1. A couple has had several pregnancies which end in early miscarriages. During the next pregnancy a fetus reaches the second trimester of pregnancy. A karyotype reveals an unbalanced translocation involving chromosomes 8 and 21. The fetus has a severe heart defect and does not survive to term. A karyotype is performed on both the mother and the father. The father is discovered to carry a balanced translocation between chromosomes 8 and 21 while the mother's karyotype is normal. In their next pregnancy what possible outcomes could occur? Draw each possible outcome showing the meiotic event responsible for this outcome.

2. For each of the following sex chromosome abnormalities 47 XXY, 47 XXX, and 45 X, address the following issues:

a. At which stages of life could medical intervention lead to the discovery that an individual carried this sex chromosome abnormality?

b. What clinical findings would be most likely to lead a physician to recommend karyotypic analysis at each stage in life for individuals who have each of these conditions?

Use the following source material for this problem.

47 XXY: http://www.nichd.nih.gov/publications/pubs/klinefelter.cfm

47 XXX: http://www.aaa.dk/TURNER/ENGELSK/TRIPLEX.HTM

45 X: Please see:
Reiser, P. A., and L. E. Underwood. *Turner Syndrome: A Guide for Families*. Wayzata, MN: Turner Syndrome Society, 1992.

3. A 32 year old woman is married to a 38 year old man. She has had several miscarriages prior to her first full term pregnancy. She has just given birth to a child with Downs syndrome. The child is found to carry a Robertsonian translocation chromosome involving chromosomes 14 and 21. The couple is concerned about having a second child with Down syndrome.
Give an explanation to the couple of the relationship of the translocation to the occurrence of Downs syndrome in their child.
The couple each have several siblings who are married but do not yet have children. Explain to the couple how a karyotype for each of them would give information which might be helpful to the other members of their family in assessing their risk of having a child with Down syndrome.

4. Use Online Mendelian inheritance in Man (OMIM) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM) as a source for information on Prader-Willi and Angelman syndrome to answer the following questions:
a. Explain how either condition could be the consequence of non-disjunction events in both paternal and maternal meiosis for chromosome 15.
b. Explain how a chromosomal deletion could cause either condition
c. Explain how a balanced translocation could contribute to the etiology of either condition.
d. What evidence suggests that the genes responsible for the two syndromes are distinct?

5. Ron and Lucinda Smith have a family of ten children. Ron's mother Mabel has a mild form of myotonic dystrophy with radial cataracts and adult onset of muscle wasting and weakness. Ron's father. Michael did not have myotonic dystrophy. Ron himself has the adult onset form of myotonic dystrophy while Lucinda is not affected. Five of the children, Ann, Bobby, Charles, Diane and Edward have myotonic dystrophy, while the remaining five children Frank, Grace, Herb, Iris and Jane have no symptoms of myotonic dystrophy. Calculate a LOD score for linkage between a marker gene and the myotonic dystrophy gene in each of the cases given below assuming a model in which myotnic dystrophy is transmitted in an autosomal dominant pattern with 100% penetrance.

A.

Family member	Genotype at the marker locus
Mabel	1,1
Ron	1,2
Lucinda	2,3
Ann	1,2
Bobby	1,2
Charles	1,3
Diane	1,2
Edward	1,3
Frank	2,3
Grace	2,2
Herb	2,3
Iris	2,2
Jane	2,2

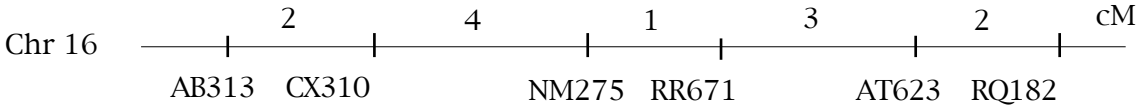
What is the lod score for linkage between the myotonic dystrophy locus and the marker locus at $\theta=0$ for this data set?
What is the lod score for linkage between the myotonic dystrophy locus and the marker locus at $\theta=0.1$ for this data set?

B.

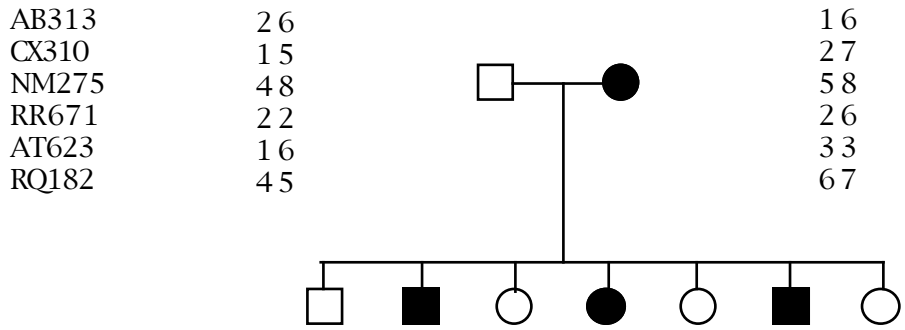
Family member	Genotype at the marker locus
Mabel	1,1
Ron	1,2
Lucinda	2,3
Ann	1,2
Bobby	1,2
Charles	2,3
Diane	1,2
Edward	1,3
Frank	2,3
Grace	2,2
Herb	2,3
Iris	2,2
Jane	2,2

What is the lod score for linkage between the myotonic dystrophy locus and the marker locus at $\theta=0$ for this data set?
What is the lod score for linkage between the myotonic dystrophy locus and the marker locus at $\theta=0.1$ for this data set?

6. Adult polycystic kidney disease (APKD) is responsible for about 20% of all patients on kidney dialysis. It is inherited in an autosomal dominant pattern with 100% penetrance. Two families were analyzed with microsatellite markers which map onto chromosome 16. What is the most likely position of the APKD gene on this map based on this data? Explain your reasoning.

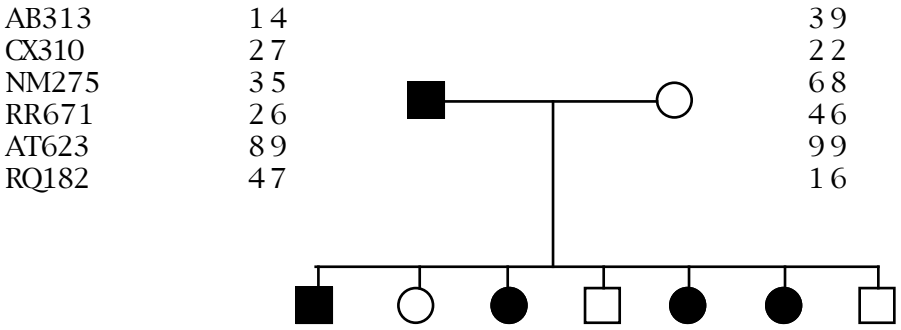


Family 1



AB313	12	62	16	66	12	66	16
CX310	75	25	71	21	75	21	71
NM275	58	88	54	84	58	84	54
RR671	22	62	22	22	22	62	22
AT623	36	36	31	31	31	31	36
RQ182	64	74	65	65	75	75	64

Family2



AB313	13	49	19	49	43	13	49
CX310	72	22	72	22	22	72	22
NM275	38	56	36	56	58	38	56
RR671	24	66	26	66	24	24	66
AT623	99	89	99	89	99	99	89
RQ182	76	46	71	41	76	76	41