrow$ C

Answer: (C) Go Back to Q22

Q23.

Solution

Concept — Three terms in sperm production: "Spermatogenesis", "spermiogenesis", and "spermiation" refer to different parts of the same overall process.

Step 1 — Spermatogenesis (the overall process):

- The complete process from diploid spermatogonia to mature spermatozoa.
- Takes place in seminiferous tubules of testis.
- Duration in humans: $\sim$ 64–74 days.
- Continuous in adult males; $\sim$ 100 million sperm/day.

Step 2 — Cellular sequence:

- Spermatogonia (diploid stem cells, Types A and B).
- Primary spermatocytes ($2n$, $4c$) $\rightarrow$ meiosis I.
- Secondary spermatocytes (n, $2c$) $\rightarrow$ meiosis II.
- Spermatids (n, c).
- Spermatozoa (mature, motile-capable).

Step 3 — Spermiogenesis — the morphological transformation:

- Spermatid (round cell) $\rightarrow$ spermatozoon (streamlined for motility).
- No cell division; only remodelling.
- Golgi phase: acrosomal vesicle forms.
- Cap phase: acrosome spreads over nucleus.
- Acrosomal phase: nuclear condensation (histones replaced by protamines $\rightarrow$ tightly packed DNA); flagellum assembly; mitochondria gather at midpiece.
- Maturation: residual cytoplasm shed (phagocytosed by Sertoli cells).
- Final morphology: head (nucleus + acrosome), neck, midpiece (mitochondrial sheath), tail (axoneme).

Step 4 — Spermiation — the release step:

- The FINAL event of spermatogenesis.
- Mature spermatids (now spermatozoa) released from Sertoli cell embrace into the seminiferous tubule LUMEN.
- Involves apical actin remodelling, retraction of Sertoli cell processes, breakdown of specialised cell-cell junctions.
- Released sperm are still not yet motile; they gain motility during epididymal transit.

Step 5 — Sertoli cells — the nurse cells:

- Tall columnar cells extending from basement membrane to lumen.
- Each Sertoli cell embraces multiple germ cells at different stages.
- Form blood-testis barrier (tight junctions; immune privilege).
- Nutritional support, hormone-responsive (FSH).
- Secrete: androgen-binding protein, inhibin, AMH (fetal life), tubular fluid.

Step 6 — Leydig cells — testosterone factories:

- In interstitial spaces between tubules.
- LH (anterior pituitary) stimulates them.
- Produce testosterone from cholesterol.

Step 7 — Hormonal axis: GnRH (hypothalamus, pulsatile) $\rightarrow$ FSH + LH (pituitary) $\rightarrow$ Sertoli + Leydig $\rightarrow$ spermatogenesis + testosterone. Negative feedback by testosterone and inhibin.

Step 8 — Post-testicular events:

- Epididymis: sperm gain motility, store.
- Vas deferens: transport.
- Seminal vesicles, prostate, bulbourethral glands: contribute seminal plasma.
- Capacitation (in female tract): final preparation for fertilisation.

Final Answer: Spermiation $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q23

Q24.

Solution

Concept — Oxytocin — the parturition and lactation hormone: A 9-amino-acid neuropeptide, closely related to vasopressin (the two differ in only 2 amino acids).

Step 1 — Synthesis and release:

- Synthesised in paraventricular nucleus (PVN) and supraoptic nucleus (SON) of hypothalamus.
- Transported down axons to the POSTERIOR pituitary (neurohypophysis).
- Stored in nerve terminals; released into blood on neural signals.

Step 2 — Parturition:

- Uterine oxytocin receptors massively upregulated in late pregnancy (estrogen-driven).
- Cervical/uterine stretch triggers oxytocin release (Ferguson reflex).
- Oxytocin causes powerful uterine smooth muscle contraction.
- Positive feedback loop: stretch $\rightarrow$ oxytocin $\rightarrow$ contraction $\rightarrow$ more stretch $\rightarrow$ . . . , culminating in delivery.
- Synergy with prostaglandins (PGE_2, $PGF_{2\alpha}$).
- Pitocin (synthetic oxytocin): standard drug for labour induction/augmentation; also used post-delivery to control uterine bleeding.

Step 3 — Milk-ejection reflex:

- Suckling stimulates nipple sensory afferents.
- Signal reaches hypothalamus; triggers oxytocin release.
- Oxytocin acts on myoepithelial cells of mammary alveoli $\rightarrow$ contraction $\rightarrow$ milk pushed from alveoli into ducts.
- Distinct from milk PRODUCTION (which depends on prolactin from ANTERIOR pituitary).
- Conditioned “let-down”: mother’s response to baby’s cry or other cues.

Step 4 — Other roles:

- Pair-bonding, social behaviour, parent-infant bonding (“love hormone” in popular media).
- Sexual behaviour, orgasm-associated release.
- Trust and prosocial behaviour (intranasal oxytocin studies; results context-dependent).

- Anxiolytic in some contexts.

Step 5 — Vasopressin (ADH) — the close cousin:

- Also a 9-amino-acid peptide; differs from oxytocin in 2 residues.
- Also made in PVN/SON; also released from posterior pituitary.
- Main effects: water retention (kidney V_2 receptors $\rightarrow$ aquaporin-2); vasoconstriction (V_1).
- Diabetes insipidus: ADH deficiency (central) or resistance (nephrogenic) $\rightarrow$ polyuria/polydipsia.

Step 6 — Posterior vs anterior pituitary:

- Posterior: neural extension of hypothalamus; stores/releases oxytocin and ADH (no synthesis here; just released from axon terminals).
- Anterior: true endocrine gland; produces GH, prolactin, ACTH, TSH, FSH, LH. Controlled by hypothalamic releasing factors via hypothalamic-pituitary portal blood system.

Step 7 — Compare prolactin (milk production):

- Anterior pituitary lactotrophs.
- Stimulates milk synthesis in mammary glands during pregnancy and lactation.
- Suppressed by dopamine from hypothalamus (a unique inhibitory control).
- Dopamine D_2 agonists (bromocriptine, cabergoline) suppress prolactin (treat hyperprolactinaemia, prolactinomas).

Final Answer: Oxytocin $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q24

Q25.

Solution

Concept — The Reproductive and Child Health (RCH) programme: India's flagship initiative for maternal-child health, integrating multiple health domains.

Step 1 — Maternal mortality — the burden:

- Maternal mortality ratio (MMR): deaths per $100{,}000$ live births.
- India MMR: ~ 437 in early 1990s $\rightarrow \sim 97$ in recent reports; substantial de-

cline.
- Major causes globally: haemorrhage, sepsis, hypertensive disorders (pre-eclampsia/eclampsia), unsafe abortion, obstructed labour.

Step 2 — Skilled birth attendance — the centerpiece:

- Delivery by trained personnel (doctors, nurses, ANMs — auxiliary nurse midwives) able to recognise and manage complications.
- Institutional delivery (in a health facility) preferred over home delivery without skilled support.
- Janani Suraksha Yojana (JSY, 2005): cash incentive for institutional delivery.
- Janani Shishu Suraksha Karyakram (JSSK, 2011): free delivery, diagnostics, drugs, blood, transport, food for mother and sick newborns at public facilities.

Step 3 — Antenatal care package:

- Early registration (within 12 weeks).
- At least 4 antenatal check-ups.
- Tetanus toxoid immunisation (TT1 early, TT2 a month later; booster if previously vaccinated).
- Iron-folic acid supplementation (180 tablets through pregnancy; prevent anaemia, neural tube defects).
- Calcium supplements (later).
- Screening: blood pressure (for pre-eclampsia), Hb, urinalysis, blood group, HIV, syphilis, hepatitis B, gestational diabetes.
- Ultrasound for dating and anomaly screening.
- Birth preparedness: identify facility, transport plan.

Step 4 — Intrapartum care:

- Partograph use (graphical labour progress monitoring).
- Active management of third stage of labour (uterotonics like oxytocin to prevent postpartum haemorrhage).
- Clean delivery practices.
- Refer to higher centre for complications.

Step 5 — Postnatal care:

- Postnatal home visits by ASHA worker (1, 3, 7, 14, 21, 28, 42 days post-delivery in Home Based Newborn Care, HBNC).

- Detect maternal complications: postpartum haemorrhage, sepsis, hypertension.
- Newborn care: early initiation of breastfeeding, skin-to-skin contact (Kangaroo Mother Care), warmth, infection prevention.
- Birth weight monitoring.
- Postnatal contraceptive counselling.

Step 6 — Child health components:

- Universal Immunisation Programme (UIP): BCG, OPV, pentavalent (DPT-HepB-Hib), measles-rubella, rotavirus, PCV, JE in endemic areas.
- Vitamin A supplementation.
- Integrated Management of Neonatal and Childhood Illness (IMNCI).
- ORS + zinc for diarrhoea.
- Anaemia Mukt Bharat: combat childhood anaemia.
- POSHAN Abhiyan: nutrition.

Step 7 — Family-level workers:

- ASHA (Accredited Social Health Activist): village-level female community health worker; promotes institutional delivery, immunisation, contraception.
- ANM (Auxiliary Nurse Midwife): provides antenatal, delivery, immunisation services.
- AWW (Anganwadi Worker): nutrition, pre-school education.

Step 8 — Adolescent reproductive sexual health: RKSK (Rashtriya Kishor Swasthya Karyakram) addresses adolescent issues: nutrition, mental health, sexual reproductive health, substance abuse, non-communicable diseases, gender-based violence.

Final Answer: Skilled birth attendance with institutional delivery $\Rightarrow$ $\boxed{\text{C}}$

Answer: (C) Go Back to Q25

Q26.

Solution

Concept — Long-acting reversible contraceptives (LARCs): The most effective reversible contraceptive methods; failure rates similar to or lower than female sterilisation.

Step 1 — Norplant — the first hormonal implant:

- Six small Silastic capsules ($\sim$ 34 mm long, 2.4 mm diameter) placed subdermally in the inner upper arm.
- Each capsule contains levonorgestrel (a progestin).
- Slow release over 5 years.
- Approved in US 1990; widely used in 1990s but withdrawn 2002 (commercial reasons, not safety).
- Removal of 6 capsules could be difficult; required experienced clinician.

Step 2 — Newer implants:

- Jadelle (Norplant-2): only 2 rods; 5-year duration.
- Implanon / Nexplanon: single rod containing etonogestrel; lasts 3 years; much easier insertion/removal.
- These newer single-rod implants are now the standard.

Step 3 — Mechanism of action:

- Continuous low-dose progestin.
- Suppresses LH surge $\rightarrow$ inhibits ovulation (primary mechanism).
- Thickens cervical mucus $\rightarrow$ blocks sperm penetration.
- Thins endometrium $\rightarrow$ impairs implantation.
- Failure rate $< 0.05\%$ per year — among the most effective methods.

Step 4 — Side effects:

- Menstrual disruption: irregular bleeding, amenorrhoea (some welcome this, others find it bothersome — main reason for discontinuation).
- Headache, weight changes, mood, acne (variable).
- No estrogen-related cardiovascular risks (unlike combined oral pill).

Step 5 — Other LARC methods:

- Copper-T IUD (e.g. ParaGard, multiload Cu-375): copper toxic to sperm and ova; 10+ year duration; no hormones; can cause heavier menses; first choice in many settings.

- Levonorgestrel IUS (Mirena, Liletta): progestin slowly released within uterus; 5–7 year duration; markedly reduces menstrual blood loss (used therapeutically for menorrhagia).

Step 6 — Other contraceptive categories:

- Combined oral pills (estrogen + progestin).
- Progestin-only pills (mini-pill).
- Patch, vaginal ring.
- Depot injections (DMPA, 3-monthly).
- Barrier: condoms (male, female), diaphragm.
- Natural methods: calendar/rhythm, basal body temperature, cervical mucus.
- Sterilisation: tubal ligation (female), vasectomy (male) — generally considered permanent.
- Emergency contraception (post-coital): levonorgestrel pill, ulipristal, copper IUD.

Step 7 — India context: National Family Welfare Programme; emphasis on choice and "cafeteria approach". Reversible methods (condoms, oral pills, IUCDs, implants, injectables — recent addition Antara, DMPA) plus permanent methods (vasectomy, tubectomy). Implants becoming more available.

Final Answer: Norplant $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q26

Q27.

Solution

Concept — From ovule to seed — the development of seed coat: After fertilisation, the ovule undergoes a series of transformations to become a seed.

Step 1 — The ovule structure:

- Nucellus: central mass of tissue; contains the megasporocyte/embryo sac.
- Integuments: one or two protective layers around the nucellus (one in basal angiosperms; two in most others).
- Funicle: stalk connecting ovule to placenta within ovary.
- Micropyle: small opening at the ovule apex (where pollen tube enters).
- Chalaza: opposite end of the ovule.

Step 2 — After fertilisation:

- Egg + sperm → zygote → embryo.
- Polar nuclei + second sperm → primary endosperm → endosperm tissue.
- Ovule itself transforms into the SEED.
- Ovary wall transforms into the FRUIT pericarp (in angiosperms).

Step 3 — Integuments → seed coat:

- Integuments harden and become the seed coat.
- Outer integument → **testa** (outer seed coat; usually tougher, often pigmented).
- Inner integument → **tegmen** (inner seed coat; thinner).
- Micropyle remains as a small pore through which water enters during germination.
- Hilum: scar where the funicle was attached.

Step 4 — Mature seed components:

- Embryo: derived from zygote; has radicle (future root), plumule (future shoot), cotyledon(s).
- Endosperm: derived from triple fusion; nutritional tissue. May be persistent (cereals, castor) or consumed during seed development (most legumes, beans, peas — food stored in cotyledons instead).
- Seed coat: derived from integuments.
- Sometimes: perisperm (derived from nucellus, persistent in some seeds like coffee, black pepper).

Step 5 — Functional roles of testa:

- Mechanical protection of embryo.
- Resistance to desiccation (some seeds remain viable for years/centuries).
- Some seeds have hard impermeable seed coats → require scarification (mechanical/chemical) or fire to germinate.
- Some seed coats are designed for dispersal: hooks (cocklebur), wings (maple), arils (yew), edible fleshy seed coat (pomegranate).

Step 6 — Fruit development:

- Ovary wall → pericarp (fruit wall).
- Pericarp has three layers: epicarp (skin), mesocarp (fleshy middle), endocarp (innermost, sometimes hard like in stone fruits).
- True fruits: only from ovary.

- False fruits (accessory fruits): involve other floral parts (apple — mainly receptacle; strawberry — receptacle is the fleshy edible part, the "seeds" are actually achene fruits).
- Simple fruits (mango), aggregate fruits (raspberry), multiple fruits (pineapple, fig).

Step 7 — Seed dispersal:

- Wind: dandelion (pappus), maple (samara), orchid (dust seeds).
- Water: coconut, mangrove.
- Animals: ingested (juicy fruits, seeds pass through gut); attached (burrs, sticky seeds).
- Mechanical: explosive dehiscence (touch-me-not, witch hazel).

Final Answer: Integuments of the ovule $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q27

Q28.

Solution

Concept — Polyembryony and nucellar embryony: The presence of multiple embryos in a single seed; an example of apomixis (asexual seed formation).

Step 1 — Polyembryony in citrus and mango:

- Common in *Citrus* species (oranges, mandarins, lemons) and *Mangifera indica* (mango).
- A single seed often contains 1 zygotic embryo + several adventitious embryos.
- The adventitious embryos arise from somatic cells of the nucellus (the maternal tissue surrounding the embryo sac).
- They are genetically IDENTICAL to the mother plant (clones).
- The zygotic embryo (from sexual fertilisation) may also be present; it is genetically a hybrid of mother and pollen donor.
- Typically, the nucellar embryos out-compete and replace the zygotic embryo.

Step 2 — Nucellar embryony — a type of apomixis:

- Apomixis: asexual production of seeds with embryos genetically identical to the mother.

- Nucellar (or adventive) embryony: nucellar cells, which are diploid sporophytic tissue, begin to divide and develop into embryos within the existing ovule, without meiosis or fertilisation.
- These embryos have $2n$ from the start (no meiosis-fertilisation cycle), thus identical to the mother.
- The embryo sac itself may also develop a sexual embryo, leading to polyembryony.

Step 3 — Other types of apomixis:

- Diplospory: megaspore mother cell skips meiosis; develops directly into embryo sac.
- Apospory: a somatic cell forms the embryo sac (skipping the megasporocyte stage entirely).
- All produce $2n$ embryos clonal to mother.
- Examples beyond citrus/mango: *Hieracium* (hawkweed; classic case studied by Mendel that gave confusing results), dandelion (*Taraxacum*), some grasses, blackberries.

Step 4 — Horticultural significance:

- Citrus rootstocks: produced from nucellar embryos $\rightarrow$ true-to-type clones from seed (rare in seed-propagated plants); reliable rootstock for grafting.
- Maintains favourable cultivar genotypes through generations.
- Hybrid seed production: if a system can be engineered to make hybrid plants set apomictic seed, the F_1 hybrid genotype could be maintained indefinitely (the "holy grail" of hybrid agriculture; could dramatically reduce hybrid seed cost). Active research target.

Step 5 — Compare with twinning (animals):

- Polyembryony in mammals: armadillo always has 4 identical quadruplets (single zygote splits).
- Monozygotic human twins: similar mechanism.

Step 6 — Parthenocarpy — different concept:

- Development of fruit WITHOUT fertilisation $\rightarrow$ seedless fruit.
- Examples: bananas, seedless grapes, navel oranges, pineapple (in commercial cultivars).
- Distinct from apomixis (which produces seeds without sexual fertilisation).

- Triggered naturally or by hormone treatments (auxin, GA).

Final Answer: Nucellar cells (nucellar embryony) $\Rightarrow$ D

Answer: (D) Go Back to Q28

Q29.

Solution

Concept — Brassinosteroids — the plant steroid hormones: A class of hormones discovered late in the history of plant hormone biology but now recognised as central regulators of growth and stress response.

Step 1 — Discovery:

- Mitchell et al. (1970): noticed that pollen extracts from *Brassica napus* (rapeseed) promoted plant growth.
- Grove et al. (1979): isolated brassinolide (the most active brassinosteroid) from 40 kg of bee-collected pollen — a heroic chemical purification.
- Subsequent identification of many natural brassinosteroids.

Step 2 — Chemistry:

- Polyhydroxylated C_{27}, C_{28}, C_{29} steroids.
- Derived from sterols (just like animal steroid hormones).
- Most active: brassinolide; others include castasterone, 24-epibrassinolide.
- Active at very low concentrations (nM range).

Step 3 — Receptor and signalling:

- Receptor: BRI1 (Brassinosteroid Insensitive 1) — a leucine-rich-repeat receptor kinase at the PLASMA MEMBRANE. (Animal steroid receptors are intracellular — a major difference.)
- Co-receptor: BAK1.
- BR binding $\rightarrow$ receptor activation $\rightarrow$ phosphorylation cascade.
- Downstream: BIN2 (GSK3-like kinase) inactivated; transcription factors BZR1/BES1 activated.
- Massive transcriptional response: cell wall biosynthesis, growth-related genes, defence responses.

Step 4 — Physiological roles:

- Cell elongation and division — key growth promoters.

- Vascular differentiation (xylem development).
- Pollen tube growth.
- Stomatal development.
- Senescence (some contexts).
- Stress responses: tolerance to heat, cold, salt, drought, pathogens.
- Cross-talk with auxin, GA, ethylene, jasmonate signalling.

Step 5 — BR-deficient mutants are dwarfs:

- Mutations in BR biosynthesis or signalling (*det*2, *cpd*, *dwarf*4, *bri*1) give dwarf phenotypes.
- Often dark-green, compact, with short hypocotyl in dark (lack the etiolation response).
- Applying exogenous BR rescues biosynthesis mutants; not signalling mutants (*bri*1).

Step 6 — Agricultural use:

- Commercial BR analogues (e.g. 24-epibrassinolide) used as plant growth regulators in agriculture.
- Applied as seed treatment, foliar spray.
- Reported benefits: yield increase, stress tolerance, fruit quality.
- More widely used in China and South Asia than in some other regions.

Step 7 — The major plant hormone classes (compare):

- Auxins (IAA): cell elongation, apical dominance, tropisms.
- Cytokinins: cell division, delay senescence.
- Gibberellins (GAs): stem elongation, germination.
- Abscisic acid (ABA): stress responses, dormancy, stomatal closure.
- Ethylene (gas): fruit ripening, senescence, abscission.
- Brassinosteroids: growth, stress tolerance.
- Jasmonates: wounding/herbivore defence.
- Salicylates: pathogen defence (systemic acquired resistance).
- Strigolactones: branching inhibition; mycorrhizal communication.

Final Answer: Brassinosteroids $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q29

Q30.

Solution

Concept — Thigmotropism — directional growth in response to touch: A specialised tropism that allows climbing plants to exploit support structures without dedicating biomass to thick stems.

Step 1 — Examples:

- Tendrils: peas, cucumber, grapevine, passion flower, sweet pea. Specialised filamentous organs (modified leaves or stems) that coil around any support they touch.
- Twining stems: morning glory, beans (*Phaseolus*), hops, honeysuckle. The whole stem helically coils around a support.
- Clinging roots: ivy (*Hedera*), Virginia creeper — short adventitious roots adhere to surfaces.

Step 2 — Mechanism (in tendrils):

- Touch on one side of a tendril activates mechanosensitive ion channels.
- Differential growth: slower on the touched (contact) side, faster on the opposite side.
- Result: tendril bends toward and around the support.
- Once coiled, the tendril contracts and stiffens, pulling the plant body close to the support.

Step 3 — Hormonal involvement:

- Auxin redistribution similar to phototropism: auxin accumulates on the non-touched side, accelerating growth there.
- Ethylene is also involved.
- Jasmonate signalling activated in some cases.

Step 4 — Speed: Some tendrils respond within minutes; visible coiling can occur in ~ 20 minutes after contact. Darwin's son Francis did the first detailed studies.

Step 5 — Thigmonasty — distinguished from thigmotropism:

- NASTIC movements: response not dependent on direction of stimulus.
- Examples:
  - *Mimosa pudica* (touch-me-not): leaflets fold and the whole leaf droops on touch. Driven by turgor changes in pulvinar cells (potassium and water flux); seismonasty.

- *Dionaea muscipula* (Venus flytrap): rapid closure when prey touches trigger hairs (twice within 20 seconds, to filter out random contacts).
- Sundews (*Drosera*): tentacles fold around prey.

Step 6 — Other tropisms (recap):

- Phototropism: response to light direction; shoots positive (toward), roots usually negative.
- Gravitropism (geotropism): response to gravity; shoots negative, roots positive.
- Hydrotropism: response to water gradient; roots positive.
- Chemotropism: response to chemicals; pollen tubes toward synergid signals.
- Thermotropism: response to temperature gradient.
- Skototropism: response toward darkness (some tropical vines climbing to find host tree trunks).

Step 7 — Adaptive value of thigmotropism:

- Vines achieve great height while investing minimal biomass in supporting structures.
- Reach light in canopy without standing on their own.
- Can rapidly recolonise gaps and disturbed areas.
- Some are invasive (*Mikania micrantha* "mile-a-minute weed").

Step 8 — Mechanosensitivity in plants more broadly:

- Plants sense mechanical signals: touch, wind, rain, herbivory.
- Thigmomorphogenesis: plants exposed to repeated mechanical stress (wind) grow shorter, sturdier — adaptive response.
- Mechanosensitive channels (MCAs, MSLs in plants) underlie sensing.

Final Answer: Thigmotropism $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q30

Q31.

Solution

Concept — Prions — the protein-only infectious agents: The most heretical idea in modern biology when proposed: an infectious agent without any nucleic acid. Now fully accepted; Stanley Prusiner awarded the 1997 Medicine Nobel.

Step 1 — The two conformations of PrP:

- PrP^{C} (cellular prion protein): the NORMAL form; widely expressed in mammals, abundant in brain; GPI-anchored to plasma membrane; mostly α-helical secondary structure; protease-sensitive.
- PrP^{Sc} (scrapie prion protein): the MISFOLDED, pathogenic form; same primary sequence but mostly β-sheet; aggregation-prone; partly protease-resistant; insoluble.
- PrP^{Sc} can induce PrP^{C} to misfold into more PrP^{Sc} — the propagation mechanism.

Step 2 — Diseases caused (transmissible spongiform encephalopathies, TSEs):

- Human:
  - Creutzfeldt-Jakob disease (CJD): sporadic (85%), familial (15%, PRNP mutations), iatrogenic (contaminated growth hormone, dura mater grafts, corneal transplants), variant CJD (from BSE-infected beef).
  - Kuru: famously studied in Papua New Guinea Fore people; transmitted by ritualistic cannibalism. Carleton Gajdusek (Nobel 1976). Disease has now disappeared.
  - Gerstmann-Sträussler-Scheinker syndrome (GSS): familial.
  - Fatal familial insomnia: familial; progressive insomnia, dementia.
- Animal:
  - Scrapie in sheep (known for centuries).
  - Bovine spongiform encephalopathy (BSE, "mad cow disease"): UK epidemic in 1980s-90s from contaminated meat-and-bone-meal cattle feed; led to public-health crisis when transmission to humans (vCJD) confirmed.
  - Chronic wasting disease in deer and elk (North America, spreading).
  - Transmissible mink encephalopathy.
  - Feline spongiform encephalopathy.

Step 3 — Clinical features (CJD):

- Long incubation (years to decades) followed by rapid clinical course.
- Progressive dementia.
- Myoclonus (sudden involuntary jerks).
- Ataxia, visual disturbances, motor abnormalities.
- Characteristic EEG (periodic sharp wave complexes in sporadic CJD).
- MRI: "cortical ribboning", basal ganglia signal abnormalities.
- CSF: elevated 14-3-3 protein, total tau.
- RT-QuIC assay (Real-time Quaking-Induced Conversion): sensitive and specific for PrP^{Sc}.
- Always fatal; usually within months of clinical onset.
- Definitive diagnosis: brain biopsy or autopsy showing spongiform vacuolation and PrP^{Sc} amyloid plaques.

Step 4 — Resistance to standard sterilisation:

- PrP^{Sc} is remarkably resistant to: heat (survives normal autoclaving at $121\,^{\circ}\mathrm{C}$), formaldehyde, alcohol, common disinfectants, UV light, proteases.
- Effective decontamination requires: prolonged autoclaving at $134\,^{\circ}\mathrm{C} + 1\,\mathrm{M}$ NaOH or $\geq 20{,}000$ ppm sodium hypochlorite.
- This is why iatrogenic transmission (surgical instruments, dura mater) was problematic before recognised.

Step 5 — The protein-only hypothesis:

- Originally proposed by Tikvah Alper (1967) noting scrapie agent resistant to radiation that would destroy nucleic acid.
- Prusiner formulated and named the prion concept (1982).
- Long resisted; called heretical for not requiring nucleic acid.
- Confirmed by transgenic mouse experiments showing strain inheritance through protein.
- Recombinant PrP can be folded to infectious form in vitro — definitive proof.

Step 6 — Strain diversity:

- Different prion "strains" have different conformations, incubation periods, brain pathology distributions.
- Strain identity encoded in protein structure (not nucleic acid).
- A heritable conformation: the most profound biological consequence of prion biology.

Step 7 — Beyond classical prions:

- Similar "prion-like" propagation now recognised in many neurodegenerative diseases:
  - Alzheimer's disease: amyloid-β and tau aggregates spread from neuron to neuron.
  - Parkinson's disease: α-synuclein aggregates (Lewy bodies) spread.
  - Huntington's: huntingtin aggregates.
  - ALS: TDP-43, FUS, SOD1 aggregates.
- These are NOT infectious between individuals, but they spread within an organism in a prion-like fashion.

Step 8 — Functional prion-like proteins:

- Yeast prions: [PSI+], [URE3] — non-infectious, but heritable through cytoplasm; may have adaptive roles.
- CPEB (cytoplasmic polyadenylation element binding protein) in *Aplysia* neurons: prion-like behaviour involved in long-term memory storage.
- TIA-1 and other RNA-binding proteins with prion-like domains drive phase separation in stress granules.

Final Answer: Misfolded prion protein (PrP^{Sc}) $\Rightarrow$ $\boxed{D}$

Answer: (D) Go Back to Q31

Q32.

Solution

Concept — Phylum Chordata — the four diagnostic features: The phylum containing humans and all vertebrates plus their closest relatives. Defined by four embryonic features present at some stage of life.

Step 1 — The four chordate hallmarks:

- **Notochord:** a flexible rod-like structure dorsal to the gut, providing skeletal support and developmental signalling. Present in all chordate embryos.
- **Dorsal hollow nerve cord:** forms by neurulation from ectoderm; ventral solid nerve cord is the protostome pattern.
- **Pharyngeal slits** (gill slits): paired openings from the pharynx to the exterior; serve filter-feeding (basal chordates) or gas exchange (fish).
- **Post-anal tail:** extension of the body past the anus, containing notochord and muscle.

Step 2 — Three subphyla:

- **Cephalochordata** (lancelets, e.g. *Amphioxus / Branchiostoma*):
  - Small (~ 5 cm) marine filter feeders.
  - All four chordate features retained throughout life.
  - Notochord extends the entire body, even into the head.
  - Considered close to the ancestral chordate body plan.
- **Urochordata** (Tunicata; sea squirts, salps):
  - Adults: sessile filter feeders enclosed in a cellulose-containing tunic; lose most chordate features.
  - LARVAE ("tadpole larva"): show all four chordate features.
  - Adult retains pharyngeal slits for filter feeding.
- **Vertebrata**: have a vertebral column derived in part from notochord; the dominant chordate group.
  - Major classes: Agnatha (jawless: hagfish, lampreys), Chondrichthyes (cartilaginous fish: sharks, rays), Osteichthyes (bony fish), Amphibia, Reptilia, Aves, Mammalia.

Step 3 — The notochord:

- A rod of vacuolated cells with a fibrous sheath.
- Dorsal to the gut, ventral to the neural tube.
- Provides:
  - Mechanical support (flexible but rigid; allows myomeric body wall muscle to bend body without compression).
  - Developmental signalling: secretes Sonic hedgehog (Shh), patterns the neural tube (ventral identity), somites, and other tissues.
- In vertebrates: replaced during development by the vertebral column; remnants persist as:
  - Nucleus pulposus of the intervertebral discs (centrally placed gel).
  - Some embryonic and adult tissues.
- Chordoma: a rare malignancy arising from notochord remnants.

Step 4 — Fate of chordate features in mammals:

- Notochord $\rightarrow$ replaced by vertebrae; remnant in intervertebral disc.
- Dorsal hollow nerve cord $\rightarrow$ brain and spinal cord.
- Pharyngeal slits $\rightarrow$ become structures of head/neck: Eustachian tube, middle ear cavity, palatine tonsils, parathyroid glands, thymus, thyroid.
- Post-anal tail $\rightarrow$ tail in many mammals; coccyx in humans.

Step 5 — Position in animal phylogeny:

- Chordates are deuterostomes (along with echinoderms, hemichordates).
- Defining deuterostome features: radial cleavage (often), enterocoely (mesoderm pouches off from gut), blastopore becomes anus (not mouth), regulative development.
- Protostomes (most other invertebrates): spiral cleavage, schizocoely, blastopore $\rightarrow$ mouth, mosaic development.
- Recent molecular phylogeny groups together: Chordata + Hemichordata + Echinodermata = Deuterostomia.

Step 6 — Other relevant phyla (compare):

- Hemichordata (acorn worms, pterobranchs): have pharyngeal slits and a stomochord (notochord-like but probably not homologous); shared deuterostome ancestor with chordates.
- Echinodermata (starfish, sea urchins): radially symmetric adults, bilaterally symmetric larvae; secondarily lost notochord.

Final Answer: Notochord $\Rightarrow$ $\boxed{\text{C}}$

Answer: (C) Go Back to Q32

Q33.

Solution

Concept — Phylum Echinodermata: $\sim 7{,}000$ extant species; exclusively marine; remarkable for their water vascular system and pentaradial symmetry.

Step 1 — Diagnostic features:

- **Pentaradial (five-fold radial) symmetry in adults** (a derived condition; larvae are bilateral, revealing the deuterostome bilaterian ancestry).
- **Water vascular system**: unique hydraulic network of canals filled with sea water (and a few coelomocytes). Provides locomotion, food capture, gas exchange, sensory function.
- **Calcareous endoskeleton:** plates of $CaCO_3$ (ossicles) embedded in mesoderm; in some classes (sea stars), the ossicles form a flexible armour; in sea urchins, fused into a rigid test.
- **Spines and pedicellariae:** extending from ossicles; defensive structures.
- **Tube feet (podia):** the visible end-points of the water vascular system; used for locomotion, attachment, feeding.

- Deuterostome development (like chordates).
- No segmentation, no head, no brain (instead, a circumoesophageal nerve ring with radial nerves).
- Remarkable regenerative capacity (sea star can regrow an arm or even a whole body from a piece with central disc).

Step 2 — The water vascular system:

- **Madreporite:** sieve-like plate on the upper (aboral) surface; sea water enters here.
- **Stone canal:** from madreporite down to ring canal.
- **Ring canal:** around the mouth.
- **Radial canals:** extend from ring canal along each arm (or equivalent axis).
- **Lateral canals:** branch off to each tube foot.
- **Tube foot** (podium) + **ampulla** (muscular bulb): water displacement between ampulla and podium extends or retracts the podium; sucker at the tip for adhesion.
- Movement: coordinated extension and contraction of hundreds of tube feet, with attachment via suckers or chemical adhesion (in some species without suckers).

Step 3 — Five major classes:

- **Asteroidea** (sea stars / starfish): 5 arms (or more); central mouth on oral side; predators (some can evert stomach to digest prey externally).
- **Ophiuroidea** (brittle stars, basket stars): distinct central disc with thin flexible arms; arms can shed (autotomise) when grasped.
- **Echinoidea** (sea urchins, sand dollars, sea biscuits): globular or flattened; spines; complex jaw apparatus called Aristotle's lantern; herbivorous grazers (urchin grazing maintains kelp forests vs "urchin barrens").
- **Holothuroidea** (sea cucumbers): elongated body; tentacles around mouth; less obvious pentaradial; some defend by extruding sticky Cuvierian tubules; commercial fishery (bêche-de-mer).
- **Crinoidea** (sea lilies, feather stars): mouth and anus on upper surface; ancient (some still resemble Paleozoic fossils); "living fossils".

Step 4 — Reproduction:

- Usually separate sexes (rarely hermaphrodite).
- External fertilisation: broadcast spawning.

- Bilaterally symmetric ciliated larvae (different forms for each class: bipinnaria/brachiolaria in sea stars, pluteus in sea urchins/brittle stars, auricularia in sea cucumbers).
- Metamorphosis: dramatic; larva's bilateral body plan reorganised into radial adult.

Step 5 — Ecological importance:

- Keystone species: many sea stars regulate community structure (Paine's classic experiment with *Pisaster*).
- Bioerosion: sea urchin grazing on coral reefs.
- Sea cucumbers as deep-sea detritivores.
- Population explosions of crown-of-thorns starfish (*Acanthaster*) damaging coral reefs.

Step 6 — Phylogenetic position:

- Deuterostome.
- Closest sister group: Hemichordata.
- Together (Echinodermata + Hemichordata) = Ambulacraria, sister to Chordata.
- Adult radial symmetry is a derived condition; ancestor was bilaterally symmetric (as larvae still are).

Step 7 — Model organisms:

- Sea urchins (*Strongylocentrotus purpuratus*): foundational in developmental biology; first model for cell-cycle (cyclin discovery in sea urchin), fertilisation studies, gene regulatory networks; first invertebrate genome sequenced (2006).
- Sea stars: regeneration studies.

Final Answer: Echinodermata $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q33

Q34.

Solution

Concept — Lymphatic filariasis: A debilitating tropical disease; the world's leading cause of long-term disability after mental illness; subject of a major global elimination effort.

Step 1 — Causative agents:

- *Wuchereria bancrofti*: $\sim 90\%$ of cases; pan-tropical (Asia, Africa, Pacific, Americas).
- *Brugia malayi*: South and Southeast Asia.
- *Brugia timori*: limited to Timor and Indonesia.
- All are filarial nematodes (thread-like roundworms).

Step 2 — Life cycle:

(a) Adult worms (4–10 cm long, threadlike) live in human lymphatic vessels. Live 5–15 years.
(b) Female adults produce microfilariae (larval stage) that circulate in blood with strong nocturnal periodicity (peak between 10 PM and 2 AM in most strains) — matches biting time of *Culex* mosquito vectors.
(c) Mosquito (*Culex quinquefasciatus* for bancroftian; *Mansonia, Anopheles* for brugian) takes up microfilariae during blood meal.
(d) In mosquito, microfilariae develop through L1, L2, L3 stages over 1–2 weeks.
(e) L3 larvae migrate to mosquito mouthparts.
(f) On next bite, L3 larvae enter human skin; migrate to lymphatic vessels.
(g) Mature to adult; mate; produce new microfilariae — cycle continues.

Step 3 — Clinical course:

- **Asymptomatic** stage: microfilaraemia without symptoms (many infected people remain in this stage).
- **Acute attacks** (adenolymphangitis): episodes of fever, lymph node swelling, lymphangitis (red streaks); from immune reaction to dying worms or secondary bacterial infections.
- **Chronic** stage:
  - Lymphoedema of extremities, often legs (also arms, scrotum, breasts).
  - Hydrocele (fluid in scrotum): common in bancroftian filariasis.
  - Elephantiasis: severe disfiguring oedema with skin thickening and fibrosis, especially of legs.
  - Tropical pulmonary eosinophilia: occult filariasis with cough, wheezing, eosinophilia.

- Disability is the main clinical concern, not mortality.

Step 4 — Diagnosis:

- Nocturnal blood film: see microfilariae on Giemsa-stained thick smear (collected between 10 PM and 2 AM).
- Antigen testing (immunochromatographic card test for *W. bancrofti* antigen): more sensitive; can be done in daytime.
- Ultrasound: "filaria dance sign" — visualises moving adult worms in scrotal lymphatics.
- PCR.

Step 5 — Treatment:

- Diethylcarbamazine (DEC): the classical drug; kills microfilariae and some adults.
- Albendazole: enhances DEC efficacy in combination.
- Ivermectin: very effective against microfilariae; not against adults.
- Doxycycline: kills *Wolbachia* (intracellular bacterial endosymbiont essential for filarial reproduction) over weeks $\rightarrow$ sterilises adult worms; promising adjunct.
- Surgery for hydrocele.
- Hygiene and skin care for established elephantiasis (prevent secondary bacterial infections that worsen lymphoedema).

Step 6 — Global Programme to Eliminate Lymphatic Filariasis (GPELF):

- Launched by WHO (2000): aims to eliminate as public health problem by 2030.
- Strategy: annual mass drug administration (MDA) with DEC + albendazole (or ivermectin + albendazole in onchocerciasis-co-endemic areas, where DEC can cause adverse reactions) to entire at-risk populations.
- Aim: interrupt transmission by reducing microfilarial load below threshold required to sustain mosquito transmission.
- Several countries (Bangladesh, Cambodia, Egypt, etc.) have been certified as having eliminated LF.
- In India: MDA with DEC + albendazole conducted in endemic states; substantial progress; certification for several states.

Step 7 — Compare with onchocerciasis (river blindness):

- Caused by *Onchocerca volvulus*; another filarial nematode.
- Transmitted by blackflies (*Simulium*).
- Adult worms in subcutaneous nodules.
- Microfilariae migrate through skin and to eyes $\rightarrow$ skin disease (onchocercal dermatitis) and blindness.
- Concentrated near rivers (where blackflies breed).
- Treated with ivermectin (donated by Merck through Mectizan Donation Programme; a major public-health success since 1987).
- William Campbell and Satoshi Omura (ivermectin discovery): Nobel 2015.

Final Answer: *Wuchereria bancrofti* $\Rightarrow$ D

Answer: (D) Go Back to Q34

Q35.

Solution

Concept — Systemic lupus erythematosus (SLE): The classic multi-system autoimmune disease; a prototype for understanding broken immune tolerance.

Step 1 — Definition: A chronic autoimmune disease in which the immune system produces autoantibodies against many self-antigens (especially nuclear components), leading to immune complex deposition, complement activation, and inflammation in multiple organs.

Step 2 — Epidemiology:

- Strongly female-predominant: female:male ratio $\sim 9{:}1$.
- Peak age of onset: 15–45 years (reproductive age).
- More common and more severe in African, Asian, and Hispanic populations than European.
- Genetic susceptibility: HLA-DR2, DR3; many other risk loci.
- Environmental triggers: UV light, infections, drugs, hormonal changes.

Step 3 — Autoantibodies:

- Anti-nuclear antibody (ANA): present in $> 95\%$; sensitive screening test but not specific.
- Anti-double-stranded DNA (anti-dsDNA): highly specific for SLE; correlates with disease activity and lupus nephritis.
- Anti-Smith (anti-Sm): highly specific.
- Anti-Ro/SSA, anti-La/SSB: also seen in Sjögren syndrome; cross placenta and cause congenital heart block in fetus.

- Anti-histone: drug-induced lupus.
- Anti-phospholipid (lupus anticoagulant, anti-cardiolipin, anti-β_2-glycoprotein I): cause thrombosis (arterial/venous), miscarriage, thrombocytopenia.
- Complement consumption: low C3, C4 (used up in immune complex formation).

Step 4 — Clinical manifestations (multi-system):

- **Skin:**
  - Malar ("butterfly") rash across cheeks and bridge of nose.
  - Discoid rash (chronic scarring lesions).
  - Photosensitivity.
  - Oral ulcers.
  - Alopecia.
- **Joints:** non-erosive arthritis; symmetric, small and large joints.
- **Kidneys: lupus nephritis.** Classified by WHO/ISN into 6 classes; mesangial, focal, diffuse, membranous, advanced sclerosing; major determinant of prognosis.
- **Haematology:** cytopenias (anaemia of chronic disease, autoimmune haemolytic anaemia, leukopenia, lymphopenia, thrombocytopenia).
- **Serositis:** pleuritis, pericarditis.
- **Neuropsychiatric (NPSLE):** headache, seizures, psychosis, cognitive dysfunction, stroke, peripheral neuropathy.
- **Cardiovascular:** accelerated atherosclerosis (a major cause of late mortality), Libman-Sacks endocarditis.
- **Lungs:** pleurisy, pneumonitis, pulmonary hypertension.
- **GI:** mesenteric vasculitis, hepatitis.

Step 5 — Diagnosis:

- Combination of clinical and serological criteria (EULAR/ACR 2019): a set of clinical and immunological criteria with weighted scoring.
- Renal biopsy if nephritis suspected.

Step 6 — Treatment:

- Universal: sun protection (UV is a trigger).
- Antimalarials: hydroxychloroquine — backbone therapy; reduces flares, fatigue, joint and skin symptoms; protective against thrombosis and organ damage.

- Glucocorticoids (prednisolone): for moderate-severe flares; minimise long-term use.
- Conventional immunosuppressants: methotrexate, azathioprine, mycophenolate mofetil, cyclophosphamide (severe nephritis).
- Biologics: belimumab (anti-BAFF/B-cell stimulator), anifrolumab (anti-IFN type I receptor).
- Rituximab (anti-CD20): off-label, used in refractory disease.
- Anticoagulation for antiphospholipid syndrome (warfarin for thrombosis).

Step 7 — Prognosis:

- Highly variable; relapsing-remitting course typical.
- 10-year survival now $> 90\%$ in developed countries (was 50% in 1950s).
- Late mortality often from cardiovascular disease (premature atherosclerosis) or infection (immunosuppression).
- Lupus nephritis is the main organ-specific prognostic factor.

Step 8 — Drug-induced lupus:

- Distinct from idiopathic SLE.
- Triggered by medications: procainamide, hydralazine, isoniazid, minocycline, anti-TNF agents.
- Anti-histone antibodies; ANA positive; usually resolves on drug withdrawal.

Final Answer: Autoantibodies + multi-system involvement $\Rightarrow$ $\boxed{\text{C}}$

Answer: (C) Go Back to Q35

Q36.

Solution

Concept — Cocaine — a powerful CNS stimulant with major public health impact: A natural alkaloid from coca leaves (*Erythroxylum coca*), used by Andean indigenous peoples for millennia, but the purified or processed forms are highly addictive.

Step 1 — Source and forms:

- Coca leaf: chewed traditionally in South America for stimulant and altitude-sickness relief; low cocaine bioavailability.
- Cocaine hydrochloride (powder): snorted, dissolved for injection.
- Cocaine base (crack, free-base): smokable; rapid onset and severe addiction.

Step 2 — Mechanism in the brain:

- Cocaine blocks reuptake of monoamine neurotransmitters by inhibiting the dopamine transporter (DAT), noradrenaline transporter (NET), and serotonin transporter (SERT).
- Strongest effect at DAT → massive accumulation of dopamine in the synaptic cleft of mesolimbic pathway (ventral tegmental area → nucleus accumbens).
- This DA surge in reward circuitry produces intense euphoria.
- Excessive activation of the brain's reward system drives reinforcement and addiction.
- Other CNS effects: arousal, alertness, decreased appetite, increased confidence/aggressivity, paranoia at high doses.

Step 3 — Peripheral sympathomimetic effects (via increased NA):

- Tachycardia, hypertension.
- Vasoconstriction (skin pallor, cool extremities, increased risk of MI even in young users from coronary spasm).
- Mydriasis (pupil dilation).
- Hyperthermia (increased metabolic rate, vasoconstriction prevents heat loss).

Step 4 — Acute toxicity:

- Cardiovascular: myocardial infarction (coronary vasospasm even without atherosclerosis), arrhythmias, sudden death.
- Stroke (hypertensive cerebral haemorrhage; vasospastic infarcts).
- Seizures.
- Hyperthermia, rhabdomyolysis, kidney failure.
- Aortic dissection in some.
- Particularly dangerous when combined with alcohol: liver converts both to cocaethylene, a longer-acting cardiotoxic metabolite.

Step 5 — Chronic effects:

- Strong psychological dependence (less prominent physical dependence than opioids).
- Cognitive impairment, mood disturbance, depression.
- Paranoid psychosis.
- Nasal septum perforation (snorting; vasoconstriction → tissue necrosis).
- Crack lung (smoking).

- Endocarditis, HIV/hepatitis transmission (injection).
- Wider problems: violence, family/social breakdown, criminal justice involvement.

Step 6 — Cocaine in pregnancy:

- Vasoconstriction reduces placental blood flow $\rightarrow$ growth restriction, preterm birth, placental abruption.
- Neonatal effects: irritability, feeding problems, possible long-term neurodevelopmental deficits (though effects often smaller than initially feared in "crack baby" era).

Step 7 — Treatment:

- Acute intoxication: supportive (cooling for hyperthermia, benzodiazepines for agitation/seizures, nitroglycerin/CCB for cardiac symptoms; AVOID β-blockers alone as they leave α-agonism unopposed).
- Addiction: no specific pharmacotherapy approved (unlike opioids, alcohol); behavioural therapies, contingency management, residential rehab.
- Cocaine vaccine: under research.

Step 8 — Historical context:

- Late 19th century: cocaine widely used (in Coca-Cola until 1903; as topical anaesthetic; Sigmund Freud advocated medical use).
- Was the original local anaesthetic (Koller's eye surgery 1884); led to development of newer safer agents (procaine, lidocaine).
- Cocaine HCl still has limited legitimate use as topical anaesthetic for ENT procedures (vasoconstrictor + anaesthetic).

Step 9 — Other major drugs of abuse (compare):

- Cannabis (THC): CB_1 receptor agonist; lower addiction potential but increasing potency raises concerns.
- Heroin (an opioid): μ-opioid receptor; profound respiratory depression risk.
- Methamphetamine: also dopaminergic; releases DA from terminals (mechanism different from reuptake block); longer half-life than cocaine.
- LSD: 5-HT_{2A} agonist; hallucinogen.
- MDMA (Ecstasy): serotonergic; releases serotonin.
- Alcohol: GABA-A potentiation, NMDA inhibition.
- Nicotine: nicotinic ACh receptors; very high addiction potential.

Final Answer: Cocaine $\Rightarrow$ B

Answer: (B) Go Back to Q36

Q37.

Solution

Concept — The greenhouse effect and global warming: A natural and necessary phenomenon that has become destabilising due to human emissions.

Step 1 — The natural greenhouse effect:

- Sunlight (mostly shortwave: visible + UV) passes through atmosphere; reaches Earth's surface; is absorbed and warms surface.
- Surface re-emits energy as longwave (infrared) radiation.
- Atmospheric greenhouse gases (water vapour, CO_2, methane, N_2O, ozone) absorb IR and re-emit in all directions, including back to surface.
- Net: surface heated more than it would be by sunlight alone.
- Without greenhouse effect: Earth's mean surface temperature would be $\sim -18\,^\circ\mathrm{C}$ instead of $\sim 15\,^\circ\mathrm{C}$ — frozen, mostly uninhabitable.

Step 2 — The enhanced greenhouse effect (anthropogenic):

- Human activities since the Industrial Revolution have substantially increased atmospheric greenhouse gas concentrations.
- Atmospheric CO_2: ~ 280 ppm (pre-industrial) $\rightarrow > 420$ ppm now (highest in ~ 3 million years).
- Methane: ~ 700 ppb $\rightarrow \sim 1900$ ppb (more than doubled).
- N_2O: increased by $\sim 20\%$.
- Industrial fluorinated gases (CFCs, HFCs, SF_6): no natural background; have very high warming potential.

Step 3 — Major sources of anthropogenic GHGs:

- Fossil fuel burning (coal, oil, gas): main source of CO_2 from electricity, transport, industry, heating.
- Deforestation and land-use change: releases stored carbon; reduces future sequestration capacity.
- Agriculture: livestock (methane from enteric fermentation), rice paddies (methane), fertilisers (N_2O).
- Industrial processes: cement (calcination of limestone), some chemicals.
- Waste: methane from landfills.

Step 4 — Global Warming Potential (GWP):

- Compares warming effect of 1 kg of gas to 1 kg of CO_2 over 100 years.
- CO_2: 1 (reference).
- Methane: ~ 28 (per IPCC AR5 values).
- N_2O: ~ 265.
- SF_6: $\sim 23{,}500$.
- Some HFCs/CFCs: thousands.

Step 5 — Observed effects:

- Global mean surface temperature has risen $\sim 1.2\,^{\circ}\mathrm{C}$ above pre-industrial levels.
- Sea level rise: thermal expansion + melting glaciers and ice sheets.
- Polar ice loss; permafrost thawing (releases more methane $\rightarrow$ positive feedback).
- Glacier retreat globally.
- More frequent and intense heatwaves, droughts, wildfires, heavy precipitation, hurricanes.
- Ocean acidification (CO_2 dissolves in seawater): threatens calcifying organisms (corals, molluscs).
- Shifting species distributions; phenology changes; biodiversity loss.
- Crop yield impacts.
- Human health: heat illness, vector-borne disease spread, food/water insecurity, displacement.

Step 6 — Climate change mitigation:

- Energy: shift to renewables (solar, wind, hydro, geothermal); nuclear.
- Efficiency: building retrofits, efficient appliances, public transport, electric vehicles.
- Industry: decarbonisation; carbon capture and storage (CCS); green hydrogen.
- Agriculture: dietary shifts, reduced food waste, regenerative practices.
- Land use: prevent deforestation, restore forests, peat bog conservation.
- Direct air capture, nature-based solutions.

Step 7 — International agreements:

- UNFCCC (1992): framework convention.
- Kyoto Protocol (1997): first binding emission targets for developed countries.

- **Paris Agreement** (2015): all countries submit Nationally Determined Contributions (NDCs); aim to limit warming to "well below" $2\,^{\circ}\mathrm{C}$ above pre-industrial, with efforts toward $1.5\,^{\circ}\mathrm{C}$.
- IPCC (Intergovernmental Panel on Climate Change): assesses science; periodic Assessment Reports.
- Global Stocktake and COP meetings (COP28 in 2023).

Step 8 — Adaptation: Even with rapid mitigation, some warming is locked in. Need adaptation: coastal defences against sea-level rise, drought-resilient crops, improved health systems, climate-smart cities, water management. The poorest countries are most vulnerable and historically least responsible.

Step 9 — Other environmental issues (compare):

- Ozone depletion (stratospheric ozone hole): caused by CFCs; addressed by Montreal Protocol (1987, widely seen as the most successful environmental treaty); ozone layer recovering.
- Acid rain: SO_2, NO_x emissions $\rightarrow$ acidified precipitation; damages forests, lakes, monuments; reduced by scrubbers and clean-fuel standards in many countries.
- Eutrophication: nutrient pollution (P, N) causing algal blooms and dead zones.
- Air pollution: $PM_{2.5}$, NO_2, ozone — major public health burden in urban India.
- Plastic pollution: marine and terrestrial.

Final Answer: The greenhouse effect $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q37

Q38.

Solution

Concept — Deforestation: The clearing of forests for other land uses; among the most pressing environmental issues of our time.

Step 1 — Scale and trends:

- Pre-agricultural Earth: estimated ~ 6 billion hectares of forest.
- Today: ~ 4 billion hectares (30% of land area).
- Loss accelerated in the 20th century; recent global rate ~ 10 million hectares per year (FAO), although the rate has slowed slightly.

- Heaviest losses: tropical forests (Amazon, Congo basin, Southeast Asia).
- Temperate forests are stable or recovering in some regions (Europe, North America).

Step 2 — Drivers of deforestation:

- Conversion to agriculture: **the dominant driver globally**.
  - Cattle ranching (especially in Brazilian Amazon).
  - Soy cultivation (much for animal feed).
  - Oil palm plantations (Indonesia, Malaysia; replacing rainforest).
  - Cocoa, coffee, rubber.
  - Small-holder shifting cultivation.
- Logging: legal and illegal timber extraction.
- Mining: forest cleared for mineral extraction and roads.
- Infrastructure: roads, dams, settlements.
- Fuel-wood collection: persistent pressure in low-income regions.
- Fires: both deliberate clearing and accidental wildfires (exacerbated by climate change).

Step 3 — Ecological consequences:

- **Biodiversity loss:** tropical rainforests contain $\sim 50\%$ of terrestrial species but only $\sim 6\%$ of Earth's land area. Deforestation directly causes extinctions.
- **Carbon release:** $\sim$ 10–15% of anthropogenic CO_2 emissions; conversion of forest (high biomass) to pasture/cropland (low biomass) releases stored carbon.
- **Hydrological disruption:** forests transpire vast amounts of water; "flying rivers" from Amazon supply rainfall to agricultural regions of southern South America. Deforestation reduces regional rainfall.
- **Soil erosion:** tropical soils are often nutrient-poor and held in place by vegetation; once cleared, erosion is rapid.
- **Microclimate changes:** loss of cooling shade; increased local temperatures.
- **Disrupted nutrient cycles.**

Step 4 — Social consequences:

- Displacement of indigenous and forest-dependent peoples.
- Loss of traditional knowledge.
- Conflict over land rights.
- Health impacts of smoke from forest fires.

- Spillover of zoonotic diseases (forest fragmentation brings humans into contact with wildlife reservoirs).

Step 5 — India context:

- Forest cover: $\sim 22\%$ of land area (Forest Survey of India 2021).
- Has roughly stabilised since 1990s after long historical losses.
- Pressures: agriculture expansion, infrastructure projects, mining, urbanisation.
- Compensatory Afforestation Fund Management and Planning Authority (CAMPA): legal mandate for replanting when forest is diverted.
- Joint Forest Management (JFM): involves local communities in protection.
- Forest Rights Act (2006): recognises rights of forest-dwelling tribes.

Step 6 — Mitigation strategies:

- REDD+ (Reducing Emissions from Deforestation and forest Degradation, plus conservation, sustainable management, enhancement of forest carbon stocks): a UNFCCC framework for paying developing countries to preserve forests.
- Protected areas and indigenous-managed lands (consistently among the best-conserved forest regions).
- Sustainable certification: FSC (Forest Stewardship Council) for sustainable timber; RSPO for sustainable palm oil.
- Agroforestry: integrating trees with crops/livestock.
- Restoration: large-scale reforestation projects (China's Great Green Wall, Bonn Challenge).
- Reducing demand: alternative materials, reduced meat consumption (less feed needed, less cattle pasture).
- Satellite monitoring: Global Forest Watch and similar platforms enable near-real-time detection of clearing.

Step 7 — Tropical rainforests — the lungs of Earth?:

- Tropical rainforests are major carbon stocks and biodiversity reservoirs.
- The Amazon alone covers ~ 5.5 million km^2.
- Concern about "Amazon tipping point" — where deforestation + climate change shift the system into savanna.
- About ~ 17–20% of original Amazon has been lost.

Step 8 — Related concepts (distinguish):

- Eutrophication: nutrient enrichment of water bodies $\rightarrow$ algal blooms, dead zones.
- Biomagnification: accumulation of persistent pollutants up the food chain (DDT in raptors).
- Biological oxygen demand (BOD): a measure of organic pollution in water (microbial oxygen consumption).
- Acidification: ocean acidification from CO_2, soil/lake acidification from acid rain.

Final Answer: Deforestation $\Rightarrow$ C

Answer: (C) Go Back to Q38

Q39.

Solution

Concept — The dawn of human gene therapy: ADA-SCID was the first inherited disease successfully treated by gene therapy in humans; opened a field that has had setbacks and is now flourishing.

Step 1 — ADA-SCID disease biology:

- Adenosine Deaminase deficiency $\rightarrow$ Severe Combined Immunodeficiency.
- ADA enzyme normally converts adenosine $\rightarrow$ inosine, and deoxyadenosine $\rightarrow$ deoxyinosine.
- Without ADA: deoxyadenosine accumulates; phosphorylated to dATP; high dATP is toxic to lymphocytes (inhibits ribonucleotide reductase).
- Result: profound deficiency of T cells, B cells, NK cells.
- Affected infants present with severe recurrent infections (PCP pneumonia, candidiasis, viral infections), failure to thrive, often death within first year without treatment.
- Autosomal recessive; ~ 1 in $200{,}000$ births; one cause of "bubble baby disease" (children kept in protective isolation, exemplified by David Vetter, the "bubble boy", who lived 1971–1984).

Step 2 — Conventional treatments:

- Allogeneic haematopoietic stem cell transplantation (HSCT) from matched sibling donor: curative when available; less successful with unrelated donors.
- Enzyme replacement therapy with PEG-ADA: pegylated bovine ADA injected periodically; not perfect immune reconstitution.

- These were unsatisfactory for many patients.

Step 3 — The first gene therapy trial (1990, NIH):

- French Anderson, Michael Blaese, Kenneth Culver.
- Patient: **Ashanti DeSilva**, a 4-year-old girl with ADA-SCID.
- Started: 14 September 1990.
- Procedure:
  (a) Withdrew patient's own T lymphocytes.
  (b) Transduced T cells in vitro with retroviral vector carrying functional ADA cDNA.
  (c) Re-infused the genetically modified T cells back to patient.
  (d) Repeated periodically.
- Patient improved; second patient (Cindy Cutshall) also did well.
- However, simultaneous PEG-ADA was continued, so the relative contribution of gene therapy was debated.

Step 4 — Subsequent trials:

- HSC-based gene therapy: collect patient's own bone-marrow $CD34^+$ cells, transduce with vector carrying ADA, reinfuse after myelosuppression. More durable than the T-cell approach.
- Italian San Raffaele trial (Aiuti et al.) and others showed sustained immune reconstitution and clinical benefit without need for ongoing PEG-ADA.

Step 5 — Setbacks in the field:

- X-linked SCID gene therapy trials (1999, Paris): used γ-retroviral vectors to deliver IL2Rγ gene; cured many children, but a fraction developed leukaemia due to insertional mutagenesis (vector integrated near LMO2 or other oncogenes, activating them). Set the field back.
- Jesse Gelsinger (1999, Penn): adenovirus-based gene therapy for OTC deficiency; massive immune reaction; died at age 18. Led to closer regulation of gene therapy trials.

Step 6 — Modern gene therapy — success stories:

- Safer vectors: self-inactivating (SIN) lentiviral vectors largely supplanted γ-retroviruses; AAV (adeno-associated virus) vectors for many in vivo applications.

- **Strimvelis** (2016, EU): the first commercial ex vivo gene therapy — γ-retroviral ADA gene therapy.
- **Luxturna** (2017, US): AAV-RPE65 for Leber congenital amaurosis; restores vision in a specific inherited retinal disease.
- **Zolgensma** (2019): AAV9-SMN1 for spinal muscular atrophy; single dose; extremely expensive but transformative.
- **Casgevy** (2023): CRISPR-edited HSCs for sickle cell disease and β-thalassaemia.
- Hemophilia A and B: AAV-factor VIII/IX, approved 2022/2023.
- CAR-T therapy: T cells engineered with chimeric antigen receptor to fight cancers (B-cell leukaemias and lymphomas).

Step 7 — Approaches in gene therapy:

- Gene addition: deliver a functional copy of a defective gene.
- Gene editing: CRISPR/Cas9, base editors, prime editors to correct mutations in situ.
- Gene knockdown/replacement: RNAi or antisense (e.g. patisiran for transthyretin amyloidosis).
- Ex vivo (cells modified outside body, then transplanted) vs in vivo (vector administered directly).
- Somatic gene therapy (not heritable) is widely accepted; germline editing remains ethically contested.

Step 8 — Challenges remaining:

- Cost: many gene therapies are extraordinarily expensive ($2–3 million for some).
- Delivery to specific tissues.
- Immune responses to vectors or transgene products.
- Durability of expression.
- Off-target effects of editing.
- Equity of access.

Final Answer: ADA-SCID $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q39

Q40.

Solution

Concept — The knockout mouse — a foundational tool of mammalian genetics: The targeted disruption of a specific gene in a living mouse, enabling rigorous study of gene function. Capecchi, Smithies, Evans: Nobel Medicine 2007.

Step 1 — The breakthrough technology — gene targeting in mouse ES cells:

- Martin Evans (1981): isolated and cultured mouse embryonic stem (ES) cells from inner cell mass; could maintain pluripotency in vitro.
- Mario Capecchi, Oliver Smithies (1980s): developed homologous recombination in mammalian cells to precisely modify specific genes.
- Combining the two technologies: introduce a precisely mutated allele into ES cells, select cells with successful gene targeting, then re-introduce these ES cells into a normal embryo to make a chimera that can germline-transmit the engineered allele.

Step 2 — Standard knockout protocol:

(a) Design a targeting vector: typically replaces an essential exon of the target gene with a neomycin-resistance (neo) selectable marker, flanked by homologous arms of the target locus.
(b) Electroporate the vector into mouse ES cells.
(c) Select with G418 (kills cells without neo).
(d) Pick clones; screen by PCR or Southern blot for homologous recombination vs random integration.
(e) Inject heterozygous-targeted ES cells (typically derived from agouti-coat-colour strain) into blastocysts (typically albino strain).
(f) Transfer to pseudo-pregnant foster mothers.
(g) Pups born are chimeras (mixture of agouti and albino patches in coat).
(h) Breed chimeric males; if germline transmitted the targeted ES-cell genome, offspring will be heterozygous $+/-$.
(i) Intercross $+/- \times +/- \rightarrow 1/4 + /+,\ 1/2 + /-,\ 1/4 - /-$ (homozygous knockout).

Step 3 — Conditional / tissue-specific knockouts:

- Many genes are essential for development $\rightarrow$ constitutive knockouts are embryonic lethal.
- Solution: Cre-loxP system.
  - Engineer a "floxed" allele: target gene flanked by loxP sites (which are recognised by Cre recombinase but otherwise inert).

  - Cross with a Cre-expressing line where Cre is under control of a tissue-specific or inducible promoter.
  - Cre excises the floxed sequence ONLY in cells expressing Cre.
  - Result: gene knocked out only in specific tissue or at specific time.
- Variations: Flp-FRT system, tamoxifen-inducible CreERT2, dox-inducible systems.

Step 4 — Knockout consortia — toward a complete catalogue:

- International Knockout Mouse Consortium (IKMC) and International Mouse Phenotyping Consortium (IMPC): generated and phenotyped knockouts for thousands of genes; aim to cover the entire mouse protein-coding genome.
- Resource available to researchers worldwide.

Step 5 — CRISPR/Cas9 revolution:

- Since ~ 2013, CRISPR-Cas9 has largely replaced ES-cell-based targeting for routine knockout generation.
- Inject Cas9 + sgRNA into one-cell mouse zygotes; double-strand break at target locus; NHEJ repair causes frameshift indels $\rightarrow$ knockout.
- Much faster: founder mice in ~ 1 month vs 1–2 years for ES-cell-based.
- Allows multiplex (knockout several genes simultaneously), knock-in (with HDR repair using template), conditional alleles by inserting loxP sites.
- Charpentier and Doudna: Nobel Chemistry 2020.

Step 6 — Other types of engineered mice:

- **Transgenic mouse**: a foreign gene (transgene) inserted into the genome (usually random integration of a microinjected DNA construct). Adds something.
- **Knockout mouse**: a specific gene disrupted/deleted.
- **Knock-in mouse**: a specific gene replaced with a modified version (e.g. humanised version, point mutation, GFP reporter).
- **Conditional knockout**: tissue- or time-specific gene disruption.
- **Humanised mouse**: carrying human cells or genes (immunology research, drug testing); e.g. NSG mice engrafted with human immune system.
- **Cloned mouse**: produced by somatic cell nuclear transfer (rare for mice; first cloned mouse was Cumulina, 1998).
- **Chimeric mouse**: composite of cells with different genotypes; an intermediate step in knockout creation.

Step 7 — Impact on biomedical science:

- Thousands of disease models created.
- Insights into mammalian development, immunology, neuroscience, cancer, metabolism, behaviour.
- Tested countless drug candidates pre-clinically.
- Identified essential genes (knockouts that are lethal pinpoint critical functions).
- Mouse genome ENCODE-style projects.

Step 8 — Limitations:

- Mice are not humans: some pathways differ; some drugs/disease mechanisms don't translate.
- Knockouts can show compensation by paralogous genes (mild phenotypes when "backup" genes can substitute).
- Strain background effects (C57BL/6 vs BALB/c vs 129 strains).
- Cost and welfare considerations; alternatives (organoids, cell culture, computational models) increasingly used to reduce animal use.

Step 9 — Other model organisms (compare):

- *Saccharomyces cerevisiae* (yeast): basic eukaryotic biology; gene deletion is straightforward.
- *Caenorhabditis elegans*: development, neurobiology, ageing; small body, transparent, exact cell lineage known.
- *Drosophila melanogaster*: genetics, development; balancer chromosomes; FLP/FRT system.
- Zebrafish (*Danio rerio*): vertebrate development, transparent embryos.
- Mouse: closest practical mammalian model; the workhorse of mammalian biology.

Final Answer: Knockout mouse $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q40

Answer Key

Q	Ans	Q	Ans	Q	Ans	Q	Ans	Q	Ans
1	B	2	A	3	D	4	C	5	A
6	D	7	C	8	B	9	D	10	C
11	B	12	A	13	C	14	B	15	A
16	D	17	A	18	D	19	C	20	B
21	D	22	C	23	B	24	A	25	C
26	B	27	A	28	D	29	B	30	A
31	D	32	C	33	A	34	D	35	C
36	B	37	D	38	C	39	B	40	A