Medical Biochemistry Examination IV

March 17, 2000
Kresge Auditorium

Please follow these directions:

1. Do not begin the exam until all students have received a copy of the exam. You will be instructed as to when to break the seal.

2. The exam consists of 113 questions on 23 pages, with this title page considered page 1. There are 150 points on this exam. The point value for each question is indicated by the question. There are a defined number of answers for each question. Questions 1-82 are answered on one answer sheet (pages 2-15). The second set of questions (1-31, pages 16-23) should be answered on the second answer sheet.

3. Place your ID number on every page of the exam booklet and on the answer sheets you will hand in. Also, print your name on the line provided on the answer sheets.

4. TWO computer graded answer sheets will be used for this exam. Fill in both your ID number and your name in the indicated areas of the answer sheets. You should convert your number to a three digit number (001, 010, etc) and use the three leftmost boxes to insert your number. When using the answer sheet use a No. 2 pencil only. Fill in the circle for the correct answer(s) completely. If you wish to change an answer, be sure to erase cleanly. Make sure that you use your biochemistry ID number to fill in the ID box. The first answer sheet is used for questions 1-82; the second answer sheet is used for questions 83-113. For your convenience the second set of questions begins with number 1 (1-31).

5. When you are finished with the exam, return both the test booklet and the answer sheets. The test booklet and a copy of the answer sheet will be returned to you when the grading is complete.

6. Questions will not be allowed during the exam. If you believe there is a typographical error do the best you can with the information available. Do not spend extra time on the question. If it is determined that the information presented is ambiguous, or in error, then the question will not be counted in the final scoring.

7. Attached to the exam booklet after page 23 are two blank pages for you to use for calculations, and then two final answer sheets for your own use. You can take these sheets with you from the exam, and use them to check your answers against the posted answers (outside of room 3109 MSB). Answers will be posted after all students have taken the exam, estimated to be on Monday, March 27, 2000.

8. You will have 2.5 hours (until 12:30 pm) to complete this exam. Good luck.
QUESTIONS 1-82 GO ON ANSWER SHEET NUMBER 1

Questions 1-3 (1 point each) are matching questions. Match the question with the ONE best answer from the list A through F. An answer may be used more than once.

1. Primary normal cell strain
   A. Mortal cells which induce tumors when injected into athymic mice.

2. Established normal cell line
   B. Cells which display a prolonged M phase relative to the other two cell types.

3. Transformed cell line
   C. Mortal cells with a reduced serum requirement for growth.

Questions 4-6 (1 point each) are also matching questions. Match the question with the ONE best answer from the lettered list A through F. An answer may be used more than once.

4. An adenosine deaminase deficiency would be expected to arrest cells in this part of the cell cycle.
   A. $G_0$
   B. $G_1$
   C. $S$
   D. $G_2$
   E. $M$
   F. $P$

5. The location within the cell cycle at which cells arrest growth upon reaching their saturation density.
   A. $G_0$
   B. $G_1$
   C. $S$
   D. $G_2$
   E. $M$
   F. $P$

6. The portion of the cell cycle in which the cells divide.
   A. $G_0$
   B. $G_1$
   C. $S$
   D. $G_2$
   E. $M$
   F. $P$

7. (1 point) Evidence suggesting that cell proliferation is regulated, in part, by cell-cell interactions, came from which TWO of the following?
   A. Altering the density of the cell culture medium.
   B. Dulbecco’s wounding experiment.
   C. Altering the ability of the cell to adhere to the substrata by coating the cell culture dish with a non-toxic polymer.
   D. Adding cell membrane fragments to growing cells, which induced the cells to stop growing.
   E. Adding conditioned cell culture media to growing cells, and inducing the cells to stop growing.
   F. Observing that the final cell saturation density was inversely proportional to the serum concentration.
Questions 8-10 (1 point each) should be answered True or False based on the following situation. Consider the following chimeric receptor, in which the insulin receptor alpha chain has been altered to contain an EGF binding domain instead of an insulin binding domain. This chimeric receptor is then expressed in cells which lack normal EGF receptors, but do express normal insulin receptors. It is demonstrated that the transduced cells will bind EGF to these chimeric receptors, and in addition, that the binding of EGF activates the tyrosine kinase domain of the beta subunits of the chimeric receptors. With this background, answer the following three questions either true or false (T or F on the answer sheet).

8. The response to EGF in this transduced cell line will depend upon IRS-1 function.
9. The addition of insulin to this cell line will result in a diminished response to subsequent administration of EGF.
10. Ras will not be required for EGF to stimulate these cells to grow.

11. (1 point) The growth factors FGF and PDGF are similar to each other in which ONE of the following ways?

   A. Target cell specificity
   B. Concentration of growth factor required for one half maximal activity
   C. Molecular weight of the intact growth factor
   D. Activation of a G-protein linked receptor
   E. Activation of a tyrosine kinase containing receptor

Questions 12-14 (1 point each) should be answered True or False concerning the cellular response to EGF binding to the EGF receptor in normal fibroblasts.

12. The intracellular pH decreases due to the activation of a sodium proton antiporter.
13. Phospholipase-C-gamma is activated, leading to PIP₂ hydrolysis to produce PA and IP₃.
14. A temporal pattern of gene expression is induced, due to the alteration of certain transcription factor activities.

15. (1 point) Oxidized LDL stimulates smooth muscle cell proliferation through the activation of ALL of the following EXCEPT for which ONE?

   A. Sphingomyelinase
   B. Ceramidase
   C. Sphingosine kinase
   D. Phospholipase C
Match the following questions (16-20, 1 point each) with the **ONE** best answer concerning the MAP kinase cascade, from the choices A through J. An answer may be used more than once.

16. Ras is activated with the direct help of this protein. A. GAP
17. Ras is de-activated with the direct help of this protein. B. Grb1
   C. Grb2
18. This protein contains both SH2 and SH3 domains, which allows it to act as an adaptor protein for proteins which cannot bind directly to activated growth factor receptors. D. MAP kinase
   E. MAP kinase kinase
   F. MAP kinase kinase kinase
   G. SOS
19. This protein is also a MAP kinase kinase kinase (note that answer F will NOT be accepted as an answer to this question). H. Raf
   I. Rap
   J. Ras
20. This protein needs to be phosphorylated on both Y and T residues to be active.

21. (1 point) Nitric oxide, NO, a potent vasodilator, is produced from which **ONE** amino acid via the action of nitric oxide synthase?
   A. The amino acid designated by the letter “A”
   B. The amino acid designated by the letter “B”
   C. The amino acid designated by the letter “D”
   D. The amino acid designated by the letter “E”
   E. The amino acid designated by the letter “G”
   F. The amino acid designated by the letter “R”

22. (1 point) All of the cell cycle transitions are carefully regulated. Which **ONE** statement below is **INCORRECT** concerning the G2 to M phase transition?
   A. A cyclin B/p34cdc2 complex, with an active kinase activity, is required.
   B. A phosphatase is activated at the G2/M transition, which activates the cyclin B/p34cdc2 complex.
   C. The cyclin B/p34cdc2 complex is kept inactive by the wee1 kinase activity, which has activity similar to a MAP kinase kinase.
   D. The MAP kinase kinase kinase initially phosphorylates cyclin B, allowing it to complex with p34cdc2.

23. (1 point) Which **ONE** of the following is **NOT** a characteristic of transformed cells in culture?
   A. Reduced serum requirement for growth.
   B. Ability to grow in soft agar.
   C. Form tumors when injected into athymic mice.
   D. Loss of growth-inhibitory molecules from the cell surface.
   E. Ability to form multi-layers in cell culture dishes.
Questions 24-27 (1 point each) are matching. Match the oncogene listed in the answers (choices A through I) with the question. There is only ONE answer per question, although an answer may be used once, more than once, or not at all.

<table>
<thead>
<tr>
<th>Question</th>
<th>Description</th>
<th>Answer</th>
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<tbody>
<tr>
<td>24.</td>
<td>A GTP binding protein</td>
<td>A. ErbB</td>
</tr>
<tr>
<td>25.</td>
<td>A truncated growth factor receptor</td>
<td>B. Hst</td>
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<tr>
<td>26.</td>
<td>A growth factor similar to PDGF</td>
<td>C. Jun</td>
</tr>
<tr>
<td>27.</td>
<td>A slightly mutated transcription factor</td>
<td>D. Plc</td>
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<td></td>
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<td>E. Raf</td>
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<td>F. Ras</td>
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<td>G. Sis</td>
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<td>H. Sos</td>
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<td>I. Src</td>
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28. (1 point) An established “normal” cell line differs from a primary cell strain by which ONE of the following?

- B. Requirement of amino acids and vitamins for growth.
- C. Number of mutations required to reach a transformed state.
- D. Cell saturation density.

29. (1 point) Human tumors can arise from mutations within all of the following enzyme systems EXCEPT for which ONE?

- A. The MAP kinase cascade
- B. DNA repair enzymes
- C. Transcription factors
- D. Growth factors and/or receptors
- E. Tumor suppressors
- F. Energy-generating pathways

30. (1 point) The combination of TGF-beta and EGF will allow a normal fibroblast cell line to do which ONE of the following?

- A. Form tumors in nude mice
- B. Grow in soft agar
- C. Increase cell saturation density
- D. Arrest cell growth at a specific point in the cell cycle
Questions 31-39 (1 point each) are **True or False. Darken either T or F on the answer sheet.**

31. Isoschizomers are restriction enzymes which are isolated from different sources but recognize and cut the same nucleotide sequence.

32. A bacterial plaque is caused by lysis of infected bacteria by bacteriophage.

33. cDNA libraries represent all the genes which are present in a specific organism.

34. Diseases caused by expansion of trinucleotide repeat sequences always amplify sequences in the protein coding portion of the gene.

35. The size of the transcript detected in a Northern blot is full length.

36. SDS-PAGE (polyacrylamide gel electrophoresis) separates proteins on the basis of isoelectric charge of the protein.

37. Transgenic animals can be used as model systems for understanding the function of specific genes/proteins and their role in disease.

38. Chromosome walking can be used to isolate stretches of contiguous DNA.

39. Dystrophin functions as a linkage molecule between cytoskeletal proteins and sarcomeric proteins.

40. (1 point) Restriction endonucleases are enzymes that cut which of the following? Choose the **ONE** best answer.

   A. double stranded DNA  
   B. single stranded DNA  
   C. DNA in a RNA-DNA hybrid  
   D. double stranded RNA  
   E. answers A, B, and C

41. (1 point) All of the following vectors would be preferred while constructing a genomic library, **EXCEPT** for which **ONE**?

   A. bacteriophage  
   B. YACs  
   C. BACs  
   D. cosmids  
   E. plasmids
42. (1 point) Western blot analysis is used to detect which of the following? Choose the **ONE** best answer.
   A. protein  
   B. DNA  
   C. RNA  
   D. All of the above  

43. (1 point) All of the following are true about the dystrophin protein, EXCEPT for which **ONE**?
   A. it is associated with the sarcolemma  
   B. it is a mutant protein only produced in Duchenne's muscular dystrophy  
   C. it links the actin cytoskeleton with the plasma membrane  
   D. it is a truncated protein in Becker's muscular dystrophy  

44. (1 point) Which **ONE** of the following sets of reagents are necessary for nucleotide sequencing reactions via the dideoxy chain termination method?
   A. complementary primer, deoxy nucleotides, DNA polymerase  
   B. dideoxy nucleotides, reverse transcriptase, complementary primer  
   C. DNA polymerase, deoxy nucleotides, ligase enzyme  
   D. Hydrazine, formic acid, dimethylsulfate  

45. (1 point) Current problems with gene therapy include which of the following? Choose the **ONE** best answer.
   A. controlled regulation of the expression vector  
   B. methods for delivering the expression vector  
   C. widespread transfer of the vector within the host  
   D. all of the above  
   E. none of the above  

46. (2 points) Electrophoresis resolves DNA fragments based on which **ONE** of the following?
   A. sequence  
   B. molecular weight  
   C. isoelectric point  
   D. frequency of CTG repeats
47. (1 point) Familial hypertrophic cardiomyopathy is caused by mutations in which ONE of the following?

A. sarcomeric proteins  
B. sarcoplasmic reticulum proteins  
C. sarcolemma proteins  
D. cardiac muscle protein kinases

48. (1 point) Which ONE of the following procedures may be performed during construction of a genomic library?

A. partial endonuclease restriction digest to generate overlapping DNA fragments  
B. reverse transcription to generate the first strand of DNA synthesis  
C. packaging of the vector-insert DNA into retroviral particles  
D. Southern blotting of mRNA with restricted pieces of DNA

49. (1 point) The Cot\(_{1/2}\) value of two complementary DNA sequences depends upon all of the following EXCEPT for which ONE?

A. the amount of repetitiveness within the sequences  
B. the amount of DNA in the genome under study  
C. the amount of ethidium bromide in the reannealing reaction  
D. the amount of salt in the reannealing reaction

50. (2 points) Which ONE of the following nucleotide sequences would most likely be an endonuclease restriction site?

A. (5') AUGCAU (3')  
   UACGUA

B. (5') CGGGGC (3')  
   GCCCCG

C. (5') TAATAA (3')  
   ATTATT

D. (5') GCTAGC (3')  
   CGATCG
51. (1 point) All of the following properties are associated with cloning vectors EXCEPT for which ONE?

A. they contain regions of DNA not essential for propagation which can be replaced with foreign DNA
B. they can replicate autonomously in bacteria
C. some carry antibiotic resistance genes
D. their DNA is not easily separated from the host bacterial DNA

52. (2 points) Southern blot hybridization is used to detect which ONE of the following?

A. RNA
B. DNA
C. Protein
D. Isoelectric point

53. (1 point) All of the following statements are true about PCR (polymerase chain reaction) EXCEPT for which ONE?

A. it is a cyclical process of denaturation of template DNA, renaturation of primers to DNA, and synthesis of DNA strands
B. it requires a heat stable DNA polymerase
C. it requires deoxy and dideoxy nucleotides
D. it can be used to amplify genomic DNA or cDNA

54. (1 point) The coding region of a single copy gene would be expected to reassociate its separated DNA strands with which ONE of the following kinetics?

A. fast kinetics
B. intermediate kinetics
C. slow kinetics

Questions 55-58 (1 point each) requires matching the protein with the associated disease. Each answer is used only once.

55. Myosin binding protein C A. Becker's Dystrophy
56. dystrophin protein B. Myotonic Dystrophy
57. protein kinase C. Familial Hypertrophic Cardiomyopathy (FHC)
58. α-dystroglycan protein D. Limb-girdle Dystrophy
The R1-R1 insert DNA fragment is cloned into the R1 site of the vector. The vector alone is 2500 bp.

Questions 59-61 refer to the following figure.

59. (1 point) How many fragments would you expect if the vector + insert DNA were fully restricted with both H and R enzymes?
   A. 2
   B. 3
   C. 4
   D. 5

60. (2 points) What size fragments would you expect to see if the vector + insert DNA is fully restricted with the S enzyme?
   A. 900 bp, 1800 bp, and 1000 bp
   B. 1800 bp, and 1900 bp
   C. 400 bp and 800 bp
   D. 400 bp, 800 bp, and 2500 bp

61. (1 point) Assume that the filled-in boxes in the insert DNA fragment are exon sequences for a cardiac-specific myosin heavy chain gene. In which of the following tissues would you expect hybridization of the insert DNA to occur in a Northern blot? Choose the ONE best answer.
   A. liver
   B. heart
   C. kidney
   D. all of the above
   E. none of the above
62. (2 points) The exacerbation of the symptoms of neurofibromatosis type I following pregnancy is an example of which ONE of the following?

A. Variable expressivity  
B. An environmental contribution to phenotype  
C. Sex-linked inheritance  
D. Delayed age of onset

63. (2 points) The mutation rate of the mitochondrial genome is elevated as compared to the nuclear genome due to which ONE of the following?

A. Heteroplasmym  
B. Free radical formation due to the TCA cycle  
C. A lack of a DNA repair system in the mitochondria  
D. None of the above

64. (2 points) Meiosis I reduces the number of sister chromatids from

A. Four to two  
B. Two to one  
C. Eight to four  
D. None of the above is correct

65. (2 points) Spectral karyotyping is most useful for evaluation of which ONE of the following?

A. Trisomies and changes in chromosome number  
B. Translocations and changes in chromosome structure  
C. Linkage analysis  
D. Genomic imprinting

66. (2 points) A young patient presents with many of the characteristics of Down’s syndrome. Cytogenetics reveals that only half of the fifty cells examined carried an extra chromosome 21. This is best explained by which ONE of the following?

A. Laboratory error  
B. Failure of meiosis I  
C. Failure of meiosis II  
D. Germline mosaicism in one of the parents  
E. Mitotic non-disjunction
67. (1 point) Parents of an individual with Prader-Willi syndrome donate skin cells which are evaluated by cytogenetics using FISH with a probe directed against the deleted region of chromosome 15. The analysis is also done with the patient's cells. Which ONE of the following results should be observed?

A. The probe reveals one spot in maternal cells
B. The probe reveals one spot in paternal cells
C. The probe reveals two spots in the patient's cells
D. The probe is unable to distinguish between cells from either parent or the patient

68. (1 point) Increases in genomic instability are associated with cancer predisposition. This best reflects which ONE of the following?

A. The inability to repair DNA in the mitochondria
B. The fact that cells lacking DNA repair are malignant
C. The clonal nature of cancer
D. The accumulation of mutations in growth regulatory genes

69. (1 point) A 21 year old woman in a BRCA1 family is tested for the mutation and does not carry a mutation. The best thing to tell her is which ONE of the following?

A. She does not carry any risk of developing breast cancer
B. That age-appropriate screening is necessary to identify early tumors
C. That her children may be affected with the BRCA1 allele
D. She needs to continue annual screening anyway

70. (1 point) The protein truncation test is capable of detecting all but ONE of which of the following types of mutations.

A. Frameshift
B. Insertion
C. Deletion
D. Premature stop codon
E. Missense mutation

71. (1 point) The Icelandic populations studied for cancer susceptibility are useful because of which of the following? Choose the ONE best answer.

A. Genetically homogenous
B. Represent a genetic isolate
C. Allow identification of founder mutations
D. All of the above
E. None of the above
72. (1 point) DNA chips will rapidly provide low cost mutation detection for numerous genetic diseases. This technology is based on which ONE of the following?

A. Nucleic acid hybridization
B. Protein-protein interactions
C. Fluorescent activation of circuits
D. The PCR reaction
E. Primer extension

73. (2 points) The pedigree represented to the right best displays which ONE of the following types of inheritance patterns?

A. Autosomal Dominant
B. Autosomal Recessive
C. Paternal imprinting
D. X-linked
E. Mitochondrial

74. (1 point) The key distinguishing factor between X-linked and autosomal dominant inheritance patterns is which ONE of the following?

A. Absence of male to male transmission
B. Absence of male to female transmission
C. Absence of female to female transmission
D. Absence of female to male transmission

75. (2 points) Considering the pedigree shown to the right, what is the probability that individual IV-1, with the question mark, is the carrier of the rare autosomal disorder which is also carried by individual III-2. You also know that individual III-1, the sister of the carrier, does not carry the defective allele. There is a closely linked marker with two polymorphic forms within the population, designated A and B. The genotypes are indicated in the figure. Assume that no recombination has occurred in the pedigree shown.

A. 100%
B. 75%
C. 50%
D. 25%
E. 0%
76. (1 point) A typical Robertsonian translocation results in the loss of chromosomal material, yet the individuals with this translocation are phenotypically normal. This is due to which ONE of the following?

A. All chromosomes contain extra DNA which can be lost with no effect
B. Ribosomal RNA genes are located on many chromosomes, so losing some of these redundant genes has no effect
C. The long chromosomes which participate in Robertsonian translocations have regions with no DNA, which are lost when the chromosomes fuse
D. The environmental impact due to the lost DNA is minimal

77. (2 points) Assume a person has a balanced translocation between chromosomes 10 and 12. When these chromosomes line up during meiosis a cross structure is formed, as shown in the figure. Of the six possible combinations of chromosomes which can form the germline of the individual, how many would carry the balanced translocation?

A. One
B. Two
C. Three
D. Four
E. Five
F. Six
G. None

78. (2 points) In the pedigree indicated to the right Individual II-3 has a rare autosomal recessive disorder. What is the probability that Individual III-1 is a carrier of this disease?

A. 0%
B. 12.5%
C. 25%
D. 33%
E. 50%
F. 67%
G. 75%
H. 100%
Questions 79-82 (1 point each) are matching questions. Answer the questions from the lettered list A through G. Each question only has **ONE** best answer, and an answer may be used more than once.

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
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<tbody>
<tr>
<td>79. Gene product is involved in DNA repair</td>
<td>A. AAPC</td>
</tr>
<tr>
<td>80. Alters gene transcription depending on its phosphorylation state</td>
<td>B. BRCA1</td>
</tr>
<tr>
<td>81. Disease gene cloned through use of a subtractive hybridization procedure</td>
<td>C. Rb</td>
</tr>
<tr>
<td>82. A form of a hereditary based colon cancer which has a small number of polyps prior to the malignancy developing</td>
<td>D. CF</td>
</tr>
</tbody>
</table>

**THIS ENDS THE QUESTIONS FOR THE FIRST ANSWER SHEET. THE QUESTIONS ON THE NEXT PAGE BEGIN AGAIN WITH QUESTION #1, AND REQUIRES THE USE OF THE SECOND ANSWER SHEET.**
Questions 1-5 (1 point each) are True or False. Indicate your answer by darkening either T or F on the answer sheet. **USE ANSWER SHEET TWO TO ANSWER THESE QUESTIONS.**

1. Estimates indicate that greater than 50% of hospitalized patients have a significant genetic component to their disease process.

2. Generally, genetically caused diseases manifest earlier in life (childhood), whereas diseases with genetic susceptibility manifest later in life (adulthood).

3. As the heritability of a disease decreases toward zero, the number of informative individuals needed to determine the genetic contribution to the disease also decreases.

4. Gaucher disease is an autosomal recessive trait due to mutations at the glucocerebrosidase locus.

5. A heritability of 50% implies an autosomal dominant mode of inheritance.

6. (2 points) The following table provides information about somatic cell hybridization experiments to map a gene of interest, R. These are stable hybrids derived from murine/human cell fusions. All the normal murine chromosomes are present, the test for R is specific for the human gene/gene product, and the chromosome numbers refer to the human chromosomes present. The +++ or - refer to the presence or absence of gene R or a specific human chromosome in the cell hybrid(s). To which human chromosome does Gene R map?

<table>
<thead>
<tr>
<th>Somatic Cell Hybrid Panel</th>
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<tbody>
<tr>
<td><strong>Cell Hybrid</strong></td>
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<td>1</td>
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A. 1
B. 2
C. 3
D. 4
E. 5
Questions 7-10 refer to the following paragraph and pedigree.

Two siblings with Niemann-Pick (NP) disease, an autosomal recessive disease due to the mutations at the sphingomyelinase locus, come to you because the family and the local physician are confused. The youngest child has a neuronopathic form of the disease (type A) and the older sibling has a non-neuronopathic form of the disease (type B). You take a family history and develop a pedigree that is shown below. At first you are very confused, but then you ask if NP disease has ever occurred in the family before, and the mother tells you that she was diagnosed with the type B form early in life and had a splenectomy at age 10 yrs. She now has earned her Ph.D. in pure mathematics from Princeton University and on the basis of that you can assume that she indeed has a non-neuronopathic variant of the disease. The father also has a Ph.D., and has no medical problems. [By the way, this is a real case]. Their issues relate to the explanation of how these two variants could occur in separate pregnancies and what the risks are for future pregnancies since they would like to have more children. You know no other information than the above and what is given in the pedigree. In particular, you know nothing about the genetic status of the affected or unaffected individuals. The following questions relate to this family. Non-paternity is not an issue for this family.

7. (1 point). Answer True or False. The pedigree proves that the assumption of NP disease as an autosomal recessive disease is incorrect.

8. (2 points) What is the risk of this family having an affected child with NP disease?
   A. 25%
   B. 50%
   C. 66.7%
   D. 75%
   E. 100%

9. (2 points) What is the risk of this family having another pregnancy with the neuronopathic form of NP?
   A. 25%
   B. 50%
   C. 66.7%
   D. 75%
   E. 100%
10. (2 points) The good explanation for the findings in this family (discussed on the previous page) is which ONE of the following?

A. Interlocus heterogeneity  
B. Intra-allelic heterogeneity  
C. Metabolic cooperativity  
D. Variable penetrance  
E. Environmental differences

11. (2 points) A major goal of the Human Genome Project is to determine the sequence of the entire human genome. Once this sequence is completed there will be a need to continue to sequence genomes from many other individuals from many different ethnic and demographic groups. Why is this important? Choose the ONE best answer.

A. Normal variation in genes of different populations is required for the interpretation of genetic data  
B. Genetic susceptibility to disease states involve different genetic polymorphisms in various populations  
C. Group variation in genetic structure will provide insight into important conserved regions and sequences in the human population  
D. This will likely confirm the expectation that the greatest variation in the human genomic sequences are in sub-Saharan Africa since human populations have been established there for the longest time  
E. All of the above

12. (2 points) Viral tropism can be exploited for gene therapy vector development since this property implies that viruses can do which ONE of the following?

A. spread throughout the body and add genes to all cells in the body  
B. attack and kill a variety of cell types and will be useful for cancer therapy  
C. integrate their genomes into the human genome for stable expression  
D. preferentially enter various cell types to provide genes to selected cells  
E. selectively overexpress genes in many different cell types

13. (1 point) Heritability (H) is a key concept in population genetics and identification of disease-related genes. All of the following are true about H, in the additivity model, except [do not view choice E as self-contradictory] for which ONE?

A. As H tends to 0, VE increases  
B. As H tends to 1, VG increases  
C. \( H = \frac{VP}{VG+VE} \)  
D. VG, VP and VE refer to the variance in genotype, phenotype and environment, respectively  
E. None of the above are false
14. (2 points) An individual is a carrier for a Mendelian autosomal recessive disorder. Her spouse is unaffected by the disease and is not a carrier. The couple is expecting twins. If we assume that the twins are dizygotic (fraternal), what is the probability that BOTH babies will be carriers?

A. 50%  
B. 33%  
C. 25%  
D. 0%  
E. none of the above

15. (2 points) In the above example (question 14), if we assume that the twins are monozygotic (identical), what is the probability that BOTH babies will be carriers?

A. 50%  
B. 33%  
C. 25%  
D. 0%  
E. none of the above

16. (2 points) A woman and her spouse are planning to start a family. Her spouse is affected by an autosomal dominant disease. What is the probability that the child they are planning to have will be affected by that disease?

A. 0%  
B. 25%  
C. 33%  
D. 50%  
E. 75%

17. (2 points) The Hardy Weinberg principle can be used to estimate the carrier frequency of cystic fibrosis. Which ONE of the following assumptions is true about the Hardy Weinberg equilibrium?

A. The frequency of alleles at each genotype must be equal  
B. The population being studied should be small  
C. There should be interconversion of alleles  
D. Individuals of all genotypes must be equally capable of reproduction  
E. Mating should not be random

18. (2 points) A polymorphic marker is being tested in a family. Which ONE of the following would be the MOST "informative"?

A. Father is 1,2, mother is 1,1  
B. Father is 1,1, mother is 2,3  
C. Father is 1,1, mother is 1,1  
D. Father is 2,2, mother is 2,2
19. (2 points) Which **ONE** of the following parameters can BEST be used to find out whether two markers are "linked"?

A. the frequency of mitotic recombination between the markers.
B. the rate of mutation at each marker.
C. the allele frequency for each marker.
D. the frequency of each gene in the population.
E. the frequency of meiotic recombination between the markers.

20. (2 points) Based on the genetic information for two loci A and B in the pedigree shown below, which **ONE** of the following individuals is a "recombinant"?

![Pedigree Diagram]

A. II-1
B. III-1
C. III-2
D. III-3
E. None of the above

21. (2 points) Genetic counseling is a major issue for families tested for cystic fibrosis after molecular screening for mutations. The most problematic scenario, where mutation screening results in knowledge of increased apparent risk, yet offers nothing further by way of prenatal diagnosis is when :

A. Neither partner is found to be a carrier
B. Both partners are found to be carriers for the identical mutation
C. Each partner is found to be a carrier for a different mutation
D. All of the above
E. None of the above
22. (2 points) In which of the following disorders might the phenomenon of anticipation be seen? Choose the ONE best answer.

A. Fragile X syndrome  
B. Huntington disease  
C. Myotonic Dystrophy  
D. spino-bulbar muscular atrophy  
E. All of the above

23. (2 points) A newly discovered gene is thought to be an example of a "tumor suppressor". For this mechanism to be true, which ONE of the following observations must be demonstrated?

A. One mutant allele is necessary for tumor formation.  
B. One mutant allele is sufficient for tumor formation.  
C. The gene must be expressed at different levels in tumor and blood.  
D. The gene product must be non-functional or absent.  
E. None of the above.

24. (2 points) A couple has a son with a single retinoblastoma tumor in one eye. Both parents are clinically normal, and neither of their families shows a positive family history. The son grows up and has two adult children, none of whom have retinoblastoma. The BEST explanation for retinoblastoma in the son is which ONE of the following?

A. The son inherited a mutation in the Rb gene from his father.  
B. The son has a germline mutation that he did not transmit to either child.  
C. The son has inherited one mutant Rb gene from his germline and gets one somatic mutation that inactivates the normal allele in a retinoblast.  
D. The son has somatic mutations that inactivate both copies of the Rb gene in a retinoblast.  
E. The son has germline mutations that inactivate both copies of the Rb gene.

25. (2 points) The process of chromosome walking to go from the linked marker to the disease gene requires screening which ONE of the following type of libraries?

A. A human cDNA library  
B. A human genomic DNA library  
C. A tissue specific RNA blot  
D. A library of polymorphic markers  
E. None of the above
26. (2 points) At a LOD score of 1, the odds in favor of linkage are which ONE of the following?

A. 1:1  
B. 10:1  
C. 100:1  
D. 100,000:1  
E. None of the above

27. (2 points) Which ONE of the phenomena listed below would be characteristically observed in pedigrees as a result of expansion of triplet nucleotide repeats?

A. All progeny of affected individual will be affected  
B. 25% of progeny from an affected individual will be affected  
C. Increased severity of the disease in successive generations  
D. The trait will be influenced by factors such as diet and exercise  
E. None of the above

28. (2 points) Loss of heterozygosity can be used to detect the location of tumor suppressor genes such as retinoblastoma. Which ONE of the following can result in the loss of heterozygosity?

A. Nondisjunction and loss of the "normal" copy, while retaining the mutant copy.  
B. Nondisjunction and loss of the normal copy and duplication of the mutant copy.  
C. Mitotic recombination that results in the loss of the "normal" copy.  
D. Gene conversion that results in the loss of the "normal" copy.  
E. All of the above mechanisms.

29. (2 points) Which ONE of the following is true for diseases that involve genomic imprinting?

A. The expression of the disease depends on the sex of the transmitting parent.  
B. The transmission of the disease is always through the paternal lineage.  
C. The transmission of the disease is always through the maternal lineage.  
D. The transmission of the disease follows an autosomal recessive mechanism.  
E. All of the above
30. (2 points) "W" and "K" are unrelated multifactorial traits. The frequency of disease "W" in the general population is 1 in 500, and the frequency of disease "K" in the population is 1 in 1000. Which ONE of the following is true about RELATIVE risk concerning traits W and K?

A. The relative risk for first degree relatives of a person with "W" is less than the relative risk for first degree relatives of a person with disease "K".
B. The relative risk for first degree relatives of a person with "W" is greater than the relative risk for first degree relatives of a person with disease "K".
C. The relative risk for first degree relatives of a person with "W" is equal to the relative risk for first degree relatives of a person with disease "K".
D. The relative risk for first degree relatives of a person with "W" cannot be compared to the relative risk for first degree relatives of a person with disease "K".
E. None of the above.

31. (2 points) In cleft palate, congenital hip dislocations and congenital pyloric stenosis, the trait is more common in males than females. If we compare a male child whose mother is affected to a male child whose father is affected, the risk when the mother is affected is which ONE of the following?

A. Greater
B. Smaller
C. Equal
D. Cannot be estimated.
Answers Med Biochem Exam IV

1. D 45. D 4. T
2. E 46. B 5. F
5. A 49. C 8. B
8. T 52. B 11. E
12. F 56. A 15. A
20. D 64. A 23. D
24. F 68. D 27. C
26. G 70. E 29. A
27. C 71. D 30. A
28. C 72. A 31. A
29. F 73. E
30. B 74. A
31. T 75. C
32. T 76. B
33. F 77. A
34. F 78. D
35. T 79. B
36. F 80. C
37. T 81. E
38. T 82. A
39. F
40. A
END ANSWER SHEET
41. E ONE
42. A 1. T
43. B 2. T
44. A 3. F