BioMed 130 Midterm Examination
March 23, 2001

NAME

Dr. Dahlberg's section
(5 points for each of 8 questions; 40 points total)

1. A three year old child is brought to the ER by his parents with complaints of abdominal pain, loss of appetite, constipation, disorientation and fatigue. Lead poisoning is suspected and a urine sample gives a bright florescence with a UV lamp. Briefly explain how lead causes the positive urine test?

LEAD INHIBITS FERROCHELATASE, THE ENZYME INVOLVED IN THE FINAL STEP IN HEME SYNTHESIS. THIS LEADS TO ACCUMULATION OF PORPHYRINS (PROTOPORPHYRIN IX TO BE EXACT, BUT NOT NEEDED IN ANSWER) WHICH FLUORESCENCE WHEN EXPOSED TO UV LIGHT.

2. The liver has an essential role in regulating the concentration of all 20 amino acids in the blood. This is achieved by sensing the concentration and then either synthesizing or degrading each of the 20 different amino acids. If a diet high in alanine were injected, describe the paths by which the nitrogen and keto acid of excess alanine would be disposed of in the liver. (Answer with names; chemical structures are not necessary)

TRANSAMINATION OF ALANINE WITH \( \alpha \)-KETOGLUTARATE TO GIVE PYRUVATE + GLUTAMATE. THE KETO ACID, PYRUVATE, CAN ENTER SEVERAL PATHWAYS, PRIMARILY THE KREB CYCLE. THE NITROGEN IS REMOVED FROM GLUTAMATE BY OXIDATIVE DEAMINATION IN THE LIVER MITOCHONDRIA (TO YIELD \( \alpha \)-KETOGlutARATE AND NITROGEN), WHERE THE NITROGEN THEN ENTERS THE UREA CYCLE.

3. Dr. Goltz's patient, Nigel Hartnup, developed niacin deficiency (pellagra) due to a defect in processing which amino acid and by which two organs?

TRYPTOPHAN (A FRACTION OF WHICH CAN BE CONVERTED TO NIACIN). HARTNUP'S DISEASE IS CAUSED BY A DEFECT IN RECEPTORS FOR ABSORBING MONOAMINO, MONOCARBOXYLIC AMINO ACIDS (INCLUDING TRYPTOPHAN) IN THE INTESTINE AND REABSORBING THEM FROM THE GLOMERULAR FILTRATE IN THE KIDNEY.
4. Phenylketonuria (PKU) results from mutations in phenylalanine hydroxylase, an enzyme which converts phenylalanine to tyrosine. If these patients are provided sufficient tyrosine in the diet for the synthesis of dopa, dopamine, norepinephrine, epinephrine, melatonin and thyroxin, is this adequate therapy to allow these patients to live normal lives? Why or why not?

IT IS NOT ADEQUATE THERAPY. BLOOD LEVELS OF PHENYLALANINE BECOME ELEVATED WITH A NORMAL DIET AND MUST BE LOWERED BY LIMITING PHENYLALANINE INTAKE SINCE ELEVATED LEVELS ARE TOXIC TO THE NERVOUS SYSTEM AND LEAD TO PERMANENT BRAIN DAMAGE.

5. An elevated level of homocysteine, which accumulates in the blood of patients with pernicious anemia, cannot be reduced by excessive amounts of folic acid but the extra folic acid does cause the patients to develop neurological symptoms before they develop anemia. Explain.

FOLIC ACID IS USUALLY “TIED UP” AS 5-METHYL TETRAHYDROFOLATE IN PATIENTS WITH B12 DEFICIENCY SINCE THE CELLS ARE TRYING TO CONVERT HOMOCYSTEINE TO METHIONINE. EXCESS DIETARY FOLIC ACID PROVIDES ENOUGH FOLIC ACID FOR SOME TO BE CONVERTED TO 5,10-METHYLENE TETRAHYDROFOLATE, WHICH IS REQUIRED FOR THE CONVERSION OF DUMP TO dTMP (ESSENTIAL FOR DNA SYNTHESIS AND PREVENTION OF ANEMIA). A BLOCK IN THE OTHER B12 REQUIRING REACTION (METHYLMALONYL COA TO SUCINYL COA) THEN CAUSES NEUROLOGICAL SYMPTOMS AS ELEVATED LEVELS OF METHYLMALONYL COA INTERFERE WITH PROPER MYELIN SYNTHESIS.

6. Both DNA and RNA synthesis occur in the 5’ to 3’ direction. The analogue of deoxythymidine, AZT, has an N3 group substituted for the 3’ OH in the deoxyribose. Why is this an effective drug in the treatment of AIDS?

THE ABSENCE OF A 3’OH PREVENTS FURTHER ELONGATION OF THE GROWING DNA STRAND AND HALTS FURTHER DNA SYNTHESIS OF THE VIRUS.
7. A great many modifications occur during the processing of HnRNA. One of these is RNA editing, which involves the substitution of one base for another. As an example, in the small intestine the codon CAA is converted to UAA in apolipoprotein mRNA resulting in a different apoB protein than in the liver, where this process does not occur. What is the name of this process and what is the effect on the protein synthesized in the small intestine relative to that in the liver?

RNA EDITING. CHANGING CAA TO UAA CREATES A STOP CODON AND THUS apoB IS SHORTER IN THE INTESTINE THAN IN THE LIVER.

8. Cystic Fibrosis is a genetic disorder in the CF transmembrane conductance regulator protein (CFTR). There are more than 800 different mutations in the 1480 amino acids in CFTR. Why is it important to determine the type of mutation if they all affect the same protein?

THE TYPE OF MUTATION WILL DETERMINE THE TYPE OF THERAPY. FOR EXAMPLE GENTAMYCIN SUPPRESSES MUTATIONS CAUSING PREMATURE TERMINATION, ALLOWING READ-THROUGH OF STOP CODONS. BUTYRATE BINDS CHAPERONINS WHICH OTHERWISE TARGET POORLY FOLDED CFTR MUTANT PROTEINS FOR PROTEOLYSIS.
True/False (21 points)

- DNA replication is bidirectional, semi-conservative and always goes 5' to 3'.
- DNA synthesis is much slower in eucaryotic cells than procaryotic cells but there are more origins of replication.
- Some topoisomerases in bacteria can increase the twisting of double stranded DNA.
- DNA polymerase III can work in both directions; synthesizing DNA 5' to 3' and cleaving DNA 3' to 5' (as an exomuclease).
- Nucleotide excision repair enzymes can repair the wrong strand and create a mutation, unlike mismatch repair.
- RNA repair enzymes function basically by the same mechanisms as DNA repair enzymes.
- Transcription factors can actually bind and bend the DNA helix.
- HnRNA transcripts are modified primarily in the cytoplasm.
- Mutations in the 5' or 3' non-coding regions can affect the stability of mRNAs.
- The wobble base enables two or more amino acids to use the same codon.
- A missense mutation signals the ribosome to terminate translation.
- A c-DNA library from liver cells only contains introns from liver cell mRNAs.
- Restriction sites used in RFLP are most often outside the gene being probed.
- Non-polar amino acids cluster on the surface of membrane proteins.
- Transamination reactions occur only in liver, gut and muscle cells.
- ADP and GDP are allosteric activators of glutamate dehydrogenase in the liver mitochondria, stimulating conversion of glutamate to ammonia and ketoglutarate.
- Folate contributes one carbon moieties (or units) in several different states of oxidation but only 5'-adenosyl-methionine can provide methyl groups.
- The iron in hemoglobin is converted from the ferrous to the ferric state when it binds oxygen.
- Heme iron binds carbon monoxide much better than it binds oxygen.
- Acute intermittent porphyria causes photosensitivity.
- Fortunately in newborns bilirubin cannot cross the blood-brain barrier.
Fill In The Answer (24 points)

Damage to the liver by a chemical toxin such as dioxan would cause a rise in the level of **INDIRECT** bilirubin. (1 pt)

**OR**

**UNCONJUGATED**

Part of the treatment during an attack of acute intermittent porphyria is a high carbohydrate diet because **GLUCOSE REPRESSES ALA SYNTHASE**. (2 pts)

Important products of decarboxylation of the following amino acids are:

Tyrosine: **DOPAMINE**

Tryptophan: **SEROTONIN**

The decarboxylases involved in these reactions require the cofactor **PYRIDOXAL PHOSPHATE**. (3 pts)

Check those diseases where children appear normal at birth: (3 pts)

- Phenylketonuria
- alpha thalassemia major
- beta thalassemia major

Transaminases in the gut transfer nitrogen from the absorbed amino acids onto pyruvic acid to form **ALANINE**, which is transported to the liver.

This reaction involves the co-factor **PYRIDOXAL PHOSPHATE**. (2 pts)

The three main sources of the body's amino acid pool are: (3 pts)

- DIETARY PROTEIN
- BREAKDOWN OF BODY PROTEINS
- SYNTHESIS OF NON-ESSENTIAL AMINO ACIDS

Draw the tripeptide ValylAlanylglycine. (2 pts)

**Amino acid** | **R group**
--- | ---
Valine | $-\text{CH}_2\text{CH}_3$
Alanine | $-\text{CH}_2\text{H}_2$
Glycine | $-\text{H}$

$\text{Val} - \text{Ala} - \text{Gly}$

$\text{NH}_3 - \text{C} - \text{C} - \text{C} - \text{C}_3\text{H}_7 - \text{OH}$
The nitrogen for urea synthesis comes from the amino acid \textbf{GLUTAMATE} in the mitochondria and from the amino acid \textbf{ASPARTATE} in the cytoplasm of the liver cell. (2 pts) (OR \textbf{GLUTAMIC ACID} AND \textbf{ASPARTIC ACID})

It is thought that liver failure leads to coma because the excess nitrogen \textbf{Binds & Ketoglutarate to Form Glutamate, Depleting a Citric Acid Cycle} (2 pts)\textbf{Intermediate, Reducing Oxidation and ATP Synthesis.}

The most likely reason that \textbf{beta thalassemia} is not found in utero is; (2 pts)\textbf{There are Two \& Globin Genes on Each Chromosome (\textit{XY and XXY\text}).}

If an antibiotic blocks translocation, then the growing peptide is likely to be found associated with tRNA in the \textbf{A} site. (2 pts) \textbf{(OR ACCEPTOR)}