ANANTAM IAS · OPTIONAL NOTES

Anthropology Optional The Biological Basis of Life and Mendelian Genetics

Paper 1 · Unit 4

The molecular and cellular foundation the rest of Paper 1 stands on: the cell, the Watson-Crick DNA double helix and its replication, the gene and protein synthesis, mitosis versus meiosis, Mendel's laws with the monohybrid and dihybrid ratios, and the four methods (pedigree, twin, cytogenetic, population) by which human genetics is actually studied.

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UPSC SYLLABUS

The biological basis of life: The Cell, DNA structure and replication, Protein Synthesis, Gene, Mutation, Chromosomes, and Cell Division. [With, from Human Genetics - Methods and Application:] Mendelian genetics in man - family study, twin study, foster child, co-twin method, cytogenetic method, chromosomal and karyotype analysis.

The Cell: the Unit of Life and Heredity

Genetics is unintelligible without the cell, because chromosomes, DNA and cell division all happen inside it. Lead with the cell theory and the prokaryote-eukaryote divide, then locate the organelles that carry heredity and make proteins. Keep it functional: name each structure with the job it does.

- The cell theory, established by Matthias Schleiden and Theodor Schwann (1838 to 1839) and completed by Rudolf Virchow's dictum 'omnis cellula e cellula' (every cell from a pre-existing cell, 1855), states that all living things are made of cells, the cell is the basic unit of structure and function, and all cells arise from existing cells. This last clause is what makes cell division the mechanism of inheritance.
- Two grades of cell: prokaryotic (bacteria, archaea), lacking a true nucleus and membrane-bound organelles, with a single circular DNA molecule in a nucleoid; and eukaryotic (protists, fungi, plants, animals, including humans), with a membrane-bound nucleus holding DNA organised into chromosomes, plus specialised organelles. Human cells are eukaryotic.
- The plasma membrane is a selectively permeable phospholipid bilayer with embedded proteins, described by Singer and Nicolson's fluid mosaic model (1972); it controls what enters and leaves and carries recognition molecules.
- The nucleus is the genetic control centre: bounded by a double nuclear envelope with pores, it contains the chromatin (DNA plus histone proteins) that condenses into chromosomes at division, and the nucleolus, where ribosomal RNA is made and ribosomes are assembled.
- The organelles that matter most for this unit: ribosomes, the sites of protein synthesis, free in the cytoplasm or studded on the rough endoplasmic reticulum; the endoplasmic reticulum (rough for protein processing, smooth for lipid synthesis); the Golgi apparatus, which modifies, packages and dispatches proteins; and lysosomes, the digestive vesicles.
- Mitochondria are the powerhouses, generating ATP by aerobic respiration. For anthropology they carry a second significance: they contain their own small circular DNA (mtDNA), inherited almost exclusively through the mother, which makes mtDNA the tool used to trace maternal lineages and the 'Mitochondrial Eve' evidence for a recent African origin.
- Chromosomes are the packaged form of the hereditary material. Humans are diploid with 46 chromosomes in somatic cells: 23 pairs, comprising 22 pairs of autosomes and one pair of sex chromosomes (XX in females, XY in males). Gametes are haploid, with 23 chromosomes. Each chromosome has a centromere and, at its tips, telomeres.

KEY TERMS

Cell theory — The principle (Schleiden, Schwann, Virchow) that all organisms are made of cells, cells are the unit of life, and every cell arises from a pre-existing cell.

Prokaryote / Eukaryote — Cells without a true nucleus (bacteria, archaea) versus cells with a membrane-bound nucleus and organelles (including human cells).

Mitochondrial DNA (mtDNA) — The small circular genome inside mitochondria, maternally inherited, used in anthropology to reconstruct matrilineal descent and support the recent-African-origin model.

DNA: the Watson-Crick Double Helix and Its Replication

This is the anchor topic of the unit. Two things must be delivered precisely: the structure of DNA as Watson and Crick described it in 1953, with correct attribution, and the semiconservative mechanism of replication. Get the base-pairing and the antiparallel strands exactly right, since that is where marks are won or lost.

- DNA (deoxyribonucleic acid) is the molecule of heredity. Its double-helical structure was proposed by James Watson and Francis Crick in a one-page paper in Nature on 25 April 1953. Their model rested critically on the X-ray diffraction work of Rosalind Franklin (the celebrated 'Photo 51') and Maurice Wilkins, and on Erwin Chargaff's rules. Watson, Crick and Wilkins shared the Nobel Prize in 1962; Franklin had died in 1958 and the prize is not awarded posthumously. Attribute the discovery to Watson and Crick 1953, and credit Franklin's data honestly.
- The building block is the nucleotide, made of three parts: a deoxyribose sugar, a phosphate group, and one of four nitrogenous bases. The bases are the two purines, adenine (A) and guanine (G), and the two pyrimidines, cytosine (C) and thymine (T). Nucleotides are joined by phosphodiester bonds into a strand with a sugar-phosphate backbone.
- The structure is a double helix of two strands. The sugar-phosphate backbones run on the outside; the paired bases point inward like the rungs of a twisted ladder. The two strands are antiparallel, one running 5' to 3' and the other 3' to 5', and they are complementary.
- Base pairing follows Chargaff's rules and is fixed: adenine pairs with thymine (A-T) by two hydrogen bonds, and guanine pairs with cytosine (G-C) by three hydrogen bonds. Hence A equals T and G equals C in amount. The G-C pair, with three hydrogen bonds, is the more stable, so GC-rich DNA needs more energy to separate.
- The standard B-form dimensions are worth memorising for a structure question: about 2 nanometres in diameter, one complete turn every 10 base pairs or about 3.4 nanometres, with bases stacked about 0.34 nanometres apart. The helix is right-handed.
- DNA replication is semiconservative, the key Watson-Crick prediction: each old strand serves as a template for a new complementary strand, so each daughter molecule has one parental and one new strand. This was demonstrated by Matthew Meselson and Franklin Stahl (1958) using density-gradient centrifugation of nitrogen isotopes, often called 'the most beautiful experiment in biology'.
- The mechanics of replication, named as a sequence: helicase unwinds the double helix at an origin, breaking the hydrogen bonds; single-strand binding proteins hold the strands apart; primase lays down an RNA primer; DNA polymerase adds new nucleotides only in the 5' to 3' direction. This makes one strand (the leading strand) synthesise continuously and the other (the lagging strand) synthesise in short Okazaki fragments, later joined by DNA ligase. Replication is bidirectional from the origin and highly accurate through proofreading.

- Mutation is best introduced here as an error in the DNA. A mutation is a heritable change in the DNA sequence: gene (point) mutations such as substitutions (transitions and transversions), insertions and deletions causing frameshifts; and chromosomal mutations affecting structure (deletion, duplication, inversion, translocation) or number (aneuploidy, polyploidy). Mutation is the ultimate source of all new genetic variation and thus the raw material of evolution, even though most mutations are neutral or harmful. Sickle-cell haemoglobin, from a single base substitution, is the standard anthropological example.

The four DNA bases and their pairing

Base	Type	Pairs with	Hydrogen bonds
Adenine (A)	Purine	Thymine (T)	2
Guanine (G)	Purine	Cytosine (C)	3
Cytosine (C)	Pyrimidine	Guanine (G)	3
Thymine (T)	Pyrimidine	Adenine (A)	2

KEY TERMS

Complementary base pairing — The rule that A always pairs with T (two H bonds) and G with C (three H bonds), which underlies both the double helix and the copying of DNA.

Antiparallel strands — The two DNA strands run in opposite 5'-to-3' orientations, a fact that forces leading- and lagging-strand synthesis during replication.

Semiconservative replication — Each daughter DNA molecule keeps one original strand and one newly made strand; predicted by Watson-Crick and proven by Meselson and Stahl (1958).

PREVIOUS YEAR QUESTIONS

- Write a note on Genes. [1992]

The Gene and the Genetic Code

The gene concept has shifted from an abstract 'factor' to a stretch of DNA, and a good answer traces that change and then states the modern molecular definition. Fold in the genetic code here, since it is the dictionary that connects gene to protein.

- The gene concept evolved in identifiable stages, and narrating them is itself examinable. Mendel (1866) inferred abstract hereditary 'factors'. Wilhelm Johannsen coined the word 'gene' in 1909 and drew the gene (genotype) versus trait (phenotype) distinction. Thomas Hunt Morgan's Drosophila work located genes on chromosomes in a linear order (the chromosome theory of inheritance). Beadle and Tatum's 'one gene, one enzyme' hypothesis (1941) tied genes to specific proteins. Since 1953 the gene is understood molecularly.
- The modern definition: a gene is a segment of DNA that carries the information to make a functional product, usually a polypeptide (protein) but sometimes a functional RNA. In eukaryotes a gene includes coding regions (exons) interrupted by non-coding regions (introns), plus regulatory sequences such as promoters.
- The genetic code is the set of rules by which the base sequence of DNA/mRNA is translated into the amino acid sequence of a protein. It is read in triplets called codons, each three bases specifying one amino acid.
- The properties of the code are a compact, high-yield list: it is triplet (three bases per codon); there are 64 codons for 20 amino acids; it is degenerate or redundant (most amino acids have more than one codon); it is

non-overlapping and comma-less (read continuously in fixed frame); it is nearly universal (the same in almost all organisms, evidence of common descent); and it is unambiguous (each codon specifies only one amino acid).

- The punctuation of the code: AUG is the start codon and also codes for methionine; UAA, UAG and UGA are the three stop (nonsense) codons that terminate translation. The code was deciphered by Marshall Nirenberg, Har Gobind Khorana and Robert Holley, who shared the Nobel Prize in 1968.
- Link the gene back to mutation: because the code is triplet and read in frame, an insertion or deletion not in multiples of three causes a frameshift that garbles everything downstream, whereas a single substitution changes at most one amino acid (or, thanks to degeneracy, sometimes none, a silent mutation). This is why the structure of the code has direct medical and evolutionary consequences.

KEY TERMS

Gene (modern) — A segment of DNA encoding a functional product (usually a polypeptide), including exons, introns and regulatory sequences.

Codon — A triplet of mRNA bases specifying one amino acid or a stop signal; the reading unit of the genetic code.

Degeneracy of the code — The property that most amino acids are specified by more than one codon, which cushions the effect of many point mutations.

PREVIOUS YEAR QUESTIONS

- Write a note on Genes. [1992]

Protein Synthesis: Transcription and Translation

Protein synthesis is the cell putting the genetic code to work, and it is asked directly (a 2008 note). Deliver Crick's central dogma as the frame, then the two stages, transcription and translation, in order, naming the molecules that do each job.

- The central dogma of molecular biology, articulated by Francis Crick (1958), states the direction of information flow: DNA to RNA to protein. DNA is transcribed into RNA, and messenger RNA is translated into protein. (The later discovery of reverse transcription in retroviruses, RNA back to DNA, is a recognised exception worth a line.)
- Three RNAs do the work, and their roles must be distinguished: messenger RNA (mRNA) carries the coded message from gene to ribosome; transfer RNA (tRNA) brings the correct amino acid, matching its anticodon to the mRNA codon; ribosomal RNA (rRNA) is the structural and catalytic core of the ribosome. RNA differs from DNA in being single-stranded, using ribose sugar, and carrying uracil (U) in place of thymine.
- Transcription (in the nucleus in eukaryotes): the enzyme RNA polymerase binds the gene's promoter, unwinds the DNA, and synthesises a complementary mRNA strand in the 5' to 3' direction using one DNA strand as template. In eukaryotes the primary transcript is then processed: a 5' cap and a 3' poly-A tail are added, and the introns are spliced out so that only exons remain in the mature mRNA.
- Translation (at the ribosome in the cytoplasm): the ribosome reads the mRNA codon by codon. It begins at the start codon AUG; tRNAs deliver amino acids whose anticodons pair with successive codons; peptide bonds link the amino acids into a growing polypeptide chain (initiation, elongation, termination). Translation stops at a stop codon, and the finished polypeptide folds into a functional protein.
- Fix the vocabulary correspondence, since a clean answer keeps the terms straight: a triplet of DNA/mRNA is a codon; the complementary triplet on tRNA is the anticodon; a codon specifies an amino acid; a chain of

amino acids is a polypeptide, which folds into a protein.

- Why this matters for anthropology: proteins (enzymes, structural proteins, haemoglobins, blood-group antigens) are the phenotype in molecular form. Variation in protein-coding genes underlies human biological diversity, from the haemoglobinopathies (sickle cell, thalassaemia) linked to malaria selection, to the blood-group and enzyme polymorphisms used as genetic markers of populations.

KEY TERMS

Central dogma — Crick's principle that genetic information flows DNA to RNA to protein; the master frame for protein synthesis.

Transcription — Synthesis of an mRNA copy of a gene by RNA polymerase in the nucleus, followed in eukaryotes by capping, tailing and splicing.

Translation — Decoding of mRNA at the ribosome, where tRNA anticodons match codons and amino acids are joined into a polypeptide.

PREVIOUS YEAR QUESTIONS

- Write a note on Protein Synthesis. [2008]

Cell Division: Mitosis versus Meiosis

Cell division is where genetics becomes mechanical, and the comparison of mitosis and meiosis is a recurring, high-yield question. Present both as ordered phase sequences, then draw the contrast in a table, and finish with the genetic significance, because that is what the examiner is really asking about.

- Mitosis is the division of somatic (body) cells: one parent cell divides once to produce two genetically identical diploid daughter cells, each with the full 46 chromosomes. Its purposes are growth, tissue repair and asexual replacement of cells. It preserves the chromosome number and the genome unchanged.
- The phases of mitosis, in order, are prophase, metaphase, anaphase and telophase (mnemonic PMAT), preceded by interphase in which the DNA is replicated. In prophase chromosomes condense and the spindle forms; in metaphase chromosomes line up on the equatorial plate; in anaphase the sister chromatids are pulled to opposite poles; in telophase two nuclei re-form, followed by cytokinesis, the division of the cytoplasm.
- Meiosis is the division that produces gametes (sperm and ova) in the reproductive organs: one diploid cell undergoes two successive divisions (meiosis I and II) to yield four haploid cells, each with 23 chromosomes. It is a reduction division: it halves the chromosome number so that fertilisation restores the diploid number in the next generation.
- The two divisions have distinct characters. Meiosis I is the reductional division, in which homologous chromosomes pair (synapsis) and separate; meiosis II is the equational division, resembling mitosis, in which sister chromatids separate. The long prophase I has named sub-stages (leptotene, zygotene, pachytene, diplotene, diakinesis).
- Two events in meiosis generate genetic variation and are the reason meiosis matters for both genetics and evolution: crossing over (recombination), the physical exchange of segments between homologous chromosomes at the chiasmata during pachytene of prophase I; and independent assortment, the random orientation and separation of the homologous pairs at metaphase I, which shuffles maternal and paternal chromosomes. Together with random fertilisation, these produce the near-infinite genetic uniqueness of individuals.

- State the genetic significance explicitly, since it is the marking point: mitosis conserves (identical cells, constant chromosome number, faithful growth and repair), while meiosis both maintains the species chromosome number across generations (by halving it before fertilisation restores it) and generates the variation on which natural selection acts. A species that reproduced by mitosis alone would be clonal and evolutionarily static.
- Meiosis also connects directly to Mendel: the Law of Segregation is the cellular consequence of homologous chromosomes (carrying allele pairs) separating in meiosis I, and the Law of Independent Assortment is the consequence of non-homologous pairs assorting independently at metaphase I. This is why UPSC has linked Mendel's laws to meiotic cell division (1987, 1988).

Mitosis versus Meiosis

Feature	Mitosis	Meiosis
Cell type	Somatic (body) cells	Germ cells (gamete formation)
Number of divisions	One	Two (meiosis I and II)
Daughter cells	2	4
Chromosome number of products	Diploid (2n, 46), unchanged	Haploid (n, 23), halved
Genetic outcome	Identical to parent cell	Genetically variable
Crossing over	Absent	Present (prophase I)
Homologues pair (synapsis)	No	Yes (in meiosis I)
Function	Growth, repair, replacement	Sexual reproduction, variation

KEY TERMS

Diploid / Haploid — Diploid (2n) cells carry both members of each chromosome pair (46 in humans); haploid (n) gametes carry one of each (23).

Crossing over — Exchange of segments between homologous chromosomes at chiasmata during prophase I of meiosis, a major source of recombinant genetic variation.

Reduction division — Meiosis I, which halves the chromosome number by separating homologous chromosomes, so fertilisation can restore diploidy.

PREVIOUS YEAR QUESTIONS

- Give an outline of the anthropological perspective of genetics and critically evaluate the genetic significance of meiotic cell division. [1988]

Mendel's Experiments and Laws: Monohybrid and Dihybrid Crosses

Mendel is the foundation of genetics and one of the most reliably examined topics in Paper 1. Attribute carefully (Gregor Mendel, work 1856 to 1863, paper 1866), explain why the pea was the ideal choice, then state the three laws with the monohybrid and dihybrid ratios, which the examiner expects to see written out.

- Gregor Johann Mendel, an Augustinian friar at Brno (then in Austria, now Czech Republic), carried out breeding experiments on the garden pea (Pisum sativum) between about 1856 and 1863. He presented the work in 1865 and published it as 'Versuche uber Pflanzen-Hybriden' ('Experiments on Plant Hybrids') in

1866. It was ignored for 34 years and rediscovered independently in 1900 by Hugo de Vries, Carl Correns and Erich von Tschermak. Attribute the laws to Mendel 1866, and the rediscovery to 1900.

- Why the pea was the right organism, a favourite sub-question: it has clear-cut contrasting characters (seven were used, such as tall versus dwarf, round versus wrinkled seed, yellow versus green cotyledon), it is normally self-pollinating so pure lines are easy to keep, it can be artificially cross-pollinated, it produces many offspring in a single generation, and it has a short generation time. Mendel's other great advance was quantitative: he counted large numbers of offspring and analysed the ratios statistically.
- The monohybrid cross (one character) gives the first two laws. Crossing pure tall (TT) with pure dwarf (tt) gives an F1 generation that is all tall (Tt): this is the Law of Dominance, that in a heterozygote one allele (dominant) masks the other (recessive). Self-crossing the F1 gives an F2 generation in the ratio 3 tall : 1 dwarf by phenotype, and 1 TT : 2 Tt : 1 tt by genotype.
- The Law of Segregation (Mendel's first law, also called the Law of Purity of Gametes) states that the two alleles of a gene separate cleanly during gamete formation, so each gamete carries only one allele, and they reunite at random in fertilisation. Its cellular basis is the separation of homologous chromosomes in meiosis I. The reappearance of the dwarf trait in the F2 is the proof that the recessive allele was hidden, not lost, in the F1.
- The test cross confirms the mechanism: crossing an organism of dominant phenotype with a homozygous recessive (tt) reveals the unknown genotype. A pure dominant (TT) gives all dominant offspring; a heterozygote (Tt) gives a 1:1 ratio of dominant to recessive. This is how a hidden genotype is read off from the phenotypes of the offspring.
- The dihybrid cross (two characters together) gives the third law. Crossing pure round-yellow (RRYY) with wrinkled-green (rryy) gives an all round-yellow F1 (RrYy); self-crossing the F1 gives an F2 phenotypic ratio of 9 round-yellow : 3 round-green : 3 wrinkled-yellow : 1 wrinkled-green, the famous 9:3:3:1.
- The Law of Independent Assortment (Mendel's second law) states that the alleles of different genes assort independently of one another during gamete formation, so the inheritance of one character does not affect another. Its cellular basis is the independent orientation of different homologous pairs at metaphase I of meiosis. The 9:3:3:1 ratio is the visible signature of two genes assorting independently.
- State the crucial caveat that turns a good answer into a precise one: independent assortment holds only for genes on different chromosomes (or far apart on the same chromosome). Genes lying close together on the same chromosome are linked and tend to be inherited together, an exception discovered by Morgan. Mendel's seven characters happened to behave independently, which was partly good fortune.

Mendel's crosses at a glance

Cross	F1	F2 phenotypic ratio	Law illustrated
Monohybrid (Tt x Tt)	All dominant (Tt)	3 : 1	Dominance and Segregation
Monohybrid genotypes	-	1 TT : 2 Tt : 1 tt	Segregation
Test cross (Tt x tt)	-	1 : 1	Confirms heterozygous genotype
Dihybrid (RrYy x RrYy)	All round-yellow	9 : 3 : 3 : 1	Independent Assortment

KEY TERMS

Law of Segregation — Mendel's first law: the two alleles of a gene separate during gamete formation so each gamete carries only one; cellular basis is meiosis I.

Law of Independent Assortment — Mendel's second law: alleles of different genes assort independently in gamete formation, giving the 9:3:3:1 dihybrid ratio; holds only for unlinked genes.

Test cross — A cross of a dominant-phenotype individual with a homozygous recessive to reveal the unknown genotype; a 1:1 ratio indicates a heterozygote.

PREVIOUS YEAR QUESTIONS

- Discuss the laws of inheritance propounded by Mendel on the basis of his classic experiments. Explain how these laws are applied in the study of human genetics. [1986]
- Critically discuss the Mendelian principles and their application to human populations. [2016]
- Discuss how the laws of heredity propounded by Mendel can be understood in the context of meiotic cell division and their application on Man. [1987]

Mendel in Man: Extensions, Exceptions, and Human Application

The UPSC framing almost always adds 'and their application to man'. Inheritance in humans is more complicated than pea colour, so the strong answer shows both that Mendel's laws do operate in humans and where they need extending. This is exactly the ground the 2016 'critically discuss' question tests.

- Mendel's laws do apply to humans, and the clearest cases should be named: single-gene traits inherited in Mendelian fashion include autosomal recessive conditions (phenylketonuria, cystic fibrosis, sickle-cell anaemia in the homozygote), autosomal dominant conditions (Huntington's disease, achondroplasia), and X-linked recessive conditions (haemophilia, red-green colour blindness, Duchenne muscular dystrophy). The ABO and Rh blood groups are textbook Mendelian markers.
- But strict Mendelian dominance is often incomplete, and the extensions are what 'critically discuss' rewards. Incomplete dominance: the heterozygote is intermediate, as in the pink flowers of Mirabilis or the sickle-cell trait carrier. Codominance: both alleles are fully expressed, as in the AB blood group and the MN blood groups. These modify the Law of Dominance without overturning segregation.
- Multiple alleles: a gene can have more than two alleles in the population though any individual has only two, the classic human case being the ABO system with alleles I-A, I-B and i, where I-A and I-B are codominant and both dominant to i. This is the standard demonstration that Mendelian analysis extends to humans.
- Polygenic (quantitative) inheritance is the most important extension for anthropology: many human traits (stature, skin colour, intelligence test scores, blood pressure) are controlled by many genes of small additive effect together with the environment, producing continuous variation on a bell curve rather than discrete Mendelian classes. Skin colour, governed by several genes, is the exam-standard example and connects to the study of human adaptation and 'race'.
- Further complications to acknowledge briefly: pleiotropy (one gene affecting several traits, as in sickle-cell), epistasis (one gene masking another), lethal genes (genotypes that die, distorting expected ratios, a 2012 question), and linkage (Morgan's exception to independent assortment). Environmental effects and variable penetrance and expressivity further blur simple ratios in man.
- Why humans are genetically harder to study, the point that motivates the whole 'methods' section next: we cannot arrange controlled matings, generations are long (about 25 years), family sizes are small so ratios are

statistically noisy, and there are ethical limits on experiment. Human geneticists therefore cannot breed test crosses and must fall back on indirect methods, which is exactly what the syllabus lists.

- The balanced conclusion for a 'critically discuss' answer: Mendel's principles remain the foundation of human genetics and correctly predict single-gene inheritance, but most anthropologically interesting human variation is polygenic and environmentally modulated, so Mendelism is necessary but not sufficient, and it must be combined with population genetics, cytogenetics and biometry to understand human heredity.

KEY TERMS

Codominance — Both alleles of a heterozygote are fully and simultaneously expressed, as in the human AB and MN blood groups; a modification of simple dominance.

Multiple alleles — The existence of more than two alleles of a gene in a population, though each individual carries only two; the human ABO blood-group system is the classic case.

Polygenic inheritance — A trait controlled by many genes of small additive effect (plus environment), producing continuous variation; skin colour and stature in humans are examples.

PREVIOUS YEAR QUESTIONS

- Discuss the laws of inheritance propounded by Mendel on the basis of his classic experiments. Explain how these laws are applied in the study of human genetics. [1986]
- Critically discuss the Mendelian principles and their application to human populations. [2016]
- Discuss monogenic and polygenic inheritance in man, citing suitable examples. [2011]

Methods of Studying Human Genetics: Pedigree, Twin, Cytogenetic, Population

Because humans cannot be bred experimentally, human genetics uses four principal indirect methods, and UPSC asks for them by name (2017, and repeatedly the twin method). Give each method its purpose, procedure, and its characteristic limitation, and the answer organises itself.

- Family or pedigree study is the first method: the tracing of a trait through a family tree across generations to establish its mode of inheritance. Standardised symbols are used (squares for males, circles for females, filled for affected, a horizontal line for a mating, a Roman-numbered generation for each row), and the individual through whom the family is ascertained is the proband or propositus. Pedigree analysis distinguishes autosomal dominant, autosomal recessive, X-linked recessive and X-linked dominant patterns from the way affected individuals are distributed by sex and generation. Its limitations: human families are small, records are often incomplete or unreliable, and late-onset or low-penetrance traits are easily missed.
- The twin study is the classic method for separating heredity from environment (nature versus nurture), pioneered in principle by Francis Galton. It rests on two kinds of twins: monozygotic (MZ, identical) twins, formed from one fertilised egg, who are genetically identical; and dizygotic (DZ, fraternal) twins, formed from two eggs, who share on average half their genes, like ordinary siblings.
- The logic of the twin method: compare the concordance (both twins showing a trait) of MZ versus DZ pairs. If a trait is largely genetic, MZ concordance will be much higher than DZ concordance; if environmental, the two will be similar. Because MZ twins are genetically identical, differences between them (discordance) point to environmental causes. The co-twin method compares MZ twins reared apart, or subjects one twin to a treatment and uses the other as a matched genetic control, to isolate environmental effects.

- Diagnosing zygosity ('diagnosis of twins', a 1998 question) uses similarity in genetic markers (blood groups, and today DNA fingerprinting), fingerprints, and physical resemblance; examining the placenta and membranes is suggestive but not decisive. The limitations of the twin method: MZ twins may share a more similar environment than DZ twins (violating the equal-environments assumption), samples are small, twins reared apart are rare, and prenatal environments differ.
- The cytogenetic method studies chromosomes directly. A karyotype is the systematic arrangement of an individual's chromosomes by size and shape, prepared from dividing cells (often blood lymphocytes) arrested at metaphase, stained (for example by Giemsa banding), photographed and arranged in pairs. It reveals chromosomal abnormalities: numerical anomalies (aneuploidy) such as Down syndrome (trisomy 21), Turner syndrome (45,X, monosomy) and Klinefelter syndrome (47,XXY); and structural anomalies (deletions, duplications, inversions, translocations). The sex chromatin (Barr body) test is a quick screen for the number of X chromosomes. This method links genotype to visible chromosome structure.
- The population (or biochemical and statistical) method studies the distribution and frequency of genes in whole populations rather than single families. It measures allele and genotype frequencies for markers such as blood groups and enzyme polymorphisms and analyses them against the Hardy-Weinberg equilibrium (p squared plus 2pq plus q squared equals 1), which predicts genotype frequencies in an idealised non-evolving population. Deviations from the expected frequencies reveal the action of the evolutionary forces (selection, mutation, migration or gene flow, genetic drift, and non-random mating such as consanguinity). This is the bridge from Mendel to the population genetics that dominates the rest of Paper 1.
- Related methods worth a mention to show range: the foster child or adoption method (comparing adopted children with their biological versus adoptive parents to separate heredity from upbringing), dermatoglyphics (fingerprint and palm patterns as heritable markers), immunological and biochemical assays, and modern molecular techniques (DNA fingerprinting, sequencing) that now underpin most human-genetic research.
- Close with the integrating point the examiner wants: no single method is sufficient. Pedigrees establish patterns of single-gene inheritance, twin and foster-child studies partition genetic and environmental variance for complex traits, cytogenetics detects chromosomal disorders, and population studies reveal evolutionary dynamics. Together they compensate for the impossibility of experimental breeding in humans.

KEY TERMS

Pedigree / Proband — A family tree in standard symbols used to trace inheritance; the proband (propositus) is the affected individual through whom the family is identified.

Concordance — The degree to which both members of a twin pair share a trait; higher MZ than DZ concordance indicates a genetic component.

Karyotype — The ordered display of an individual's chromosomes by size and shape, used in the cytogenetic method to detect numerical and structural abnormalities.

Hardy-Weinberg equilibrium — The population-genetic baseline (p squared + 2pq + q squared = 1) of stable allele frequencies in a non-evolving population; deviations reveal evolutionary forces.

PREVIOUS YEAR QUESTIONS

- Briefly describe the various methods used in the genetic study of man. [2017]
- Define twins. Describe the method of diagnosis of twins. In what ways are twins useful in the study of human genetics? [1998]
- Discuss the role of twins in nature-nurture problems and illustrate your answer with suitable examples. [1999]
- Write a note on Pedigree Analysis. [2007]
- Write a note in 150 words on Twin method in human genetics. [2013]

Last-mile revision

- Cell theory (Schleiden, Schwann, Virchow): all life is cellular, cells are the unit of life, every cell from a pre-existing cell. Human cells are eukaryotic (nucleus + organelles). Somatic cells are diploid (46 = 22 autosome pairs + XX/XY); gametes haploid (23). mtDNA is maternally inherited (basis of Mitochondrial Eve).
- DNA structure: Watson and Crick, 1953, Nature, using Franklin's X-ray (Photo 51) and Chargaff's rules. Double helix, antiparallel strands, sugar-phosphate backbone outside, bases inside. A-T (2 H bonds), G-C (3 H bonds). Purines A, G; pyrimidines C, T. About 2 nm wide, 10 bp per turn.
- Replication is semiconservative (each daughter = one old + one new strand), proven by Meselson and Stahl (1958). Helicase, primase, DNA polymerase (5' to 3' only), leading strand continuous, lagging strand in Okazaki fragments joined by ligase.
- Gene concept: Mendel's 'factor' (1866), Johannsen's 'gene' (1909), Morgan (genes on chromosomes), Beadle-Tatum 'one gene one enzyme' (1941), modern DNA-segment definition with exons/introns/promoters.
- Genetic code: triplet codons, 64 codons for 20 amino acids, degenerate, non-overlapping, comma-less, nearly universal, unambiguous. Start AUG (methionine); stop UAA, UAG, UGA. Cracked by Nirenberg, Khorana, Holley (Nobel 1968).
- Protein synthesis = central dogma (Crick 1958): DNA to RNA to protein. Transcription (RNA polymerase, promoter, mRNA; eukaryotes add cap, poly-A tail, splice out introns). Translation (ribosome, tRNA anticodon matches mRNA codon, peptide bonds, start at AUG, stop at stop codon). RNA: single-stranded, ribose, uracil for thymine.
- Mutation = heritable DNA change: point (substitution, frameshift from insertion/deletion) and chromosomal (structural: deletion/duplication/inversion/translocation; numerical: aneuploidy/polyploidy). Ultimate source of variation; sickle cell = single base substitution.
- Mitosis: somatic cells, one division, 2 identical diploid daughters, no crossing over; growth and repair. Phases PMAT. Preserves genome.
- Meiosis: germ cells, two divisions, 4 variable haploid gametes; reduction division. Meiosis I reductional (homologues pair and separate), meiosis II equational. Crossing over (pachytene of prophase I) + independent assortment (metaphase I) generate variation; halving lets fertilisation restore diploidy.
- Mendel: Gregor Mendel, pea (Pisum sativum), work ~1856 to 1863, paper 1866, rediscovered 1900 (de Vries, Correns, Tschermak). Pea chosen for contrasting characters, self-pollination, easy crossing, many offspring.
- Three laws: Dominance (F1 shows dominant allele); Segregation (first law, alleles separate into gametes, cellular basis meiosis I) giving monohybrid 3:1 (genotype 1:2:1); Independent Assortment (second law, unlinked genes assort independently, basis metaphase I) giving dihybrid 9:3:3:1. Test cross (x tt) gives 1:1 for a heterozygote. Linkage (Morgan) is the exception to independent assortment.
- Mendel in man: single-gene cases (autosomal recessive PKU/sickle cell; autosomal dominant Huntington; X-linked haemophilia, colour blindness; ABO/Rh markers). Extensions: incomplete dominance, codominance (AB, MN), multiple alleles (ABO), polygenic inheritance (skin colour, stature), pleiotropy, epistasis, lethal genes.
- Four methods of studying human genetics (because we cannot breed humans): (1) family/pedigree study (mode of inheritance, proband, symbols); (2) twin study (MZ identical vs DZ ~50%; compare concordance; co-twin method; nature vs nurture; Galton); (3) cytogenetic method (karyotype, Barr

body; detects Down trisomy 21, Turner 45,X, Klinefelter 47,XXY); (4) population study (allele frequencies, Hardy-Weinberg p2+2pq+q2=1, reveals evolutionary forces).

- Also: foster child / adoption method and dermatoglyphics and DNA fingerprinting. No single method suffices; they are combined because controlled mating is impossible in humans.

Common errors to avoid

- Mis-attributing DNA structure. It is Watson and Crick, 1953, and Franklin's X-ray data and Wilkins were essential; Franklin is not on the 1962 Nobel because it was awarded after her death, not because her work was minor. Do not credit the double helix to anyone else.
- Getting base pairing wrong: A pairs with T (two hydrogen bonds), G pairs with C (three hydrogen bonds). Purines are A and G; pyrimidines are C and T (and U in RNA). Reversing the bond counts or the purine/pyrimidine labels is a needless lost mark.
- Confusing transcription and translation, or forgetting that RNA uses uracil not thymine and ribose not deoxyribose. Transcription makes mRNA in the nucleus; translation makes protein at the ribosome.
- Mixing up mitosis and meiosis outcomes. Mitosis: 2 identical diploid cells, one division, no crossing over. Meiosis: 4 variable haploid cells, two divisions, crossing over and independent assortment. Only meiosis reduces the chromosome number.
- Stating Mendel's ratios loosely. Monohybrid phenotype is 3:1 (genotype 1:2:1); dihybrid is 9:3:3:1; a test cross of a heterozygote is 1:1. Write the ratios out; do not just gesture at them.
- Dating and naming Mendel wrongly. The experiments are ~1856 to 1863, the paper is 1866 (not 1865, when it was only read aloud), and the rediscovery is 1900. Mendel worked on Pisum sativum, the garden pea.
- Claiming independent assortment is universal. It holds only for genes on different chromosomes; linked genes (Morgan) are inherited together. Note that Mendel's seven characters were fortunately unlinked or far apart.
- Answering 'application to man' with pea genetics alone. The marks are in the extensions: codominance and multiple alleles (ABO), polygenic inheritance (skin colour, stature), and the reason humans need indirect methods (no controlled mating, small families, long generations).
- Blurring the twin method's logic. It compares MZ versus DZ concordance; discordance in MZ twins points to environment. Do not say twins 'prove' a trait is genetic from a single pair; it is a statistical comparison across many pairs, and the equal-environments assumption is a real limitation.
- Confusing the cytogenetic disorders: Down is trisomy 21 (47), Turner is 45,X (monosomy, female), Klinefelter is 47,XXY (male). A karyotype detects chromosomal, not single-gene, disorders.