Question 1

Alkaptonuria is an extremely rare disease. The gene for Alkaptonuria (ALK) is on human chromosome 9 and is linked to the gene encoding the ABO blood group, with a recombination frequency of 11% between the loci.

A pedigree of a family with the disease is shown below, with affected individuals indicated in black. In addition, the blood type of family members is given.

The two alleles at the ALK locus will be denoted ALK^+ and ALK^- . The three alleles at the ABO blood group locus will be denoted I^A, I^B (which are co-dominant) and i (which is recessive to I^A and I^B).

i) What is the genotype of individual 1 at the ALK and ABO loci?

ii) What is the genotype of individual 2 at the ALK and ABO loci?

iii) What is the genotype of individual 3 at the ALK and ABO loci? Which alleles of each gene are carried on the chromosome he inherited from his father and which alleles are carried on the chromosome he inherited from his mother?

iv) Individuals 3 and 4 are expecting their fifth child. A physician draws a prenatal blood sample and determines that the child has blood type B. Is it likely that the child will have alkaptonuria? Explain your answer.
Question 2

Consider the pedigree below showing the inheritance of two X-linked diseases, hemophilia A and hemophilia B. Hemophilia A is due to a lack of one clotting factor, and hemophilia B is due to a lack of a different clotting factor. These two clotting factors are encoded by two different genes, located at different positions on the X chromosome. Note that no individual shown in this pedigree is affected with both hemophilia A and hemophilia B.

- □ = phenotypically normal
- ■ = affected with hemophilia A
- ■ = affected with hemophilia B

i) Write the genotypes for the following individuals at both the hemophilia A and hemophilia B disease loci. Clearly define your genotype symbols.

<table>
<thead>
<tr>
<th>Individual</th>
<th>Genotype</th>
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<tbody>
<tr>
<td>1</td>
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<tr>
<td>2</td>
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<tr>
<td>3</td>
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<td>4</td>
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<td>5</td>
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ii) How do you account for individual 5 not being affected with either hemophilia A or hemophilia B?
Solutions

Question 1

i and ii)

\[
\begin{align*}
\frac{i^o_{ALK+}}{i^A_{ALK-}} & \quad \text{or} \quad \frac{i^o_{ALK-}}{i^A_{ALK+}} \\
\end{align*}
\]

iii) To be type B, individual 3 must have gotten an \(i^o_{ALK-}\) chromosome from Dad and an \(I^B_{ALK+}\) chromosome from Mom.

iv) Individual 4 got an \(I^A_{ALK-}\) chromosome from Mom and an \(i^o_{ALK-}\) chromosome from Dad. If no recombination occurred, then for this impending child the chance of getting \(I^B_{ALK+}\) chromosome from Dad is 50%. The chance of getting the other chromosome, \(i^o_{ALK-}\) is also 50%. There would be no chance of getting \(I^B_{ALK-}\). However, you have been told that recombination frequency is 11%, so there is some chance that this child will have alkaptonuria.
Question 2

i) **Individual** | **Genotype**
--- | ---
1 | $X^{aB}Y$
2 | $X^{Ab}X^{AB}$
3 | $X^{Ab}Y$
4 | $X^{Ab}X^{aB}$
5 | $X^{AB}Y$

$X^{aB}$ X chromosome with allele for hemophilia A, recessive phenotype

$X^{AB}$ X chromosome with wild-type alleles, dominant phenotype

$X^{Ab}$ X chromosome with allele for hemophilia B, recessive phenotype

$X^{ab}$ X chromosome with alleles for hemophilia A and hemophilia B, recessive phenotype

ii) During meiosis, there was recombination between the X chromosomes in individual #4.

![X chromosomes of Individual #4 diagram]

A cross-over between the A and B loci resulted in two new recombinant gametes:

$A^b_-- (X^{AB})$ and $a^B_-- (X^{ab})$

Individual #5 received the $X^{AB}$ chromosome from his mother (#4) and the Y chromosome from his father (#3), thus he is not affected with either hemophilia A or hemophilia B.