METABOLISM III 14OCTOBER 2005

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Goals:

- To appreciate that different tissues have very different metabolic rates
- To understand basic physiological correlates of large vs. small animals and of endotherms vs. ectotherms

I. Do all tissues (within an individual) have the same metabolic rate?

A. No, rates of metabolism differ strikingly among tissues. Internal organs don't occupy much of total mass, but do use most of energy. For a human at rest:

Organ	% total mass		% total $\dot{E}$	
kidney	0.45		7.7	
heart	0.45		10.0	
brain	**2.1**	$\Sigma = 7.7$	**16.0**	$\Sigma = 71.7\%$
abdom. organs (except kidney)	3.8		33.6	
lungs	0.9		4.4	
muscle	**41.5**		**15.7**	
other	50.7		11.9	

B. Obviously metabolic rate per gram varies dramatically among tissues. [Brain high because of cost of maintaining ionic gradients.]

C. *N.B. These values change dramatically during activity, also with feeding, or with temperature. Thus, the concept of a single, mass-specific metabolic rate is artificial.*

II. What are the physiological correlates of high mass-specific rates for small animals?

A. High mass-specific metabolic rates of small animals means that they must "gear up" their physiology and morphology to provide adequate nutrient and gas exchange.

B. Because cell size is independent of body size (~$M^{?}$), a single cell of a small animal must be metabolizing relatively intensively.

C. How can small animals meet demands of very high gas and nutrient exchange? For example, they must get lots of oxygen into the lung, into the blood, to the tissues, and to the mitochondria.

1. Small animals have relatively high respiratory rates (b = -.25).
2. Also have relatively high heart rates (b = -.25) (Perhaps 900 to 1000 beats per minute in the smallest mammals but only 30 per minute in an elephant!). Thus can rapidly transport O_2, nutrients, and wastes to the cells

[3. Hemoglobin is relatively concentrated in small animals, and O_2 dissociation curves shifted to the right, and greater "Bohr shift." See future Respiration lectures.]

4. Capillary density is relatively high in small mammals. (Why is this important?)
5. Mitochondrial volume densities, mitochondrial surface areas, & enzyme activities are all greater in small animals. Why does this make sense?

6. Relative size of organs (% of total mass) varies with size. "b" for blood and muscle volume ~1, for gut & liver < 1, for skeleton > 1.
7. Enzyme activities may scale negatively (citrate synthase, a key aerobic enzyme), thus enzymes can be more active in small animals.

C. Overall, small animals live life "in the fast lane."

III. What are the physiological correlates of high metabolic rates of endotherms?

A. Endothermy and high metabolic rates in vertebrates evolved at least twice, in ancestors of mammals ("mammal-like reptiles") and in those of birds (dinosaurs). What are the physiological/morphological differences [2] that account for the **huge** difference in metabolic rates between endotherms vs. ectotherms?
   1. Not surprisingly, endotherms have large, complex lungs (high surface areas for gas exchange) and big (4-chambered) hearts
   2. Size of metabolically active organs (liver, kidney, heart, brain) in mammals are almost twice the size of same organs in a lizard.
   3. Mitochondrial membrane surface areas 4 to 5 times that of a lizard. (W. Fig. 8.31)
   4. Enzyme activity (e.g., cytochrome oxidase, a mitochondrial enzyme important in O_2 consumption) is 4 to 5 X that of a lizard. (W Fig. 8.31)

B. Conclusion: much of the huge difference in SMR between endo- & ectotherms may be accounted for by differences in (i) size of metabolically active organs (above), (ii) greater enzyme activity, as well as (ii) greater sodium/potassium transport. In effect, "there is more there there."

[2] A very readable paper on this topic is Else & Hulbert, 1981, Am. J. Phys. 204:R3-R9.

C. Do thyroid hormones play a role in this?
   1. Thyroid hormones influence above activities (mitochondrial surface area, ion permeability, membrane fatty acid composition, growth rate, metabolic rate).
   2. Thyroid activity and hormones are lower in reptiles, suggesting a key role for the thyroid in the evolution of endothermy in mammals.

IV. Control of Resting Metabolism in Vertebrates

A. Sympathetic influences

   1. Direct influence --can increase BMR of infants or SMR of lower animals as much as 100%, but only that of adult humans by 10 to 15%. A short-term mechanism.
   2. Indirect effect of sympathetic--stimulates adrenal medulla to release epinephrine and norepinephrine into blood. This increases metabolic rate, but the effects last about 10X longer than those of sympathetic stimulation. Thus a long-term mechanism.

B. Parasympathetic stimulation does not influence metabolic rate.

C. Thyroid hormone (thyroxine) increases resting metabolic rate, primarily in endotherms. When ambient temperatures are low for long periods, hypothalamus stimulates the thyroid gland to produce thyroxine, which increases heat production to help balance heat loss to the cold environment. This is a long-term <u>thermoregulatory</u> response.

   1. Lag in response (several hours to days).
   2. May increase O_2 consumption by stimulating sodium-pump activity and the number of pump units. Also, increases mitochondrial membrane surface area.

D. Thyroid hormones have limited effects on SMR of ectotherms, especially at low temperature. However, they increase maximum levels of oxygen consumption, thereby increasing stamina (see future locomotion lectures).

E. Thus metabolic rate of an individual can be modulated by both short- and long-term mechanisms.

   5. Role of sodium pump (W 242) -- mammalian cell membranes seem "leakier" and thus require greater pumping activity (hence more ATP/time) to maintain similar transmembrane gradients. Mammalian cells 8 times more permeable to Na^+ ions than were lizard cells.
      a. Why (mechanistically) are membranes leakier? Unsaturated membrane lipids are correlated with increased permeability to ions, and mammalian phospholipids contain relatively more polyunsaturated fatty acids.
      c. Why (evolutionarily) did leakier membranes evolve? May increase diffusive capacity of membranes to other molecules.