

How does the Ketogenic Diet Work?

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The Ketogenic Diet

- ❑ The Ketogenic Diet is high fat, adequate protein and low carbohydrate diet.
- ❑ It is administered to children whose seizures have resisted control by the anticonvulsant drugs.

The Ketogenic Diet

- The Ketogenic Diet often stops seizures that resist drug control.
- Kirk Nysten discussed the Diet this morning in his discussion of dietary seizure control.

Mechanism of Action

- The Ketogenic Diet is effective but difficult to maintain.
- If we knew how the Ketogenic Diet worked, we might be able to invent drugs that would have the same anticonvulsant effects in people on a normal diet.

Theories of the Ketogenic Diet

- There are currently a number of theories that try to explain how the Ketogenic Diet works to stop seizures.

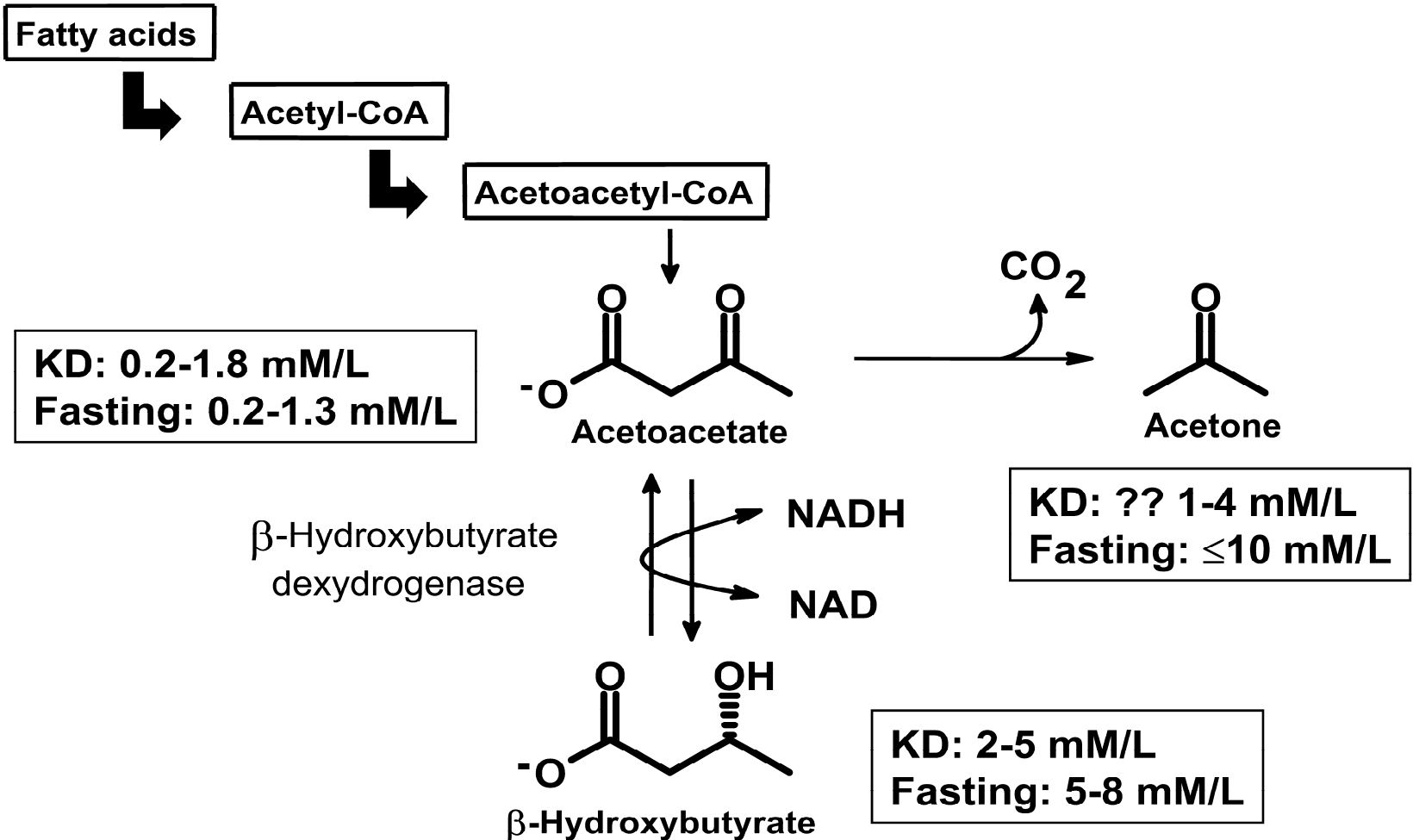
- It's a "hot" research area.

Our Own Work

- Our own group at the University of Toronto has been investigating the possible contribution of elevations in blood acetone levels to the anticonvulsant effects of the ketogenic diet (KD).

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- The Ketogenic Diet forces the body to use fat as a major source of energy.
 - This leads to the metabolism of fat, and the elevation of blood levels of three fat metabolites.
 - These are called the “ketone bodies”: acetoacetate, b-hydroxybutyrate and acetone.

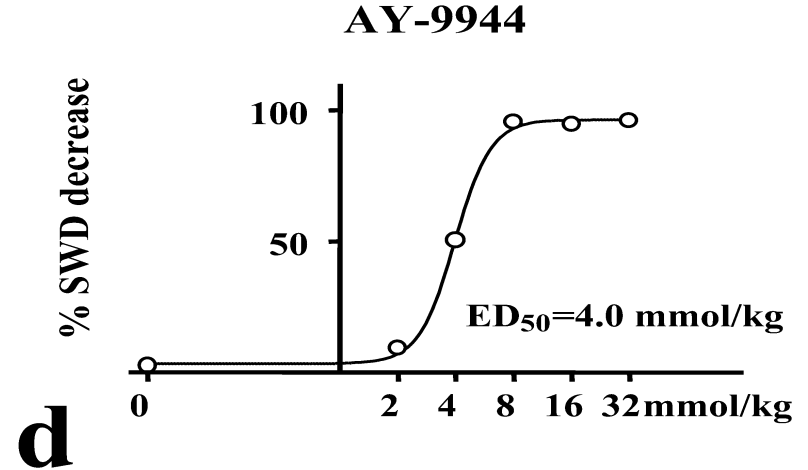
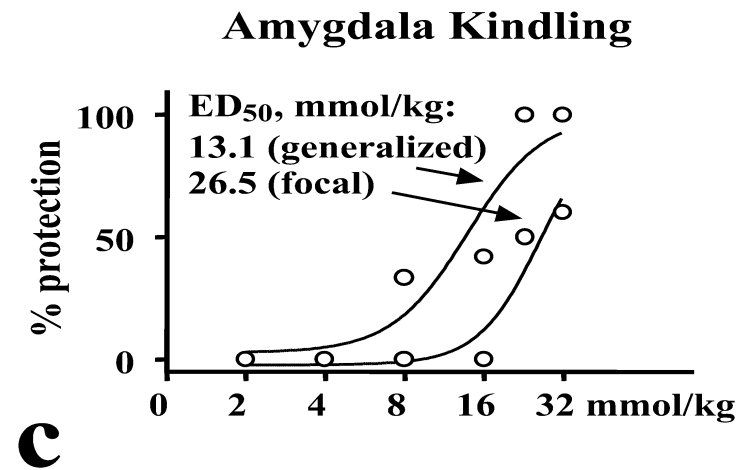
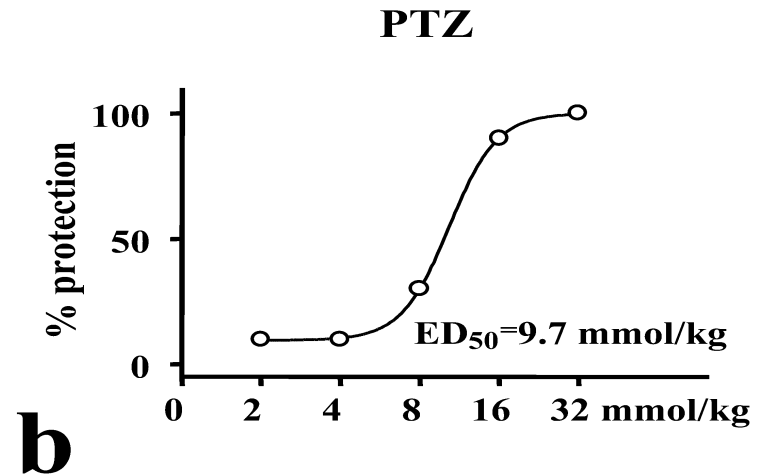
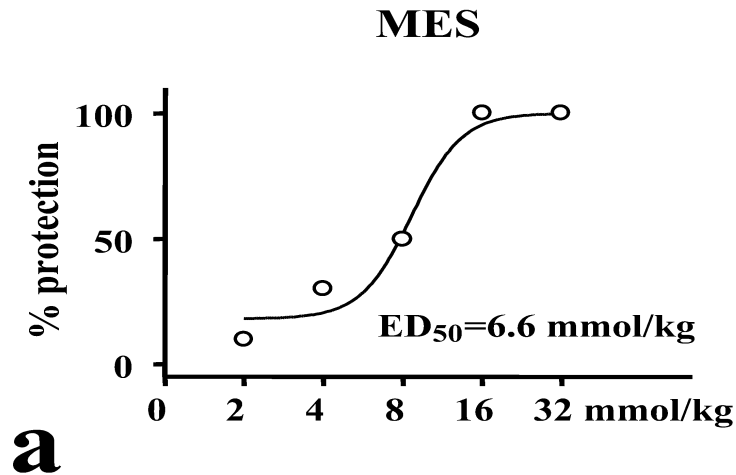
Metabolism of fat



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- We have been testing the hypothesis that one of the ketone bodies might have direct anticonvulsant effects....
 - And that these might contribute to the anticonvulsant effects of the Diet.

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- In our hands, neither acetoacetate nor b-hydroxybutyrate has proven to be anticonvulsant.
 - Acetone, however, has clear-cut anticonvulsant effects in a variety of animal seizure models.

Acetone: Dose-Response



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- These anticonvulsant effects occur in rats at blood concentrations of acetone of about 1-30 mM and higher.
 - The Ketogenic Diet produces blood levels of acetone in the range of 1-8 mM.
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Conclusion

- We have therefore concluded that the Ketogenic Diet may stop seizures because it raises blood levels of acetone.
- We are now exploring acetone-like molecules for their anticonvulsant effects.

Conclusion

- Our eventual hope is to produce new drugs that will have the effects of the Diet, without the Diet itself.
- We are hoping to produce the “Ketogenic Diet in a pill”.

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