Year 1 Medical Genetics
Final Exam
March 3, 1997

DIRECTIONS: Select the single best answer or completion of the statement.

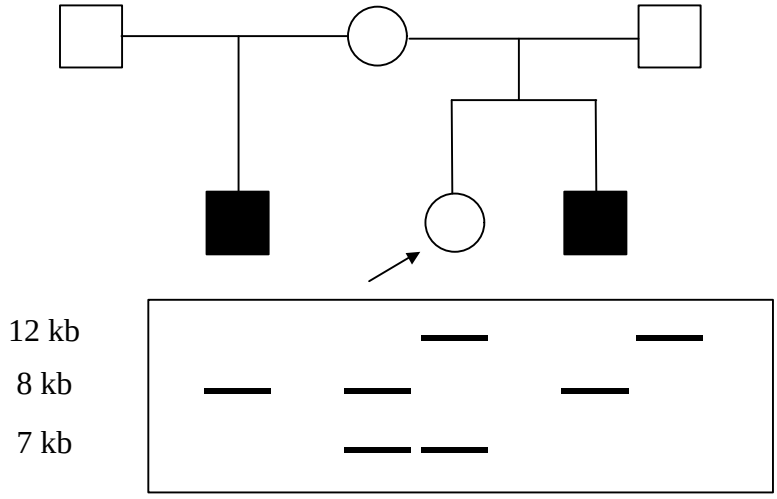
1. Examine the facial features of the infant in the slide being projected. The most likely diagnosis is:
   a) trisomy 13 syndrome
   b) trisomy 18 syndrome
   c) trisomy 21 syndrome
   d) 45,X syndrome
   e) 47,XXY syndrome

2. For multifactorial threshold traits, first degree relatives of an affected individual have a higher genetic liability because:
   a) they share the same environment
   b) they have 25% of their genes in common with the affected individual
   c) they have 50% of their genes in common with the affected individual
   d) the threshold is higher for first degree relatives than for the general population
   e) they have the same correlation coefficient as the affected individual

3. Pedigrees are a valuable tool for understanding the inheritance pattern of a disease within a family. At times it can be difficult to decipher the pattern because of ascertainment problems and the variation in severity of the disease among family members. The most significant clue a pedigree represents an autosomal dominant inheritance pattern rather than an X-linked pattern is:
   a) there will clearly be an affected person in each generation
   b) there are equal numbers of affected males and females
   c) all males live long enough to be able to father children
   d) there is male-to-male transmission evident at least once
   e) the females are more severely affected than the males

4. A woman 12 weeks into her first pregnancy comes to you requesting genetic counseling. She is concerned because her sister has a son with severe muscle weakness, similar to the condition from which her younger brother and a maternal uncle had died. Your preliminary assessment of the risk of this muscle disorder in the current pregnancy is:
   a) 1/2
   b) 1/4
   c) 1/8
   d) 1/16
   e) 1/32

5. A young woman has a brother and a half-brother who are both profoundly mentally retarded. Further assessment reveals both have severe hydrocephalus due to stenosis of the aqueduct of Sylvius. In some families, including this one, this kind of hydrocephalus is inherited as an X-linked recessive trait. DNA linkage studies are performed using a marker within the gene.



What is the status of the consultand (individual marked with an arrow)?

a) she is not a carrier
b) she is a heterozygous carrier
c) she is a hemizygous carrier
d) the studies are not informative
e) she has a chromosome abnormality

6. Infantile Tay-Sachs disease is
   a) treatable by liver transplantation
   b) treatable by enzyme replacement therapy
   c) universally fatal
   d) treatable by bone marrow transplantation
   e) treatable by a specific vitamin cofactor

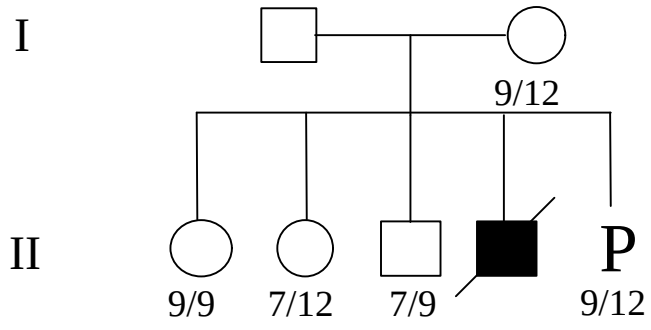
7. The presence of two chromosomally different cell lines originating within a single organism is known as:
   a) aneuploidy
   b) chimerism
   c) disomy
   d) mosaicism
   e) polyploidy

8. You and a resident are called to help in the delivery a woman in the emergency room. She is 42 years old, has 5 healthy children, very sporadic prenatal care, and no prenatal testing or ultrasounds. She thinks she is 1 week early from her assigned due date. The infant rapidly delivers and is very small based on the mother's expected gestational age. During the exam, the resident freaks out and leaves the room. You and the nurse examine the infant and find polydactyly, midfacial clefting, cyclopia and a nose-like structure on its forehead region. You explain that the facial findings appear to represent a developmental field defect, predict there are major malformations of the forebrain and suggest blood from the umbilical cord be sent for karyotyping to confirm your working diagnosis of :
    a) trisomy 13 syndrome
    b) trisomy 18 syndrome
    c) trisomy 21 syndrome
    d) 4p - syndrome
    e) 5p - syndrome

9. Fetuses with congential obstructive uropathies, usually due to urethral atresia or posterior urethral valves, develop progressive oligohydramnios because the fetal urine cannot pass into the amniotic space. This is associated with renal dysplasia and failure, with other developmental consequences responsible for the <u>majority</u> of newborn deaths. The primary purpose for prenatal *in utero* therapy in such cases is to prevent:
    a) pulmonary hypoplasia
    b) severe joint contractures
    c) hepatic dysplasia
    d) duodenal atresia
    e) vesico-rectal fistula

Questions 10-11:

Prenatal diagnosis is attempted for an autosomal recessive condition in the family shown below. The results are from genotyping using a VNTR marker located within the gene. The father (I-1) was not available for testing.



10. 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) the paternity is not clear
    d) the child is most likely unaffected
    e) the phenotype depends on the sex of the child

11. Which of the children 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

12. The severity of a particular mitochondrial disease such as MERRF can vary within a family because of:
    a) uniparental disomy
    b) chromosomal nondisjuntion
    c) allelic heterogeneity
    d) varying mutations in proto-oncogenes
    e) heteroplasmy

13. Cell proliferation is usually not associated with:
    a) early stages of embryogenesis
    b) a response to environmental ques
    c) the activity of stem cell populations
    d) determination of embryonic cells
    e) terminal differentiation

14. Which of the following would be descriptive of fragile sites within chromosomes:
    a) regions which are susceptible to breakage when exposed to cold temperature
    b) randomly distributed throughout the genome in a highly variable manner that differs from cell to cell
    c) the majority of such sites have clinically significant phenotypic expression
    d) many occur adjacent to proto-oncogenic regions
    e) are induced cytogenetically when cells are grown in culture media containing two or more antibiotics

15. The goal of the Human Genome Project (HGP) is to identify all the human genes. This project has enabled the development of many new screening and diagnostic tools for genetic conditions and also the potential for their treatment. There are also potential risks associated with HGP which include:
    a) possible misuse of genetic information
    b) potential for discrimination in jobs, insurance, and schools
    c) over commercialization of genetic research without proper safeguards
    d) uneven access to services based on location or ability to pay
    e) all of the above

16. The effects from maternal PKU can currently be prevented by:
    a) placing the woman on a protein-free diet
    b) supplementing the woman's diet with folic acid
    c) supplementing the woman's diet with phenylalanine
    d) placing the woman on a diet which limits her phenylalanine intake
    e) supplementing the woman's diet with the phenylalanine hydroxylase

17. You are asked to consult on a newborn infant who has multiple malformations and the following chromosomal abnormality: **46,XX,-6,+der 6,t(6;10),(p12;p11)pat**. Based on the karyotype results, which of the following is correct:
    a) the infant is a male
    b) the father carries an apparently balanced translocation involving chromosomes 11 and 12
    c) the infant has a partial deficiency for chromosome 6
    d) the infant has a partial deficiency for chromosome 10
    e) the chromosomal rearrangement involves the short arms of chromosomes 12 and 11

18. A 15 year old high school basketball player has developed progressive myopia, has very long arms and legs, scoliosis, and a recent physical found slight dilatation of the root of the aorta. Which of the following is the most likely explanation for these findings?
    a) homocystinuria
    b) Marfan syndrome
    c) Ehlers Danlos syndrome
    d) familial tall stature
    e) Klinefelter syndrome

19. The chromosomes begin the process of condensation from their diffuse interphase distribution into well defined chromosome structures in which phase of mitosis:
    a) prophase
    b) metaphase
    c) anaphase
    d) telophase
    e) cytokinesis

20. A man has a son by his first wife with ornithine transcarbamylase (OTC) deficiency. His new wife is concerned about having an affected child. The disease frequency in the general population is 1/20,000 ($\sqrt{20{,}000} \cong 140$). You would tell her her risk to have an affected child is:
    a) 1/2
    b) 1/4
    c) 1/10,000
    d) 1/20,000
    e) 1/40,000

21. A couple requests genetic counseling because the husband's brother has Becker muscular dystrophy. You can tell them:
    a) the chance of a son being affected is 50%
    b) the chance of a daughter being a carrier is 50%
    c) the chance of a son being affected virtually 0%
    d) the chance of a son being a carrier is 50%
    e) the chance of a son being affected is 25%

22. The most *accurate* genetic counseling can be provided if
    a) there is an extended family history of a problem
    b) there is a definite diagnosis
    c) both members of a couple are present at the session
    d) the initial counseling session is scheduled one month after the proband is evaluated
    e) the proband is present at the session

23. You are studying a child with nondisjunctional trisomy 21 and are curious about the origin of the extra chromosome. Using a polymorphic marker for a gene located on chromosome 21, you find the following genotypes for the infant and parents and conclude the nondisjunctional event occurred in:

    child: A B D **mother: A B** **father: B D**

    a) maternal meiosis I
    b) paternal meiosis I
    c) maternal meiosis II
    d) paternal meiosis II
    e) the results are uninformative

24. First trimester sonographic evaluation may prove to be a useful early, noninvasive screening tool for aneuploid fetuses. The finding of a nuchal membrane (simple hygroma, nuchal translucency) in the *first* trimester is most often associated with an increased risk for:
    a) trisomy 21 syndrome
    b) trisomy 13 syndrome
    c) 5p- syndrome
    d) 45,X syndrome
    e) XXY syndrome

25. After studying your genetics handouts, you are exhausted and decide to take a long, relaxing hot bath for a break. After 20 minutes you burst into fatigue induced laughter after looking at the deep creases in your wrinkled hands and feet because you have diagnosed yourself as being transiently affected with:
    a) mosaic trisomy 8 syndrome
    b) trisomy 18 syndrome
    c) trisomy 21 syndrome
    d) Klinefelter syndrome
    e) Turner syndrome

26. A 9 month old infant has had progressive enlargement of his tongue along with rapid weight gain. His facial features otherwise do not appear coarse, and he seems to be developing normally. His liver or spleen is not enlarged, however, a tumor-like mass is felt on his left kidney. Which of the following is his likely diagnosis?
    a) hypothyroidism
    b) lysosomal storage disorder
    c) overgrowth syndrome due to maternal diabetes
    d) Beckwith-Wiedemann syndrome
    e) Prader-Willi syndrome

27. Fluorescent In Situ Hybridization (FISH) technology is based on the use of highly specific unique sequence molecular probes and a signal amplification process that makes probe recognition possible at the light microscopy level. Which of the following would be components of a typical FISH probe / recognition system:
    a) a complementary RNA (cRNA) probe to the target sequence
    b) a hapten, such as Biotin integrated into the cRNA probe
    c) fluorochrome labeled anti-Biotin IgA molecules to allow direct probe recognition
    d) non-fluorochrome labeled cross-linking proteins that stabilize the affinity protein-immunoglobulin complex
    e) fluorochrome labeled antibodies against the affinity molecule

28. In families at known high risk for 21-hydroxlase deficiency, which medication given during pregnancy has been shown to be effective in preventing the masculinization of female fetuses:
    a) vitamin A
    b) vitamin B-12
    c) betamethasone
    d) folic acid
    e) digoxin

29. An infant is born with holoprosencephaly, midfacial clefting, and cyclopia. There is no family history of this anomaly. G-banded blood karyotype analysis reveals a 46,XY, normal male. There is no polydactyly. The best explanation for these findings would be:
    a) an autosomal dominant gene mutation involving skull development
    b) a mutation in a single gene that directs facial differentiation
    c) a deletion of a small chromosomal segment, not obvious on G-banding, that contains a series of linked genes that control facial and ocular development
    d) a developmental field defect which interferes with normal forebrain development
    e) an X-linked mutation in the maternal germline that interferes with closure of the mandibular and maxillary facial plates

30. A newborn baby has ambiguous external genitalia, intrauterine growth retardation, overlapping fingers, microcephaly, upturned nose and a cleft palate. There is no lymphedema, the neck appears normal and the extremities are normal in length. Laboratory studies are most likely to show:
    a) 45,X karyotype
    b) 46,XX karyotype
    c) increased serum 7-dehydrocholesterol
    d) increased 17 hydroxyprogesterone (Androgen precursor)
    e) 46,XY / 45,X karyotype

Questions 31-33:

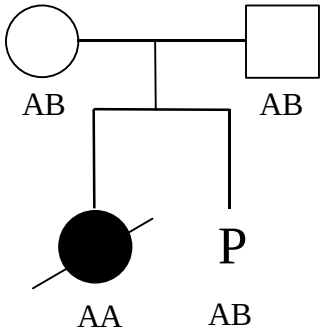
Mary is a 27 year old woman who is very involved in the mucopolysaccahidosis (MPS) support group. Mary's sister, Jane, died of Hurler syndrome (alpha-L-iduronidase deficiency) at age 8 years. Mary met two very nice men at the support group meeting, Joe and Bob, both of whom are affected with a MPS disorder. Joe has Scheie syndrome (alpha-L-iduronidase deficiency) and Bob has a mild form of Hunter syndrome (iduronate sulfatase deficiency). All of the defects are verified by enzyme testing. Mary is actively dating both Joe and Bob and wants to know her chances of having a child affected with a MPS disorder before deciding which man to marry.

31. If Mary marries Joe, what is the chance they would have a child affected with a MPS disorder:
    a) negligible
    b) 1/8
    c) 1/4
    d) 1/3
    e) 1/2

32. If Mary and Joe have a child affected with a MPS disorder, the child's genotype and clinical findings would be an example of which genetic principle(s):
    a) allelic heterogeneity
    b) locus heterogeneity
    c) inbreeding
    d) random mating
    e) uniparental disomy

33. If Mary marries Bob, what is the chance they would have a child affected with a MPS disorder:
    a) negligible
    b) 1/8
    c) 1/4
    d) 1/3
    e) 1/2

34. Two parents of Ashkenazi Jewish descent have had a child with Tay-Sachs disease. They are now expecting another child and wish to have prenatal diagnosis for this disorder. The pedigree shows the results of DNA analysis.



The most likely interpretation of the results for this pregnancy is the fetus is:
    a) homozygous affected
    b) homozygous normal
    c) a heterozygous carrier
    d) unable to determine from results
    e) unlikely to be the offspring of these parents

35. Elevations in maternal serum alpha-fetoprotein (MSAFP) levels are associated with an increased risk for:
    a) poor pregnancy outcome due to placental dysfunction
    b) trisomy 18 syndrome
    c) fetal cyclopia
    d) fetal holoprosencephaly
    e) 5p- syndrome

36. Retinoblastoma, a malignant tumor of the eye, can be inherited as an autosomal dominant trait. Penetrance in such families is 80% (4/5'ths). Ms. R's paternal grandmother, father, and brother had retinoblastoma, but Ms. R herself is unaffected. She is 12 weeks pregnant. What is the risk of retinoblastoma in Ms. R's fetus?
    a) virtually 0
    b) 1/4
    c) 1/6
    d) 1/12
    e) 1/15

37. While on your Pediatric Cardiology rotation, you are asked to consult on a newborn infant who has a loud heart murmur. On examination you document a flow murmur in the region of the aortic valve and aortic arch. The infant is a female and the pediatric resident you are working with wonders if the puffiness found in the hands and feet might be a sign of cardiac failure. You comment that there appears to be mild redundancy of skin in the nuchal region and suggest a banded blood karyotype to the surprise of the pediatric resident. This suggestion is based on your suspicion of:
    a) trisomy 13 syndrome
    b) trisomy 21 syndrome
    c) triploidy
    d) 45,X syndrome
    e) 4p - syndrome

38. A woman is seen for genetic counseling because her brother is said to have Marfan syndrome. She also tells you he is moderately mentally retarded and has scoliosis. You can tell her:
    a) based on the family history, she should have an echocardiogram and ophthalmologic exam to rule out Marfan syndrome
    b) because she is only 5'2" tall, she does not have Marfan syndrome and the risk to have an affected child is low
    c) her brother needs a formal genetic evaluation to confirm the diagnosis of Marfan syndrome
    d) a prenatal ultrasound evaluation can diagnose Marfan syndrome in the fetus
    e) the risk of having a son affected is higher than having a daughter affected with Marfan syndrome

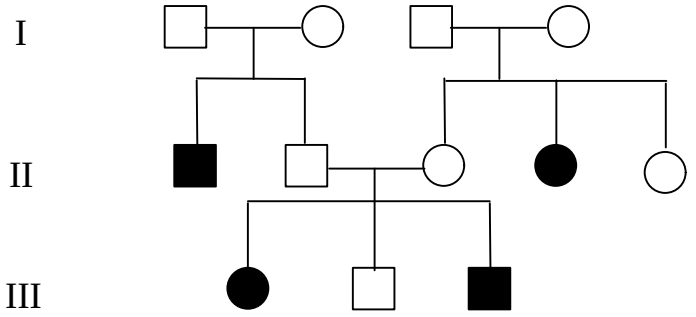
39. If the population incidence of a certain X-linked dominant condition in males is 1/20,000, then the expected incidence in the population of affected females is:
    a) 1 in 1,000
    b) 1 in 10,000
    c) 1 in 20,000
    d) 1 in 40,000
    e) 1 in 80,000

40. Which of the following pairs of signal transduction molecules are least likely to interact with each other:
    a) transcription factor: enhancer
    b) transcription factor: promoter
    c) growth factor: membrane receptor
    d) growth factor: promoter
    e) growth factor receptor: protein kinase

41. A young woman comes for genetic counseling because her only brother had Duchenne muscular dystrophy (DMD). He had DNA testing for the eight most common deletions associated with DMD which did not identify a deletion. He also had dystrophin histochemical studies following a muscle biopsy which showed the characteristic absence of this protein. Unfortunately this brother died last year and was cremated. DNA was not saved nor are tissue blocks available. No other family members are affected with DMD. The young woman is presently 8 weeks pregnant and wants to know whether or not her fetus has DMD. The best approach to carrier and/or prenatal testing is:
    a) DNA linkage studies on the woman and other family members to determine if she is a carrier; if she is a carrier, chorionic villus sampling and subsequent linkage studies on the fetus, if a male
    b) creatine phosphate kinase (CPK) levels in the woman and subsequently in the amniotic fluid if she is a carrier and the fetus a male
    c) chorionic villus sampling and subsequent deletion analysis if the fetus is a male
    d) determination of fetal sex by either chorionic villus sampling, amniocentesis, or ultrasound and in utero fetal muscle biopsy if the fetus is a male
    e) carrier testing is not necessary and prenatal diagnosis not appropriate in this case since the brother was a new mutation and the young woman is not at increased risk for having a son with DMD

Questions 42-43:

An autosomal recessive disease has a population frequency of 1/40,000. The pedigree below describes a family in which all affected individuals have the same disease.



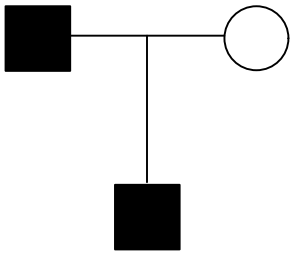
42. What is the probability of their first child being affected if individual II-1 marries the sister of his sister-in-law (II-5).
    a) 1/8
    b) 1/6
    c) 1/4
    d) 1/3
    e) 1/2

43. What is the probability of their first child being affected if individual II-1 marries someone from the general population.
    a) 1/100
    b) 1/200
    c) 1/400
    d) 1/600
    e) 1/800

44. Which of the following types of mutations would be expected to produce a more severe phenotype in osteogenesis imperfecta?
    a) a mutation which causes reduced production of a structurally normal protein
    b) a mutation which causes the production of normal quantities of a structurally abnormal protein
    c) a mutation which causes a neutral change in an amino acid
    d) a mutation that interferes with mRNA synthesis
    e) a mutation towards the N terminus of the protein

45. A 23 year old man suffers painless loss of central vision in his right eye. Three months later, he suffers similar visual loss in the left eye. He has no other symptoms and has been healthy throughout his life. A careful family history looking for sudden visual loss reveals a maternal uncle who suffered the same problem at a similar age. You suspect Leber's hereditary optic neuropathy and testing confirms the mitochondrial mutation. The patient is very worried about the possibility his two sons may be affected by the same problem he and his uncle have had. You tell him risks to his two sons is:
    a) virtually zero
    b) 100%
    c) 50 %
    d) each has a 50% risk of being a carrier
    e) each will be an obligate carrier

46. In the following pedigree, the chromosomally normal son has inherited hemophilia A from his father. The most likely mechanism which explains this is:



    a) paternal isodisomy
    b) paternal heterodisomy
    c) maternal isodisomy
    d) maternal heterodisomy
    e) nonpaternity

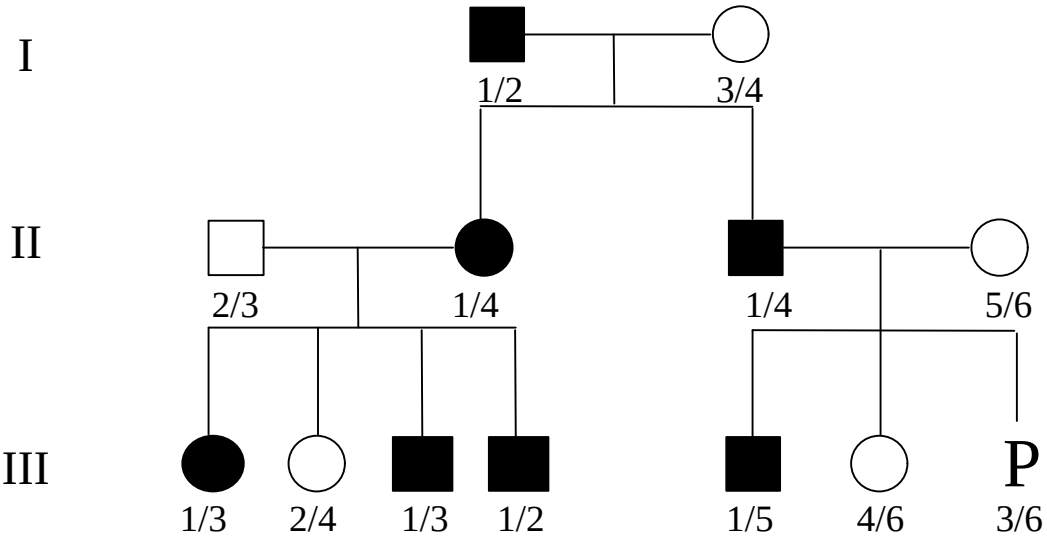
47. A healthy couple is seen for genetic counseling because the woman's father has hemophilia A. To provide this couple with an accurate risk for having a child affected with hemophilia A, you need to:
    a) do nothing further
    b) obtain a blood sample on the woman for factor VIII studies
    c) obtain a blood sample on the woman for DNA studies
    d) obtain a blood sample from the woman's mother for DNA studies
    e) obtain a more detailed family history

48. You are asked to counsel a couple who underwent chorionic villus sampling because of advanced maternal age. Chromosome analysis has revealed an abnormal 45,X/46,XY karyotype. You tell them their fetus might have:
    a) Turner syndrome
    b) ambiguous genitalia
    c) normal male genitalia
    d) a, b, and/or c
    e) Klinefelter syndrome

49. A 24 year old woman is referred for genetic counseling because she had a baby who was born with Down syndrome and died of complications following open heart surgery to correct an endocardial defect. Based on this information you can tell her:
    a) she has a 1% risk for having another child with a chromosome anomaly
    b) her risk is greater than 1% risk for having another child born with a chromosome anomaly because her previous child had severe complications of Down syndrome
    c) she is not at increased risk of recurrence
    d) prenatal diagnosis is not routinely offered to someone in her age group despite her history
    e) you cannot provide her with accurate counseling at this time without her previous child's karyotype result

Relax, take a deep breath
You're 2/3'rds there!!!!

50. Genotyping gives the following results in an autosomal dominant disorder when using a VNTR marker:



What is the phenotype of the unborn child III-7 likely to be?

a) the pedigree is not informative enough to answer the questions
b) the child is most likely affected
c) the paternity is not clear
d) the child inherited the gene, but is unaffected because of nonpenetrance
e) the phenotype depends on the sex of the child

51. If only women 35 years of age and older underwent prenatal testing, what percentage of trisomy 21 fetuses would be detected:

a) 5%
b) 20%
c) 35%
d) 40%
e) 65%

52. Mutations in the BRCA1 gene are associated with the increased risk of developing breast and ovarian cancer. In such cases, one mutation in the BRCA1 gene is transmitted through the germline. A second mutation at the other BRCA1 locus is necessary for tumor formation. Which of the following is not characteristic of an inherited cancer syndrome:
    a) earlier age of onset for tumors
    b) multiple family members affected by different types of cancer
    c) bilateral involvement of tissues with symmetric distribution like the breast
    d) multiple tumor foci within the same organ or tissue
    e) decreased risk of tumor development in individuals if the cancer is found in family members of a sex in which that tumor is rare (i.e., the risk to a particular women would be less for developing breast cancer because, besides her mother and aunt, a maternal uncle had breast cancer

53. A child is stillborn with multiple congenital anomalies. Skin was sent for karyotyping and returned 46,XX,-14,+rob(13;14)mat. The recurrence risk for subsequent pregnancies would be:
    a) not increased
    b) 1-2%
    c) 10-12%
    d) 65%
    e) 100%

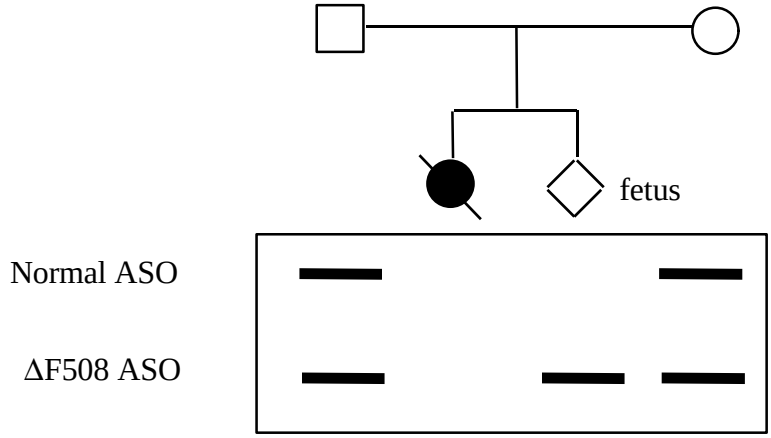
54. A couple who recently moved to Detroit from Belfast, Ireland have a child with isolated spina bifida. They are planning to have more children, but are concerned about the recurrence of this disorder and inquire about their options for prenatal testing. You would offer which of the following as the *most accurate* prenatal test for their particular concern:
    a) maternal serum alpha-fetoprotein screening
    b) high resolution ultrasound at 15 weeks gestation
    c) chorionic villus sampling at 10 weeks gestation
    d) amniocentesis at 15-16 weeks gestation
    e) cordocentesis at 20 weeks gestation

55. Which of the following medications should be avoided by individuals with a family history of malignant hyperthermia:
    a) primaquine
    b) naphthalene
    c) phenobarbitol
    d) halothane
    e) dantrolene

56. A couple seeks genetic counseling because their first child, a girl, was born with pyloric stenosis. You tell them:
    a) their risk for recurrence is not increased in future pregnancies
    b) their risk for recurrence is 3% based on multifactorial inheritance
    c) their risk for recurrence will depend on the sex of the next child
    d) their risk is 25%
    e) if the next child is a boy the risk will be lower than if the next child is a girl

57. Genetic recombination occurs during which phase of the cell cycle:
    a) metaphase I
    b) mitotic prophase
    c) meiotic prophase I
    d) meiotic prophase II
    e) both mitotic and meiotic prophase

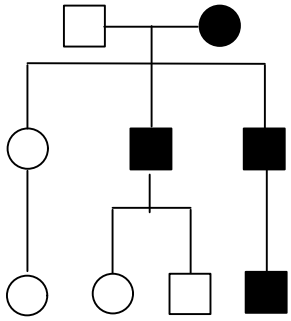
58. The family illustrated below has lost one child to cystic fibrosis. No DNA is available from the affected daughter. Below the pedigree are the results of the allele-specific oligonucleotide probe (ASO) for the ΔF508 mutation and the corresponding normal allele. Interpret the result of the prenatal studies.



    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 sister was not available
    e) the diagnosis of CF should be questioned in this case

59. The Philadelphia chromosome is a cytogenetic abnormality often observed in chronic myelogenous leukemia. The genetic basis for the development of this cancer is:
    a) the deletion of the *abl* proto-oncogene
    b) translocation and duplication / amplification of the *bcr* proto-oncogene
    c) loss of genetic heterogeneity at a tumor suppressor locus
    d) a deletional mutation adjacent to the *bcr* proto-oncogene causing autonomous expressing and subsequent unregulated cell growth
    e) repositioning of the *abl* proto-oncogen from the long arm chromosome 9, into the regulatory regions of the *bcr* cluster region of chromosome 22

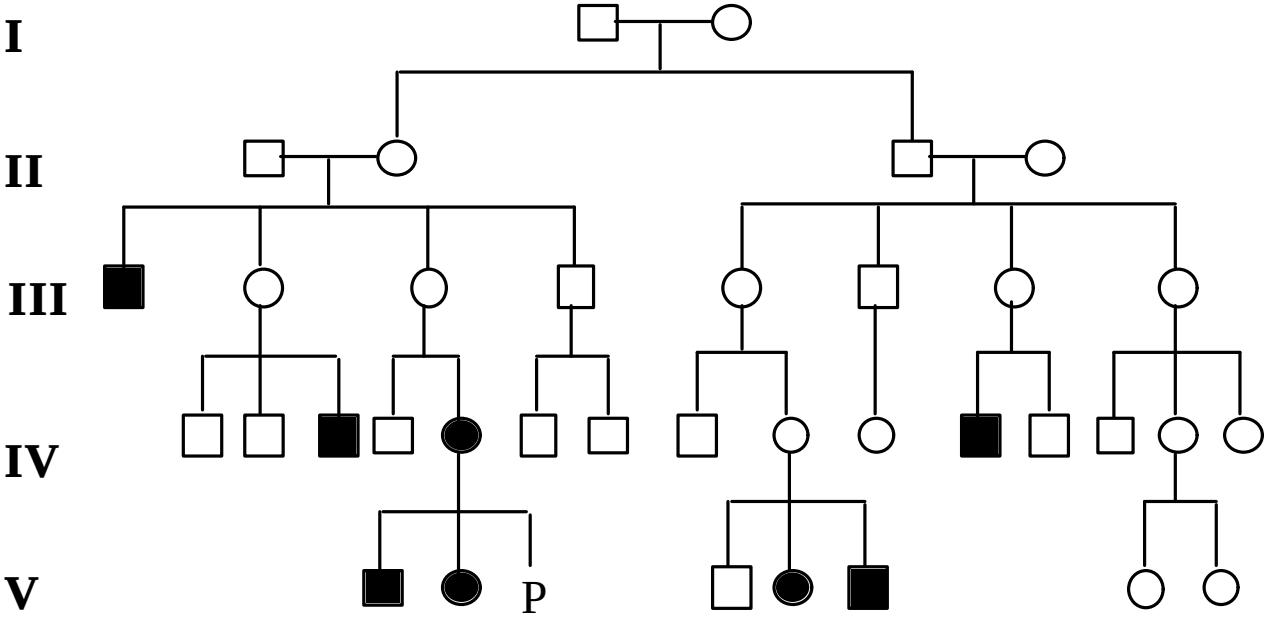
60. The following pedigree is <u>best</u> described by which of the following patterns of inheritance:



    a) autosomal dominant
    b) autosomal dominant with nonpenetrance
    c) autosomal recessive
    d) X-linked recessive
    e) mitochondrial

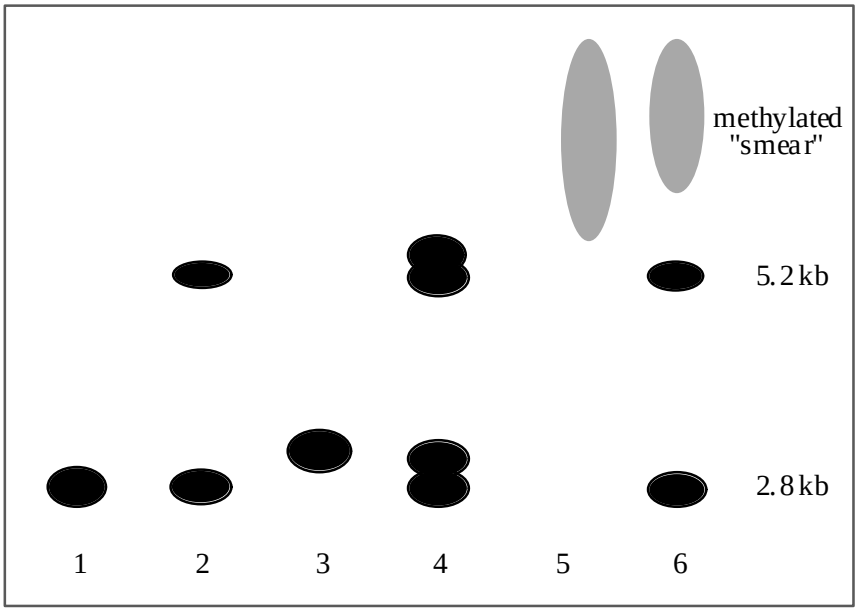
Questions 61-63:

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



61. Normally, the FMR-1 gene contains 6 to 52 repeats of the CGG, expansions from approximately 53 to 200 repeats are regarded as premutations, and those over 200 are full mutations. Individual III-8 undergoes DNA analysis to determine the number of CGG repeats in each of her FMR-1 genes. Which is the correct result?
    a) 24 / 29
    b) 51 / 29
    c) 160 / 29
    d) 230 / 29
    e) 3,490 / 29

62. Several family members in the pedigree above undergo DNA analysis. The restriction enzyme Eag 1 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. Individual IV-5 undergoes prenatal diagnosis. The results of the studies done on her fetus (V-3) are in lane 2 of the following Southern blot analysis. The fetus is:



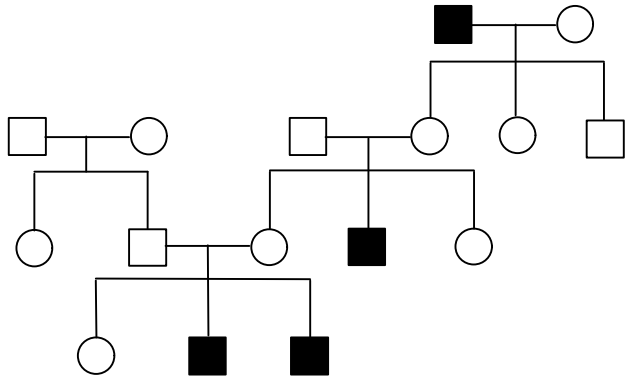
a) normal male
b) normal female
c) premutation female
d) affected male
e) affected female

63. Individual IV-9 has:
a) a normal gene
b) a premutation
c) a full mutation
d) either a premutation or a full mutation
e) two premutations

64. The Upper Slobivian Olympic Committee tried to substitude Oleg Vichnakov for his sister Olga on the women's weight lifting team. They got caught, of course, when a chromosomal check of the buccal smear cells revealed that Oleg/Olga had the wrong number of Barr bodies. Assuming that Oleg is a normal male, how many Barr bodies were seen in his buccal mucosal cells?
a) none
b) one
c) two
d) three
e) four

65. Anticipation is characteristic of conditions caused by:
    a) microdeletions
    b) mitochondrial inheritance
    c) genomic imprinting
    d) trinucleotide repeat expansions
    e) germline mosaicism

66. The following pedigree is <u>best</u> described by which of the following patterns of inheritance:



    a) autosomal dominant
    b) autosomal dominant with nonpenetrance
    c) autosomal recessive
    d) X-linked recessive
    e) mitochondrial

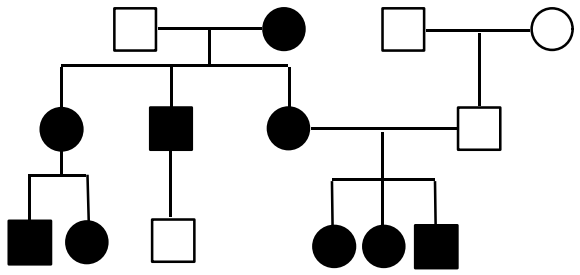
67. Open fetal surgery has been successful in the prenatal treatment of:
    a) congenital obstructive uropathy
    b) severe combined immunodeficiency syndrome (SCIDs)
    c) congenital diaphragmatic hernia
    d) neural tube defects
    e) plastic surgical repair of cranial-facial defects in syndromes such as Treacher-Collins

68. During the last century, a group of French Canadians moved to southern Louisiana. One of the members of this community was a gentleman who had an Ashkenazi Jewish heritage, but had converted to Catholicism and joined the group, the Arcadians, in their move. He was a carrier of Tay-Sachs disease. He fathered many children and now Tay-Sachs disease has an increased frequency among the Arcadian population in Louisiana. This phenomenon is referred to as:
    a) allelism
    b) balanced polymorphisim
    c) founder effect
    d) gene flow
    e) heterozygote advantage

69. Patients with mitochondrial myopathies do not usually improve spontaneously because:
    a) muscle is not highly aerobic and can go into oxygen debt
    b) mitochondrial turnover in muscle is very low
    c) muscle cells do not divide
    d) most mitochondrial proteins are encoded by nuclear DNA
    e) muscle cells are multinucleated

70. Multiple myeloma is a malignancy arising from antibody producing cells. Generally, a single class of antibody is produced by a given tumor, rather than a mixture of different antibody types. The best explanation for this is:
    a) the monoclonal basis of cancers
    b) multiple myeloma can only occur due to a series of mutations in cells that produce IgA
    c) mutations within B-cells lead to generalized abnormal cell grow, but the production of IgM in cells programmed to produce this particular immunoglobulin class results in the final step needed for malignant transformation
    d) the oncogene responsible for this malignant transformation causes down-regulation and suppression of the regulatory regions of the other immunoglobulin genes
    e) other classes of immunoglobulins have been clonally depleted by a series of mutations involving immunoglobulin expression over successive generations in the early stages of this malignancy

71. The following pedigree is best described by which of the following patterns of inheritance:



    a) autosomal dominant
    b) autosomal dominant with nonpenetrance
    c) autosomal recessive
    d) X-linked recessive
    e) mitochondrial

72. Which of the following clinical features would NOT indicate an inborn error of metabolism?

a) a child who is the second pregnancy to parents who are known to be consanguineous

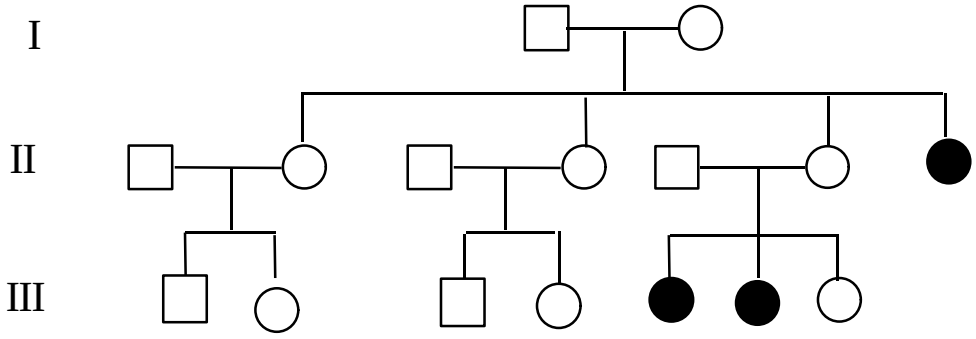
b) the parents of a child with mental retardation who have also had two early miscarriages, as did the maternal grandmother

c) an infant who was initially bright and alert and is now losing skills and paying little attention to the external environment

d) a previously well male infant with no dysmorphic features who suffers vascular collapse at 2 days of age

e) recurrent episodes of vomiting associated with elevated levels of ammonia in a 3 month old female

For questions 73-74, use the following pedigree of a family with testicular feminization and the risks (A-E).

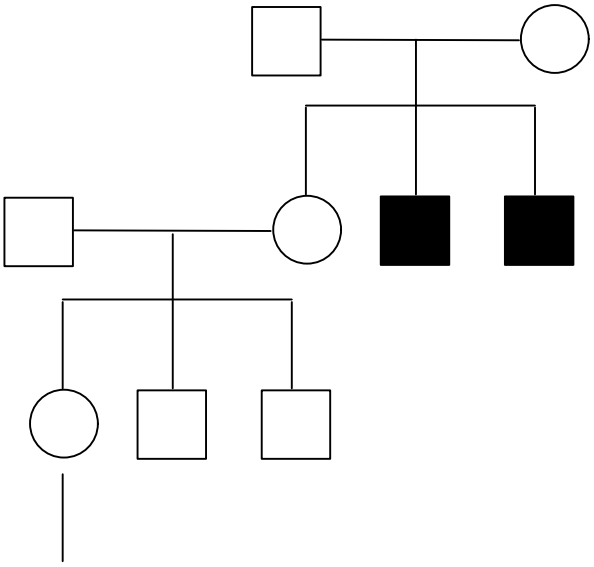


A. 100%
B. 50% (1/2)
C. 25% (1/4)
D. 12.5% (1/8)
E. virtually 0

73. What is the chance III-4 carries the testicular feminization gene?

74. What is the chance III-5 will have a child affected with testicular feminization?

75. What is the risk of hemophilia A in the male fetus?



a) 1 / 5
b) 1 / 8
c) 1 / 10
d) 1 / 20
e) 1 / 40