

Year 1 Medical Genetics

Final Exam

March 6, 1998

DIRECTIONS: Select the single best answer to each question.

1. Examine the phenotype of the child on the right in the slide being projected. The diagnosis is:
 - A. Angelman syndrome
 - B. Down syndrome
 - C. myotonic dystrophy
 - D. mosaic trisomy 8 syndrome
 - E. William syndrome
2. Daniel Rader, M.D., who shared his experiences doing genetic testing on patients with us in the PBS documentary, "A question of Genes: Inherited Risks," does apolipoprotein E (APOE) testing on his patient Kathleen Clayton to better understand her risk for heart disease. The testing reveals that Kathleen has a "double dose" of APOE-4, indicating she has a high risk. Dr. Rader also learns that the APOE-4 gene is a marker for Alzheimer's disease, a condition that currently has no effective treatment. The finding presents a dilemma for Dr. Rader--Kathleen was concerned about heart disease, not Alzheimer's. This experience leads Dr. Rader to what conclusion?
 - A. genetic testing is very cost effective since one test can give you information about more than one condition
 - B. Kathleen shouldn't worry about Alzheimer's disease since she will probably die first from heart disease
 - C. he is not sure if he should offer genetic testing to his patients until the ethical, social, and financial issues are resolved
 - D. Kathleen's extended family members must be told immediately they probably also have a risk for heart disease and Alzheimer's
 - E. knowledge is power and even though Kathleen may not initially want the information about her risk for developing Alzheimer's disease, in the long run it is best that she be told
3. In human triploids, the extra set of chromosomes may be contributed by either parent. When the extra set is paternal in origin, there is overgrowth of the placenta. When the extra set is maternal in origin, placenta development tends to be very poor. The phenomenon which explains these findings is:
 - A. anticipation
 - B. heterodisomy
 - C. imprinting
 - D. isodisomy
 - E. loss of heterozygosity

4. The carrier frequency of Tay Sachs disease is estimated to be 1 in 30 in the Ashkenazi Jewish population. The disease incidence in this population would therefore be:
- A. 1 in 30
 - B. 1 in 60
 - C. 1 in 360
 - D. 1 in 900
 - E. 1 in 3600
5. Epidemiological studies of a multifactorial threshold trait reveal the incidence of the trait is 2/1000 in females and 1/1000 in males. During the past month you have seen two couples in the Genetics Clinic, both of whom have a child affected with this trait. Couple A has an affected daughter and couple B an affected son. Each couple wanted information about recurrence risks for this trait. Based on your knowledge of multifactorial threshold traits, you concluded:
- A. couple A has a higher recurrence risk than couple B
 - B. couple B has a higher recurrence risk than couple A
 - C. couple A and couple B have a 25% recurrence risk
 - D. neither couple has an increased recurrence risk
 - E. the risk to each couple is the square root of twice the general population incidence of the trait
6. The woman you saw this morning in the Genetics Clinic has the following clinical features: difficulty releasing her hand after turning the door knob, distal muscle atrophy, and facial muscle weakness. While taking her family history you discover she lost two babies shortly after birth because of respiratory insufficiency. The woman's father also has "muscle problems," cataracts, and developed frontal baldness at an early age. Although you sent a blood sample from her to the DNA Diagnostic Laboratory to confirm your diagnosis, you are fairly certain she has:
- A. Becker muscular dystrophy
 - B. Charcot-Marie-Tooth Disease
 - C. Marfan syndrome
 - D. myotonic dystrophy
 - E. spinal and bulbar muscular dystrophy
7. The type of mutation which has been found in all patients with the condition described in question #6 is a/an:
- A. deletion
 - B. duplication
 - C. inversion
 - D. point mutation
 - E. trinucleotide repeat

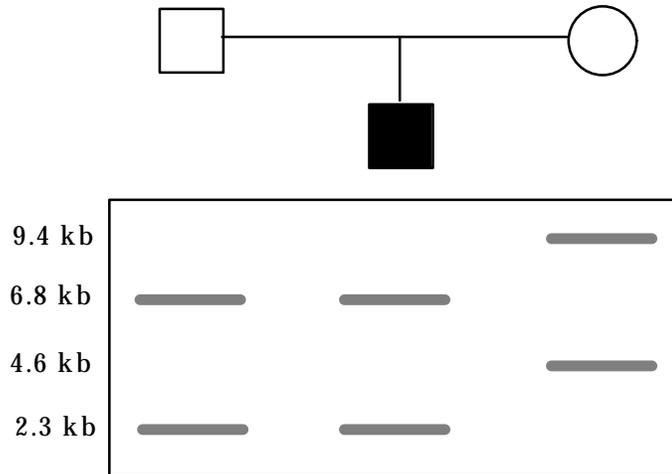
Questions 8-10. Select the BEST answer from the following (each answer may be used more than once):

- | | |
|---------------------------------|--------------------------------|
| A. neuroblastoma | E. retinoblastoma |
| B. chronic myelogenous leukemia | F. breast carcinoma |
| C. familial polyposis coli | G. Burkitt lymphoma |
| D. neurofibromatosis I | H. Li-Fraumeni syndrome |
| E. Wilm's tumor | I. adenocarcinoma of the colon |

8. The concepts of tumor promotion, initiation, and transformation were demonstrated by the description and recognition of a series of linked events involving activation of proto-oncogenes and loss of suppressor gene systems in this type of cancer.
9. Loss of heterozygosity in neoplastic cells for the *p53* tumor suppressor locus in these hereditary cancer families can result in tumor formation in a variety of cell types (including sarcomas, carcinomas, and other malignancies) as opposed to other hereditary cancers where the genetic alterations are more tissue specific.
10. A chromosomal rearrangement brings enhancer and transcriptional activating sequences of the *myc* proto-oncogene adjacent to an immunoglobulin heavy chain gene locus.

11. The Wilson family was evaluated and counseled in Case Study II. A diagnosis of Duchenne muscular dystrophy was suspected in Tim and Sara Wilson's son, Tyler. Pertinent laboratory results revealed markedly elevated CK levels in Tyler as well as the absence of dystrophin on a muscle biopsy. Multiplex PCR analysis of DNA from Tyler failed to identify one of nine common deletions within the DMD gene. You conclude:
- A. since a deletion was not identified in Tyler's DMD gene, he must be a new mutation and the risk to other family members is not increased
 - B. since a deletion was not identified in Tyler's DMD gene, he probably has Becker and not Duchenne muscular dystrophy
 - C. even though a deletion was not identified in Tyler's DMD gene, other family members may be at increased risk for having sons with DMD
 - D. because the diagnosis of DMD in Tyler is questionable, linkage analysis to determine other family member's gene status would be useless
 - E. linkage analysis would be useful to determine the carrier status of females in the family, but of little use for prenatal diagnostic purposes
12. Specific principles have been clearly formulated which determine whether a genetic disease is a candidate to be included in state programs for newborn screening. You are the director of the Michigan Newborn Screening Program and have been asked to determine whether a new disease should be added for newborn screening. Based on your understanding of these principles, what is the most important criteria in making your decision to add a new genetic disease?
- A. a disease which has a high frequency in only a specific ethnic population
 - B. a disease in which the age of onset of symptoms is during late adolescence
 - C. a disease in which the test has no false negatives and a high number of false positives
 - D. a disease in which the test has many false negatives, but no false positives
 - E. a disease in which irreversible damage is produced if untreated early in life

13. Shown below is a diagram of a Southern blot for a child affected with a well described multiple malformation syndrome and mental retardation. His parents were also studied. One RFLP on chromosome 15 has alleles 2.3, 4.6, 6.8 and 9.4 kb. What is the diagnosis in the child?

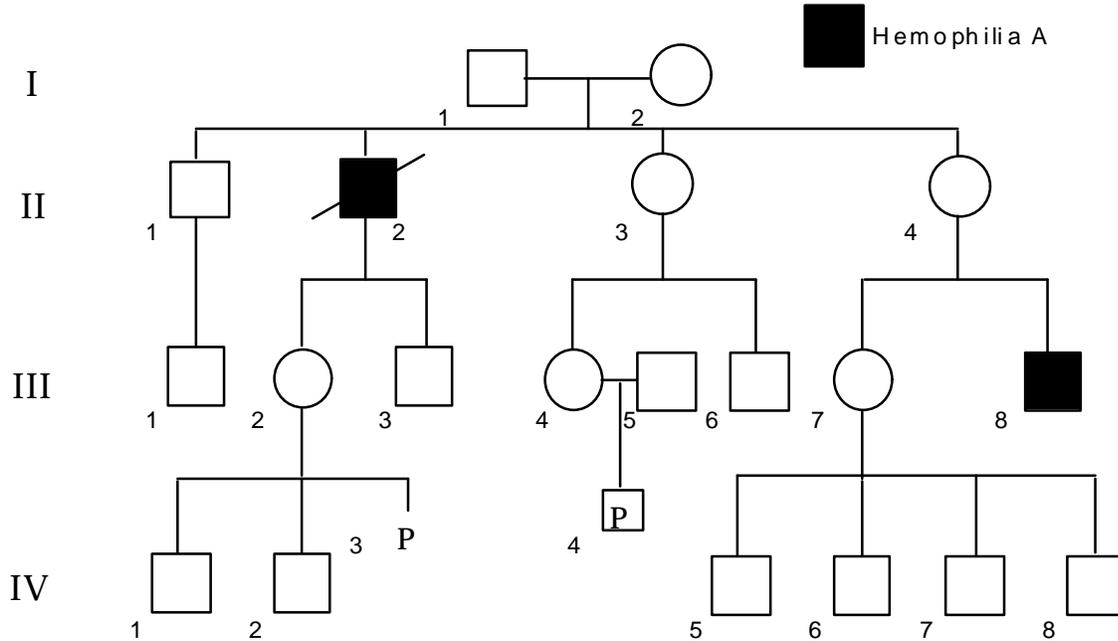


- A. Angelman syndrome
 B. fragile X syndrome
 C. Prader-Willi syndrome
 D. trisomy 15
 E. William syndrome
14. Anhidrotic ectodermal dysplasia is an X-linked recessive condition in which affected males lack sweat glands. Other structures derived from the ectoderm, such as the hair, teeth, and nails, are also affected. Mothers of affected sons often have patchy areas of anhidrotic skin. This mosaic pattern results because of:
- A. anticipation
 B. enhancer genes
 C. loss of heterozygosity
 D. heteroplasmy
 E. X inactivation
15. Which of the following parameters in maternal serum is the most useful for detecting Down syndrome in the second trimester?
- A. AFP (alpha-fetoprotein)
 B. hCG (human chorionic gonadotropin)
 C. estriol
 D. PAPP-A (pregnancy associated placental protein A)
 E. fetal cells in maternal blood

Questions 16-19. Select the BEST answer from the following (each answer may be used more than once):

- A. multiplex PCR analysis
 - B. fluorescence in situ hybridization
 - C. allele specific oligonucleotide hybridization
 - D. Southern blot analysis
 - E. linkage analysis
16. A segment of DNA is amplified by PCR, divided into aliquots, dotted onto separate filter membranes, and hybridized with a probe.
17. A method of identifying DNA fragments separated by electrophoresis, transferred onto a membrane, and hybridized with a labeled nucleic acid probe.
18. The simultaneous amplification of different sequences in a single reaction using sets of primers specific for each sequence.
19. A method of localizing a cloned segment of DNA on a chromosome by the binding of labeled complementary DNA and visualization by specialized microscopy.
20. Twin studies comparing monozygotic and dizygotic twins are useful for trying to sort out how much of the total phenotypic variance is due to genetic factors. The reason twin studies are useful is because monozygotic and dizygotic twins:
- A. have the same genetic differences
 - B. have the same environmental differences
 - C. have the same genetic and environmental differences
 - D. have different environmental differences
 - E. have different environmental and genetic differences

Questions 21-26. Refer to the following pedigree of a family with hemophilia A:

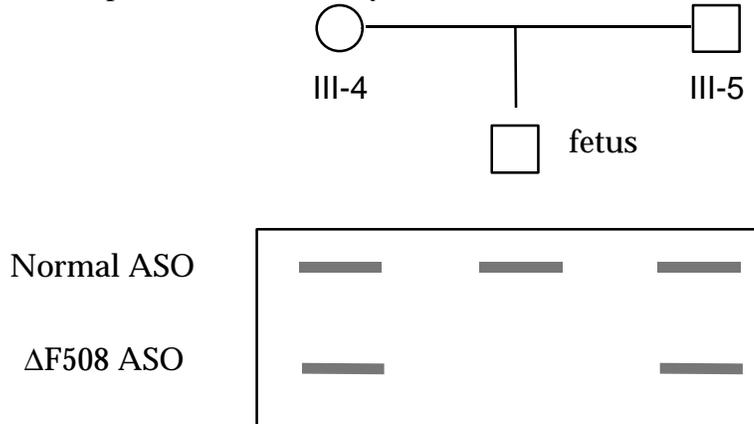


21. Individual III-2 is currently 6 weeks pregnant. She recently established contact with her biological father's family and discovered he died at age 20 from complications of hemophilia A. She comes for genetic counseling and wants to know the chance her fetus will be affected with hemophilia A? The risk you give her is:
- A. virtually 0
 - B. 1/20
 - C. 1/10
 - D. 1/4
 - E. 1/2
22. The woman you counseled in the previous question brings in her cousin (individual III-4) to the next genetic counseling appointment. Because of your excellent explanation of how hemophilia is inherited, the woman realizes her cousin (who is 20 weeks pregnant with a **male** fetus) is also at risk for having a child with hemophilia. You tell individual III-4 her risk for having a son with hemophilia is:
- A. virtually 0
 - B. 1/2
 - C. 1/4
 - D. 1/8
 - E. 1/16

23. In your efforts to do a thorough job after discussing with individual III-4 her chances of having a child with hemophilia, you diligently ask questions about her husband's family history. You discover her husband (individual III-5) had a 23 year old brother who died from complications of cystic fibrosis (not indicated in the pedigree). There is not a family history of cystic fibrosis in III-4's family. The incidence of cystic fibrosis in the general population is $1/2500$. After your calculations, you now have to tell III-4 the chances her unborn son is also affected with cystic fibrosis is:
- A. $1/16$
 - B. $1/20$
 - C. $1/75$
 - D. $1/125$
 - E. $1/150$
24. Individual III-3 calls you again a few weeks later wanting to bring in another cousin (III-7) who is thinking about becoming pregnant. She isn't sure, however, if this is necessary because this cousin has had four sons, none of whom have hemophilia A. You tell her this cousin should make an appointment because her risk for having a child with hemophilia is:
- A. $1/4$
 - B. $1/8$
 - C. $1/34$
 - D. $1/36$
 - E. $1/68$

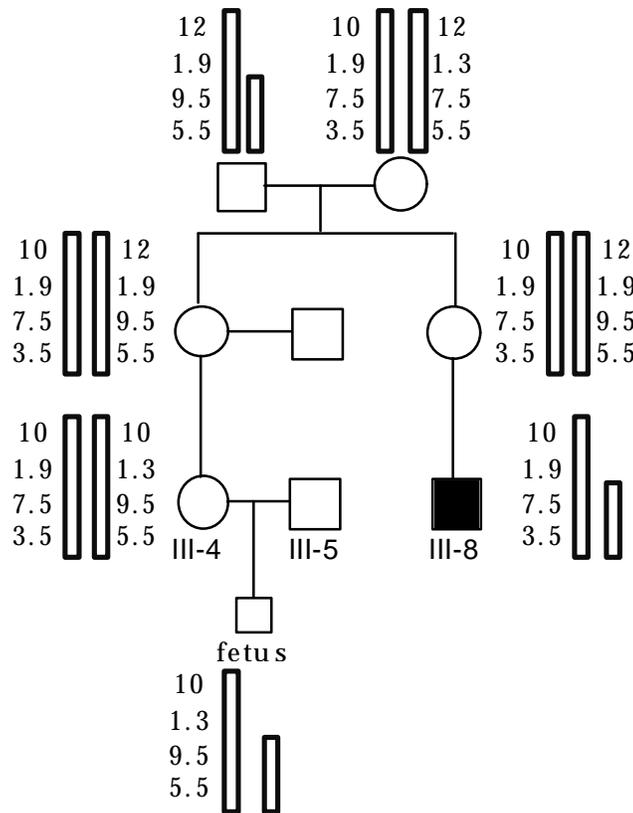
Meanwhile, you are still trying to help individual III-4 who is panic stricken about the prospect of her son having hemophilia A and/or cystic fibrosis. She is interested in prenatal diagnosis for both conditions. You yourself are a bit overwhelmed by this case and contact the molecular geneticist in the DNA Diagnostic Laboratory for help. He tells you to get a blood sample on the cousin with hemophilia A (individual III-8) to try and identify the mutation in this family. Since the brother with cystic fibrosis is not available for testing, he suggests getting blood samples on your couple (individual III-4 and III-5) to test for the more common mutations associated with cystic fibrosis. Because of time constraints, a sample is also taken from the fetus for DNA analysis. The DNA Diagnostic Laboratory has luck with the CF testing, but not with the hemophilia testing.

25. Below are the results of the allele-specific oligonucleotide probe (ASO) for the $\Delta F508$ mutation and the corresponding normal allele for individuals III-4, III-5, and their fetus. Interpret the results of the prenatal studies for cystic fibrosis.



- A. the fetus is homozygous unaffected
- B. the fetus is a heterozygous carrier
- C. the fetus is homozygous affected
- D. the results cannot be determined since DNA from the affected brother was not available
- E. the diagnosis of CF should be questioned in this case

26. Since the mutation within the hemophilia gene was not identified in individual III-8, linkage analysis is performed using four markers located very close to the hemophilia A gene. Your interpretation of the results of the following linkage studies is:



- A. the fetus is most likely affected with hemophilia A
 - B. the fetus is most likely unaffected with hemophilia A
 - C. the results of the linkage studies are uninformative
 - D. the results of the linkage studies have identified nonpaternity in this family
 - E. the results of the linkage studies have identified a crossover in the fetus
27. You are treating a young boy who has lactic acidosis, encephalomyopathy, and ragged red fibers seen on muscle biopsy. A careful family history shows the boy's mother has minimal muscle weakness and his older sister has recurrent headaches as well as seizures. DNA analysis was performed on muscle tissue from the boy and he was found to have a point mutation within his mtDNA. The inheritance of the disorder in this family is:
- A. autosomal dominant
 - B. autosomal recessive
 - C. mitochondrial
 - D. X-linked dominant
 - E. X-linked recessive

28. The major reason for the clinical variability of symptoms in the different family members described in question #27 is because of:

- A. allelic heterogeneity
- B. anticipation
- C. heterodisomy
- D. heteroplasmy
- E. imprinting

Questions 29-32. Select the BEST answer from the following (each answer may be used more than once):

- | | |
|---------------|--|
| A. 47,XX,+13 | F. 69,XXX |
| B. 47,XX,+18 | G. 46,XX,4p- |
| C. 47,XX,+21 | H. 46,XX,5p- |
| D. 47,XXY | I. 46,XX,-6,+der 6,t(6;12),(p13;q26) |
| E. 45,X/46,XY | J. 46,XX,-12,+der 12,t(6;12),(p13;q26) |

29. An obstetrical ultrasound at 20 weeks gestation shows a fetus that measures approximately 18 weeks in size with holoprosencephaly, cleft lip and palate, and an extra small finger on each hand.

30. While on Peds Cardiology, your chief resident asks you to stop by the neonatal intensive care unit to see a newborn transferred from upstate with a significant flow murmur and a preliminary echocardiogram diagnosis of a large ventriculoseptal defect. The female infant was born quite small-for-gestational age and is very irritable with increased general muscle tone despite medications. During your exam, you confirm the grade III ventricular flow murmur but also notice clinodactyly in the infant's hand that is not taped onto an IV board. You suggest a karyotype to your impressed chief resident to rule out this possibility.

31. You are asked to counsel a couple with a child recently born with multiple congenital anomalies in which the wife was found to carry a balanced translocation. Which of the above choices would reflect the karyotype of their daughter who has a partial duplication of the long arm of chromosome 12 and partial deletion of the short arm of chromosome 6?

32. While on Obstetrics, you participate in the delivery of a 20 week stillborn infant that apparently died within the past 7-10 days. The fetus is small for gestational age and the placenta is rather large and unusual in appearance containing numerous grape-like cystic clusters. A brief exam of the infant finds syndactyly in the right hand and left foot. You suggest trying to obtain a karyotype from the fetus or placenta to rule out this chromosomal cause for the pregnancy loss.

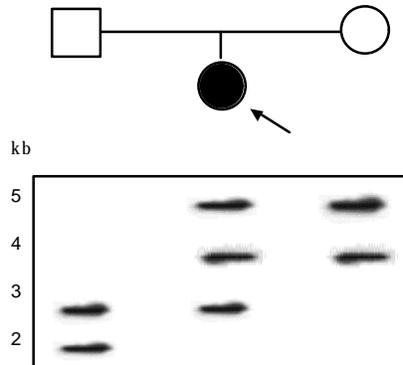
33. During which period of intrauterine development is the embryo/fetus most susceptible to malformations caused by teratogens:
- A. 1-3 weeks postconception
 - B. 4-6 weeks postconception
 - C. 10-12 weeks postconception
 - D. 2nd trimester
 - E. 3rd trimester
34. You are asked to evaluate a newborn male infant in the Neonatal Intensive Care Unit because of the sudden onset of lethargy progressing to coma. The symptoms began within 24 hours after the onset of formula feeding. The blood ammonia is markedly elevated, though the sodium, potassium, blood pH, and CO₂ are normal. The family history is significant in that the mother's brother died at 2 days of age of unknown causes and the mother had 1 previous son who died with similar clinical findings. Physical exam revealed no dysmorphic features. The most likely diagnosis is:
- A. deficiency of galactose 1-phosphate uridyl transferase
 - B. deficiency of phenylalanine hydroxylase
 - C. deficiency of 21-hydroxylase
 - D. deficiency of ornithine transcarbamylase
 - E. deficiency of propionyl CoA carboxylase
35. Hardy-Weinberg equilibrium is observed under certain conditions. One population phenomenon that is required for Hardy-Weinberg to be effective is a large population that mates randomly. If a population is small, there is a greater chance for random fluctuations in gene frequency. This is referred to as:
- A. genetic drift
 - B. heterozygote advantage
 - C. inbreeding
 - D. migration
 - E. selection
36. Prenatal therapy using diverting shunts to date is most effective in improving the outcome in which fetal condition:
- A. diaphragmatic hernia
 - B. endocardial cushion defect
 - C. hydrocephaly
 - D. obstructive uropathy
 - E. spina bifida

37. If both parents are carriers of a recessive allele which is lethal *in utero* in the homozygous state, what proportion of their liveborn offspring will be genetic carriers for this allele?
- A. 1/4
 - B. 1/2
 - C. 1/3
 - D. 2/3
 - E. 3/4
38. Ruth and Tom Robin are the young couple who came to see you during Case Study II because they are anxious to start a family. Their obstetrician has referred them because he realizes they have a greater risk for having children with a specific group of inherited conditions. Tom and Ruth are first cousins and Ruth has phenylketonuria (PKU). Ruth is clinically normal and was treated with a strict low phenylalanine diet through the age of fifteen. You discuss with them their risk for having a child with PKU as well as other autosomal recessive disorders because of the consanguinity. You also realize they have a potentially significant risk for having children with other birth defects, so you talk to them about:
- A. maternal age
 - B. maternal imprinting
 - C. maternal inheritance
 - D. maternal PKU
 - E. maternal uniparental disomy

Questions 39-41. Select the BEST prenatal test from the following options to offer to the patient in each of the following clinical descriptions (each answer may be used more than once) to address the clinical issued raised in each case.

- A. maternal serum screening for biochemical markers
 - B. chorionic villus sampling
 - C. traditional amniocentesis
 - D. fetal blood sampling (cordocentesis)
 - E. fetal endoscopy
39. A 24 year old woman, 14 weeks pregnant, with no family history of birth defects, mental retardation, or miscarriages.
40. A 30 year old woman at 18 weeks gestation that has a screening ultrasound which shows mild ventriculomegaly, nuchal thickening, and an endocardial cushion defect present in her fetus.
41. A 19 year old woman, presently at 17.5 weeks gestation, who has had two elevated maternal serum alpha-fetoprotein (MSAFP) values on prenatal screening at 15 and 16 weeks gestation.

42. A child has Patau syndrome (trisomy 13). One RFLP on chromosome 13 near the centromere has alleles of 5, 4, 3, or 2 kb. Shown below is a diagram of a Southern blot for the child, her father, and her mother. What is the parental origin and stage of meiosis of the error leading to this case of trisomy 13?



- A. maternal meiosis I
- B. maternal meiosis II
- C. paternal meiosis I
- D. paternal meiosis II
- E. cannot be determined from the information given

Questions 43-45. Select the BEST answer from the following (each answer may be used more than once):

- A. nucleosome
- B. centromere
- C. telomere
- D. 30 nm chromatin fiber

43. directly participates in meiotic segregation

44. helps to control the positions and interactions of chromosomes within the interphase nucleus, and is essential for normal chromosomal replication

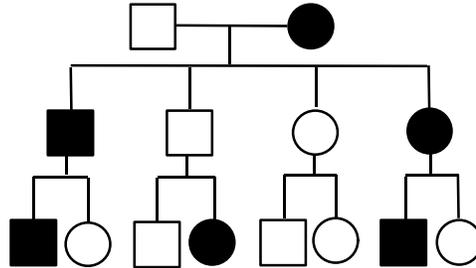
45. the presence of histone 1 leads to the formation of this basic chromatin structure

46. Extended family members of Mr. R's (the man and his wife who you counseled in Problem Set 1) come for genetic counseling because of the Robertsonian translocation in their family. A first cousin of Mr. R's who is currently 6 weeks pregnant is karyotyped. Ten days later you receive the following result from the cytogenetics laboratory: 45,XX,-13,-14,+t(13;14). You tell her she has an increased risk for having a liveborn child with which of the following chromosome abnormalities?

- A. monosomy 13
- B. trisomy 13
- C. monosomy 14
- D. trisomy 14
- E. all of the above

47. What is the actual risk for the woman you counseled in question # 46 to have a liveborn child with a chromosome abnormality?
- A. 1%
 - B. 10-12%
 - C. 25%
 - D. 50%
 - E. 67%
48. Mr. R's cousin comes back to see you at 8 gestational weeks. You counsel her about her increased risk for having a child with a chromosome abnormality. You also talk to her about the pros and cons of various prenatal diagnostic procedures. She understands all the information and tells you she is very anxious about having a child with a chromosome abnormality and wants definitive prenatal diagnosis as soon as possible. You schedule her for which prenatal diagnostic procedure?
- A. amniocentesis
 - B. chorionic villus sampling
 - C. cordocentesis (fetal blood sampling)
 - D. fetal muscle biopsy
 - E. maternal serum biochemical screening
49. Whether or not there is a cause and effect relationship between a potential human teratogen and a structural anomaly in a baby can be difficult to ascertain. A complete prenatal history of the exposure must be collected and other causes for the anomaly need to be considered. Also, experience with other women who have been exposed to the agent in question and information about their reproductive outcomes is critical when trying to answer the question about cause and effect because:
- A. if the agent in question has been previously associated with any type of birth defect, its' teratogenicity is proven
 - B. genetic factors do not play *any* role in the underlying causative mechanism of a drugs' teratogenic potential and, therefore, you can directly apply the experiences of other women and their reproductive outcomes when counseling patients
 - C. if the agent in question is a teratogen, it will cause a birth defect in every woman who is exposed to this agent during pregnancy
 - D. it is important to look for patterns or combinations of birth defects since all known human teratogens produce reasonably well-defined patterns of defects
 - E. the resulting birth defect in the offspring of different women will be the same even if the exposure occurred at different times during the pregnancy

50. The following pedigree is best described by which of the following pattern of inheritance:



- A. autosomal dominant
- B. autosomal recessive
- C. X-linked dominant
- D. X-linked recessive
- E. mitochondrial

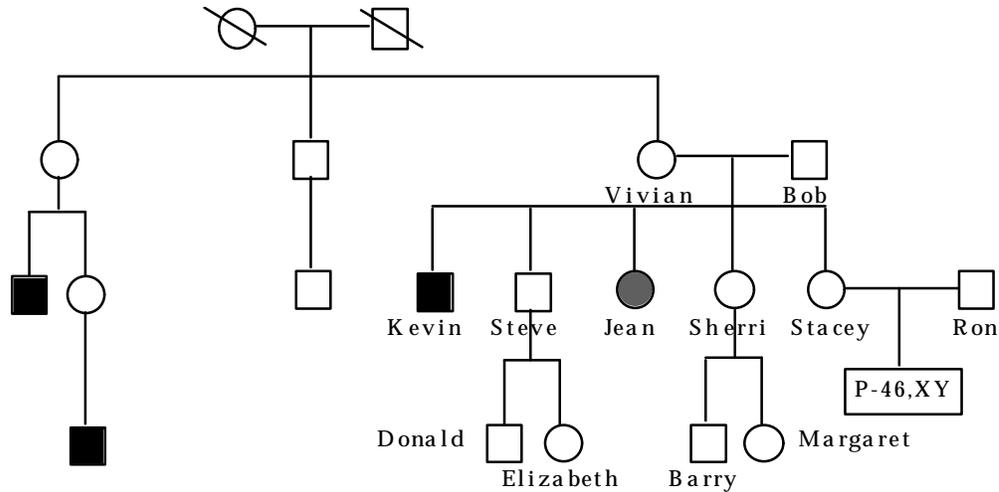
Questions 51-55. Match each of the following clinical situations with the term that best describes it (each term may be used more than once):

- A. allelic heterogeneity
- B. locus heterogeneity
- C. variable expression
- D. nonpenetrance
- E. anticipation
- F. new mutation

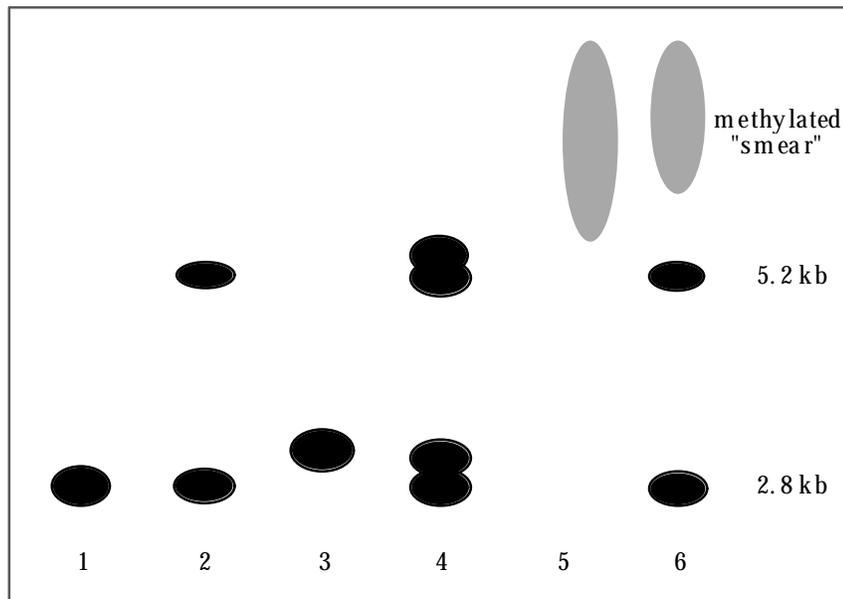
- 51. A family with neurofibromatosis type I, where the father has 7 large cafe au lait spots and axillary freckling, but his daughter has an optic glioma, many cutaneous neurofibromas and cafe au lait spots.
- 52. X-linked spinal and bulbar muscular dystrophy and testicular feminization syndrome, both caused by mutations in the androgen receptor gene.
- 53. Autosomal dominant, autosomal recessive, and X-linked forms of Charcot-Marie-Tooth disease, a disorder of peripheral nerves.
- 54. A phenotypically normal father whose son and mother have the same autosomal dominant condition.
- 55. A man who developed Huntington disease at age 40 has a son with a movement disorder at age 12.

Question 56-58 refer to the following information about the family you counseled in Case Study I.

The affected individuals in the pedigree below have mental retardation due to an expanded trinucleotide (CGG) repeat in their FMR-1 gene.



Several family members in the pedigree above undergo DNA analysis. The restriction enzyme Eag I cuts at the restriction site only if the gene is not methylated. If the normal gene is cut, a 2.8 kb fragment is detected on Southern blot, if it is not cut, a 5.2 kb fragment is detected. The results of the studies from different family members are indicated in the following Southern blot analysis.

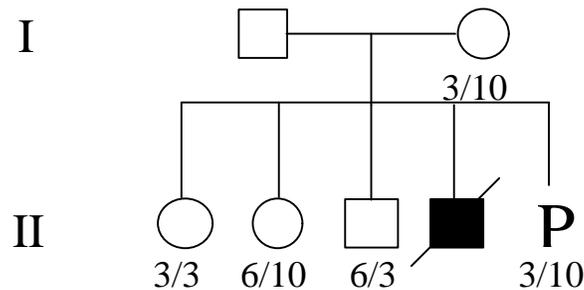


56. Elizabeth undergoes carrier testing. The results of her studies are in lane 4 of the Southern blot analysis. She is a:
- A. normal male
 - B. normal female
 - C. premutation female
 - D. affected male
 - E. affected female
57. Elizabeth's father, Steve, refuses to give a blood sample for DNA analysis. He is a physician and states he completely understands X-linked inheritance and it is impossible for him to carry a FMR-1 mutation since he is normal. Without even having to do DNA analysis on Steve, you are certain he:
- A. is absolutely correct and must have a normal gene
 - B. doesn't understand the inheritance of fragile X mental retardation since he must have a premutation
 - C. could never have completed medical school since he must have a full mutation
 - D. is not Elizabeth's father
 - E. has some type of deleterious mutation on his Y chromosome
58. You previously studied Stacey during Case Study 1 and identified a premutation in her FMR-1 gene. Other family members studied included Kevin and Jean who both have full mutations, and Sherri who has a normal gene. Elizabeth was studied recently. During Stacey's first pregnancy the male fetus was found to have a normal FMR-1 gene. She comes back to see you a year later because she is pregnant with her second baby. The results of the prenatal studies are found in lane 6. You talk to her about the clinical manifestations of this result explaining her unborn baby's phenotype will most likely resemble which family member?
- A. her brother Kevin
 - B. her brother Steve
 - C. her sister Jean
 - D. her sister Sherri
 - E. her niece Elizabeth

59. You are asked to evaluate a 9 month old female infant who recently moved to the United States from South America. She is the offspring of first cousin parents. She has unexplained developmental delay, seizures, an eczema-like rash, and metabolic acidosis. A survey of various biochemical parameters indicates that she has a deficiency of four carboxylase enzymes. The most likely diagnosis is:

- A. arginase deficiency
- B. biotinidase deficiency
- C. congenital cytomegalovirus infection
- D. propionyl CoA carboxylase deficiency
- E. tyrosinemia

Prenatal diagnosis is attempted for an autosomal recessive condition in the family shown below. The results are from genotyping using a VNTR marker located in the gene in which mutations causing the phenotype have been identified. The father (I-1) and affected child (II-4) were not available for testing.



60. What is the phenotype of the unborn child II-5 likely to be?

- A. the pedigree is not informative enough to answer the question
- B. the child is most likely affected
- C. there is nonpaternity
- D. the child is most likely unaffected
- E. the phenotype depends on the sex of the child

61. Which of the children in the above pedigree are likely to be carriers of the disease?

- A. II-1 and II-3
- B. II-2 and II-3
- C. II-1 and II-5
- D. II-2 and II-5
- E. II-1 and II-2

Questions 62-64. Select the BEST answer from the following (each answer may be used more than once):

- A. meiosis I
- B. meiosis II
- C. mitosis

62. genetic recombination occurs

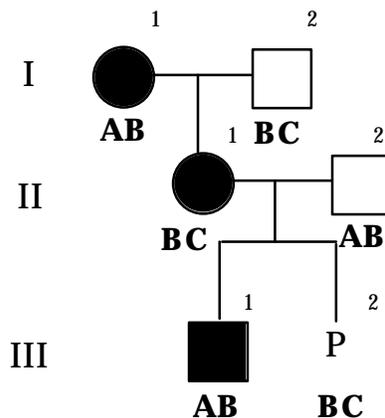
63. a nondisjunctional event would result in two genetically identical chromosomes within the gamete

64. chromosomal bivalents are observed

65. When screening populations for genetic disorders, it is important screening tests have relatively high sensitivity and specificity, a relatively low rate of false-positive and false-negative results, and a relatively good positive predictive value. Whether or not your screening test fits this criteria depends largely on your target screening population because:

- A. the sensitivity will vary depending on your population
- B. the specificity will vary depending on your population
- C. the false-negative rate will vary depending on your population
- D. the false-positive rate will vary depending on your population
- E. the positive predictive value will vary depending on your population

66. The following is a pedigree in which the affected individuals have neurofibromatosis I.



The mother (II-1) of the affected son (III-1) is pregnant and has had prenatal testing based upon a set of markers closely linked to the NF1 gene. Haplotypes are given for each relative and the fetus. What is the probability that the fetus will be affected?

- A. less than 1 in 100
- B. 1 in 4
- C. 1 in 2
- D. 2 in 3
- E. greater than 99 in 100

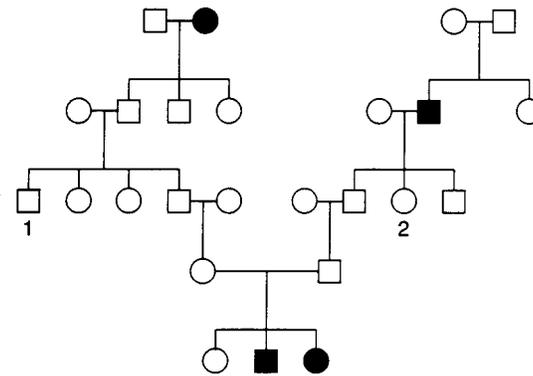
67. The Human Genome Project is a federally funded research effort to map and sequence all of the approximately 100,000 genes. The purpose behind mapping and sequencing all human genes is:
- A. to obtain a DNA profile on all inmates in state prisons
 - B. for human cloning purposes
 - C. so insurance companies can improve their profit margins
 - D. to provide diagnostic tests and to develop better treatments for human diseases
 - E. to remove deleterious genes from the gene pool
68. In the first trimester, the ultrasound marker that has the highest sensitivity for detection of Down syndrome is:
- A. choroid plexus cyst
 - B. hyperechogenic bowel
 - C. omphalocele
 - D. nuchal translucency
 - E. urinary tract abnormalities

Questions 69-71. For each clinical situation select the most likely diagnosis from the following (each answer may be used more than once):

- | | |
|-------------------------------------|--------------------------------------|
| A. cystic fibrosis | F. Tay-Sachs disease |
| B. fragile X syndrome | G. hypohydrotic ectodermal dysplasia |
| C. Sanfilippo mucopolysaccharidosis | H. hereditary baldness |
| D. propionic acidemia | I. Marfan syndrome |
| E. pneumonia | J. Stickler syndrome |

69. A 5 year old was developing normally up to the age of 2 years. She was prescribed Ritalin for hyperactivity at age 3 years. She has progressive developmental delay, slowly enlarging head, thickened gums, and bushy eyebrows. Her spine x-rays show beaking of a few vertebrae. Her urine contains increased amounts of heparan sulfate.
70. Two year old Michael was brought to the pediatrician because only two teeth have erupted so far. His motor and mental development is normal. He has very sparse hair on the scalp, and has not needed a haircut yet. He used to get frequent high fevers during his first year of life.
71. Thirty year old Samantha started wearing eyeglasses at 2 years of age. She has started to have pain in her knees and hips after a day's work. She has just given birth to a baby boy who has a cleft of the palate and a small chin. Her family physician is wondering if the mother/child have a common condition.

72. Examine the following pedigree. What is the most likely pattern of inheritance?



- A. autosomal dominant
- B. autosomal recessive
- C. X-linked recessive
- D. X-linked dominant
- E. X-linked dominant with nonpenetrance

73. For the pedigree in question #72, what is the risk of having an affected child if individuals 1 and 2 are married?
- A. 1/16
 - B. 1/12
 - C. 1/8
 - D. 1/4
 - E. 1/2
74. Alice Ward, a pregnant 43 year old who was counseled during Case Study II, has a family history of spina bifida. Alice's nephew, Joshua, was born with spina bifida at the L1-L2 level. She wants to know if there is an increased risk for spina bifida in her current pregnancy and if there are any tests that can detect spina bifida prenatally. She is currently 10 weeks pregnant. Based on your complete risk assessment, you tell her:
- A. her chances of having a child with spina bifida is 3-5% and this birth defect can be detected if she undergoes chorionic villus sampling or amniocentesis
 - B. her chances of having a child with spinal bifida is 3-5% and this birth defect can be detected only if she undergoes chorionic villus sampling
 - C. her chances of having a child with spina bifida is 3-5% and this birth defect can be detected only if she undergoes amniocentesis
 - D. her chances of having a child with spina bifida are not increased above the general population incidence and she is at an increased risk for having a child with a chromosome abnormality which can be detected if she undergoes chorionic villus sampling or amniocentesis
 - E. her chances for having a baby with spina bifida is 3-5% and she has an increased risk for having a child with a chromosome abnormality; both of these disorders can be detected if she undergoes amniocentesis
75. Medical genetics is deeply committed to patient autonomy and informed decision making. We provide patients and their families with information and support so they can make informed decisions about child bearing, prenatal testing, abortion, presymptomatic genetic testing, medical management, and lifestyle. The reasons why different families faced with the same genetic diagnosis make different decisions are respected and valued in the field of medical genetics. As we got a sense of from the patient panel on Tuesday and the videoclips from the PBS documentary at the beginning of this course, individuals and their families react differently because:
- A. there is a spectrum of belief and value systems within our society
 - B. of differences in how risks are perceived
 - C. previous life-changing experiences vary
 - D. the coping mechanisms differ from family to family
 - E. of all of the reasons stated above

