**INFLUENCE OF THE ENVIRONMENT ON PHENOTYPE**

Some traits in humans are inherited in a relatively straightforward manner. For example, the ABO blood group is determined by alleles of a single gene, the ABO gene, situated on chromosome 9. However, in general, there is no simple pattern of inheritance for many traits. Many genes may be involved for a single trait and environmental factors also play a part. It is often very difficult to establish the relative importance of each of the genetic factors and environmental factors.

One method for trying to establish the relative importance of genetics and the environment in determining a particular trait is to study the incidence of the trait in twins.

When both members of a twin have the same form of a trait they are said to be concordant for the trait. For example, if each twin has haemophilia, they are said to be concordant for haemophilia. On the other hand, if one twin has haemophilia whilst the other twin does not, then the twins are discordant for the trait.

A concordance rate for a particular form of a trait can be calculated as follows:

Concordance rate = number of pairs in which both twins show the train / number of

pairs in which at least one member of the pair shows the trait

1. What is the difference between monozygotic and dizygotic twins?
2. Would you expect monozygotic twins to be concordant or discordant for their ABO blood groups? Explain.
3. In a study of 200 people who were each one of a monozygotic twin pair and who had an operation for gallstones, it was found that in 54 cases the other member of the twin pair had also had an operation for gallstones. What is the concordance rate for gallstones in this survey? (Show working.)

Over many years, data has been collected on the frequencies of particular traits in the different types of twins. Some of this data is presented in the table below.

|  |  |  |
| --- | --- | --- |
|  | Percentage concordance in: | |
| Disorder | **Monozygotic twins** | **Dizygotic twins** |
| Diabetes mellitus | 84 | 37 |
| Epilepsy | 72 | 15 |
| Cancer | 61 | 44 |
| Cancer at the same site | 95 | 58 |
| Spina bifida | 6 | 4 |
| Multiple sclerosis | 20-30 | 6 |
| Congenital dislocation of the hip | 41 | 3 |
| Measles | 95 | 87 |

1. Suggest which disorders listed in the table have a major genetic component.
2. How would you account for the high concordance rate for measles in both kinds of twins?
3. To what extent do you think the genotype and environment contribute to spina bifida?

Height and weight data for twins are also available.

|  |  |  |
| --- | --- | --- |
|  | Percentage concordance in | |
|  | Monozygotic (same sex) twins | Dizygotic twins |
| Height | 95 | 56 |
| Weight | 98 | 46 |

1. The difference between concordance rates for weight is greater than the difference between the concordance rates for height. How do you interpret this?

**CASE STUDY 1: CYSTIC FIBROSIS**

**Part A** (See Fact Sheet 33)

1. List some of the symptoms of cystic fibrosis?
2. What is the normal function of the CTFR gene that is faulty in people suffering from cystic fibrosis?
3. Why does a fault in the CTFR gene lead to the mucous in the lungs becoming thicker?
4. Describe the two main theories used to explain the high incidence of cystic fibrosis in the population.
5. Describe the most likely way in which a person would inherit cystic fibrosis.
6. What is the most common mutation that causes cystic fibrosis?
7. Describe the newborn screening tests for cystic fibrosis.

**Part B**

Mary and John have been married for four years but so far Mary has not been able to conceive. Mary is 39 and John is 42 so they have decided to apply to take part in an IVF program.

Shortly after making their application, Mary discovers that her infant nephew Tom has been diagnosed with cystic fibrosis.

Mary remembers that her mother had two younger brothers who died in infancy and suspects that at least one of them may also have had cystic fibrosis.

John looks up cystic fibrosis on the internet and discovers that it is the most common life-limiting hereditary disease and is caused by an autosomal recessive gene that can skip generations. In light of this information Mary decides to investigate her family history.

Mary’s grandmother, Ethel married Edward in England in 1929 and migrated to Australia in 1932. They had four children Alice, Margaret (Mary’s mother) and two younger siblings who died in infancy – Richard aged 6 months (cot death?) and Peter aged 11 months (possibly from cystic fibrosis). Mary was unable to find out anything about her grandparent’s families in England.

Mary’s aunt Alice had two sons, Anthony and Paul, neither of whom has cystic fibrosis. Both Anthony and Paul are married and both have one child – neither child has the disease.

Mary’s mother, Margaret married Geoff and they had three children. Mary is the eldest.

Mary’s sister, Ruth just had her first child, Tom, who has been diagnosed with cystic fibrosis. Mary’s younger brother, Rex, has no children. There is no known history of cystic fibrosis in Geoff’s family

1. Construct the pedigree for Mary’s family in the space below.
2. Why is there doubt concerning the cause of death of Mary’s uncles, Richard and Peter?
3. Do you think it is possible that Richard had cystic fibrosis? Explain.
4. What were the genotypes of Mary’s grandparents?
5. What is the probability that Mary’s mother is a carrier for the cystic fibrosis allele?
6. What is the probability that Mary is carrying the cystic fibrosis allele? (Assume Geoff is homozygous dominant.)
7. In view of the seriousness of this condition, do you think that John should also investigate the health records of his family? Explain.
8. On what grounds should Mary and John seek genetic counselling?
9. What is the probability that Mary and John could have a child with cystic fibrosis?
10. If Mary and John were accepted into an IVF program then pre-implantation tests could be carried out to select an embryo that did not have the cystic fibrosis gene. Discuss some of the moral/ethical issues that arise from this technology.
11. It is estimated that as many as 1 in 25 people of Europeans descent carry the cystic fibrosis mutations. Suggest why a life-limiting mutant gene such as this can survive in the gene pool.

**CASE STUDY 2: HUNTINGTON DISEASE**

**Part A** (See Fact Sheet 44)

1. At what age do the symptoms of Huntington disease first appear?
2. Describe some of the symptoms of Huntington disease.
3. What is the life expectancy for a person with this disease?
4. Why does an error in the *huntingtin* gene cause neurodegeneration?
5. What type of mutation causes Huntington disease?
6. Name the inheritance pattern for this disease.
7. What is presymptomatic testing?
8. The second last paragraph of the fact sheet suggests that “…the advantages and disadvantages of having presymptomatic testing be considered before having testing.” Describe what you perceive to be some of the advantages and disadvantages of presymptomatic testing for Huntington disease.

**Part B**

The following pedigree shows the inheritance pattern for a family with Huntington’s disease.

1

2

3

10

9

15

1. Identify the evidence in the pedigree that proves that Huntington disease is caused by a dominant allele.
2. Determine the genotype of individuals 2, 4, 11 and 12.
3. Clearly show the proportion of genotypes and phenotypes for the children of a cross between Individual 13 and a person without Huntington disease.
4. What is the chance of Individual 13 having a child with Huntington disease if his partner is heterozygous?
5. What is the chance of individual 13 having a female child with Huntington disease if his partner does not have the disease?
6. Which set of parents in the pedigree could possibly have a child that is homozygous for the disease?
7. Compare the actual phenotypic ratio of the children of 3 and 4 with the expected ratio. Clearly identify any difference or similarity.
8. Explain why a lethal disease such a Huntington remains in the human population.

# CASE STUDY 3: DUCHENNE MUSCULAR DYSTROPHY

**Part A** (See Fact Sheet 41)

1. What general observation is used to distinguish between Duchenne and Becker dystrophy?
2. List some of the features of Duchenne muscular dystrophy.
3. What is the main cause of death in individuals with DMD?
4. Identify the type of mutation that causes DMD and explain how this mutation leads to muscle weakness.
5. Explain why DMD is far more common in males than in females.
6. Under what circumstances could a female be affected by DMD?
7. If genetic testing showed that a female was a carrier of DMD, what advice should she receive before starting a family?

**Part B**

Below is a family tree showing the inheritance of DMD.

1

2

1

6

1

11

1

2

I

II

III

IV

1. Give evidence from the pedigree that proves that DMD is recessive.
2. Which individuals would definitely have elevated levels of creatine kinase in their blood?
3. Which individuals might show elevated levels of creatine kinase?
4. What is the probability that II-2 is a carrier?
5. What is the probability that II-5 is a carrier?
6. If IV-1 wanted to start a family, what information should she be given by genetic counsellors?
7. If III-10 and III-11 choose to have another child, what is the probability that it would be a male with DMD?
8. Ralph is a 22-year old with terminal DMD. Specialists believe that he may only live another 6-12 months. Ralph’s fiancée, Jennifer, wants him to have some of his sperm frozen so that she can use them for artificial insemination at a later date. Describe some of the moral/ethical issues this raises.

**GENE MUTATIONS**

The following table gives all the possible combinations of nucleotides and the amino acid associated with each codon. U (for uracil) is used because this is the code that had been translated on to the RNA strand. U takes the place of T in the RNA strand.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **The RNA Codons** | | | | |
|  | **U** | **C** | **A** | **G** |
| **U** | UUU **Phenylalanine** (Phe) | UCU **Serine** (Ser) | UAU **Tyrosine** (Tyr) | UGU **Cysteine** (Cys) | **U** |
| UUC Phe | UCC Ser | UAC Tyr | UGC Cys | **C** |
| UUA **Leucine** (Leu) | UCA Ser | UAA **STOP** | UGA **STOP** | **A** |
| UUG Leu | UCG Ser | UAG **STOP** | UGG **Tryptophan** (Trp) | **G** |
| **C** | CUU **Leucine** (Leu) | CCU **Proline** (Pro) | CAU **Histidine** (His) | CGU **Arginine** (Arg) | **U** |
| CUC Leu | CCC Pro | CAC His | CGC Arg | **C** |
| CUA Leu | CCA Pro | CAA **Glutamine** (Gln) | CGA Arg | **A** |
| CUG Leu | CCG Pro | CAG Gln | CGG Arg | **G** |
| **A** | AUU **Isoleucine** (Ile) | ACU **Threonine** (Thr) | AAU **Asparagine** (Asn) | AGU **Serine** (Ser) | **U** |
| AUC Ile | ACC Thr | AAC Asn | AGC Ser | **C** |
| AUA Ile | ACA Thr | AAA **Lysine** (Lys) | AGA **Arginine** (Arg) | **A** |
| AUG **Methionine** (Met) or **START** | ACG Thr | AAG Lys | AGG Arg | **G** |
| **G** | GUU **Valine** Val | GCU **Alanine** (Ala) | GAU **Aspartic acid** (Asp) | GGU **Glycine** (Gly) | **U** |
| GUC (Val) | GCC Ala | GAC Asp | GGC Gly | **C** |
| GUA Val | GCA Ala | GAA **Glutamic acid** (Glu) | GGA Gly | **A** |
| GUG Val | GCG Ala | GAG Glu | GGG Gly | **G** |

Below is the normal code for a sequence of four amino acids and four possible mutations:

AAA CTA CAC TTC (normal code)

AAA ACT CCA CTT C

AAA TTA CAC TTC

AAA CTC CTC CAC TTC

AAA CTC ACT TC

Complete the table below by working out the complementary RNA code (C pairs with G, G with C, T with A and A with U) and then the sequence of amino acids.

|  |  |  |  |
| --- | --- | --- | --- |
|  | DNA sequence | RNA sequence | Amino acid sequence |
| Correct code |  |  |  |
| Point mutation |  |  |  |
| Repetition |  |  |  |
| Deletion |  |  |  |
| Insertion |  |  |  |