Year 1 Medical Genetics
Final Examination
March 1, 1996

DIRECTIONS: Select the <u>single best</u> answer or completion of the statement.

1. Which of the following is TRUE about meiotic nondisjunction?

   A chromosomal nondisjunction in meiosis I results in a gamete with disomy for a maternal and a paternal chromosome homolog
   B. chromosomal nondisjunction in meiosis II results in a gamete with disomy for identical maternal or paternal homologs
   C. meiotic nondisjunction resulting in disomic gametes increases with maternal age
   D. the majority of trisomic conceptions result from a chromosomal nondisjuction in maternal meiosis I
   E. all of the above answers are true!

2. A 35 y/o woman comes for prenatal genetic counseling at 12 weeks gestation because her only sib, a brother, died 4 years ago of what was described as Duchenne muscular dystrophy. No other family members have had this disorder so linkage analysis to identify which X chromosome may have been involved is not possible. A muscle biopsy done on her brother reported showed absence of a protein called dystrophin. The best approach to prenatal testing in this case would be:

   A. chorionic villus sampling to rule out aneuploidy and confirm fetal sex, followed by in utero fetal muscle biopsy for dystrophin studies at 20 weeks gestation if the fetus is still at risk
   B. early amniocentesis and dystrophin studies in amniotic fluid
   C. cordocentesis and dystrophin studies from fetal blood
   D. high resolution ultrasound at 18 weeks to confirm fetal sex, and cordocentesis at 19-20 weeks for fetal blood dystrophin studies
   E. fetal muscle biopsy alone at 20 weeks gestation

3. Which of the following is NOT true of Burkitt lymphoma?

   A. it is frequently associated with an 8q;14q reciprocal translocation
   B. chromosomal translocation brings a proto-oncogene into a new position adjacent to enhancer gene sequences resulting in inappropriate expression of the proto-oncogene
   C. requires the presence of a germline mutation as well as a somatic mutation in the normal allele before neoplasia occurs
   D. does not require a mutation within the proto-oncogene for tumor formation to occur
   E. is a soft tissue tumor of the jaw

4. Which of the following is not a numerical chromosomal abnormality?

   A. polyploidy
   B. robertsonian translocation
   C. triploidy
   D. trisomy
   E. aneuploidy

QUESTIONS 5 - 8, match the following terms with the proper definition: (a selection may be used once, more than once or not at all)

A. Variable expressivity
B. Incomplete penetrance
C. Anticipation
D. Allelic heterogeneity
E. Locus heterogeneity
F. Codominance

5. The phenomenon of increasing severity of phenotypic expression of an allele in offspring of an affected parent.

6. Defined by the presence of phenotypically normal individuals even when they carry a mutation that is associated with an autosomal dominant condition.

7. Testicular feminization and X-linked spinal and bulbar muscular atrophy (Kennedy disease).

8. A father with 7 café au lait spots over 15 mm in diameter, and iris hamartomas whose daughter has many cutaneous neurofibromas, an acoustic neuroma and axillary freckles.

9. While walking through the NICU you hear what sounds like a kitten mewing. You isolate the sound as coming from one of the infants who is hooked up to a multitude of monitoring systems. The nurse explains that the infant is 6 weeks old, was very small at birth, appears significantly mentally retarded, and has failure to thrive. An ENT consultation diagnosed laryngeal dysplasia. Examination shows microcephaly and a round appearing face. You inquire as to the infants karyotype as you suspect the following:

   A. 5p- syndrome
   B. trisomy 18 syndrome
   C. trisomy 8 syndrome
   D. 4p- syndrome
   E. fragile X syndrome

10. A couple has had an infant with an isolated open spinal defect (meningomyelocele). The infant's karyotype is 46,XY. The mother was 21 years old at the time of the infant's birth. The father was 41 years old. The couple becomes pregnant two years later. The woman began taking folic acid supplementation before becoming pregnant. The probability this child with have a neural tube defect such as spina bifida is:

    A. 1%
    B. 3 - 5%
    C. 7 - 10%
    D. greatly increased since folic acid is a teratogen
    E. no greater than the general population risk

11. Familiar cancers show all the following characteristics EXCEPT:

    A. earlier age of onset
    B. multifocal tumors
    C. multiple family members affected by rare tumors
    D. tumors of less malignant potential than their sporadic counterparts
    E occasional presence of associated phenotypic abnormalities

12. A *good* genetic screening program has all of the following characteristics except:

    A. the program should be cost effective
    B. the program includes provision for patient education regarding the risks and benefits of screening
    C. the diseases for which patients are screened are lethal or have serious adverse consequences
    D. the diseases for which patients are screened must be curable if appropriately treated
    E. the program incorporates an effective mechanism for follow-up of abnormal results

13. The mother of a boy with molecularly proven Duchenne muscular dystrophy has mild weakness and an elevated serum creatine kinase (CK). What *most likely* accounts for this?

    A. X-inactivation (Lyonization)
    B. she has testicular feminization syndrome
    C. she is 45,X
    D. she is 47,XXX
    E. she is 47,XXY

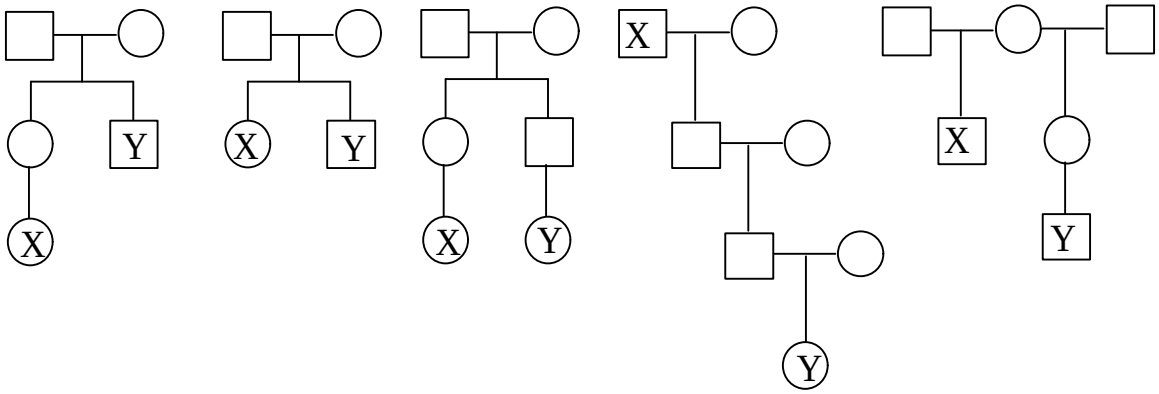
14. The principle benefit of bladder shunting for fetuses with obstructive uropathies is:

A. release the pressure from the bladder
B. lower the intra-abdominal circumference
C. restore the amniotic fluid volume
D. lower fetal blood pressure
E. there is little benefit in fetal bladder shunting

15. Mutations can affect a gene:

A in noncoding regions of the gene
B. in coding regions of a gene, disrupting the coding sense
C. in coding regions of a gene, resulting in amino acid substitutions
D. in coding regions of a gene, resulting in no change in the protein
E. within introns
F. all of the above
G. A, B, C only

16. The coefficient of relationship of grandparent-grandchild is the same as which of the following pairs of X-Y individuals?



Pair A Pair B Pair C Pair D Pair E

A. Pair A
B. Pair B
C. Pair C
D. Pair D
E. Pair E

17. Open fetal surgery has been used to treat all of the following except:

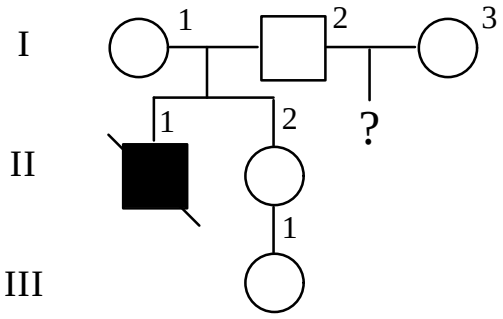
A. diaphragmatic hernia
B. aortic arch constriction
C. sacrococcygeal teratoma
D. CCAM
E. B and D

18. In a sample of 1000 African American individuals, 4 had sickle cell anemia (SS), 112 had sickle cell trait (AS) and 884 were normal (AA). The frequency of the S gene in this sample is:

A. 0.4%
B. 4.0%
C. 6.0%
D. 8.0%
E. 12.0%

QUESTIONS 19 - 20:

The proband, II-1, in the family shown below died of cystic fibrosis which has an incidence of 1 in 2500 in the general population. I-2 and I-3 are not related.



19. What is the chance that an offspring of I-2 and I-3 will be affected with cystic fibrosis?

A. 1 / 400
B. 1 / 200
C. 1 / 100
D. 1 / 50
E. 1 / 25

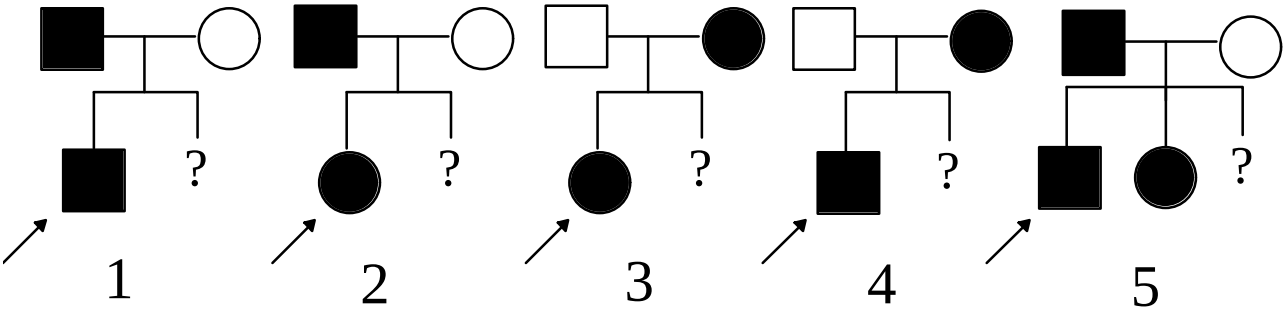
20. Assuming her father is homozygous normal, the probability III-1 is a carrier of cystic fibrosis is:

A. 1 / 2
B. 1 / 3
C. 1 / 4
D. 1 / 8
E. 1 / 16

21. Successful genetic counseling helps a patient or family to do all of the following except:

    A. adjust to and accept the disease in the family
    B. understand the nature, prognosis, and treatment of the condition
    C. understand the mode of inheritance and the recurrence risk
    D. understand the available reproductive options
    E. reduce the frequency of the abnormal gene in the population

QUESTIONS 22 - 23, assume multifactorial inheritance:



22. Which of the couples above has the greatest risk for an affected child as a result of their pregnancy? Assume the incidence is equal in both sexes and all individuals manifest with equal severity.

    A. couple 1
    B. couple 2
    C. couple 3
    D. couple 4
    E. couple 5

23. Which of the couples above (couples 1 through 4) is likely to have the greatest risk of an affected child as a result of their next pregnancy if the population incidence is 5X greater in males that in females? Assume all individuals manifest with equal severity.

    A. couple 1
    B. couple 2
    C. couple 3
    D. couple 4
    E. couples 1 and 3 both have the greatest risk

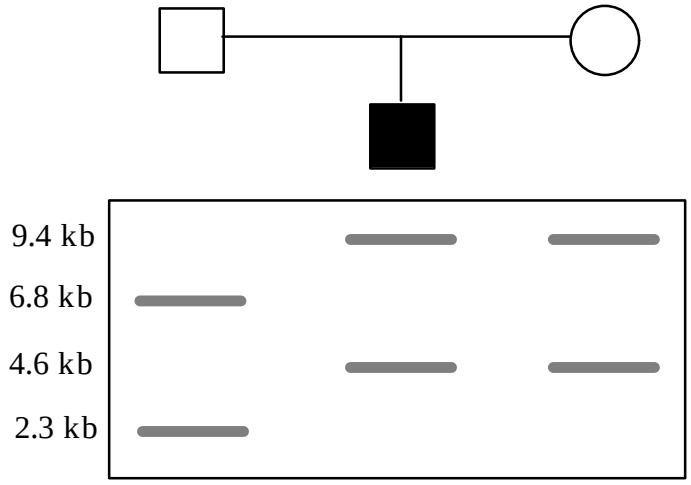
24. Ethnic differences in disease frequencies are most apparent for:

    A. autosomal dominant conditions
    B. autosomal recessive conditions
    C. X-linked recessive conditions
    D. autosomal trisomies
    E. sex chromosome aneuploidies

25. A man with a Mendelian syndrome marries a normal woman. Of their 9 children, all 4 boys are normal, whereas all 5 daughters are affected by the same syndrome. What is the most likely inheritance pattern for this syndrome?

A. autosomal dominant
B. autosomal dominant with female preponderance
C. X-linked dominant
D. Y-linked
E. autosomal recessive

26. 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. Marfan syndrome
B. Retinoblastoma
C. Prader-Willi syndrome
D. Angleman syndrome
E. Triploidy

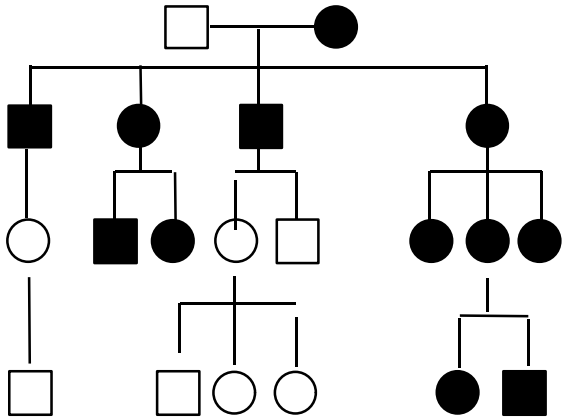
27. Morphogenesis is controlled by classes of developmental regulatory genes that are expressed in the following order during embryogenesis:

A. polarity genes - segmentation genes - homeotic selector genes
B. segmentation genes - polarity genes - homeotic selector genes
C. segmentation genes - homeotic selector genes - polarity genes
D. homeotic selector genes - polarity genes - segmentation genes
E. polarity genes - homeotic selector genes - segmentation genes

28. One of Mary's brothers and a maternal uncle are color blind for red and green. No others in her family are known to be affected, including her parents, another brother and her sister. From the most likely pattern of Mendelian transmission that can account for this disorder, what is the likelihood that her first child will be affected?

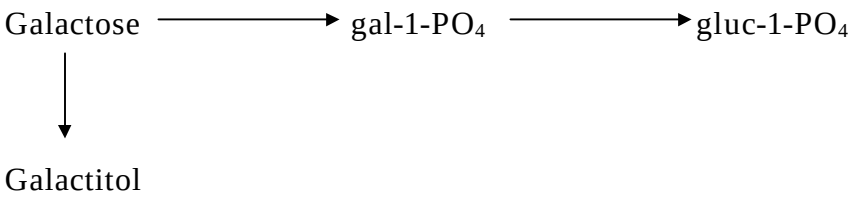
A 6.25 %
B. 12.5 %
C. 25 %
D. 50 %
E. none of the above

29. The pedigree drawn below is most characteristic of which of the following inheritance patterns:



A. autosomal dominant
B. X-linked dominant
C. mitochondrial inheritance
D. paternal imprinting
E. maternal imprinting

30. In galactokinase deficiency, galactitol in the lens causes cataracts. What is the basis for the metabolic consequences?



A. abnormal protein production
B. alternative pathway overproduction
C. protein deficit
D. both B and C
E. none of the above

31. A birth defect associated with a multiple defect syndrome and caused by a point mutation most likely arose from a gene coding for a:

    A. cytochrome
    B. cytoskeletal protein
    C. transcription factor
    D. glucose metabolizing enzyme
    E. DNA polymerase

32. Which of the following individuals has the highest risk of having a child with Down syndrome?

    A. a female with a t(13q;14q)
    B. a male with a t(14q;21q)
    C. a female who is 35 years old
    D. a male who is 45 years old
    E. a female with a t(14q;21q)

QUESTIONS 33 - 35:

An infant presents at day six of life with poor feeding, vomiting and lethargy. Initial laboratory studies show a metabolic acidosis. Further history reveals the infant was the full term product of a normal pregnancy and delivery. He did well in the first two days of life and was discharged home.

33. In evaluating for the possibility of an inborn error of metabolism, which of the following is the most non-essential piece of information?

    A. family history of neonatal deaths
    B. family history of consanguinity
    C. infant's feeding history
    D. infant's karyotype
    E. unusual odor in the infant

34. Which laboratory test would be the least likely to provide diagnostic information for this patient?

    A. urine and plasma amino acids
    B. urine organic acids
    C. urine for mucopolysaccharides
    D. plasma ammonia
    E. urine for reducing substances (i.e. sugars)

35. The family history reveals that the parents are first cousins. This disorder is most likely:

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

36. Which of the following is NOT true of genetic recombination?

A. it only occurs during prophase I of the first meiotic division
B. chiasmata represent areas of crossing over between sister chromatids
C. genetic recombination is one of the primary processes of genetic assortment
D. chromosome homologs become *physically* paired (bivalent formation) before they align on the spindle apparatus
E. during anaphase I, each of the chromosomes segregate as a unit (i.e., both chromatids remain attached at the centromere) to one of the poles of the daughter cells

37. Which of the following is NOT associated with tumor suppressor genes?

A. usually require loss of both alleles before cell transformation occurs
B. a single mutation can activate these genes to suppress vital cellular pathways resulting in aberrant cell growth and proliferation
C. loss of heterozygosity for these genes is a hallmark feature found in cancers due to tumor suppressor gene systems
D. many cancer families carry mutations for such genes in their germlines
E. behave at the molecular level in a recessive manner

38. What does a <u>lod score</u> of 3.5 mean?

A. the disease and the marker are not linked.
B. the result is uninformative
C. the DNA typing has had problems
D. the result is promising, but more members of the pedigree must be typed to get a meaningful result
E. the odds are better than 1000:1 that the disease is linked to this marker

39. All of the following are appropriate referrals to the Genetic Clinic except:

A. a couple who are both deaf and concerned about their chances of having a hearing child
B. a child suspected of having fetal alcohol syndrome
C. a couple who is expecting their first child and the man's father has myotonic dystrophy
D. a couple in which the husband is of Ashkenazi Jewish ancestry
E. all of the above are appropriate referrals

40. You are asked to counsel a couple who has a newborn daughter with an abnormal karyotype, a deletion of the short arm of chromosome 3. Her karyotype is 46,XX,del(3)(p25.5). Both parents are studied and their karyotypes are normal. The most accurate counseling is:

    A. their chance of having another child with an unbalanced karyotype is low but not zero because of the possibility of parental gonadal mosaicism
    B. the testing has detected false paternity since one parent must have a balanced translocation to explain the deletion in the child
    C. small chromosomal deletions do not usually cause severe birth defects and mental retardation
    D. the parent's normal siblings should be karyotyped to determine if they are balanced translocation carriers
    E. because the deletion is *de novo*, the proband is less likely to have birth defects and mental retardation than if it was inherited secondary to a translocation in one of the parents

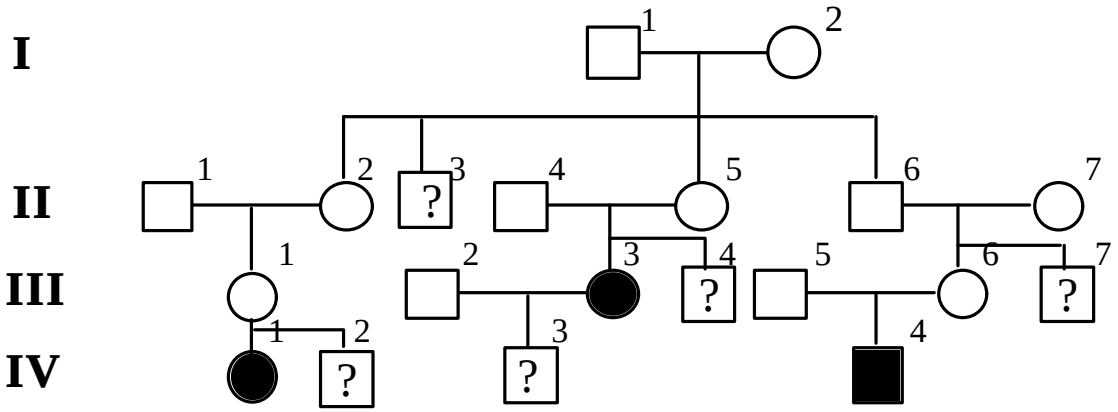
41. Loss of heterozygosity in the BRCA1 gene locus has been associated with which of the following cancers?

    A. Gardner syndrome
    B. familial polyposis coli
    C. Li-Fraumeni syndrome
    D. breast and ovarian cancer
    E. retinoblastoma

42. PKU occurs with a frequency of 1 in every 10,000 newborns. A couple is concerned about their risk of having a child with PKU. They are unrelated and each has a negative family history of PKU. Their risk of having a child affected with PKU is:

    A. 1 in 100
    B. 1 in 200
    C. 1 in 400
    D. 1 in 2500
    E. 1 in 10,000

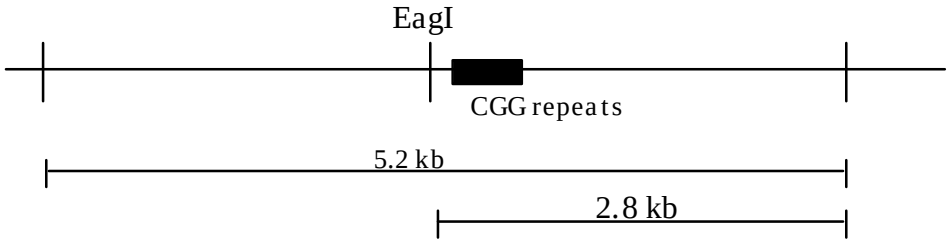
QUESTIONS 43 - 45 pertain to the following pedigree in which the affected individuals have mental retardation due to the fragile X syndrome.



43. In the pedigree above, the woman who has the highest risk of having a son affected with fragile X syndrome is:

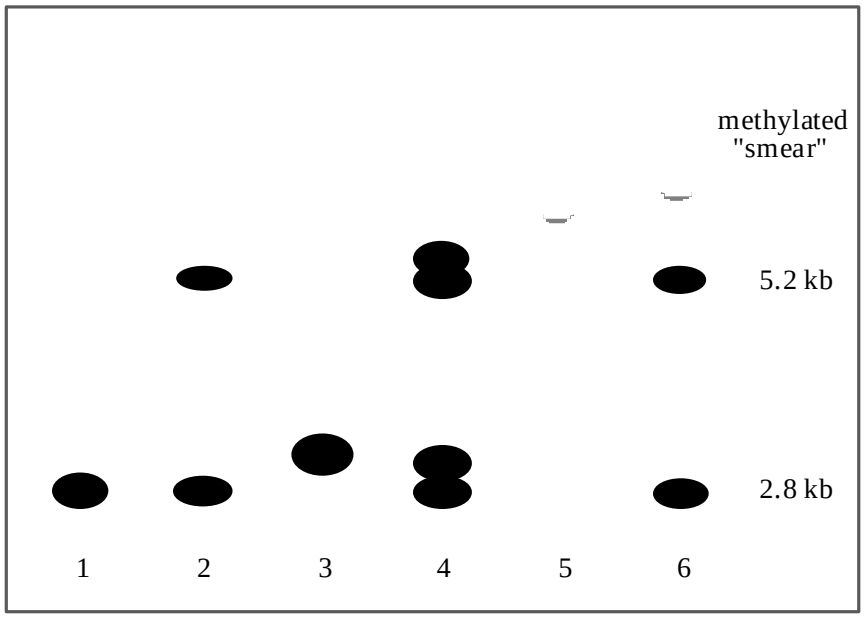
    A. I-2
    B. II-5
    C. II-7
    D. III-1
    E. III-3

44. Several family members in the pedigree above undergo DNA analysis. The restriction enzyme Eag 1 cuts at the site indicated below 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 ? is on the next page)

Which of the following patterns would represent the genotype of individual II- 6?

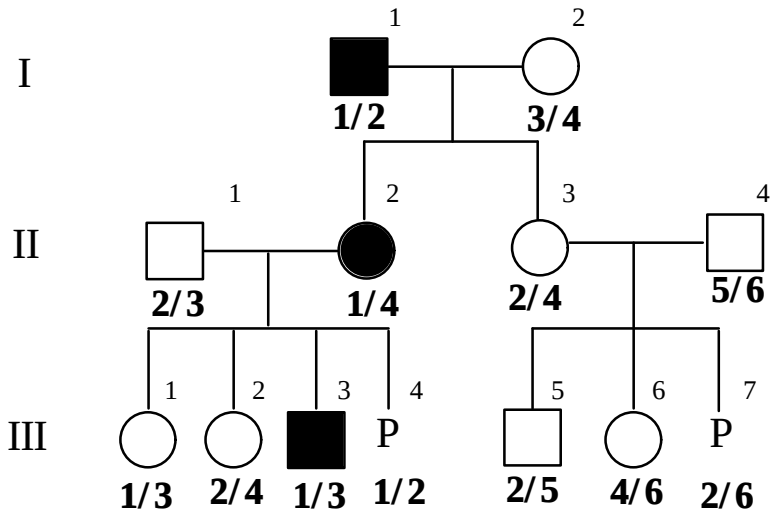


A. Lane 1
B. Lane 2
C. Lane 3
D. Lane 5
E. Lane 6

45. The phenotype of individual III-3 is best described by the following:

A. lymphedema of the hands and feet, coarctation of the aorta
B. epicanthal folds, polydactyly, and microcephaly
C. large prominent ears, long face, macroorchidism, and mental retardation
D. mental impairment ranging from learning disabilities to more severe mental retardation, as well as emotional disorders
E. prominent forehead, mitral valve prolapse, macroorchidism, and autistic features

46. DNA linkage analysis using a highly variable marker inside the disease causing gene gives the following results in an autosomal dominant disorder:



What is the <u>phenotype</u> of the unborn child III-4 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 gender of the child

47. The father of a 24-year old male patient has a diagnosis of Huntington disease and is cared for at home. Several paternal relatives are similarly affected, and most are now in long-term care facilities. The patient and his wife request predictive testing. Since the year is 1990, this was done by linkage analysis. All appropriate blood samples are obtained, and the results obtained in duplicate indicate that there is nonpaternity; that is, the patient's biologic father is not the legal and affected father. The mother is interviewed separately and gently but does not confirm the genetic interpretation. *Which one of the following approaches would best aid the patient and his wife in planing their future?*

A. respect the autonomy of the mother and tell the patient the molecular testing was not informative
B. demand that the mother divulge these results to her son
C. respect the autonomy of the mother, say nothing about the nonpaternity, but tell the patient the results indicate he has not inherited the Huntington allele
D. call the couple in and review all the results, including the nonpaternity; ask the young man not to tell his mother about the nonpaternity

48. While working with Dr. Quershi, a famous fetal pathologist at Hutzel Hospital, you are asked to assist in an autopsy on 20 week stillborn infant. The infant is small for gestational age, has bilateral syndactyly of the hands, and has unusual phenotypic facial features in which the left eye and ear are positioned lower on the face / head than the contralateral eye and ear, and there appears to be a downward droop to the left corner of the mouth. Examination of the placental demonstrates a cystic degeneration (hydatiform) of the trophoblast. You suspect the fetus had the following underlying syndrome:

    A. triploidy
    B. trisomy 18
    C. trisomy 13
    D. 4p- syndrome
    E. trisomy 16

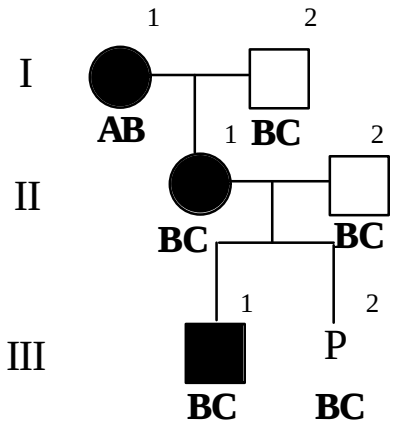
49. A woman whose father has both G6PD deficiency and X-linked color blindness has two sons. The first son has G6PD deficiency and the second has color blindness. What is the best explanation for this family history?

    A. this family demonstrates an inheritance pattern inconsistent with Mendel's law of segregation and independent assortment
    B. the first son is a recombinant; the second son is a nonrecombinant
    C. the first is a nonrecombinant; the second is a recombinant
    D. both sons are recombinants
    E. both sons are nonrecombinants

50. What is meant by "positional cloning"?

    A. mapping genes to chromosomes
    B. identifying disease causing genes and then determining the protein product ("reverse genetics")
    C. analyzing first the defective protein product and then cloning the gene(s) coding for the protein
    D. using PCR to map genes
    E. Southern blot analysis

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



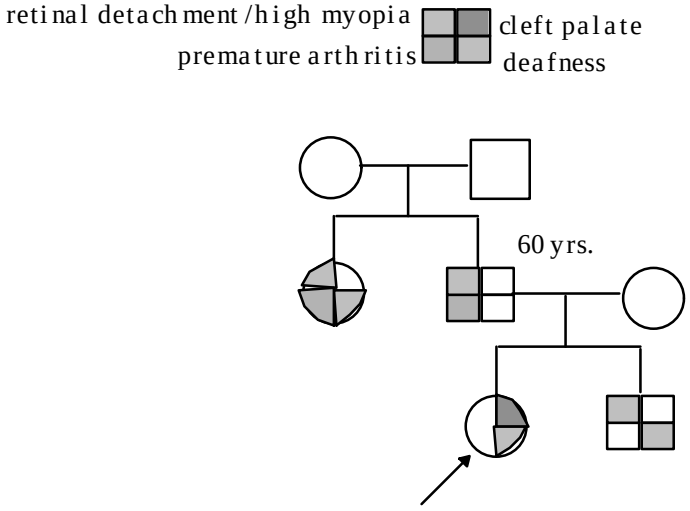
The mother (II-1) of the affected son is pregnant and has had prenatal testing based upon a set of markers closely linked to the NF1 gene. Haplotypes are given for each relative and the fetus. What is the probability that the fetus will be affected?

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

52. You are asked to look at an ultrasound scan of an 18 week fetus with an abnormal chest finding. The mother has good gestational dating parameters and the fetus is measuring small for gestational age indicating probable intrauterine growth retardation. In addition, you note sonographic features consistent with small bowel, stomach and liver in the chest cavity and therefore agree with the ultrasound tech that this fetus appears to have a diaphragmatic hernia. You also note that the fetus has overlapping fingers on both hands (clenched fist sign). You counsel the mother that the fetus may have the following chromosomal syndrome:

A. trisomy 21
B. trisomy 13
C. trisomy 18
D. 45,X syndrome
E. 46,XY,-9,+der (9q+) syndrome

53. Twenty-eight year old Pamela wants to know about her chances of having a child with deafness. She had a cleft palate as a child, but the deafness persisted even after the palate was repaired. Her hearing test shows sensorineural deafness. She is 5'8" tall. Her family history is as follows:



What is the most accurate answer to her question?

A. her fetus has a 50% chance of having sensorineural deafness, but the chance for cleft palate is 2%
B. her child may be significantly short because of epiphyseal dysplasia
C. if her child does not have a cleft palate, then the deafness would not occur
D. she probably has Stickler syndrome and there is a 50% chance for each of her children to inherit this condition
E. since cleft lip shows multifactorial inheritance, the risk for the fetus to have a neural tube defect is increased

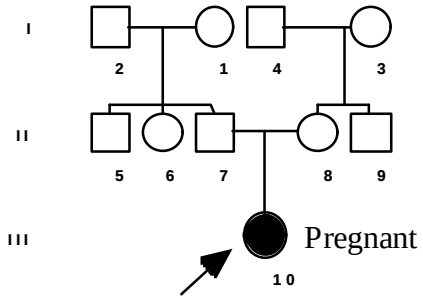
54. Which of the following is/are true about deafness?

A. congenital infections can cause deafness
B. skin pigmentation abnormalities such as Waardenburg syndrome are associated with deafness
C. all individuals with significant hearing loss should have a genetics evaluation
D. deafness can be acquired due to toxicity of antibiotics
E. all of the above are true about deafness

55. Genetic drift is primarily a result of

A. selection
B. variable fitness
C. immigration
D. small population size
E. all of the above

56. In the following pedigree, individual 10 has a Mendelian syndrome for which she is referred to a geneticist. She is also 8 weeks pregnant and wishes to know the likelihood of her future child also being affected by the same syndrome. There is no consanguinity between herself and her completely normal husband, who is not shown on the pedigree. Which patterns of inheritance need to be considered:



A. X-linked recessive
B. X-linked dominant with incomplete penetrance
C. Autosomal dominant with new mutation
D. Autosomal dominant with incomplete penetrance
E. Autosomal recessive
F. All of the above
G. A, B, C, D
H. B, C, D, E

57. Many individuals in the general population may have 1 - 2 minor anomalies. Which of the following is / are true?

A. if mental retardation is also present, a chromosome analysis should be performed
B. minor anomalies can be inherited
C. a congenital heart defect (e.g. endocardial cushion defect) is considered a minor anomaly
D. minor anomalies are never associated with serious genetic syndromes
E. A and B are both true

58. A 17 year old boy is referred for a genetics evaluation because of difficulties in school and lack of development of the secondary sexual characteristics. Physical exam reveals a eunichoid body habitus, a small penis and testes, and lack of pubic and axillary hair. Chromosome analysis reveals an abnormal karyotype. The error in meiosis that could explain this chromosome abnormality is:

A. Nondisjunction during paternal meiosis I
B. Nondisjunction during paternal meiosis II
C. Nondisjunction during maternal meiosis I
D. Nondisjunction during maternal meiosis II
E. either A or C or D

59. Which of the following is NOT characteristic of G+ (dark) chromosomal banding regions?

A. contain tissue-specific genes
B. likely contain early embryonic or vital developmental genes
C. rich in simple sequence repetitive DNA
D. rich in transcribed genes
E. contain a higher AT:GC ratio and are more condensed regions of the chromosome

60. A patient at 18 weeks gestation is referred to you for prenatal counseling following the return of a markedly elevated maternal serum alpha-fetoprotein (MSAFP) screen. A screening ultrasound shows a single fetus with no obvious anomalies. You perform an amniocentesis which returns 46,XX with a mildly elevated amniotic fluid AFP value and positive acetylcholinesterase. Which of the following is true of this scenario:

A. no further testing is necessary because fetal abnormalities have been ruled out by the screening ultrasound
B. you can reassure the patient that everything seems OK, but suggest another MSAFP screen be drawn in two weeks to monitor the pregnancy
C cordocentesis should be performed immediately to measure AFP and acetylcholinesterase levels in fetal blood
D. the results indicate a functional abnormality of the placenta
E. a subtle structural anomaly, such as a small spina bifida, must be present but was unrecognized on ultrasound evaluation

61. PAX2 gene expression is critical during morphogenesis of the otic vesical, optic nerve, ureteric bud and parts of the central nervous system. Why does the presence of only one mutant allele for this gene in heterozygotes cause a multiple defect syndrome?

A. the mutant gene product binds to inappropriate DNA regulatory regions
B. the gene product is a transcription factor and its function depends on its dosage
C. the mutant gene product is expressed in secondary oocytes when only the haploid maternal allele is present
D. the mutant gene product is expressed in spermatids when only the haploid paternal allele is present
E. the octapeptide sequence of the mutant gene product binds to promotors without activating them and competitively inhibits the wild-type gene product from binding

62. A 40 y/o patient is referred by her frustrated obstetrician following her first prenatal visit yesterday at 18 weeks gestational age. She has five children ages 20, 18, 15, 12, and 10 y/o who have no medical or genetic problems. Her family history is unremarkable except for multiple family members on the paternal side with weight problems and adult onset diabetes mellitus. The best prenatal test to offer her would be:

A. no invasive testing as there is no risk of genetic abnormalities
B. chorionic villus sampling
C. maternal serum screening
D. amniocentesis
E. diagnostic embryoscopy

63. Which of the following is NOT true of MITOSIS?

A. each of the homologous chromosomes segregate intact to the daughter cells such that both chromatids are of maternal or paternal origin
B. nondisjunction would result in two identical copies of either the maternal or paternal chromosome
C. in anaphase, kinetochore microtubules shorten to pull the chromosomes towards the spindle pole
D. in anaphase, polar microtubules elongate to push the spindle poles apart.
E. each daughter cell contains 46 chromosomes (2N)

64. A non-pregnant couple comes to you for counseling because of a previous child born with Greb-Johnson syndrome. This syndrome is characterized by severe mental retardation, muscle wasting after puberty, hypospadius in males, polydactyly with syndactyly, and facial hemangiomas. As a clinical genetics specialist, you recognize this to be a autosomal recessive disorder for which there is no recognized chromosomal aberration, no available DNA testing, and no biochemical markers to screen for in amniotic fluid. The best option for early prenatal diagnosis in this case would involve:

A sonographic evaluation at 12-13 weeks gestation
B. chorionic villus sampling
C. early amniocentesis
D. diagnostic embryoscopy
E cordocentesis

65. Genetic screening for cystic fibrosis heterozygotes is:

A. widespread
B. difficult because the tests do not detect all the mutant alleles
C. highly successful in detecting affected individuals before the onset of serious symptoms
D. difficult because there are many false positive results
E. all of the above

QUESTIONS 66 - 67: match the following clinical findings with the most likely type of alteration in protein function:

A. Enzyme deficiency
B. Abnormality of mitochondria
C. Structural protein abnormality
D. Altered cellular protein receptor
E. Abnormal control of growth and differentiation

66. A female has elevated serum cholesterol, an elevated LDL and a normal VLDL. Atheromas and xanthomas are present. Both her father and brother have similar problems.

67. An 18 year old male presents with a history of multiple fractures, beginning during infancy, blue sclerae and mild hearing loss. Both his father and grandfather have similar problems.

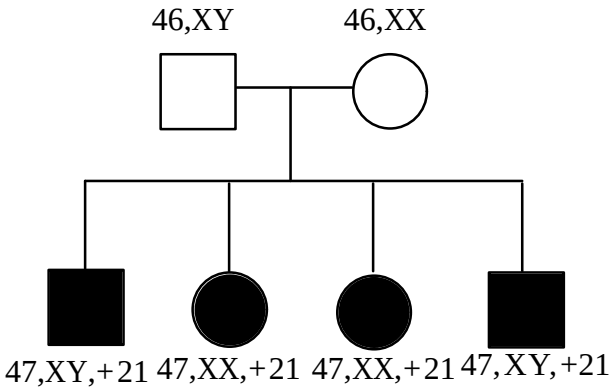
68. A newborn infant manifests typical phenotypic features of trisomy 21 and a karyotype returns showing 46,XY,-21,+rob(21;21). Which of the following is NOT true?

A. the next step in the evaluation is to karyotype the parents
B. if the translocation is *de novo*, recurrence risk is ~1%
C if the translocation is carried by the father the recurrence risk is 100%
D. the chromosome anomaly is a structural abnormality called a centric fusion
E. if the translocation is carried by the mother the recurrence risk is 10%

69. Mitochondrial DNA deletions in a given patient usually:

A. are different sizes in different tissues
B. consist of a series of stochastically determined deletions
C. consists of a unique deletion in all tissues
D. are homoplasmic
E. are inherited from the patient's mother

70. What is the most likely explanation for the observed family history and corresponding cytogenetic results?



A. chromosomal translocation
B. nondisjunction has a recurrence risk of 1%
C. autosomal recessive Down syndrome
D. gonadal mosaicism
E. paternal imprinting

71. A 5 year old boy presents with progressive muscle weakness and pseudohypertrophy of the calf muscles. He has an elevated CK level and a muscle biopsy shows complete lack of dystrophin. Multiplex PCR-deletion analysis fails to identify a deletion in the dystrophin gene. The most reasonable explanation is:

A. this patient does not have a muscular dystrophy
B. this patient has Becker muscular dystrophy
C. this patient most likely has a chromosome abnormality
D. this patient has a mutation elsewhere in the dystrophin gene
E. this patient most likely represents a new mutation

72. Genomic imprinting is best described by which of the following statements?

A. it produces differential expression of genes depending on whether they were inherited from the father or mother
B. it affects most genes except those on the sex chromosomes
C. it occurs only in female gametes
D. it is reversed or removed when a cell passes through mitosis
E. it reflects a change in the DNA sequence of affected genes

73. All of the following are true regarding first trimester stem cell transplantation with paternal bone marrow except:

    A. induces tolerance
    B. reduces risk for graft versus host disease
    C. reduces risk for rejection
    D. has a high rate of infection
    E. can be used to treat conditions such as beta thalassemia

74. All of the following are characteristics of mitochondrial genetics except:

    A. mtDNA is maternally inherited
    B. mitochondrial diseases most often affect tissues/organs with high ATP requirements
    C. nuclear DNA has a higher mutation rate compared to mtDNA
    D. mitochondrial diseases are commonly myopathies, neurologic syndromes, and cardiomyopathies
    E. mtDNA diseases can be inherited in a Mendelian inheritance pattern

75. Concerns regarding predictive genetic testing for late onset disorders such as breast and ovarian cancer are based on which of the following:

    A. genetic discrimination by health care and life insurance companies
    B. well described survivor guilt and changes in family dynamics
    C. increased cancer surveillance in woman who carry the BRCA1 mutation is not yet proven to decreased the mortality of the disease
    D. testing of children
    E. all of the above are serious concerns about predictive genetic testing

HAVE A GREAT SPRING BREAK!!!