Mendelian Genetics Practice Questions

Part 1: Using Test Crosses

In dogs, there is an hereditary deafness caused by a recessive gene, “d.” A kennel owner has a male dog that she wants to use for breeding purposes if possible. The dog can hear, so the owner knows his genotype is either DD or Dd. If the dog’s genotype is Dd, the owner does not wish to use him for breeding so that the deafness gene will not be passed on. This can be tested by breeding the dog to a deaf female (dd).

1A. Draw the Punnett squares to illustrate these two possible crosses. In each case, what percentage/how many of the offspring would be expected to be hearing? Deaf? How could you tell the genotype of this male dog?

Part 2: Sickle Cell Disease

2A. Two individuals who are heterozygous at the Sickle Cell locus have four children together. One of the children is affected with the disorder. Based on this information, is the sickle cell trait dominant or recessive?

2B. If the affected offspring has a child with an unaffected individual (who does not carry the sickle allele), what is the probability that any given child will be unaffected? Be a carrier? Be affected?

Part 3: Cystic Fibrosis

3A. If two carriers of the cystic fibrosis trait have children, what is the probability that their first child will be affected?

3B. If they eventually have three children, what is the probability that all three will be affected?
Part 4: Huntington’s Disease

Huntington’s Disease Background

Huntington's disease is a progressive disorder of the central nervous system. Intellectual impairment and severe mental disturbances are also a part of the disease. Initial symptoms include irritability, clumsiness, depression and forgetfulness. Mood, personality change and uncontrollable movements may begin ten years before diagnosis of the disease. (Folksinger Woody Guthrie, who died of the disease, was first thought to be an alcoholic and later schizophrenic, before he was properly diagnosed.)

The arrival of the gene in the New World can be traced to the 17th century. It is believed that symptoms of the disorder may have been responsible for charges made against some persons of consorting with the devil and of being witches. In 1630, three men whose families had been persecuted for witchcraft immigrated to America. One of the men settled in East Hampton, Long Island, New York. His offspring were notorious for a strange and frightening disease and it is one of them who was described in a paper first reporting the disease.

The gene for Huntington's Disease (HD) is dominant. If a person has the gene, that person will have the disease. The average age of onset is 40, though there is a wide range. The illness is progressive, with no remission, and is always fatal. Persons with the disease usually live about 20 years after first showing symptoms. It has recently been found that HD is caused by a mutation that brings about an increase in the number of repeats of three nucleotide bases, CAG, found at the end of the number 4 chromosome. The normal version of the HD gene has between 11 and 34 copies of CAG. The mutation which causes Huntington's increases the number of repeats to 37 or more. The HD repeat size rarely stays the same from one generation to the next and tends to increase. When passed on from fathers the increase is sometimes dramatic. Small increases, or sometimes decreases, have been seen when transmitted from mothers. There seems to be some relationship between the number of CAG repeats and the age at which the disease first appears. When there are more than 52 repeats, age of onset is usually much younger than the forties. One child who was diagnosed by age 3 had 86 copies of the repeat. Most persons with adult onset HD have between 37 and 52 repeats. In a few cases of new mutations to HD, repeats between 33 and 38 units have been identified. These people are unaffected, but the risk for HD in their children or grandchildren may be increased. The exact size range of repeats has not been definitely established, so repeats between 31 and 39 are considered uncertain.

The direct genetic test for the HD gene is available, but costs several hundred dollars. (A blood sample is taken and a polymerase chain reaction assay carried out.) Presently testing for HD is generally possible only when a person at risk has living relatives with the disease.

Based on this information, read through the following family history and answer the questions below.

Huntington's Disease, A Family History

John became interested in finding out more about genetic testing when he learned that his great grandfather had died of a disease that no one wanted to talk about. He also knew that his great-great grandfather, Jedediah, had come to Louisiana in 1895 from Long Island and that there were stories about his ancestors involving witchcraft. After reading the background on Huntington's disease, John became very concerned about his own family and was told that his great-grandfather had died, after suffering for 17 years, of Huntington's disease. Some members of his family agreed to volunteer for screening using the new PCR test for the CAG repeats. Your job is to analyze the findings and determine if there is a possibility that John might be at risk for this disease.

4A. Make a pedigree of John's family using the information given below. The numbers indicate how many uninterrupted CAG repeats there are on each of the two number 4 chromosomes. Write the name of the person and the number of CAG repeats beside or underneath them. (Hint: Begin the pedigree with John and work backwards.)
Most pedigrees, like the one shown above, indicate males as squares, and females as circles. Affected individuals are identified by shading in the square or circle.

*Max's parents: great-great grandmother Dovie (not tested) and great great-grandfather Jedediah (not tested)
*Osco's parents: great-grandmother Ophelia (not tested) and great grandfather Max (died of Huntington's, not tested)
*Maternal grandmother Maudie: 12, 32
*Maternal grandfather Osco: 18, 37
*Mother's brother Dink: 12, 53 (HD symptoms appeared at age 22)
*Mother’s sister Emma: 18, 12
*Mother's sister Barbara: refused to have the test
*Mother, Lucretia: 48, 12
*Father, Randolph: 35, 14
*John (is under age 18, cannot be tested)

4B. Answer the following questions using the Pedigree that you made and Background information on Huntington's

1. Using general probability, what are the chances of a parent with HD passing the gene on to any one of his or her children?

2. Indicate the number of CAG repeats you expect to see for each of the following situations:
   a. Normal Gene ______
   b. Huntington's disease _____
   c. Early onset HD ______
   d. New mutations, unaffected, but children or grandchildren may be affected _____

3. Thinking of all the ways in which the number of repeats may be passed on to children, discuss the possibility that John may get an HD gene
   a. from his mother
   b. from his father

Part 5: Dihybrid Crosses- In humans, there is a gene that controls formation (or lack thereof) of muscles in the tongue that allow people with those muscles to roll their tongues, while people who lack those muscles cannot roll their tongues. The ability to roll one’s tongue is dominant over non-rolling. The ability to taste certain substances is also genetically controlled. For example, there is a substance called phenylthiocarbamate (PTC for short), which some people can taste (the dominant trait), while others cannot (the recessive trait). The biological supply companies actually sell a special kind of tissue
paper impregnated with PTC so students studying genetics can try tasting it to see if they are tasters or non-tasters. To people who are tasters, the paper tastes very bitter, but to non-tasters, it just tastes like paper. Let’s let $R$ represent tongue-rolling, $r$ represent a non-roller, $T$ represent ability to taste PTC, and $t$ represent non-tasting.

Suppose a woman who is both a homozygous tongue-roller and a non-PTC-taster has children with a man who is a heterozygous tongue-roller and is a PTC taster, and they have three children: a homozygous tongue-roller who is also a PTC taster, a heterozygous tongue-roller who is also a taster, and a heterozygous tongue-roller who is a non-taster.

5A. If these parents would have a bunch more children so that they had 12 in all, how many of those 12 would you expect to be non-tasters who are homozygous for tongue-rolling?

Part 6: Paternity Testing Suppose you’ve been asked to help a new mother identify the biological father of her child. She is Type A, and her new baby is Type B.

Consider these three putative fathers: can any be the biological father? Why or why not?

#1 (Type A): Yes or No?
#2 (Type B): Yes or No?
#3 (Type O): Yes or No?

Part 7: Epistasis
If I cross a Brown Lab (bbEe) with a Black Lab (BbEe), can I expect any yellow puppies? If so, what proportion of the pups would I expect to be yellow?