

CHO: Mother Nature's Favorite Fuel



Disclosures

- I have consulted for governments, NGOs, Scientific Societies, trade organizations and private industry. I am completely conflicted. However, I contend that opposing vested interests cancel out potential COI.
- Regardless, virtually nothing I intend to "sell" is less than 50 years old, well beyond usual shelf life and 'best used by' pull date.

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In a galaxy long ago,
but not very far away....



- Before PubMed, in the prehistoric days of *Index Medicus*
- Scientists did not have artificial intelligence
- So they were forced to use the real thing!
- "Good experiments are right forever."
(Otto Warburg)

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Sugars are Mother Nature's Most Essential Nutrients

- Humans can make every sugar necessary for life.
- Irrespective of maternal diet, the fetus, the future of the human species, obtains essentially all of its energy supply from glucose.
- The brain, the peak of human evolutionary progression, prefers to consume only glucose.

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Where is the IRB When You Need It Most?

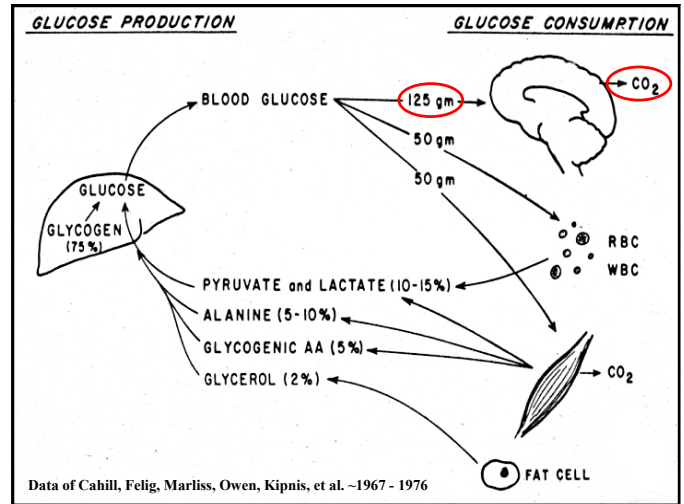
"50 males, 18 to 29 years of age, almost all of them medical students, were chosen for examination. The subjects lay quietly....The internal jugular vein was punctured....
Care was taken to see that the subjects breathed normally during and immediately preceding the taking of the sample."

Brain Arteriovenous R.Q. = 0.99

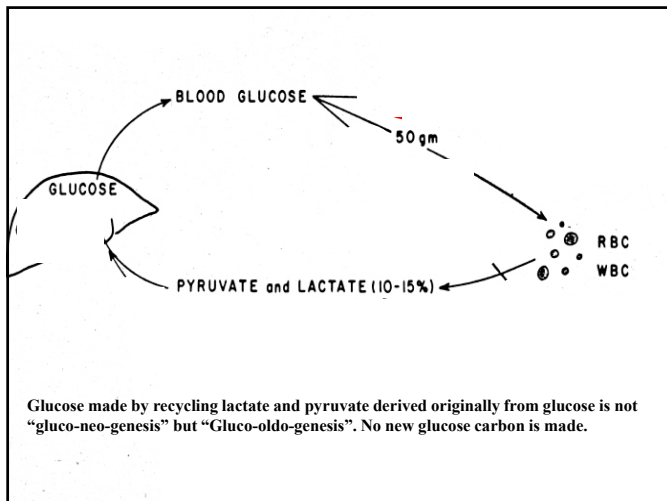
Brain Glucose Utilization ~ 5.5-5.6 mg/100 gm brain/minute

Erna Gibbs et al. *J Biol Chem* 144:325-332, 1942

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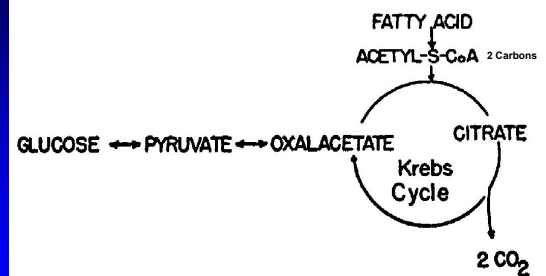


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Net Glucose Carbon Cannot Come from Oxidation of Fatty Acid Carbon



Weinman, Strisower, Chaikoff *Physiol Rev* 27:252, 1957

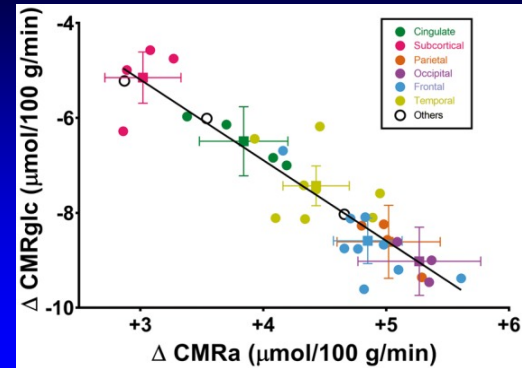
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But, some new glucose carbon can be made from lipolysis of adipose tissue

- Release of glycerol
 - Usually, a relatively minor contribution
- Hepatic Ketogenesis from FFA
 - Quantitatively important only when ketone body concentrations are elevated.

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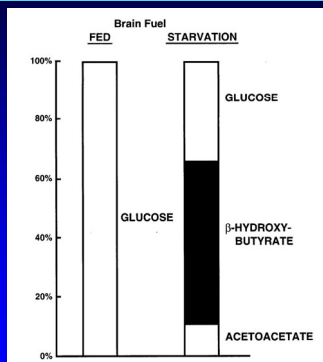
The Cerebral Metabolic Rate of Glucose is reduced in proportion to the Cerebral Metabolic Rate of Acetoacetate



Courchesne-Loyer et al. J Cerebral Blood Flow and Metabolism 37:2486, 2017

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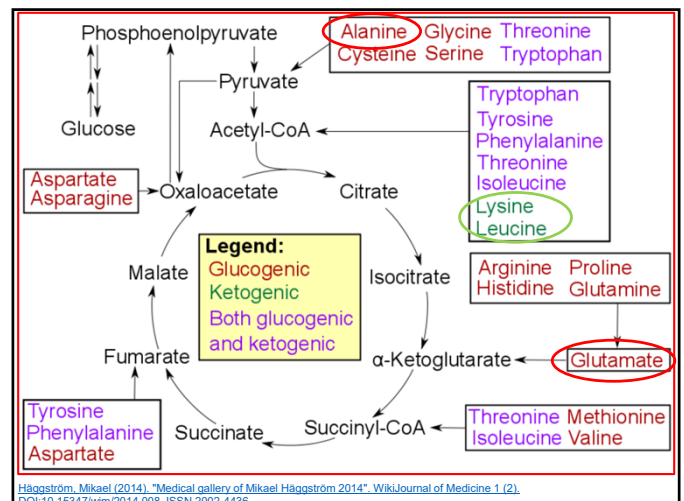
Brain Metabolism After 40 Days of Fasting



Circulating AcAc + βOHB = 7.7 mM

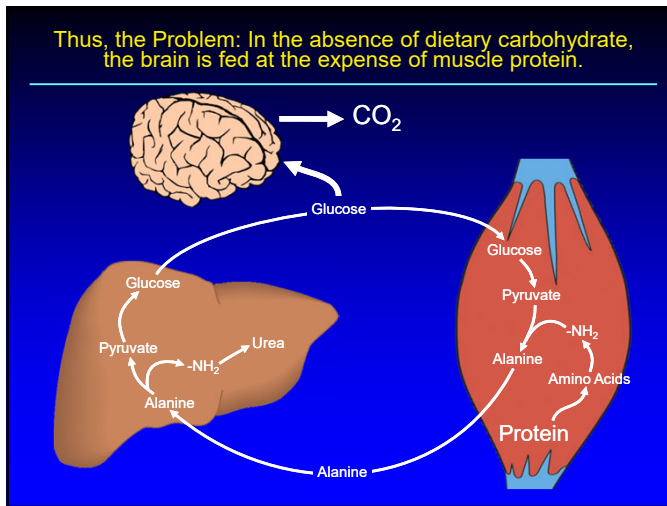
Ollie Owen, George Cahill, and others. J Clin Invest 46:1589,1967

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Thus, the Problem: In the absence of dietary carbohydrate, the brain is fed at the expense of muscle protein.



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“We find that the average respiratory quotient for 74 infants on the first day of life was 0.80.... This value of 0.80 represents a fasting value not widely different from that observed during the first 24 hours with fasting man...0.79.”

Benedict & Talbot
The Physiology of the New-Born Infant
1915

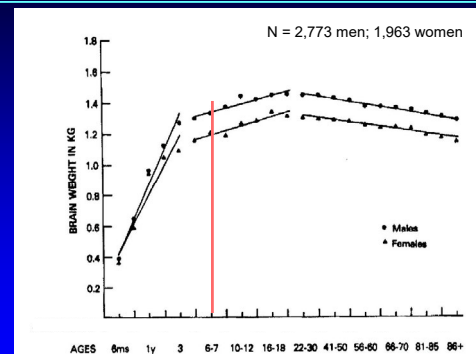
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Neonatal Cerebral Fuel Metabolism

- Amino & fatty acids are not significant CNS fuels
- Glucose is the preferred brain fuel.
 - Newborn glucose production rates can barely meet the brain's glucose requirements.
- Ketones are the principal alternative fuel.
 - Lactate may serve as a fuel in rare instances.
- Ketone utilization is proportional to arterial level.
- The human fetal brain can oxidize ketones.
 - Adam, et. al. *Acta Paed Scand* 64:17, 1975
- The newborn brain can oxidize ketones.
 - Kraus, et. al *Hoppe Seylers Z Physiol Chem* 355:164, 1974.

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Brain Weight as Function of Age



Dekaban et al. *Ann Neurol* 4:345-356, 1978

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Daily Brain Glucose Utilization Measured With Positron Emission Tomography

Age (yrs)	Brain Glucose Utilization (grams/day)
Birth	20
1	60
2	80
3	120
4 - 8	130
10 - 16	120
Adult	110

Derived from Chugani, et. al., *Ann. Neurol.* 22:487,1987.

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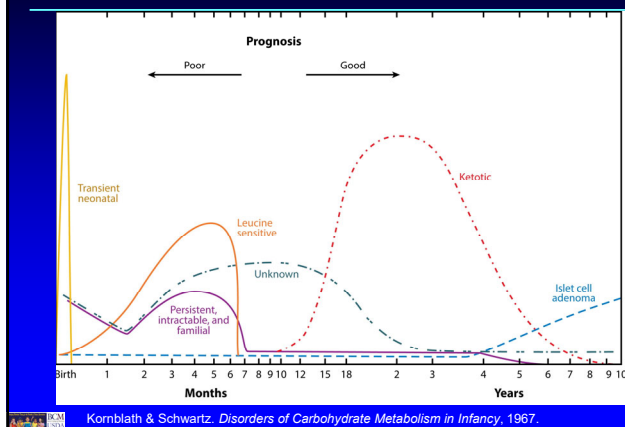
Daily Brain Glucose Utilization Measured With Positron Emission Tomography

Age (yrs)	Brain Glucose Utilization (grams/day)	Snack Equivalency Units
Birth	20	300 ml Human Milk
1	60	40 Animal Crackers
2	70	130 M&Ms
3	130	4.5 Hershey Bars
4 - 8	140	3.5 Coca Colas
10 - 16	120	3.5 Snickers Bars
Adult	100	Case of Light Beer

Derived from Chugani, et. al., *Ann. Neurol.* 22:487,1987.

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Does This Matter in Real Life?



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