1. Let M = parental mating type, G = kids' genotypes, and DSP = "discordant sibpair."

$$\begin{aligned}\Pr(\text{IBD} = v|\text{DSP}) &= \textstyle\sum_{M,G} \Pr(\text{IBD} = v|M, G, \text{DSP}) \Pr(G|M, \text{DSP}) \Pr(M|\text{DSP}) \\ &= \textstyle\sum_{M,G} \Pr(\text{IBD} = v|M, G) \Pr(G|M, \text{DSP}) \Pr(M|\text{DSP})\end{aligned}$$

Calculating $\Pr(M|\text{DSP})$ is similar to that for the affected sibpair, as calculated in class:

M	$\Pr(M)$	$\Pr(\text{DSP}\|M)$	$\Pr(M\|\text{DSP})$	$\Pr(M\|\text{DSP})$ when $p = 0.05$
DD × Dd	$4p^3(1-p)$	1/2	$\alpha \cdot 2p^3(1-p)$	~ 0.0656
Dd × Dd	$4p^2(1-p)^2$	3/8	$\alpha \cdot (3/2)p^2(1-p)^2$	~ 0.9344

where $\alpha = 1/[2p^3(1-p) + (3/2)p^2(1-p)^2]$

Then we calculate $\Pr(G|M, \text{DSP})$ and $\Pr(\text{IBD} = v|M, G)$ for all possible M, G:

M	G	$\Pr(G\|M, \text{DSP})$	$\Pr(\text{IBD} = v\|M, G)$ 0	1	2
DD × Dd	DD,Dd	1	1/2	1/2	0
Dd × Dd	DD,Dd	2/3	0	1	0
Dd × Dd	DD,dd	1/3	1	0	0

We then sum up to get $\Pr(\text{IBD} = v|\text{DSP})$:

0	1	2
0.344	0.656	0

2. Let K = IBD status at disease gene and X = IBD status at marker.

$$\begin{aligned}\Pr(X = v|\text{DSP}) &= \textstyle\sum_k \Pr(X = v|\text{DSP}, K = k) \Pr(K = k|\text{DSP}) \\ &= \textstyle\sum_k \Pr(X = v|K = k) \Pr(K = k|\text{DSP})\end{aligned}$$

For $r = 0.05$, the transition matrix $\Pr(X = x|K = k)$ is the following:

K	X = 0	1	2
0	0.819	0.172	0.009
1	0.086	0.828	0.096
2	0.009	0.172	0.819

Note that the rows sum to 1.

We multiply each row by the result for $\Pr(K = k|\text{DSP})$ from problem 1, and obtain the following for $\Pr(X = x|\text{DSP})$.

0	1	2
0.338	0.602	0.059

3. (a) $S_{\text{pairs}} = 2 + 0 + 0 + 0 + 0 + 2 = 4$
   $S_{\text{all}} = 9/4$:

h				
1	1	2	2	4
1	1	2	4	2
1	1	4	2	2
1	1	4	4	4
1	3	2	2	2
1	3	2	4	1
1	3	4	2	1
1	3	4	4	2
3	1	2	2	2
3	1	2	4	1
3	1	4	2	1
3	1	4	4	2
3	3	2	2	4
3	3	2	4	2
3	3	4	2	2
3	3	4	4	4
				ave = 36/16

   (b) $S_{\text{pairs}} = 8$, $S_{\text{all}} = 19/4$

4. (a) The distribution of each S_{ij} is

S	0	1	2
$\Pr(S)$	1/4	1/2	1/4

   So $\text{E}(S_{ij}) = 0 \cdot (1/4) + 1 \cdot (1/2) + 2 \cdot (1/4) = 1$ and $\text{var}(S_{ij}) = (0-1)^2(1/4) + (1-1)^2(1/2) + (2-1)^2(1/4) = 1/2$.
   It's easy to calculate the joint distribution of S_{ij} and $S_{ij'}$ where $i \neq j, i \neq j', j \neq j'$:

	S_{ij}		
$S_{ij'}$	0	1	2
0	1/16	1/8	1/16
1	1/8	1/4	1/8
2	1/16	1/8	1/16

This implies that S_{ij} and $S_{ij'}$ are independent and hence $\text{cov}(S_{ij}, S_{ij'}) = 0$. (To get this, assume that the parents have *ordered* genotypes (1,2) and (3,4) and that sib i has genotype (1,3). Individual j is equally likely to have genotype (1,3), (1,4), (2,3), or (2,4), as is individual j', and they're independent. The joint distribution of S_{ij} and $S_{ij'}$ follows immediately.

(b)

$$\begin{aligned}
\text{E}\left(\frac{S_{12}+S_{13}+S_{23}}{3}\right) &= \tfrac{1}{3}(\text{E}\, S_{12} + \text{E}\, S_{13} + \text{E}\, S_{23}) = 1 \\
\text{var}\left(\frac{S_{12}+S_{13}+S_{23}}{3}\right) &= \tfrac{1}{9}(\text{var}\, S_{12} + \text{var}\, S_{13} + \text{var}\, S_{23}) \\
&= 1/6 \qquad \text{[Recall, from (a), that the cov's are 0.]}
\end{aligned}$$

5. Let p = frequency of the B allele; $q = 1 - p$.

We found an expression in class for $\text{E}[(Y_1 - Y_2)^2 | k \text{ alleles IBD at QTL}]$ in terms of σ_a^2 and σ_d^2, so all we need to do is express σ_a^2 and σ_d^2 in terms of a, d and p.

$$\begin{aligned}
\mu^\star &= q^2(\mu - a) + 2pq(\mu + d) + p^2(\mu + a) \\
&= (q^2 + 2pq + p^2)\mu + (p^2 - q^2)a + 2pqd \\
&= \mu + (2p - 1)a + 2pqd \\
\alpha_A &= p(\mu + d - \mu^\star) + q(\mu - a - \mu^\star) \\
&= p[d - (2p - 1)a - 2pqd) + q(-a - (2p - 1)a - 2pqd) \\
&= pd + (1 - p)(-a) - (1 - 2p)a - 2pqd \\
&= p(d - a) - 2pdq \\
\alpha_B &= p(\mu + a - \mu^\star) + q(\mu + d - \mu^s tar) \\
&= pa + qd - (2p - 1)a - 2pqd \\
&= q(d + a) - 2pqd \\
\delta_{AA} &= \mu - a - \mu^\star - 2\alpha_A = \ldots = -2p^2 d \\
\delta_{AB} &= \mu + d - \mu^\star - \alpha_A - \alpha_B = \ldots = -pqd \\
\delta_{BB} &= \mu + a - \mu^\star - 2\alpha_B = \ldots = -2q^2 d
\end{aligned}$$

$$\begin{aligned}
\sigma_a^2 &= 2(\alpha_A^2 \cdot q + \alpha_B^2 \cdot p) = \ldots \\
&= 2pq[a + d(p - q)]^2
\end{aligned}$$

$$\begin{aligned}
\sigma_d^2 &= q^2\delta_{AA}^2 + 2pq\delta_{AB}^2 + p^2\delta_{BB}^2 = \ldots \\
&= 4p^2q^2d^2
\end{aligned}$$