Introduction

Being alive is work. Cells organize small organic molecules into polymers such as the proteins, carbohydrates, and so forth you studied last week. Cells move substances across membranes, change shape, grow and reproduce. Cells have complex structures that are intrinsically unstable; work is required to maintain this structure and order. To do work, cells must extract energy from nutritive molecules. Plants and animals both utilize the process of cellular respiration to obtain energy from complex molecules. The chemical reactions involved in this process release energy which is harnessed at the cellular level in the form of ATP. The summary chemical equation for this process is:

\[
C_6H_{12}O_6 + 6O_2 + 6H_2O \rightarrow 6CO_2 + 12H_2O + \text{Energy}
\]

Note the relationship of this equation to the photosynthesis equation. One is the reverse of the other. This relationship expresses the fact that these two processes are inextricably linked in the living world. Aerobic cellular respiration is dependent on the products of photosynthesis and photosynthesis utilizes the products of cellular respiration.

The process of respiration takes place over two distinctly different regions of the cell. First a six carbon saccharide -glucose- is break down into 2 three carbon organic acids. Step one takes place in the cytoplasm of a eukaryotic cell yielding a net of 2 ATP’s and some NADH. Chapter 7 we discussed the electron bus being NADPH. The process of respiration uses a similar electron bus: NADH. The second step in the respiratory process occurs when the three carbon organic acids produced in the first pathway of glucose breakdown (Glycolysis) is taken into the mitochondria where upon it is further degraded yielding electrons and H⁺ ions necessary to drive the third stage of respiration. Electrons stripped from carbon during the first and second stages of the respiratory process are channeled into a series of trans-spanning membranes (commonly referred to as the electron transport system) located between the inner and outer mitochondrial spaces. Here the electrons do work: pumping H⁺ ions against a concentration gradient. Finally, these electrons are absorbed by O₂ forming H₂O as H⁺ stream through a ATPase channel protein.

Course Outcomes

- Describe cellular respiration and how respiration relates to photosynthesis
- Describe the differences between aerobic and anaerobic respiration

Learning Goals

- Understand where “energy” for cellular functions originates.
- Understand the relationship between photosynthesis and cellular respiration
- Know the steps in aerobic respiration and where each occurs in the cell.
- Understand the basic features of oxidation-reduction reactions.
- Be able to describe the role of the step wise break down (extraction of electrons) of glucose in the production of ATP and account for the location and number of each CO₂ produced during aerobic and anaerobic respiration.
Master the “accounting sheet” for ATP formation found in the cytoplasm and mitochondria.

Assignments:

1. Read Chapters Chapter 8 in your text.
   Note that some portions of Chapter 7 and 8 are color-coded indicating the amount of detail in the presentation. You will not be responsible for the biochemical to biochemical detailed level of understanding. You will, however, be held responsible for the information presented in the study guides. Study guide information is fair game for lecture tests. Although you may not be asked to reproduce these biochemical pathways compound by compound you should be familiar with each of the processes (ETS and chemosmotic principle, ... etc.), such as starting and end compounds, and where energy is produced and required in the form of ATP. You should also be able fill in the ATP accounting sheet provide with this week’s study guide set.

3. Go to the following Web site:

   Study this page to augment your information and understanding of cellular respiration.

   http://www.emc.maricopa.edu/faculty/farabee/BIOBK/BioBookGlyc.html

   This link has a flow cartoon of the electron transport system. I strongly recommend this site.

   http://faculty.uca.edu/~johnc/respir1440.htm

   Great non-technical web site with diagrams and hot links to side bars for information amplification.

   http://faculty.nl.edu/jste/cellular_respiration.htm

   This site is fairly technical and to the point. If you have choose not to purchase the text book
   This chapter can easily substitute.
INTRODUCTION

There are 3 reasons for glucose metabolism:

1) All cells metabolize glucose
   a) Nerve cells in brains use glucose exclusively

2) Glucose metabolism is less complex than metabolism of other organic molecules

3) Cells converts other organic molecules to glucose
   a) Sugars, fats and to some extent proteins can release energy by oxidation
   b) Some energy is trapped as ATP
   c) Sugars and proteins have about 4 k-calories/grams of stored energy
      1. Fats have about 9 kcal/gram of energy
      2. If Sugar is burned in a one step process it will release 686 kcal/mole of energy as heat

The breakdown of glucose to ATP is not 100% efficient. Rather energy is released in the form of heat (2ND Law of Thermodynamics) as glucose is metabolized to CO₂ and H₂O

I. ATP PRODUCTION

A. ATP is the prime energy carrier for all cells

B. Comparison of three types of energy releasing pathways

1. AEROBIC RESPIRATION (O₂) is the main pathway for energy release from carbohydrate to ATP

   Sugar + Oxygen → Carbon dioxide + Water

   Oxygen is more electronegative than carbon (oxygen has a greater affinity for electrons than carbon) If carbon binds to oxygen the carbon is oxidized because electron shift toward oxygen.

   In this reaction the oxygen is reduced      Example: CO₂

2. FERMENTATION AND ANAEROBIC electron transport (both without O₂) release lesser amounts of energy for transfer to a small number of ATP (2)
3. All energy releasing pathways start with glycolysis
   a. Glucose is split into two pyruvate molecules
   b. Glycolysis reaction occur in the cytoplasm without the use of O₂

C. Overview of aerobic respiration
   1. Fermentation yields 2 ATP  aerobic respiration yield 36 ATP
   2. A simplified equation for AEROBIC respiration:

      \[ \text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2 \rightarrow 6\text{CO}_2 + 3\text{H}_2\text{O} \]

      *Note the similarities between this equation and photosynthesis*

   3. Three series of reactions are required for aerobic respiration
      a. Glycolysis is the breakdown of glucose to pyruvate; small amounts of ATP are generated in this pathway
      b. Krebs cycle degrades pyruvate to carbon dioxide, water, ATP, H⁺ ions, and electrons
      c. Electron transport phosphorylation processes the H⁺ ions and electrons to generate high yields of ATP; oxygen is the final acceptor of the electrons

II. GLYCOLYSIS The first stage of the energy-releasing pathway

A. Enzymes in the cytoplasm catalyze several steps in glucose breakdown
   1. Glucose is the first phosphorylated in energy-requiring steps, then the six-carbon intermediate is split to form two molecules of PGAL
   2. Enzymes remove H⁺ and electrons from PGAL and transfer them to NAD⁺ which becomes NADH (used later in the electron transport system)
   3. By substrate-level phosphorylation - four ATP are produced but remember two ATPs are used to initiate the catabolism process.

B. The end products of glycolysis are: 2 pyruvates, 2 ATP (net gain) and 2 NADH for each molecule of glucose degraded

III. Completing the Aerobic Pathway

A. preparatory steps and the Krebs cycle
   1. Pyruvate enters the mitochondria and is converted to acetyl-CoA
a) The first of the 3 CO₂ is lost

b) Acetyl-CoA then combines with oxaloacetate present in the mitochondria from the previous turn of the cycle to form Citric acid

2. During each turn of the Krebs cycle, the acetyl-CoA is further degraded leaving as two carbon dioxide (CO₂)

B. Functions of the second stage
   1. H⁺ and e⁻ are transferred to NAD⁺ and FAD
   2. Two molecules of ATP are produced by substrate-level phosphorylation

C. Third stage of aerobic pathway -- Electron transport phosphorylation
   1. NADH and FADH₂ give up their electrons to transport (enzyme) systems embedded in the mitochondrial inner membrane.
   2. According to the chemiosmotic theory, energy is released in the passage of electrons through components of the transport series.
      a. The energy is used to pump hydrogen ions out the inner compartment
      b. When hydrogen ions flow back through the ATP synthase in the channels, the coupling phosphate (Pᵢ) to ADP yields ATP

D. Summary of the energy harvest
   1. Electron transport yields 32 ATP; glycolysis yields 2 ATP; Krebs yields 2 ATP for a grand total of 36 ATP per glucose molecule
   2. Normally, for every NADH produced within the mitochondria and processed by the electron transport system, 3 ATP are formed; FADH₂ yields only 2 ATP
   3. NADH from the cytoplasm cannot enter the mitochondrion and must transfer its electrons
      a. In most cells (skeletal, brain) the electrons are transferred to FAD and thus yield two ATP (for a total of 36 ATP)
      b. But in liver, heart, and kidney cells, NAD⁺ accepts the electrons to yield 3 ATP; because 2 NADH are produced per glucose, this gives a total yield of 38 ATP
IV. ANAEROBIC Routes

A. Anaerobic pathways operate when oxygen is absent or limited; pyruvate from glycolysis is metabolized to produce molecules other than acetyl-CoA.

B. Fermentation Pathways

1. With an energy yield of only 2 ATPs, fermentation is restricted to single-celled organisms and cells of multi-celled organisms only at certain limited times

2. Lactate fermentation
   a. Certain bacteria (as in milk) and muscle cells have the enzymes capable of converting pyruvate to lactate
   b. No additional ATP beyond the net 2 from glycolysis is produced by NAD^+ is regenerated

3. Alcohol Fermentation
   a. Fermentation begins with glucose degradation to pyruvate.
   b. Cellular enzymes convert pyruvate to acetaldehyde, which then accepts electrons from NADH to become alcohol.
   c. Yeasts are valuable in the baking industry (CO₂ by product makes dough rise) and in the alcoholic beverage production

\[
C_6H_{12}O_6 \rightarrow CO_2 + H_2O + Alcohol
\]

TERMS:

Aerobic respiration - oxygen consumed in the process of metabolism
Anaerobic respiration - no oxygen consumed during metabolism
ATP - Adenosine Tri-phosphate
FAD - flavin adenine nucleotide
NAD - nicotiamide adenine dinucleotide
Glycolysis
Krebs cycle
The direction H+ ion diffusion is indicated by the location of ATP synthase proteins (lollipops). Mitochondria and some bacteria use chemiosmosis to make ATP during cell respiration. Chloroplasts use chemiosmosis to make ATP as part of photosynthesis.
Fill-in-the-Blanks

Virtually all forms of life depend on a molecule called (4) ______________ as their primary energy carrier. Plants produce adenosine triphosphate during (5) ______________, but plants and all other organisms can also produce ATP through chemical pathways that degrade (take apart) food molecules. The main degradative pathway requires free oxygen and is called (6) ______________. There are three stages of aerobic respiration. In the first stage, (7) ______________, glucose is partially degraded to (8) ______________. By the end of the second stage, which includes the (9) ______________ cycle, glucose has been completely degraded to carbon dioxide and (10) ______________. Neither of the first two stages produces much (11) ______________. During both stages, protons and (12) ______________ are stripped from intermediate compounds ______________ and delivered to a(n) (13) ______________ chain. This system is used in the third stage of reactions, electron transfer (14) ______________; passage of electrons along the transfer chain drives the enzymatic “machinery” that phosphorylates ADP to produce a high yield of (15) ______________. (16) ______________ accepts “spent” electrons from the transfer chain and keeps the pathway clear for repeated ATP production. Other degradative pathways are (17) ______________, in that something other than oxygen serves as the final electron acceptor in energy-releasing reactions. (18) ______________ and anaerobic (19) ______________ are the most common anaerobic pathways.

Matching   Choose the most appropriate answer for each.

22. _____ Krebs cycle
23. _____ oxygen
24. _____ mitochondrion
25. _____ electron transfer phosphorylation
26. _____ enzymes
27. _____ ATP
28. _____ glycolysis
29. _____ aerobic respiration
30. _____ cytoplasm
31. _____ fermentation pathways and anaerobic electron transport

A. Starting point for three energy-releasing pathways
B. Main energy-releasing pathway for ATP formation
C. Site of glycolysis
D. Third and final stage of aerobic respiration; high ATP yield
E. Oxygen is not the final electron acceptor
F. Catalyze each reaction step in the energy releasing pathways
G. Second stage of aerobic respiration; pyruvate is broken down into CO₂ and H₂O
H. Site of the second and third stages of the aerobic pathway
I. The final electron acceptor in aerobic pathways
J. The energy form that drives metabolic reactions
8.2. GLYCOLYSIS: FIRST STAGE OF ENERGY-RELEASING PATHWAYS

Fill-in-the-Blanks

(1) [recall Ch.7] organisms can synthesize and stockpile energy-rich carbohydrates and other food molecules from inorganic raw materials. (2) _____________ is partially broken down by the glycolytic pathway; at the end of this process some of its stored energy remains in two (3) _____________ molecules. Some of the energy of glucose is released during the breakdown reactions and used in forming the energy carrier (4) _____________ and the reduced coenzyme(5) _____________ . These reactions take place in the cytoplasm. Glycolysis begins with two phosphate groups being transferred to (6) _____________ from two (7) _____________ molecules. The addition of two phosphate groups to (6) energizes it and causes it to become unstable and split apart, forming two molecules of (8) _____________ . Each (8) gains one(9) _____________ group from the cytoplasm, then (10) _____________ atoms and electrons from each PGAL are transferred to NAD, changing this coenzyme to NADH. At the same time, two (11) _____________ molecules form by substrate-level phosphorylation; the cell’s energy investment is paid off. One (12) _____________ molecule is released from each 2-PGA as a waste product. The resulting intermediates are rather unstable; each gives up an(13) _____________ group to ADP. Once again, two (14) _____________ molecules have formed by (15) _____________ phosphorylation. For each (16) _____________ molecule entering glycolysis, the net energy yield is two ATP molecules that the cell can use anytime to do work. The end products of glycolysis are two molecules of (17) _____________ , each with a (18) -carbon _____________ backbone.

(number)

Sequence

Arrange the following events of the glycolysis pathway in correct chronological sequence. Write the letter of the first step next to 19, the letter of the second step next to 20, and so on.

19. _____ A. The first two ATPs form by substrate-level phosphorylation; the cell’s energy debt is paid off.
20 _____ B. Diphosphorylated glucose (fructose 1,6-bisphosphate) molecules split to form 2 PGALs; this is the first energy-releasing step.
21. _____ C. Two three-carbon pyruvate molecules form as the end products of glycolysis.
22 _____ D. Glucose is present in the cytoplasm.
23. _____ E. Two more ATPs form by substrate-level phosphorylation; the cell gains ATP; net yield of ATP from glycolysis is 2 ATPs.
24 _____ F. The cell invests two ATPs; one phosphate group is attached to each end of the glucose molecule (fructose 1,6-bisphosphate).
25 _____ G. Two PGALs gain two phosphate groups from the cytoplasm.
26 _____ H. Hydrogen atoms and electrons from each PGAL are transferred to NAD, reducing this carrier to NADH.
8.4. THIRD STAGE OF THE AEROBIC PATHWAY

Fill-in-the-Blanks
If sufficient oxygen is present, the end product of glycolysis enters a preparatory step, (1) ________________ - formation. This step converts pyruvate into acetyl CoA, the molecule that enters the (2) ________________ cycle, which is followed by (3) ________________ phosphorylation. During these three processes, a total of (4) ________________ (5) ________________ (number)(energy-carrier molecules) are generated. In the preparatory conversions, prior to and within the Krebs cycle, the food molecule fragments are further broken down into (6) _________________. During these reactions, hydrogen atoms (with their (7) ________________ are stripped from the fragments and transferred to the coenzymes (8) ________________ and (9) ________________

Labeling
In exercises 10—14, identify the structure or location; in exercises 15—18, identify the chemical substance involved. In exercise 19, name the metabolic pathway.
10. ________________ of mitochondrion 15. __________
11. ________________ of mitochondrion 16. __________
12. ________________ of mitochondrion 17. __________
13. ________________ of mitochondrion 18. __________
14. ___________ 19. ___________ ___________

Fill-in-the-Blanks
NADH delivers its electrons to the highest possible point of entry into a transfer chain; from each NADH, enough H\(^+\) is pumped to produce (20) ________________ ATP molecules. FADH\(_2\) delivers its (number) ________________ electrons at a lower point of entry into the transfer chain; fewer H are pumped, and (21) ________________ (number). ATPs are produced. The electrons are then sent down highly organized (22) ________________ chains located in the inner membrane of the mitochondrion; hydrogen ions are pumped into the outer mitochondrial compartment. According to the (23) ________________ model, the hydrogen ions accumulate and then follow a gradient to flow through channel proteins, called ATP (24) ________________, that lead into the inner compartment. The energy of the hydrogen ion flow across
the membrane is used to phosphorylate ADP in order to produce (25) _____________. Electrons leaving the electron transfer chain combine with hydrogen ions and (26) ____________ to form water. In eukaryotic cells, these reactions occur only in (27) ____________. From glycolysis (in the cytoplasm) to the final reactions occurring in the mitochondria, the aerobic pathway commonly produces a total of (28) ____________ (number) or (29) ____________ (number) ATP(s) for every glucose molecule degraded.

Choice
For questions 30—50, choose from the following. Some correct answers may require more than one letter.

a. preparatory steps to Krebs cycle       b. Krebs cycle       c. electron transfer phosphorylation
30. _____ Chemiosmosis occurs to form ATP molecules
31. _____ Three carbon atoms in pyruvate leave as three CO₂ molecules
32. _____ Chemical reactions occur at transfer chains
33. _____ Coenzyme A picks up a two-carbon acetyl group
34. _____ Makes two turns for each glucose molecule entering glycolysis
35. _____ Two NADH molecules form for each glucose entering glycolysis
36. _____ Oxaloacetate forms from intermediate molecules
37. _____ Named for a scientist who worked out its chemical details
38. _____ Occurs within the mitochondrion
39. _____ Two FADH₂ and six NADH form from one glucose molecule entering glycolysis
40. _____ Hydrogens collect in the mitochondrion’s outer compartment
41. _____ Hydrogens and electrons are transferred to NAD and FAD
42. _____ Two ATP molecules form by substrate-level phosphorylation
43. _____ Free oxygen withdraws electrons from the system and then combines with H to form water molecules
44. _____ No ATP is produced
45. _____ Thirty-two or thirty-four ATPs are produced
46. _____ Delivery point of NADH and FADH₂
47. _____ Two pyruvates enter for each glucose molecule entering glycolysis
48. _____ The carbons in the acetyl group leave as CO₂
49. _____ One carbon in pyruvate leaves as CO₂
50. _____ An electron transfer chain and channel proteins are involved
Matching

Match the following components of respiration to the list of words below. Some components may have more than one answer.

11. _____ lactic acid, lactate
12. ____ NAD ----------> NADH
13. _____ carbon dioxide is a product
14. ___ NADH ----------> NAD+
15. _____ pyruvate used as a reactant
16. _____ ATP produced by substrate-level phosphorylation
17. _____ glucose
18. _____ acetyl-COA is either a reactant or a product
19. _____ oxygen
20. _____ water is a product

True/False

If the statement is true, write a “T” in the blank. If the statement is false, explain why in the answer blanks below the statement.

_____ 1. Glucose is the only carbon-containing molecule that can be fed into the glycolytic pathway.

_____________________________________________________________________________
_____________________________________________________________________________
_____________________________________________________________________________

_____ 2. Simple sugars, fatty acids, and glycerol that remain after a cell’s biosynthetic and storage needs have been met are generally sent to the cell’s respiratory pathways for energy extraction.

_____________________________________________________________________________
_____________________________________________________________________________
_____________________________________________________________________________

_____ 3. Carbon dioxide and water, the products of aerobic respiration, generally get into the blood and are carried to gills or lungs, kidneys, and skin, where they are expelled from the animal’s body.

_____________________________________________________________________________
_____________________________________________________________________________
_____________________________________________________________________________
4. Energy is recycled along with materials.

5. The first forms of life on Earth were most probably photosynthetic eukaryotes.

Choice

For questions , refer to the text; choose from the following:

a. glucose  b. glucose-6-phosphate  c. glycogen  d. fatty acids  e. triglycerides
f. PGAL  g. acetyl-CoA  h. amino acids  i. glycerol  J. proteins

_______ Fats that are broken down between meals or during exercise as alternatives to glucose
_______ Used between meals when free glucose supply dwindles; enters glycolysis after conversion
_______ Its breakdown yields much more ATP than glucose
_______ Absorbed in large amounts immediately following a meal
_______ Represents only 1 percent or so of the total stored energy in the body
_______ Following removal of amino groups, the carbon backbones may be converted to fats or carbohydrates or they may enter the Krebs cycle
_______ On the average, represents 78 percent of the body’s stored food
_______ Between meals liver cells can convert it back to free glucose and release it
_______ Can be stored in cells but not transported across plasma membranes
_______ Amino groups undergo conversions that produce urea, a nitrogen-containing waste product excreted in urine
_______ Converted to PGAL in the liver; a key intermediate of glycolysis
_______ Accumulate inside the fat cells of adipose tissues, at strategic points under the skin
_______ A storage polysaccharide produced from glucose-6-phosphate following food intake that exceeds cellular energy demand (and increases ATP production to inhibit glycolysis)
_______ Building blocks of the compounds that represent 21 percent of the body’s stored food
_______ A product resulting from enzymes cleaving circulating fatty acids; enters the Krebs cycle
Self-Quiz

1. Glycolysis would quickly halt if the process ran out of , which serves as the hydrogen and electron acceptor.
   a. NADP+  b. ADP  c. NAD  d. H₂O

2. The ultimate electron acceptor in aerobic respiration is ________________ .
   a. NADH  b. carbon dioxide (CO₂)  c. oxygen (½ O₂)  d. ATP

3. When glucose is used as an energy source, the largest amount of ATP is generated by the portion of the entire respiratory process.
   a. glycolytic pathway  b. acetyl-CoA formation  c. Krebs cycle  d. electron transfer phosphorylation

4. The process by which about 10 percent of the energy stored in a sugar molecule is released as it is converted into two small organic-acid molecules is
   a. photolysis  b. glycolysis  c. fermentation  d. the dark reactions

5. During which of the following phases of respiration is ATP produced directly by substrate-level phosphorylation?
   a. glycolysis  b. Krebs cycle  c. both a and b  d. neither a nor b

6. What is the name of the process by which reduced NADH transfers electrons along a chain of acceptors to oxygen so as to form water and in which the energy released along the way is used to generate ATP?
   a. glycolysis  b. acetyl-CoA formation  c. the Krebs cycle  d. electron transfer phosphorylation

7. Pyruvic acid can be regarded as the end product of ________________ .
   a. glycolysis  b. acetyl-CoA formation  c. fermentation  d. the Krebs cycle

8. Which of the following is not ordinarily capable of being reduced at any time?
   a. NAD  b. FAD  c. oxygen, O₂  d. water

9. ATP production by chemiosmosis involves ________________ .
   a. H concentration and electric gradients across a membrane  b. ATP synthases  c. both a and b  d. neither a nor b

10. During the fermentation pathways, a net yield of two ATPs is produced from ________________ the NAD necessary for ________________ is regenerated during the fermentation reactions.
    a. the Krebs cycle; glycolysis  b. glycolysis; electron transport phosphorylation  c. the Krebs cycle; electron transport phosphorylation  d. glycolysis; glycolysis