Mendelian Genetics

Definitions:
Gene

1. Inheritable sequence of nucleotides or bases, making up a segment of DNA which codes for a polypeptide
2. A gene can be regarded as a unit of inheritance

Allele

1. An alternative form of a gene that can be present on either one or both of a pair of homologous chromosomes
2. That codes for a variant gene product
3. Alleles of a gene occupy the same locus on a pair of homologous chromosomes

Codominance

1. 2 different dominant alleles of the same gene are both expressed and influence the phenotype
2. Results in heterozygote's phenotype being different from the phenotypes of both homozygotes
3. More than 2 phenotypes possible

Locus

1. Position of a gene on a chromosome
2. Alleles occupy the same locus
3. Different genes occupy different loci

Dominant

1. Allele that shows its phenotype regardless of whether it is homozygous dominant or heterozygous
2. Masks the effects of gene products expressed by the other allele

Recessive

1. Allele that only shows its phenotype in the homozygous recessive genotype
2. Effects of its gene product are masked by that of the dominant allele

Homozygous

1. Alleles at a given locus on a pair of homologous chromosomes are identical

Heterozygous

1. Alleles at a given locus on a pair of homologous chromosomes are different

Phenotype

1. Characteristic of an organism that is expressed or observed
2. Arises from the interaction between the genotype and the environment

Genotype

1. Combination of alleles situated on homologous chromosomes at corresponding loci
2. Determines a specific trait of an organism
3. Inherited from parents via alleles

Linkage

1. 2 or more genes on the same chromosome that do not assort independently in meiosis and are thus inherited together
2. Genes closer together less likely to undergo crossing over and exchange alleles between homologous chromosomes

Crossing over

1. Homologous chromosomes pair up via synapsis to form bivalents during prophase 1 of meiosis
2. Crossing over occurs between non-sister chromatids of homologous chromosomes at chiasmata
3. Corresponding segments exchange genetic material forming non-identical sister chromatids ⇒ Recombinants form
4. Genes closer together less likely to undergo crossing over and exchange alleles between homologous chromosomes

Points to note for Genetic Diagram

1. Define Symbols
2. Parental Phenotype
3. Parental Genotype
4. Gametes (must circle)
5. Fertilisation (show punnett square/lines)

6. Offspring genotype
7. Offspring phenotype
8. Offspring phentypic ratio

Mendel's Laws

1. Law of segregation → Alleles separate from one another during meiosis to form gametes
2. Law of independent assortment → Homologous chromosomes pair up during metaphase 1 of meiosis in 2 rows ⇒ Orientation of each bivalent is completely independent from the orientation of other bivalents ⇒ New combinations of maternal and paternal chromsomes in gametes

Sex Determination

	Male	Female
Humans/Drosophila	XY	XX
Birds	ZZ	ZW
Grasshoppers/Cockroaches	XO	XX

- State whether male/female is the heterogametic/homogametic sex

Points to note for χ^2 test

1. Calculate χ^2 value = $\Sigma(O-E)^2/E$
2. Calculate degrees of freedom
3. For χ^2 value = ____ and degree of freedom value = ____, (state range of values for p)
4. (If significant) Since $p<0.05$, at level of significance of 5%, we reject the null hypothesis and conclude that there is a **significant** difference in the observed and expected results and the difference is not due to **chance** alone ⇒ Other reasons for the difference
5. (If not significant) Since $p>0.05$, at level of significance of 5%, we do not reject the null hypothesis and conclude that there is no **significant** difference between the observed and expected offspring and any difference is due to **chance**
6. (For epistasis) Ratio is close to ____ ratio, a modified 9:3:3:1 ratio which indicates epistasis

Why is it unlikely that daughters fathered by a haemophiliac will also suffer from haemophilia?

1. Haemophilia is an X-linked disease
2. Daughters will inherit the diseased X chromosome from their father, however, they will also inherit another X chromosome from their mother
3. Since haemophilia is a rare X-linked recessive allele, it is likely that the daughter will inherit a normal X chromosome from their mother. Presence of the dominant normal allele will help to mask the effects of the recessive diseased allele

Suggest how new genotypes arise

1. Crossing over between non-sister chromatids of homologous chromosomes during prophase I of meiosis resulting in new combinations of alleles on chromosomes of gametes
2. Gametes produced may have recombinant genotype of ___. Therefore, fusion of gametes will give rise to the new genotype.

Explain why there is a range of phenotypes for this characteristic

1. Range of phenotypes are due to slight phenotypic differences that vary along a continuum indicating continuous variation
2. Range of phenotypes indicate polygenic inheritance where multiple genes are involved
3. There is an additive effect of each gene where each gene has a small overall effect
4. In addition to genotypic factors, environmental factors affect the phenotype

Explain why heterozygotes of a recessive disease appear normal

1. Heterozygotes have dominant normal allele
2. Hence, the cell is able to synthesise sufficient levels of the protein/enzyme, masking the effects of the recessive diseased allele
3. Function of enzyme

Mapping units = % of recombinant genotype

Epistasis = A form of gene interaction in which a gene at one locus alters the phenotypic expression of a gene at a second locus

- Gene which is expressed is epistatic to the gene which is altered/suppressed (hypostatic)
- Only one phenotype is expressed
- Dominant epistasis = Dominant allele for one gene negates the effect of another gene
- Recessive epistasis = Recessive allele for one gene negates the effect of another gene

Types of Epistasis

1. 9:3:3:1
    - Recessive epistasis
        - aa and bb epistatic over codominant phenotype
    - 2 genes code for the same phenotype
    - Dominant alleles are codominant, producing a new phenotype
    - If only have dominant allele for one gene, that phenotype is expressed
    - If both recessive alleles are expressed, another phenotype is expressed
2. 9:7
    - Recessive epistasis
        - aa genotype epistatic over B_ genotype
        - bb genotype epistatic over A_ genotype
    - Requires dominant alleles for both genes for phenotype to be expressed
    - Biochemical pathway
        - Gene 1 codes for enzyme 1 which converts original molecule into an intermediate
        - Gene 2 codes for enzyme 2 which converts intermediate into the molecule which displays the phenotype
3. 9:3:4
    - Recessive epistasis
        - bb genotype epistatic over A locus
    - 1 gene codes for colour
    - Other gene codes for deposition of pigment
    - Biochemical pathway
        - Dominant allele for gene 1 codes for enzyme 1 which produces a black pigment
        - Recessive allele for gene 1 codes for enzyme 2 which produces a brown pigment
        - Dominant allele for gene 2 codes for pigment deposition
4. 15:1
    - Dominant epistasis
        - Duplicate dominant epistasis
    - 2 genes code for 2 enzymes which have the same function
    - Only one dominant allele required for phenotype to be expressed
5. 12:3:1
    - Dominant epistasis
        - Gene A is epistatic over B locus
    - Biochemical pathway
        - Dominant allele for gene 1 codes for an inhibitor for production of yellow pigment from precursor
        - Dominant allele for gene 2 codes for an inhibitor for the production of green pigment from yellow pigment produced in the absence of gene product of A
6. 13:3
    - Dominant epistasis
        - Gene B is epistatic over A locus

- Biochemical pathway
  - Dominant allele for gene 1 codes for enzyme which produces coloured pigments
  - Dominant allele for gene 2 codes for inhibitor of production of coloured pigments

<u>How to describe epistasis</u>

1. Epistasis
2. State which genotype is epistatic over which gene locus
3. State biochemical pathway

Linked Genes

- Situated on same chromosome
- Located close enough that they tend to be inherited together
- The closer the gene loci, the higher the chance that alleles of the genes will be inherited together as one linkage group
- The further the gene loci, the higher the chance of crossing over
- Does not show independent assortment (9:3:3:1 ratio)
- Parental phenotypes in approximately equal numbers, recombinant phenotypes in approximately equal numbers

<u>Suggest how test cross with many different pairs of characters could be used to map the position of genes on the chromosomes of fruit flies</u>

1. Recombinant frequency = Total recombinant offspring/Total offspring x 100%
2. The greater the % of recombinants, the greater the distance between genes
3. 1% recombination frequency = 1cM
4. If expected phenotypic ratio is obtained (1:1:1:1), then there is no linkagesx

Chromosomal Aberrations = Alterations in chromosome structure
<u>Deletion/Duplication</u>

- Removal/repeat of a chromosomal segment
- Occur during crossing over when non-sister chromatids of homologous chromosomes break and rejoin at the incorrect locations such that one chromatid may give up more genes than it receives ⇒ One chromosome with deletion mutation, one chromosome with duplication mutation

Inversion = Reversal of a segment within a chromosome
Translocation = Crossing over and subsequent genetic recombination between non-homologous chromosomes

- Gene's expression influenced by its new location next to regulatory elements e.g. enhancers and silencers may up/downregulate the expression of the gene

Aneuploidy

- Cell does not have a chromosome number that is a multiple of the haploid number
- Some chromosomes are present in extra/fewer copies than the wild type
    - Trisomy = Extra chromosome
    - Monosomy = Missing chromosome
- Due to non-disjuntion event where:
    - Failure of homologous chromosomes to move apart properly during anaphase 1 of meiosis 1
    - Failure of sister chromatids to separate properly during anaphase 2 of meiosis 2
    - Failure of sister chromatids to separate properly during anaphase of mitosis
        - If early on in the embryonic development, more severe
        - If in somatic adult cell, could be harmless as few daughter cells are affected or could be harmful if affected chromosomes cause imbalance in critical genes
- e.g. Down Syndrome (Trisomy 21)

Polyploidy

- 3 or more times the haploid number of chromosomes in nucleus
- Types:
    - Non-disjunction of entire chromosome sets during mitosis ⇒ Produce 4n somatic cell
    - Non-disjunction of entire chromosome sets during meiosis ⇒ Produce 2n gamete
- Fairly common in plants
- May be infertile due to inability of chromosomes to pair up during meiosis to form viable gametes

Discontinuous variation

- Distinct and discrete phenotypes
- Caused by different alleles of a single/few gene(s)
- Generally unaffected by environmental conditions

Continuous variation

- Range of phenotypes due to slight phenotypic differences that vary along a continuum indicating continuous variation
- Indicates **polygenic inheritance** where there is an additive effect of multiple genes on a single characteristic with each gene only having a small effect

- Phenotype also affected by environmental factors

How environment may affect phenotype?

- Phenotypic variation may result from the interaction of genotype and the environment
- Environment may modify or limit the expression of gene(s)
- Environment may trigger or switch on certain genes which are always present in the genome
    - Temperature
    - UV light
    - Photoperiod (wavelength of light and duration)
- Environment effect is usually greater on polygenes as frequency of phenotypes follow a normal continuous variation distribution pattern
- Environment may induce mutation which may affect phenotype e.g. exposure to UV light/carcinogens

Why is the range of variation greater in the F2 generation than the F1 generation?

- During prophase I of meiosis, crossing over occurs at chiasmata regions, between non-sister chromatids of homologous chromosomes resulting in new combinations of alleles on chromosomes
- During metaphase I and anaphase I of meiosis, independent assortment and random separation of homologous chromosomes occurs, resulting in different combinations of maternal and paternal chromosomes in gametes
- With multiple alleles for each gene, this leads to many more different combinations of alleles in gametes in F2 generation compared to F1 generation
- Random fusion of large variety of gametes leads to increased variation

	Polygenic	Multiple Alleles
Number of genes involved	Several	One
Effect of individual alleles	Additive/Quantitative	Non-additive/Qualitative
Type of variation	Continuous	Discontinuous
Effect of environment	More likely to be affected by environment	Less likely to be affected by environment