1a) \( q \), the frequency of allele \( a \), is the number of \( a \) alleles divided by the total number of alleles. Since there are 1,000,000 individuals in the population, there are 2,000,000 alleles in the population. Each \( aa \) homozygote has two \( a \) alleles, while each \( Aa \) heterozygote has one \( a \) allele. We can calculate \( q \) as follows:
\[
q = \frac{f(a)}{(2(500)+9000)/2000000} = 0.005
\]

b) \( p+q = 1 \), so \( p = 1 - q = 1 - 0.005 = 0.995 \)

c) One generation of random mating is sufficient to bring a population into Hardy-Weinberg equilibrium, regardless of whether the previous generation was in Hardy-Weinberg equilibrium. Therefore \( f(aa) = q^2 = (0.005)^2 = 2.5 \times 10^{-5} \), and the total number of \( aa \) individuals is \( 2.5 \times 10^{-5} \times 1000000 = 25 \).

Likewise, the total number of \( Aa \) individuals is:
\[
1000000(2pq) = 1000000(2 \times 0.005 \times 0.995) = 9950
\]

d) no. In the absence of selection and mutation, there will be no change in the frequency of each allele from generation to generation.

In generation one, there are 9000 + 2(500) = 10000 \( a \) alleles
In generation two, there are 9950 + 2(25) = 10000 \( a \) alleles

e) no. If generation one was in Hardy-Weinberg equilibrium, then the number of homozygous \( aa \) albino individuals would be equal to \( q^2 \). However, \( q^2 \times 1000000 = 1000000(0.005)^2 = 25 \) but there were 500 albino individuals in generation one.

f) The probability that an unaffected individual is a carrier is \( p(Aa)/(p(Aa)+p(AA)) \). For f and g, we can assume that the probability of an unaffected individual being a carrier is just \( f(Aa) \), as the number of \( aa \) albino individuals is extremely small.

The probability of an unaffected individual being a carrier is:
\[
f(Aa) = 2pq = 2(0.005)(0.995) = 9.95 \times 10^{-3}
\]
The chances that both parents are carriers and both pass on their \( a \) allele is:
\[
(1/4)(9.995 \times 10^{-3})^2 = 2.48 \times 10^{-5}
\]

g) The frequency of \( Aa \) carriers in generation one is 9000/1000000 = 9\times 10^{-3}
The chances that both parents are carriers and both pass on their \( a \) allele is:
\[
(1/4)(9.995 \times 10^{-3})(9 \times 10^{-3}) = 2.24 \times 10^{-5}
\]

h) The albino parent is \( aa \), and must therefore pass on an \( a \) allele. The probability that the other parent passes on an \( a \) allele is:
\[
(1/2)(9.995 \times 10^{-3}) = 5.00 \times 10^{-3}
\]
2a) For a rare dominant disease you can assume that all affected individuals are heterozygous. Therefore the frequency of heterozygotes is \( f(Aa) = 1/1000 \), and each of those individuals has one q allele, so \( q = 1/2000 \).

For a dominant disorder with selective disadvantage \( S \) and mutation rate \( \mu \), \( q = \mu/S \). Therefore \( 1/2000 = \mu/0.2 \), and \( \mu = 0.0001 \).

b) For a recessive mutation, the incidence of disease is equal to \( q^2 \). Therefore, \( q = (1/1000)^{1/2} = 0.032 \), plugging that into \( q^2 S = \mu \): \( (1/1000) \times 0.2 = 2 \times 10^{-4} \)

Final answer: \( \mu = 2 \times 10^{-4} \)

c) Plugging in the value for \( q \) calculated in part b into \( q S = h \), we find that \( h = 0.032 \times 0.2 = 6.4 \times 10^{-3} \). Heterozygous advantage is phenomena where the heterozygotes of a detrimental allele are better equipped to survive, thus maintaining the detrimental allele in the population. Individuals heterozygous at this particular locus are more fit by a factor of \( 1 + h \). Final answer: \( h = 6.4 \times 10^{-3} \)

3. a) Given \( \mu \) and \( S \) we can calculate \( q \) using the equation \( q = \sqrt{\mu/S} = \sqrt{10^{-5}/0.4} = 0.005 \).

The incidence of the disease in the population would be \( q^2 = (0.005)^2 = 2.5 \times 10^{-7} \); therefore, one in forty thousand people would be affected by the disease.

b) At steady state, \( \Delta q = 0 \), and \( \Delta q_{sel} = \Delta q_{mut} \). Let us call the number of affected individuals \( n_h^{total} \); \( n_h^{total} \) is the sum of homozygotes arising from inbreeding and from random mating. The number of homozygotes arising from inbreeding are described by the equation:

\[
\begin{align*}
\ n_h^{inbreeding} &= F q \\
\end{align*}
\]

where \( F \) is the inbreeding coefficient (in this case 1/16) and \( q \) is the allele frequency. The number of homozygotes arising from random mating is described by the familiar equation: \( n_h^{random} = q^2 \). Adding the respective weights, as random mating corresponds to 90% and cousin marriage corresponds to 10% of the mating, we get a final equation of:

\[
\begin{align*}
\ n_h^{total} &= 0.9 n_h^{random} + 0.1 n_h^{inbreeding} = 0.9 q^2 + 0.1 F q \\
\end{align*}
\]

We plug this modified in the \( n_h^{total} \), into the \( \Delta q_{sel} \) equation to get

\[
\Delta q_{sel} = -S (0.9 q^2 + 0.1 F q)
\]

Setting this equal to \( \Delta q_{mut} = \mu = 10^{-5} \), and plugging in values for \( F \) and \( S \), we get a final equation:

\[
\Delta q = \Delta q_{mut} - \Delta q_{sel} = \mu - S (0.9 q^2 + 0.1 F q) = 0
\]

\[
10^{-5} - 0.4 (0.9 q^2 + 0.1 \left(\frac{1}{16}\right) q) = 10^{-5} - 0.36 q^2 - 0.0025 q = 0
\]

\[
q = 0.002839 \quad \text{or} \quad q = -0.009784
\]
As we cannot have negative allele frequencies, final answer is \( q = 0.00284 \). How does this allele frequency compare to part a? To find the incidence of the disease, we plug in our \( q \) value into the \( n_h^{\text{total}} = 0.9q^2 + 0.1Fq \) equation. This gives us: \( n_h^{\text{total}} = 0.00002574 \). Final answer: incidence = 1 in forty thousand. This is the same number obtained due to random mating—why do you think this is the case?

The allele frequency is reduced because inbreeding results in a greater proportion of homozygotes, because homozygotes are selected against, those alleles fall out of the population. Why is the incidence the same? Even though the allele frequency is low, much more of the inbreeding population is homozygous at this locus relative to the randomly mating population, resulting the same incidence of disease at equilibrium.

c) The allele frequency can be calculated by

\[
q_{\text{new}} = q_{\text{old}} + \Delta q \approx q, \text{ after one generation}
\]

\[
\Delta q = -5q^2 + \mu = -0.4q^2 + 10^{-5}
\]

Assuming that our inbred population was at steady-state, we can use a \( q = 0.00284 \), giving us

\[
\Delta q = -0.4(0.00284)^2 + 10^{-5} = 6.77 \times 10^{-6}
\]

\[
q_{\text{new}} = 0.00284 + 6.77 \times 10^{-6} = 0.00285
\]

\[
q_{\text{new}}^2 = (0.00285)^2 = 8.104 \times 10^{-6}
\]

Incidence of disease right after cessation of inbreeding is approximately one in 125,000. This is much lower than at Hardy-Weinberg equilibrium.

d) The allele frequency would be expected to rise after cessation of inbreeding until \( q = 0.005 \). This is due to the fact that the mutation rate is creating more alleles than are being selected out in the population. The allele frequency, \( q \), approaches 0.005 as time approaches infinity.