(f) Eg. Uncontrollable cell division – point mutation
  (i) Proto-oncogenes – growth promoting genes
  (ii) Point mutation alters the ability of the proto-oncogene to be switched off
  (iii) RAS gene in human bladder cancer can be changed into oncogene
  (iv) RAS gene may not be able to be switched off – permanently switched on
  (v) This would promote unregulated cell division, leading to a tumour
(g) Eg. Huntington disease – stutter
  (i) Results from an expanded triple nucleotide repeat
  (ii) Normal gene has repeating CAG sequences
  (iii) Protein is altered sufficiently when CAG sequences are expanded to above a threshold number
  (iv) Symptoms manifest later in life eg. dementia and loss of motor control

(3) Chromosome Mutation – a change to parts of or whole chromosomes
(a) Ie. In the number or structure of chromosomes
(b) Includes a deletion, inversion or translocation
(c) The most common chromosome mutation is trisomy 21 aka. Downs Syndrome (increased chance of giving birth to a Downs baby as you age)

vi) Explain how mutations can have beneficial, neutral or harmful effects on the way a protein functions

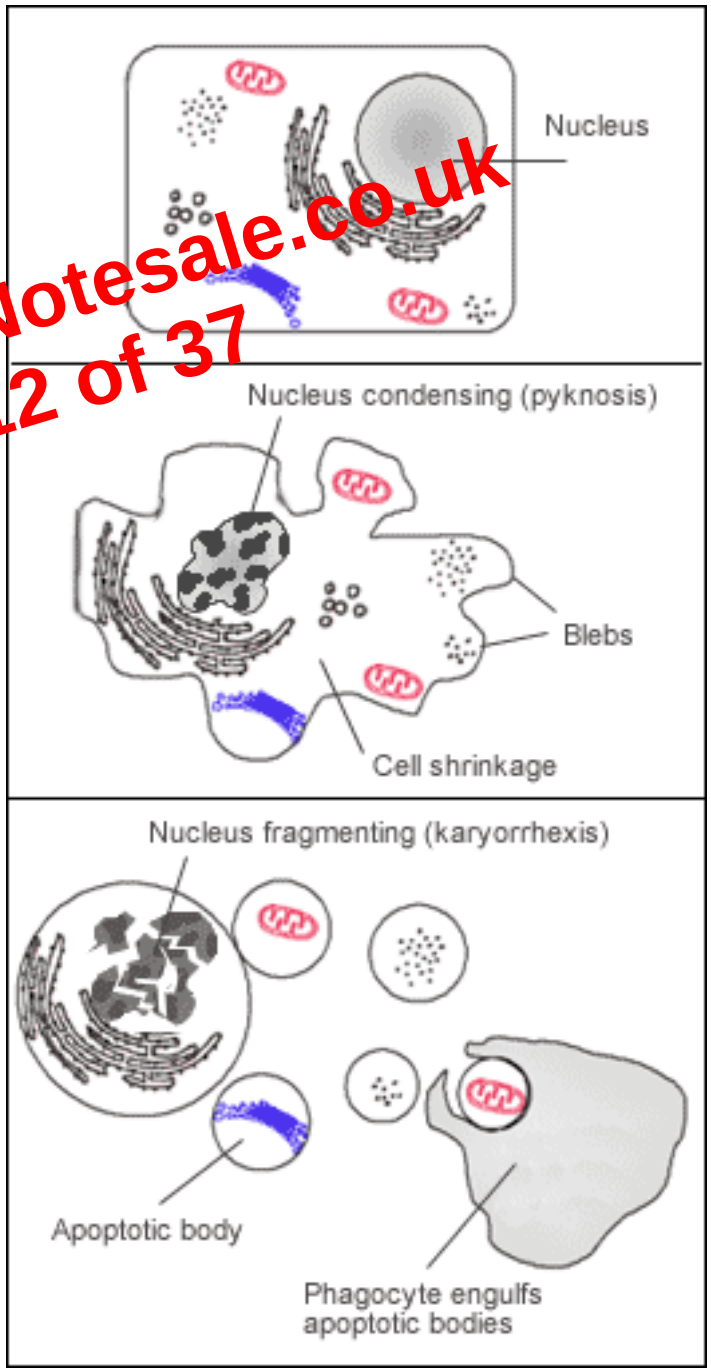
(1) Neutral effects
(a) If a gene is altered by a change to its base sequence it becomes an allele
(b) A visible change may not be produced if...
  (i) The mutation is in a non-coding region of the DNA
  (ii) It is a silent mutation ie. although the base triplet has changed, it still codes for the same or similar amino acid so the protein is unchanged
(c) The mutation may cause a change to the structure of the protein, and therefore a different characteristic, but the changed characteristic gives no particular advantage or disadvantage to the organism
  (i) Eg. Ability to smell honeysuckle
  (ii) Eg. Ability to roll your tongue (genetic trait)
  (iii) Eg. Have free or attached ear lobes

(2) Harmful/beneficial effects
(a) Eg. Melanin in skin
(b) Early humans in Africa had dark skin – pigment melanin protected them from harmful effects of UV light whilst still being able to synthesise vitamin D
(c) Any humans with mutations to some of the genes determining skin colour, producing paler skin, would have burned and suffered from skin cancer
(d) As humans migrated to more temperate climes, the sunlight was not intense enough to cause enough vitamin D to be made by those with dark skin
(e) Humans with a lack of melanin could synthesise more vitamin D

(a) Retinoic acid – derivative of vitamin A, activates homeobox genes in vertebrates in the same order that they are expressed in developing systems eg. CNS
(b) Retinoic acid is a morphogen – substance that governs the pattern of tissue development ie. plays a role in the development of morphological characteristics
(c) Too much vitamin A (retinol) taken in by pregnant women, particularly during the first month gestation, can interfere with the normal expression of these genes – causing birth defects eg. cranial deformities

x) *Outline how apoptosis (programmed cell death) can act as a mechanism to change body plans*

(1) Apoptosis – a series of biochemical events that together are a fast process of programmed cell death that occurs in multicellular organisms
(2) Hayflick constant – cells should undergo about 50 mitotic divisions and then undergo a series of biochemical events that leads to an orderly and tidy cell death
  (a) Cancer cells, on the other hand, are immortal
  (b) The rate of cells dying should balance the rate of cells produced by mitosis
  (c) Not enough apoptosis leads to the formation of tumours
  (d) Too much apoptosis leads to cell loss and degeneration
(3) Necrosis – an untidy and damaging cell death that occurs after trauma and releases hydrolytic enzymes
(4) Mechanism for apoptosis
  (a) Enzymes break down the cell cytoskeleton
  (b) Cell surface membrane changes
  (c) Cytoplasm becomes dense, with organelles tightly packed
  (d) Chromatin condenses
    (i) Nuclear envelope breaks
    (ii) DNA breaks into fragments
  (e) Blebs – cell breaks up into small vesicles
  (f) Vesicles are taken up by phagocytosis
(5) Controlling apoptosis
  (a) Events are controlled by a diverse range of internal and external cell signals



(b) Eg. Cytokines made by cells of the immune system, hormones, growth factors
(c) Such proteins can be released into the cytosol (aqueous component of cytoplasm) and bind to apoptosis inhibitors to allow the process to take place
(d) Nitric oxide – can induce apoptosis by making the inner mitochondrial membrane more permeable to hydrogen ions and dissipating the proton gradient

(6) Significance of apoptosis
(a) Weeds out ineffective or harmful T lymphocytes during the development of the immune system
(b) Limb development apoptosis – causes the digits (fingers and toes) to separate from each other
(c) Excess neurones produced during the development of the nervous system killed
(d) Cellular debris is disposed of and so does not damage any other cells or tissues
(e) Harmful, hydrolytic enzymes via necrosis aren't released into surrounding tissue
(f) Components of old cells can be reused

b) Meiosis and Variation

*i) Describe, with the aid of diagrams and photographs, the behaviour of chromosomes during meiosis, and the associated behaviour of the nuclear envelope, cell membrane and centrioles. (Names of the main stages are expected, but **not** the subdivisions of prophase)*

(1) Binary Fission – reproduction in prokaryotes producing genetically identical offspring
(a) Single DNA molecule replicates
(b) Both copies attach to the cell membrane
(c) Cell membrane begins to grow between the two DNA molecules
(d) Bacterium doubles in size
(e) Cell membrane pinches inward
(f) Cell wall forms between two DNA molecules dividing the original cell into two identical cells
(g) Genetic variation will only be introduced by mutation

(2) Mitosis – asexual reproduction in eukaryotes
(a) Produces two genetically identical cells
(b) Each daughter cell contains the same number and types of chromosomes as the original parent cell

(3) Meiosis is a reduction division – sexual reproduction in eukaryotes
(a) Occurs in the sex organs ie. gonads (testes/ovaries or anthers/ovules)
(b) Gametes are produced
(c) Halves the number of chromosomes – to ensure that, after the fertilisation of two gametes, the original chromosome number is restored (not doubled)
(d) Involves two divisions
(e) Necessary to avoid duplication of the chromosomes in successive generations
(f) Gametes will then fuse together to form a zygote during fertilisation

(4) Characteristics of genetic diseases controlled by a single recessive gene
  (a) Children born to two carriers have a 25% chance of being homozygous recessive therefore have the disorder
  (b) Carriers will not have the disorder
  (c) Eg. Cystic fibrosis
    (i) Cause
      1. Mutation disrupts the transport of chloride ions and water across the membranes of cells lining the airways, gut and reproductive tracts
      2. Changes the shape of the transmembrane chloride ion channels
      3. Cilia are not properly hydrated and cannot shift mucus
    (ii) Effect/symptoms
      1. Production of abnormally thick and sticky mucus in the lungs and airways
      2. More likely to get respiratory, bacterial infections
      3. Recurrent infections may lead to lung failure
      4. Affected gut and pancreas so food is not digested efficiently
      5. Treatments include daily physiotherapy helps to relieve congestion and antibiotics help fight infection
    (iii) Genetics
      1. Homozygous dominant – all chloride ion channels function
      2. Homozygous recessive – have cystic fibrosis
      3. Heterozygous – no symptoms but do have some abnormal chloride ion channels yet enough normal channels for their lungs to functions
  (d) Eg2. Haemophilia A
    (i) Cause
      1. Factor VIII – a blood clotting protein coded for by a gene on the X chromosome
      2. Recessive allele expresses an altered protein that doesn't function
      3. Hemizygous – males have only one X chromosome, if it has the allele for haemophilia A, the male will suffer from haemophilia
    (ii) Effect
      1. Leads to an increase in blood clotting time
      2. Internal bleeding from knocks and bleeding into joints are particularly harmful
  (e) Eg3. Duchenne muscular dystrophy (DMD)
    (i) Cause
      1. Dystrophin – DMD gene for a muscle protein on the X human chromosome
      2. A large protein involved in structures needed for muscle contraction
      3. Mutations of the gene usually result in a severely truncated dystrophin protein or no dystrophin at all (deletion mutation)
    (ii) Effect
      1. Develop muscle weakness in early childhood
      2. Usually wheelchair-bound by 10 years old

(b) Q = the relative frequency of the recessive (a) allele

(11) Given the allelic frequencies of a hypothetical gene with alleles A and a, expected frequencies of the progeny genotypes and phenotypes can be calculated

(12) Therefore – $p^2 + 2pq + q^2 = 1$

(a) p^2 is the proportion of the next generation expected to be homozygous dominant

(b) pq is the proportion of the next generation expected to be heterozygous

(c) q^2 is the proportion of the next generation expected to be homozygous recessive

		Male Gametes	
		A p	a q
Female Gametes	A p	AA p^2	Aa pq
	a q	Aa pq	aa q^2

(13) In a question, calculate the value of q (recessive allelic proportion from relative frequency of homozygous recessive organisms) and then calculate the value of p by subtracting it from 1

(14) With co-dominance, actual allele frequencies can be directly determined by counting alleles as the heterozygotes are distinguishable from both homozygotes

(15) Hardy-Weinberg Law Equilibrium Conditions

(a) Hardy-Weinberg law – in a large randomly mating population, the allele and genotype frequencies remain constant from generation to generation

(b) Hardy-Weinberg equilibrium – state of population which conforms to the expectations predicted by the Hardy-Weinberg law

(c) If the following conditions are not met, allele and genotype frequencies will change over the generations (evolution)

(i) Population is very large (eliminates sampling error)

(ii) Random-mating within the population

(iii) No selective advantage for any genotype – no selection pressures are operating and each genotype has equal fitness (no differential mortality)

(iv) Closed population – no migration of individuals from/into another population

(v) No mutation from one allele into another

1. If mutation does occur – forward and backward mutations are equal

(vi) No genetic drift – no changes in allele frequencies resulting from random, chance processes (more likely to affect smaller populations)

(vii) Characteristic being studied is not sex-linked – only for traits with dominant and recessive alleles

xiv) Explain, with examples, how environmental factors can act as stabilising or evolutionary forces of natural selection

(1) Population growth

(a) All organisms can reproduce – have the potential to increase their population size

(v) No distinction between extinct and extant (surviving) species (both may be included in cladograms) vs. distinction between extinct and extant species

(4) Linnaean system of classification – often confirmed by cladistic classification
  (a) Regarded as much less complex
  (b) Uses the groups kingdom, phylum or class – helpful to use a fixed number of levels in the classification of living organisms
  (c) Reflects phylogenies (evolutionary relationships) between the different species of organisms – helps us understand the evolutionary relationships between species
  (d) Shows both monophyletic and paraphyletic groups as taxa

(5) Characteristics used to determine ancestry
  (a) Designed to be as objective as possible
  (b) Modifications of long-standing features shared by species eg. monkeys, apes and humans have opposable thumbs = primate
  (c) Unique features may determine a species but useless for determining ancestry
    (i) Only shared by virtue of having long histories
    (ii) Evolutionary 'hangers on' that have persisted in several linages and continued to diverge so are no longer closely related eg. many animals' guts consist of a mouth and anus

xviii) Compare and contrast natural selection and artificial selection

(1) Natural selection
  (a) Mechanism for evolution
    (i) Organisms best adapted to their environment are more likely to survive
    (ii) They are therefore more likely to reproduce
    (iii) And by doing so pass on favourable alleles to their offspring
  (b) Selective agent – the environment (nature)
  (c) Advantageous to the environment/ecosystem
  (d) Relatively slow
  (e) Free of cost

(2) Artificial selection
  (a) Mechanism for selective breeding
  (b) Selective agent – humans eg. In agricultural system
  (c) Advantageous to humans
  (d) Relatively fast
  (e) Costs money

(3) Both
  (a) Involve selection of parents for advantageous traits
  (b) Involve inheritance of alleles
  (c) Change allele frequencies
  (d) Takes several generations

(4) Process of selectively breeding – artificial selection
  (a) Choose a male and female with the desired characteristic(s) and mate them