Topic 6: CELLULAR CATABOLISM

I Principles of catabolism

- A Catabolism = breakdown of complex molecules for obtaining energy
- B Energy is obtain by moving electrons in the form of hydride ions (H-)
- C Sources: carbohydrates, fats
- D Intermediate acceptors: NAD+, FAD+ (derived from B-vitamins niacin and riboflavin); they accept e- in the form of H- to become NADH and FADH2.
- E Terminal acceptors: oxygen (aerobic catabolism), pyruvic acid (anaerobic catabolism)

II Steps in Aerobic Catabolism

- A Glycolysis
  - 1 1st phase of glucose metabolism – occurs in cytosol
  - 2 1 6-carbon glucose molecule is broken down into 2 3-carbon pyruvic acid molecules
    - a yield = 2 ATPs and 2 NADHs for each glucose
  - 3 no oxygen needed (anaerobic)

- B Citric Acid Cycle
  - 1 2nd phase of glucose metabolism – occurs in mitochondrial matrix
  - 2 pyruvic acid is transported into mitochondrial matrix
  - 3 3-carbon pyruvic acid ➔ 2-carbon acetyl CoA + CO_2 (CoA derived from pantothenic acid)
    - a loss of a carbon as CO_2 is called decarboxylation
    - b enzyme that catalyzes this reaction must have thiamine (another B-vitamin) present
    - c yield = 1 NADH for each pyruvic acid
  - 4 acetyl CoA joins the citric acid cycle: 2-carbon acetyl CoA + a 4-carbon molecule ➔ a 6-carbon molecule (citric acid)
    - a yields no energy-producing molecules
  - 5 6-carbon molecule ➔ a different 6-carbon molecule
    - a yields no energy-producing molecules
  - 6 6-carbon molecule ➔ a 5-carbon molecule + CO_2
    - a yields 1 NADH for each original pyruvic acid
  - 7 5-carbon molecule ➔ 4-carbon molecule + CO_2
    - a yields 1 NADH for each original pyruvic acid
  - 8 4-carbon molecule ➔ different 4-carbon molecule
    - a yields 1 GTP for each original pyruvic acid

b GTP is “exchanged” for ATP

9 4-carbon molecule ➔ different 4-carbon molecule

a yields 1 $FADH_2$ for each original pyruvic acid

10 4-carbon molecule ➔ different 4-carbon molecule

a yields 1 NADH for each original pyruvic acid

11 4-carbon molecule ➔ 4 carbon molecule that acetyl CoA originally joined with

a this is why it’s called the citric acid **cycle**

b this final step yields no energy-producing molecules

12 Final yield:

a 4 NADH, 1 $FADH_2$, and 1 ATP (also 3 CO_2 as waste) for each original **pyruvic acid** molecule

b this means 8 NADH, 2 $FADH_2$, and 2 ATP (also 6 CO_2 as waste) for each original molecule of **glucose**

13 Although O_2 is not required during the citric acid cycle, it is necessary in order for the cycle to proceed, since O_2 is ultimately needed to process the NADH and $FADH_2$; therefore the citric acid cycle is part of aerobic catabolism

C Electron Transport Chain

1 3rd phase of glucose catabolism – occurs in inner membrane of mitochondrion

2 each NADH and $FADH_2$ “enters” the transport chain, passing electrons to the first component of the chain

3 as electrons are passed from one component to the next, the electrons lose energy, this energy is used by 3 of the components of the chain to pump hydrogen ions (H+) from mitochondrial matrix to intermembrane space

4 this establishes/maintains a concentration gradient for H+

5 H+ re-enters the matrix via ATP synthase, which uses the energy of the concentration gradient to drive the production of ATP (= chemiosmotic theory)

6 final electron acceptor = O_2 (½ O_2 ➔ H_2O, since once again, e- are passed as H-)

7 how much energy for each intermediate acceptor?

a each NADH has energy to generate 3 ATPs

b each $FADH_2$ has energy to generate 2 ATPs

c the NADHs derived from glycolysis must enter the mitochondrial matrix to pass electrons to the e- transport chain; in doing so, some of their energy is lost, therefore each NADH derived from glycolysis has energy to generate 2 ATPs

8 yield from e- transport chain

a 3 X 8 NADH from citric acid cycle = 24

b 2 X 2 FADH2 from citric acid cycle = 4
c 2 X 2 NADH from glycolysis = 4
d 32 ATPs from each original glucose

E Summary of aerobic catabolism
1 total yield (add all other ATPs) = 36 ATPs
2 final equation: glucose ($C_6H_{12}O_6$) + O_2 ➔ $6CO_2$ + $6H_2O$ + ATP

III Anaerobic metabolism
A Glycolysis only; pyruvic acid does not enter citric acid cycle
B Pyruvic acid ➔ lactic acid
1 there is a net energy loss in this reaction: 1 NADH is converted back to NAD
2 therefore 2 NADHs are lost for each glucose anaerobically catabolized
3 but remember, glycolysis total yield = 2 ATPs for each glucose
4 cells can function for short periods of time using only anaerobic metabolism
5 converting lactic acid back to pyruvic acid requires O_2, since NADH will be made in the process and NADH must have "somewhere to go"
6 this is what is meant by building up "O_2 debt" during anaerobic catabolism

IV Catabolism of fats:

A Triglycerides composed of glycerol + 3 fatty acid side chains
1 glycerol enters catabolic pathways part-way through glycolysis
2 fatty acids are broken down into 2-carbon chunks
a enter catabolic pathway as acetyl CoA, at beginning of citric acid cycle
b because each triglyceride has lots of 2 carbon chunks, catabolism of each fat molecule yields 6 to 7 times as much ATP
c but triglycerides have a higher molecular weight, so each gram of fat yields only about twice as much energy as each gram of carbohydrate
d approx 9 - 9.5 kcal (dietary calories)/gram fat vs. approx. 4 - 5 kcal/gram carbohydrate

B because fat catabolism primarily uses the citric acid cycle and electron transport chain, it is almost entirely aerobic, and fat catabolism requires more O_2 per gram food than does carbohydrate catabolism

Topic 7: DEFECTS IN MEMBRANE PHYSIOLOGY – CYSTIC FIBROSIS

I What is cystic fibrosis (CF)?
- A Heritable disorder; 1 in 2000 births
- B Characteristics
  - 1 thick, sticky mucous buildup in airways
  - 2 blockage of pancreatic ducts

II The cause of CF is a mutation in the gene for the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR)
- A Normal CFTR (protein) is made in rough ER, then transported via the Golgi to the plasma membrane
- B Normal CFTR at the plasma membrane allows for chloride (Cl-) permeability
- C Abnormal CFTR (protein) is made in rough ER, but stays there or in the Golgi; does not reach the plasma membrane
- D Cells with abnormal CFTR have decreased membrane permeability to Cl-

III In airways and in pancreatic ducts
- A Normal Cl- channel/CFTR is present on the part of the plasma membrane that faces the airway or the lumen of the pancreatic ducts
  - 1 An ion pump on the basal part of the plasma membrane pumps Cl- into the cell
  - 2 Outcome of this is a high intracellular concentration of Cl-
  - 3 Cl- leaks out through Cl-channel/CFTR on membrane that faces lumen
  - 4 Na+ “follows” Cl- by passing in between cells (via “leaky” tight junctions)
  - 5 This creates an osmotic gradient (a concentration gradient for H_2O)
  - 6 Entire process results in dilution of material in lumen
- B Abnormal Cl- channel/CFTR is not present on plasma membrane
  - 1 Although a gradient of Cl- is established, Cl- cannot leak out into the lumen
  - 2 Material in lumen is not diluted
    - a In airways, mucous becomes thick and sticky
    - b In pancreatic ducts, pancreatic secretions are too thick, and eventually plug up the ducts

IV In sweat glands
- A Normal Cl- channel/CFTR is present on the lumen-facing plasma membrane of cells that line the duct

1 An ion pump pumps Cl- out of the cell, into the extracellular fluid
2 Outcome of this is a low intracellular concentration of Cl-
3 Cl- “leaks” into cell from lumen of sweat duct
4 Na+ “follows” Cl- via Na+ channels
5 H_2O does not “follow” NaCl, since the epithelium lining the sweat ducts is not highly permeable to H_2O (tight junctions are **not** “leaky”)
6 Result is removal of NaCl from the sweat

B Abnormal Cl- channel/CFTR is not present on plasma membrane
1 Although a gradient of Cl- can still be established, Cl- cannot enter the cell from the lumen of the sweat duct
2 Material in lumen retains a high concentration of NaCl

V Other tissues are affected, since the CFTR occurs in many places in the body, but the major problems with CF are in the pancreas and airways.

VI Treatment
A Pancreatic enzymes
B Fat-soluble vitamins
C Low-fat diet
D Aggressive treatment of any lung infections

Help Session I
Exam I