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 84 questions on 15 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. For multiple answer questions without a defined number of answers 0.25 points will be deducted for each incorrect answer, although the lowest point value assigned for a question is 0. **No multiple answer question will have more than 4 correct answers. If a question has a defined number of answers, there is no penalty for guessing.**

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

4. There is one answer sheet for this exam. Fill in the circle for the correct answer(s) completely. If you believe that a question has more than one correct answer fill in all answers for that question 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. You should use the three leftmost boxes to insert your number.**

5. When you are finished with the exam, return both the test booklet and the answer sheets. The test booklet will be returned to you when the grading is complete. **You will receive your next installment of the course syllabus in your mailbox the second week of February.**

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. Following the last page of the exam are two blank pages for your use, and a third page which can be used by you to list your answers. You can take this sheet with you from the exam, and use it to check your answers against the posted answers (outside of room 3109 MSB). **You will not be given extra time to fill out this answer sheet.** Answers will be posted on December 20th, at noon, assuming that all students attend the exam at its scheduled time. You can access your grades from Blackboard beginning December 18th.

8. You will have **3.0 hours (until 11:30 am)** to complete this exam. Good luck.
Questions 1-10 (2 points each) should be answered from the list of amino acids designated by the single letter code (answers A through J). Each question may have more than one correct answer; indicate all correct answers on the answer sheet. An answer may be used once, more than once, or not at all.

1. Strictly ketogenic
2. Precursor of epinephrine
3. Precursor of dopamine
4. Essential for the human diet
5. Belongs to the fumarate family of degradation products
6. A defect in its degradation leads to maple syrup urine disease
7. Required for the synthesis of the porphyrin ring
8. Required for the synthesis of the purine ring
9. Synthesis is initiated with 3-phosphoglycerate
10. Synthesis is initiated from α-ketoglutarate

A. The amino acid designated by “A”
B. The amino acid designated by “D”
C. The amino acid designated by “E”
D. The amino acid designated by “G”
E. The amino acid designated by “K”
F. The amino acid designated by “L”
G. The amino acid designated by “S”
H. The amino acid designated by “V”
I. The amino acid designated by “W”
J. The amino acid designated by “Y”

Questions 11-16 (1.5 points each) refer to tetrahydrofolate and its derivatives. Answer each question with the ONE best answer listed. An answer may be used once, more than once, or not at all.

11. This form of tetrahydrofolate will accumulate when vitamin B12 is deficient
A. Tetrahydrofolate
B. N^5, N^10 methylene tetrahydrofolate
C. N^5, N^10 methylenyl tetrahydrofolate
D. N^5 formyl tetrahydrofolate
E. N^10 formyl tetrahydrofolate
F. N^5 formimino tetrahydrofolate
G. N^10 formimino tetrahydrofolate
H. N^5 methyl tetrahydrofolate
I. N^10 methyl tetrahydrofolate

12. This form of tetrahydrofolate is required for the biosynthesis of thymidine

13. This form of tetrahydrofolate is required for the biosynthesis of the purine ring

14. This form of tetrahydrofolate is produced by the serine hydroxymethyl transferase reaction

15. This form of tetrahydrofolate is produced when glycine is degraded

16. This form of tetrahydrofolate is produced during histidine degradation
17. (2 points) A newborn who tests positive for phenylalanine in the blood most likely has a problem in which of the following? There may be more than one correct answer to this question; indicate all correct answers on the answer sheet.

A. Phenylalanine hydroxylase
B. Tyrosinase
C. Tyrosine transaminase
D. Vitamin B6 levels
E. Vitamin B12 levels
F. Tetrahydrofolate regeneration or synthesis
G. Tetrahydrobiopterin regeneration or synthesis

18. (2 points) Parkinson’s disease results from a defect in which ONE of the following pathways?

A. Catecholamine biosynthesis
B. GABA biosynthesis
C. Serotonin biosynthesis
D. Histamine biosynthesis
E. Acetylcholine biosynthesis

19. (2 points) Increased thrombosis can result from elevated levels of homocysteine. Which enzymes might be defective to allow homocysteine levels to accumulate? This question may have more than one correct answer. Indicate all correct answers on the answer sheet.

A. Cysteine deaminase
B. Cystathionase
C. Cystathione-β-synthase
D. Glycine cleavage enzyme
E. Homocysteine decarboxylase
F. Methionine synthase
G. N⁵, N¹⁰ methylene tetrahydrofolate reductase
H. Serine hydroxymethyl transferase
20. (2 points) You are seeing a patient who is a 40 year old white woman of Dutch descent who complains of bouts of severe abdominal pain for most of her life. She has had multiple surgeries that have failed to solve her problem. She states most of the doctors who have seen her in the past think she is crazy. Most recently she has had a recurrence of her pain since being on the Adkin's (high protein) diet for weight loss. Her symptoms most likely would respond to treatment with which of the following therapies? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. High carbohydrate diet  
B. Infusion of hemin  
C. Daily ingestion of a B-complex vitamin  
D. Use of an antidepressant  
E. Increased levels of folic acid  
F. Dialysis using a chelating agent to remove lead

21. (2 points) Neonatal jaundice is most likely due to a defect in which ONE of the following processes?

A. Isoprenylation  
B. Glycosylation  
C. Acylation  
D. Farnesylation  
E. Phosphorylation  
F. Myristalation

22. (2 points) A deficiency in vitamin B6 would lead to the decreased production of all of the following EXCEPT for which ONE?

A. Epinephrine  
B. Serotonin  
C. Gamma-aminobutyric acid  
D. Dopamine  
E. Acetylcholine
23. (2 points) Amino acid degradation gives rise to a certain subset of end-products, or families. These families can be represented by all of the following EXCEPT for which ONE?

A. Fumarate  
B. Oxaloacetate  
C. Pyruvate  
D. Alpha-ketoglutarate  
E. Succinyl-CoA  
F. Malate

24. (2 points) Which of the following amino acids can only be synthesized from glucose using a pathway in which phosphoenolpyruvate is an obligatory intermediate? There may be more than one correct answer to this question; indicate all correct answers on the answer sheet.

A. Glycine  
B. Tyrosine  
C. Methionine  
D. Aspartate  
E. Threonine  
F. Glutamate

25. (2 points) Vitamin B12 deficiency can lead to methyl-malonic acidemia. Which of the following amino acids would contribute to this problem when degraded in an individual with a deficiency of B12? There may be more than one correct answer to this question; indicate all correct answers on the answer sheet.

A. Aspartate  
B. Glutamate  
C. Methionine  
D. Isoleucine  
E. Leucine  
F. Histidine  
G. Tyrosine
26. (2 points) Which of the following enzymes are NOT necessary as an isoleucine nitrogen travels from the muscle to the liver to be incorporated into urea? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. Glutamate dehydrogenase  
B. Lactate dehydrogenase  
C. Carbamoyl-phosphate synthetase I  
D. Arginase  
E. a-ketoglutarate dehydrogenase  
F. Ornithine transcarbamoylase  
G. Aspartate transcarbamoylase  
H. Citrate synthase  
I. Argininosuccinate synthetase

27. (2 points) A newborn infant presents with lethargy, and a blood test indicates hyperammonemia. In addition, hypercitrullinemia is also discovered. The most likely enzymatic defect in this infant is which ONE of the following?

A. N-acetylglutamate synthase  
B. Carbamoyl-phosphate synthetase I  
C. Carbamoyl-phosphate synthetase II  
D. Ornithine transcarbamoylase  
E. Arginase  
F. Argininosuccinate synthetase  
G. Argininosuccinate lyase

28. (2 points) Glutamate performs multiple roles in nitrogen metabolism in the body. Which of the following are NOT such roles? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. Substrate for fixing ammonia  
B. Substrate for releasing ammonia  
C. Substrate in transamination reactions  
D. Substrate to transfer nitrogen between tissues  
E. Substrate for citrulline biosynthesis  
F. Substrate for producing a regulator of the urea cycle
29. (2 points) A buildup of orotic acid is diagnostic for a defect in which urea cycle enzyme? Choose the ONE best answer.

A. Arginase  
B. Argininosuccinate lyase  
C. Argininosuccinate synthetase  
D. Carbamoyl-phosphate synthetase I  
E. N-acetylglutamate synthase  
F. Ornithine transcarbamoylase

30. (2 points) Treatments to reduce ammonia levels in individuals with urea cycle defects include which of the following? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. Statins  
B. Colestid  
C. α-ketoacids of essential amino acids  
D. Citric acid  
E. Methotrexate  
F. Phenylacetate

31. (2 points) An example of someone in positive nitrogen balance would be which of the following? There may be more than one correct answer to this question; indicate all correct answers on the answer sheet.

A. A 25 year old man with a fever of 103 degrees  
B. A 6 year old healthy girl  
C. A patient recovering from burn wounds  
D. A person lifting weights to increase strength  
E. A 20 year old anorexic woman  
F. A 26 year old man on a hunger strike
32. (2 points) Which of the following terms can be used to describe sphingomyelin? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. Cerebroside  
B. Ganglioside  
C. Glycolipid  
D. Glycosphingolipid  
E. Phospholipid  
F. Sphingolipid

33. (2 points) Sphingosine is directly synthesized from which TWO of the following precursors?

A. Glycine  
B. Serine  
C. Alanine  
D. Pyruvate  
E. Oleic acid  
F. Oleyl-CoA  
G. Palmitic acid  
H. Palmitoyl-CoA

34. (2 points) Plasmalogen synthesis originates from which ONE of the following compounds?

A. Glycerol  
B. Glycerol-3-phosphate  
C. Dihydroxyacetone phosphate  
D. Glyceraldehyde-3-phosphate  
E. 3-phosphglycerate

35. (2 points) The creation of an ether linkage in plasmalogen synthesis requires which ONE of the following?

A. Reduction of an ester linkage to an ether linkage  
B. Addition of a CDP-fatty acyl group to the one position of the carbon backbone  
C. Substitution of an ester-linked acyl chain with a fatty alcohol  
D. Substitution of a hydroxyl group with a fatty alcohol  
E. Substitution of a phosphohead group with a fatty alcohol
36. (2 points) The sugar substrate for the synthesis of gangliosides is most similar to which ONE of the following?

A. The sugar substrate for glycolysis
B. The sugar substrate for glycogen synthesis
C. The sugar substrate for the HMP shunt
D. The sugar substrate for fatty acid biosynthesis
E. The sugar substrate for purine biosynthesis

37. (2 points) Treatment of phosphatidylinositol-trisphosphate with phospholipase D will yield which TWO of the following?

A. Diacylglycerol
B. Phosphatidic acid
C. Lysophosphatidylinositol trisphosphate
D. Inositol-phosphate
E. Inositol-bisphosphate
F. Inositol-trisphosphate
G. Inositol-tetraphosphate

Questions 38-42 (2 points each) should be answered from the lettered list below (A-J). Match the disease asked in the question with the lipid species which accumulates within the cell. There is only ONE answer per question, although an answer may be used once, more than once, or not at all.

38. Most striking symptom is a cherry-red spot in the retina
39. Metachromatic leukodystrophy
40. Gaucher’s disease
41. Niemann-Pick disease
42. The only X-linked sphingolipidosis

A. Ceramide
B. Ceramide-gal-sulfate
C. Ceramide-glc-gal-gal
D. Galactocerebroside
E. Glucocerebroside
F. GM2
G. GM3
H. Sphingosine
I. Sphingomyelin
J. Lactosyl-ceramide
Questions 43-46 (1.5 points each) should be answered from the lettered list below. The biosynthesis of phospholipids required a large number of activated intermediates. Answer the following questions based on the activated intermediates which are required for the synthesis described in the question. There is only ONE answer per question, but an answer may be used once, more than once, or not at all.

43. Required to synthesize phosphatidylcholine
   A. Diacylglycerol
   B. CMP-diacylglycerol
   C. CDP-diacylglycerol
   D. Phosphatidic acid
   E. Choline

44. Required to synthesize phosphatidylinositol
   F. Phosphocholine
   G. Inositol
   H. CMP-inositol
   I. CDP-inositol
   J. UDP-inositol

45. Required to convert lactosyl-ceramide to GM₃
   K. CMP-sialic acid
   L. CDP-sialic acid
   M. UDP-sialic acid
   N. Phosphatidylglycerol

46. Required to synthesize cardiolipin

Questions 47-54 are True/False (1.5 points each). Answer by darkening either the T or F sections of the answer sheet.

47. Agonist stimulation of phospholipase C can occur via a GTP-binding protein.
48. GM₂ has a more complex structure than GM₁.
49. Lysosphingolipids have the same biological activities as the parent sphingolipids.
50. Cardiolipin is only found in mitochondrial membranes.
51. Lipid membrane asymmetry across the leaflets of the membrane allow red blood cells to be recognized as “old” and cleared by the spleen.
52. The major phospholipid associated with surfactant is dioleyl-phosphatidylethanolamine.
53. The α subunit of hexosaminidase A is responsible for recognizing globoside as a substrate.
54. Surfactant proteins are very hydrophilic, which allows for appropriate interactions at the air-water interface within the lung.
Questions 55-60 (2 points each) are based on the answers listed below (A to I). Match the base analog listed in the question with its target enzyme as the answer. There is only ONE answer per question, although an answer may be used once, more than once, or not at all.

55. 5-fluorouracil  
56. Methotrexate  
57. PALA  
58. Azaserine  
59. Azido-thymidine  
60. Aminopterin

A. Amidophosphoribosyltransferase  
B. Aspartate transcarbamoylase  
C. Dihydrofolate reductase  
D. Dihydropterin reductase  
E. Herpes virus DNA polymerase  
F. Mammalian DNA polymerase  
G. Ornithine transcarbamoylase  
H. Reverse transcriptase  
I. Thymidylate synthase

Questions 61-66 (1.5 points each) are based on the figure below. The figure indicates the general structure of a purine and pyrimidine ring, with some of the atoms of each ring numbered. The numbers refer to the question number. For each numbered atom choose its biochemical origin from the lettered list of answers available (A through G). There is only ONE answer per question, although an answer may be used once, more than once, or not at all.

A. Aspartate  
B. Carbon dioxide  
C. Glutamine  
D. Glycine  
E. N10-formyl tetrahydrofolate  
F. Ribose-5-phosphate  
G. Serine

67. (2 points) Lesch-Nyhan syndrome is due to an inability to catalyze which reaction? Choose the ONE best answer.

A. Adenine to AMP  
B. Adenosine to AMP  
C. Guanine to GMP  
D. Guanosine to GMP  
E. Thymine to TMP  
F. Thymidine to TMP
68. (2 points) Gout can result from all of the following EXCEPT for which ones? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. Von Gierke’s disease
B. Lesch-Nyhan syndrome
C. ADA deficiency
D. A super-active variant of amidophosphoribosyl transferase
E. A super-active variant of PRPP synthetase

69. (2 points) The regulated enzyme in pyrimidine biosynthesis is which ONE of the following?

A. Carbamoyl-phosphate synthetase I
B. Carbamoyl-phosphate synthetase II
C. Carbamoyl-phosphate synthetase III
D. Aspartate transcarbamoylase
E. Ornithine transcarbamoylase
F. Dihydrro-orotase
G. UMP synthase

Questions 70-73 (1.5 points each) refer to ribonucleotide reductase. Match the appropriate nucleotide (answers A through P) with the question asked. There is only ONE answer per question, although answers may be used once, more than once, or not at all.

A. ATP
B. dATP
C. ADP
D. dADP
E. GTP
F. dGTP
G. GDP
H. dGDP
I. CTP
J. dCTP
K. CDP
L. dCDP
M. UTP
N. dUTP
O. UDP
P. dUDP

70. Inhibits the activity of the enzyme
71. When bound to the substrate specificity site, stimulates the production of deoxypyrimidines
72. When bound to the substrate specificity site, adenine nucleotides will be reduced
73. Preferred substrate when dTTP is bound to the substrate specificity site

74. (2 points) A vitamin B12 deficiency will lead to the inhibition of all of the following
reactions **EXCEPT** for which ones? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. Homocysteine to methionine  
B. Homocysteine to cystathionine  
C. dUMP to TMP  
D. Serine to glycine  
E. Methylmalonyl-CoA to succinyl-CoA  
F. Phenylalanine to tyrosine

75. (2 points) Aspartate participates in purine and pyrimidine metabolism via which of the following reactions or pathways? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. IMP to AMP conversion  
B. IMP to GMP conversion  
C. Purine ring biosynthesis  
D. Pyrimidine ring biosynthesis  
E. UTP to CTP conversion  
F. dUMP to TMP conversion

76. (2 points) Which of the following vitamins are **NOT** lipid soluble? This question may have more than one correct answer; indicate all correct answers on the answer sheet.

A. Vitamin A  
B. Vitamin C  
C. Vitamin D  
D. Vitamin E  
E. Vitamin K

77. (1 point) The "pre" portion of preproinsulin mRNA codes for which **ONE** of the following?

A. A chain  
B. B chain  
C. C-peptide  
D. signal sequence  
E. None of the above
78. (1 point) Myristoylated proteins have myristic acid covalently attached to which ONE of the following?

A. N- terminal methionine residues
B. C- terminal glycine residues
C. Asparagine residues
D. N- terminal glycine residues
E. C- terminal methionine residues

79. (2 points) Which ONE of the following statements is correct regarding O-linked glycosylation?

A. Sugars are transferred from nucleotide sugar intermediates to Asn groups of the nascent peptide
B. The terminal glucose is removed from high mannose precursors of complex carbohydrates in the ER
C. A dolichol pyrophosphate carrier is required
D. Sugars are transferred one at a time using a dolichol phosphate intermediate
E. Sugars are transferred from nucleotide sugar intermediates to Ser/Thr residues of the nascent peptide.

80. (2 points) The activation and secretion of mature insulin from the preproprotein synthesized during translation requires all of the following EXCEPT for which ONE?

A. cleavage of the signal peptide by signal peptidase
B. protein disulfide isomerase to assist in the correct formation of disulfide bonds
C. endoprotease removal of the C- peptide
D. formation of a thioester linkage between Cys and the C- terminal amino acid
E. targeting of the mature insulin to a secretion site

81. (1 point) All of the following are TRUE concerning N-linked glycoprotein biosynthesis EXCEPT for which ONE?

A. transfer of the oligosaccharide core from the dolichol intermediate to the protein usually occurs during polypeptide biosynthesis
B. processing of the oligosaccharide core can occur after transfer to the nascent polypeptide
C. an oligosaccharide protein transferase is responsible for transferring the core oligosaccharide from dolichol to the protein
D. additional sugars can be added to the core oligosaccharide in the golgi
E. Asp-Y-Ser/Thr is the sequence recognized for N-linked glycosylation
82. (1 Point) Which **ONE** of the following statements regarding glycosylation is **INCORRECT**?

A. A dolichol carrier is required for O-linked glycosylation  
B. Glycosylation of the nascent peptide can begin even before its synthesis is completed  
C. Inhibition of glycosylation in the RER prevents proper sorting of the nascent protein  
D. Terminal sugars are removed from the high mannose precursors of complex carbohydrates in the ER  
E. O-linked glycosylation can occur on either serine or threonine residues

83. (2 points) Classes of proteins, synthesized initially with a sequence that binds to a signal recognition particle, include which of the following? Choose the **ONE** best answer.

A. lysosomal enzymes  
B. mitochondrial proteins  
C. integral membrane proteins at the cell surface  
D. A and B ONLY  
E. A and C ONLY

84. (2 points) The enzyme defective in I-cell disease is which **ONE** of the following?

A. protein disulfide isomerase  
B. dolichol pyrophosphatase  
C. N-acetylglucosamine phosphotransferase  
D. hexosaminadase  
E. mannose-6-phosphatase
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5. B, J  34. C  63. C
6. F, H  35. C  64. E
12. B  41. I  70. B
13. E  42. C  71. A
15. B or A  44. C  73. G
16. F  45. K  74. B, F
17. A, G  46. C  75. A, C, D
18. A  47. T  76. B
20. A, B  49. F  78. D
22. E  51. T  80. D
23. F  52. F  81. E
24. D, F  53. F  82. A
25. C, D  54. F  83. E
27. F  56. C
28. E  57. B
29. F  58. A