TEMPLE
Tools Enabling Metabolic Parents LEarning

Very-long-chain acyl-CoA dehydrogenase deficiency

Introductory information

Written by:
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Reviewed & Revised for North America
by: S. van Calcar

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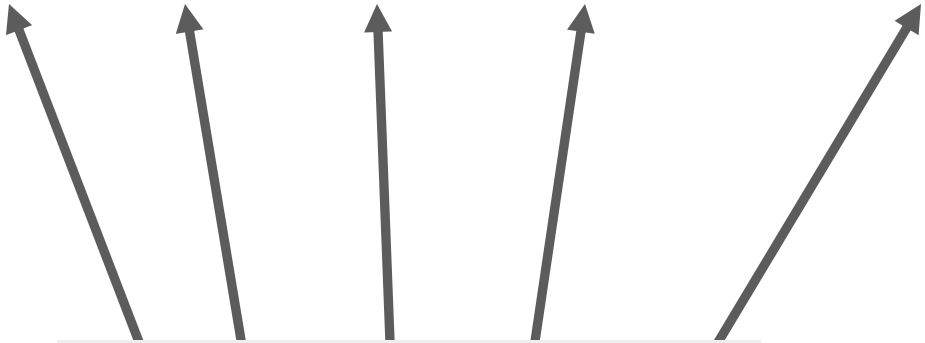
Very-long-chain acyl-CoA dehydrogenase



VLCAD deficiency

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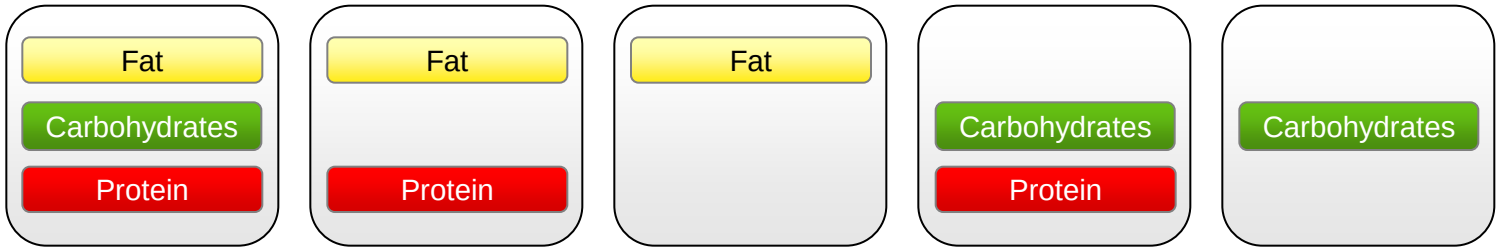
Food – Components of a typical diet

Natural Food



eg. milk, yogurt, nuts

eg. meat, poultry, fish, eggs, cheese

eg. oil, butter, margarine

eg. fruit, vegetables, potatoes, cereals, pasta, rice

eg. sugar, lemonade

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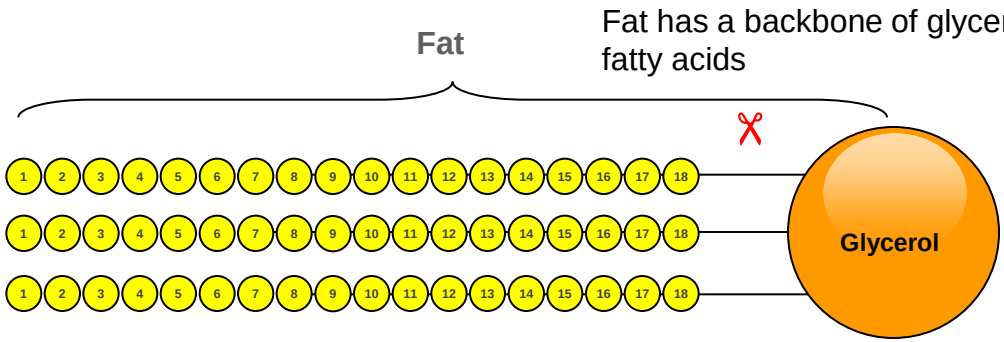
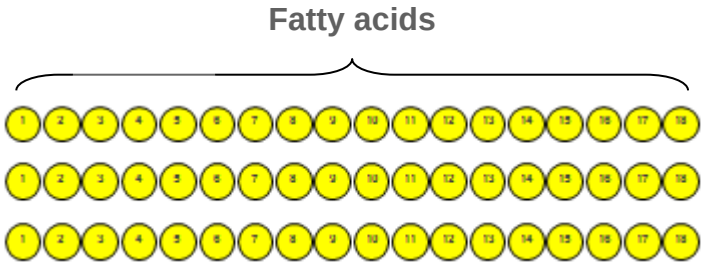
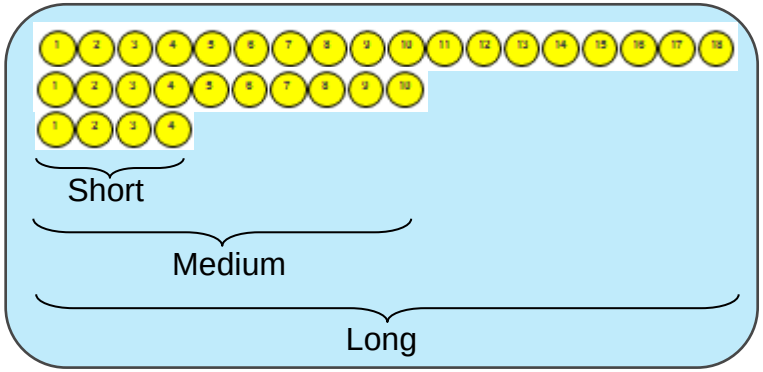
Fat vs Fatty Acids



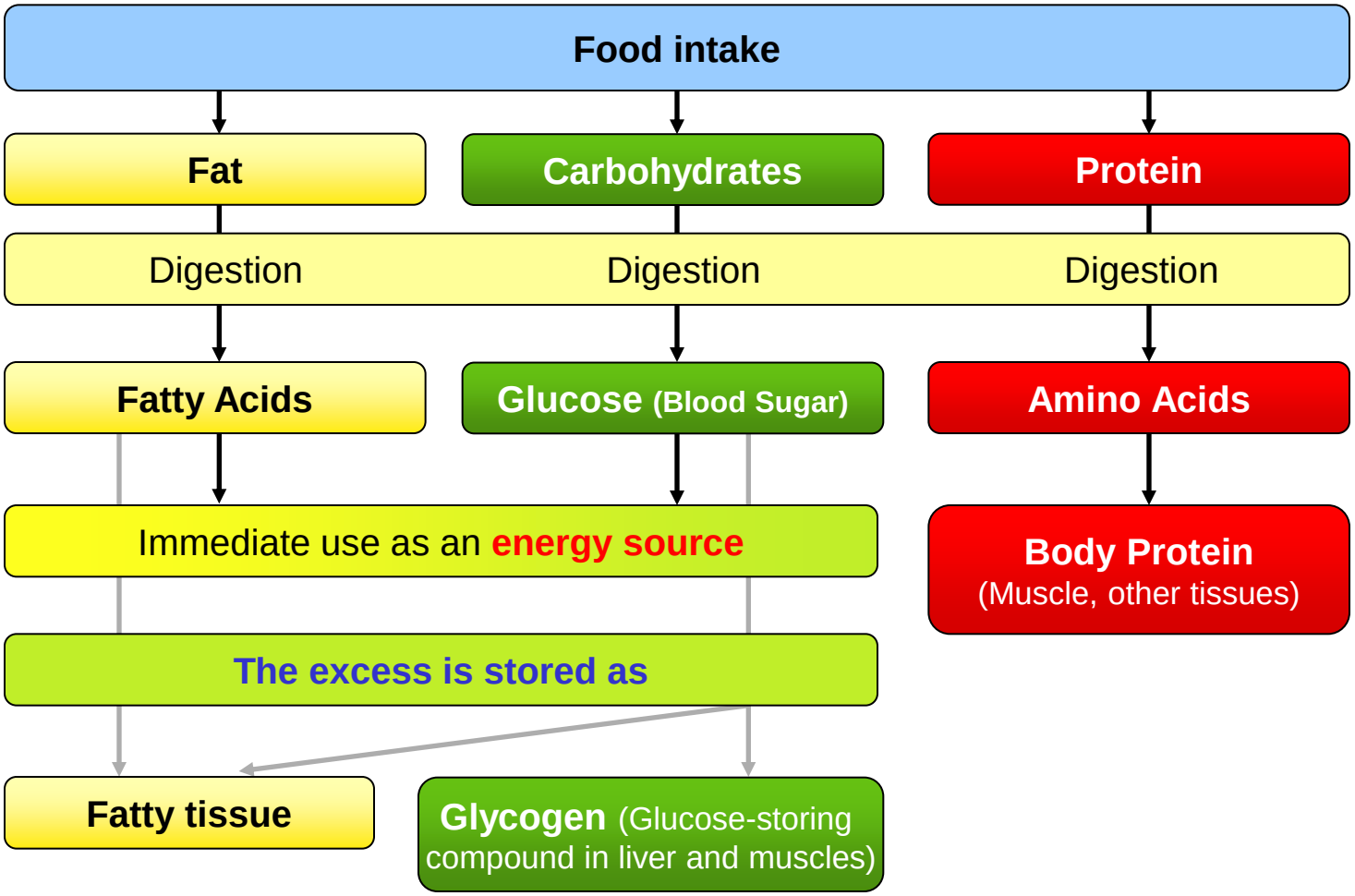
Fatty acids are made from chains of carbon atoms. There are different lengths of fatty acids; short-chain, medium-chain, and long-chain.





Long-chain fatty acids	> 12	carbon atoms
Medium-chain fatty acids	6-12	carbon atoms
Short-chain fatty acids	< 6	carbon atoms

How the body uses these nutrients



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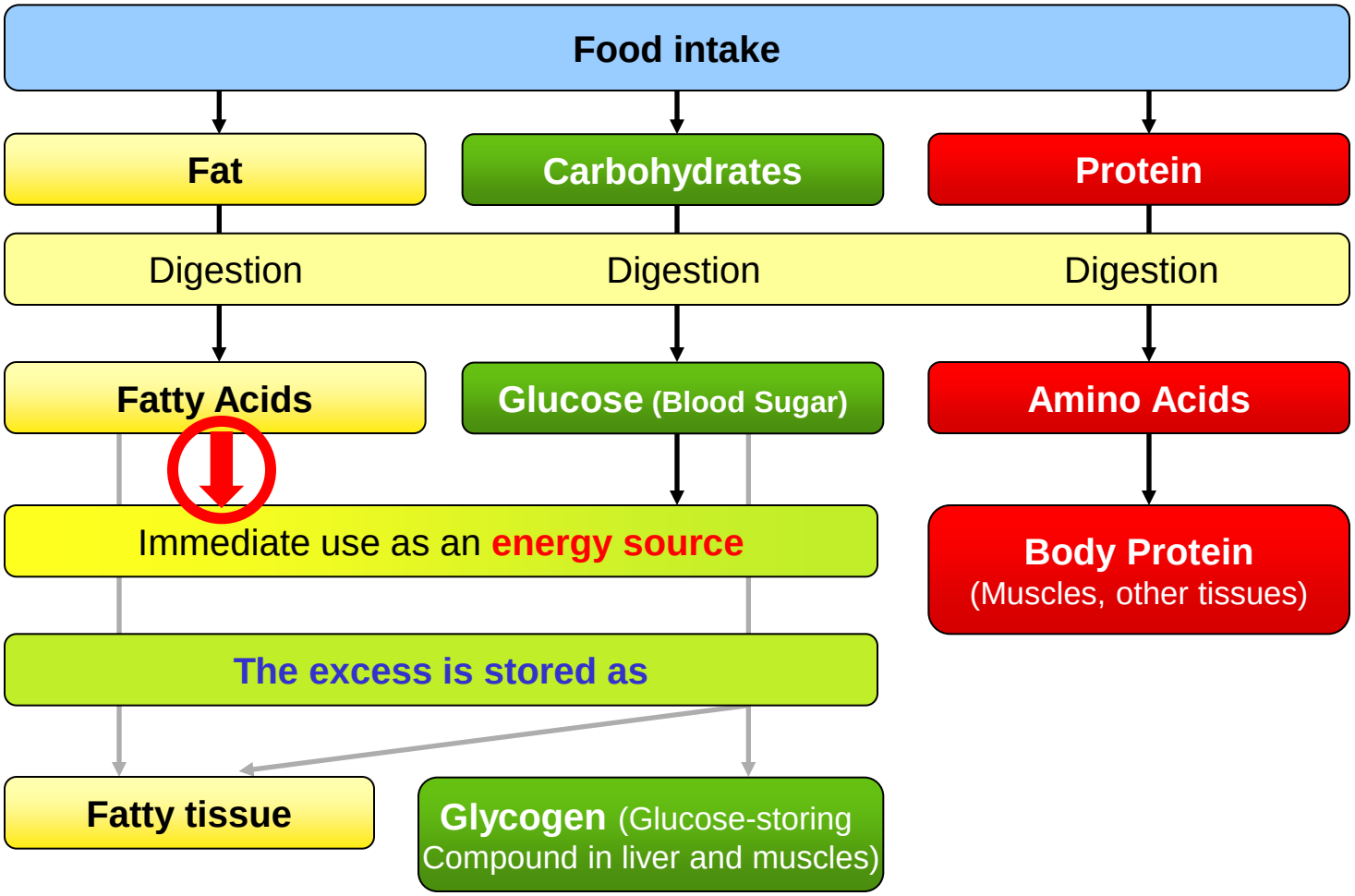
In VLCAD deficiency, there is a problem using some fatty acids



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Enzymes

Enzymes are proteins that facilitate various chemical reactions in the body. They are involved in the biosynthesis (anabolism) and the degradation (catabolism) of all the substances in the body. This is called **Metabolism**.

Acyl-CoA dehydrogenases are enzymes that break down fatty acids. The VLCAD enzyme breaks down **l**ong-**c**hain fatty acids.

In VLCAD deficiency the activity of the VLCAD enzyme is greatly reduced.

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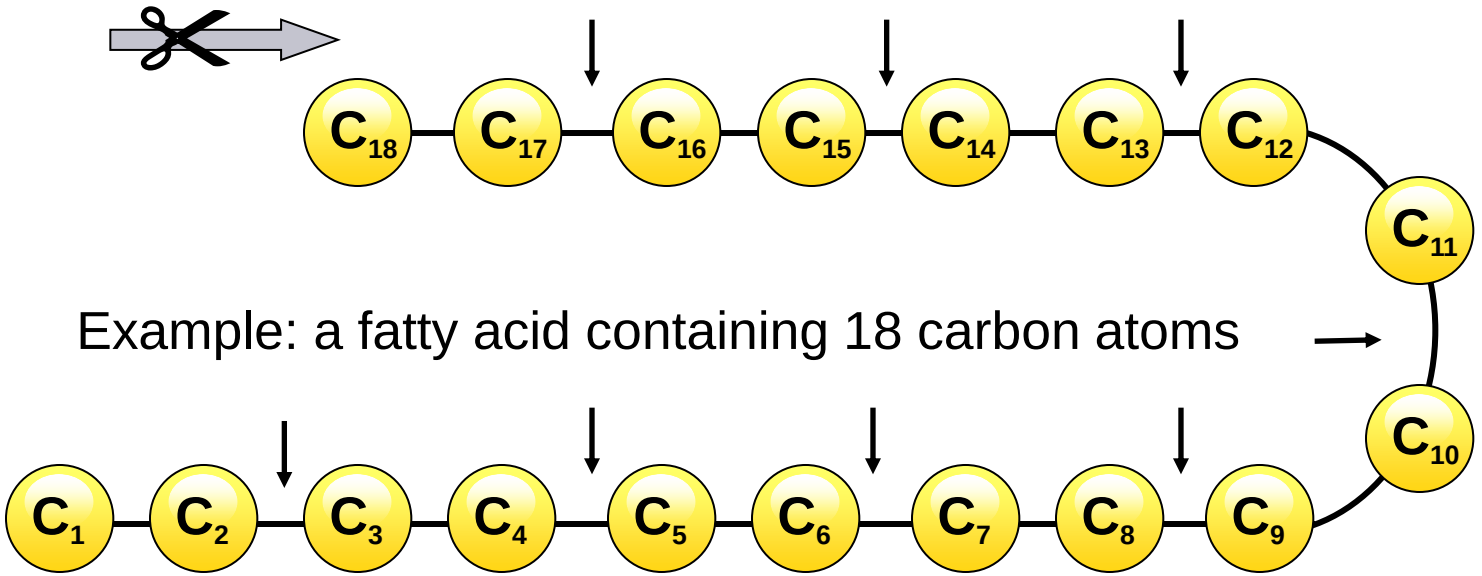
Fatty Acids

Fatty acids are made from chains of carbon (=C) atoms



Example: a fatty acid containing 18 carbon atoms

Long-chain fatty acids	> 12	carbon atoms
Medium-chain fatty acids	6-12	carbon atoms
Short-chain fatty acids	< 6	carbon atoms

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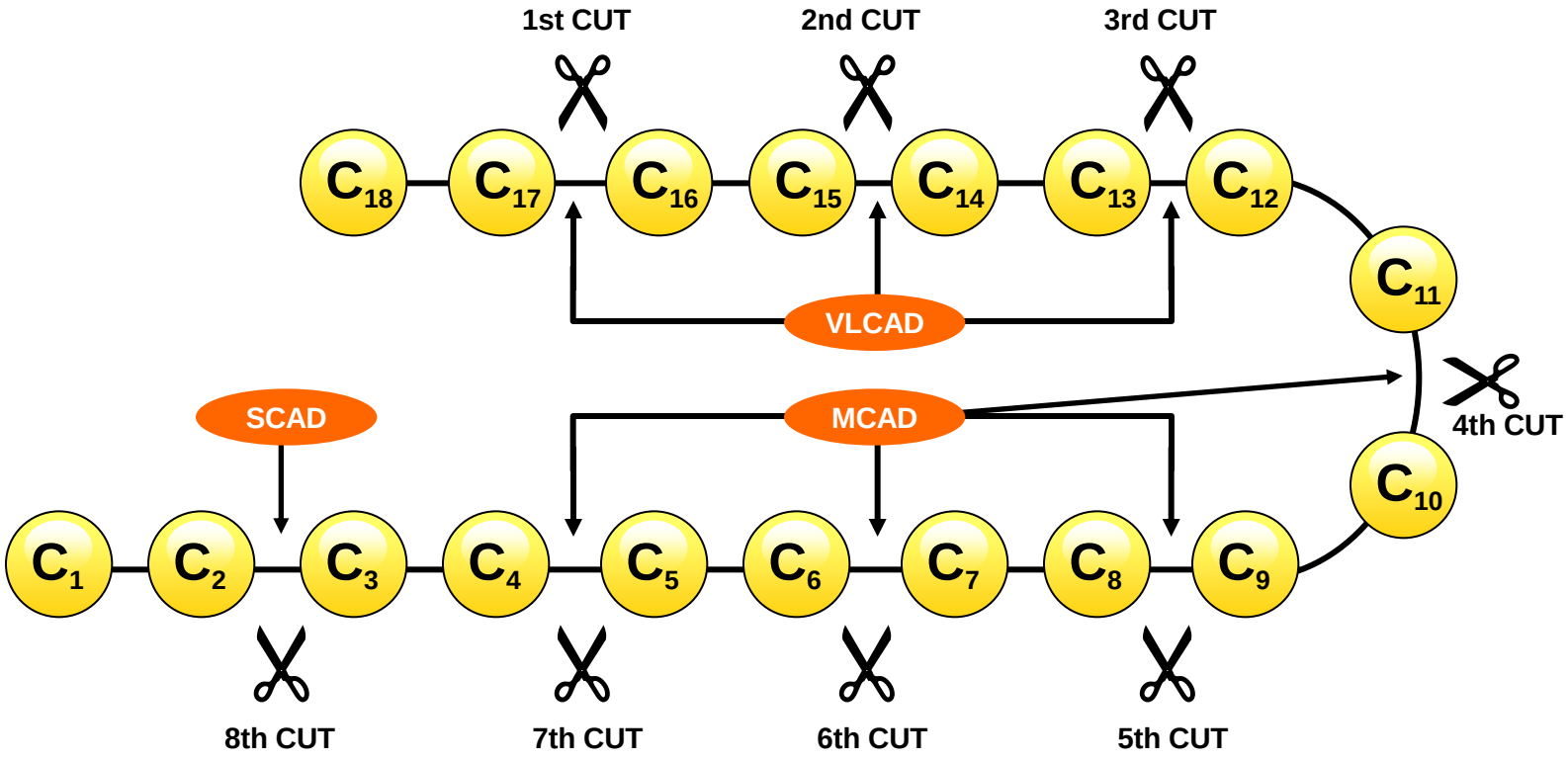
How enzymes break down a fatty acid

3 enzymes are needed for this process:

The enzyme VLCAD starts, the enzyme MCAD continues, the enzyme SCAD finishes



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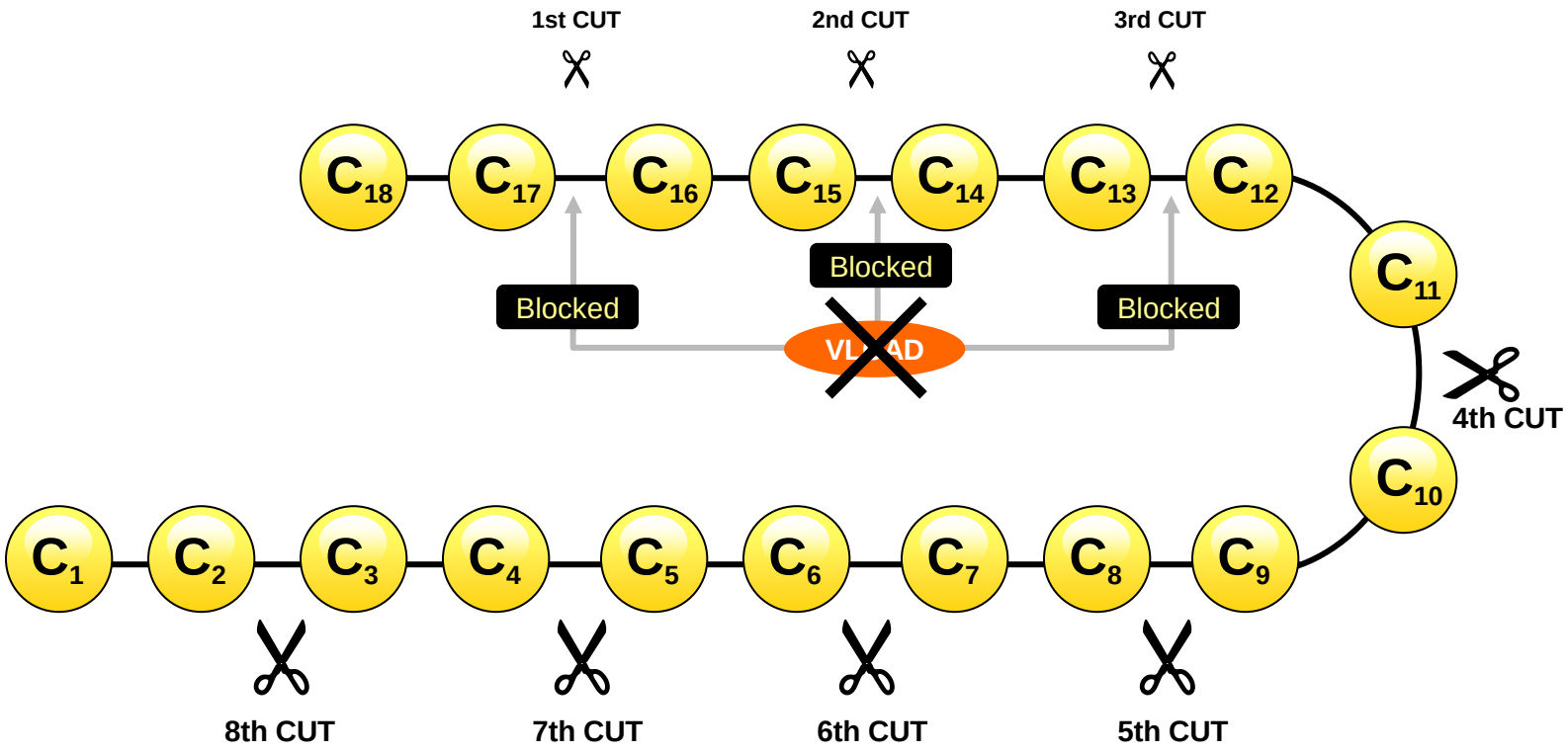
In VLCAD deficiency, long-chain fatty acids cannot be broken down in cells

Break down of the chain of carbon molecules cannot start



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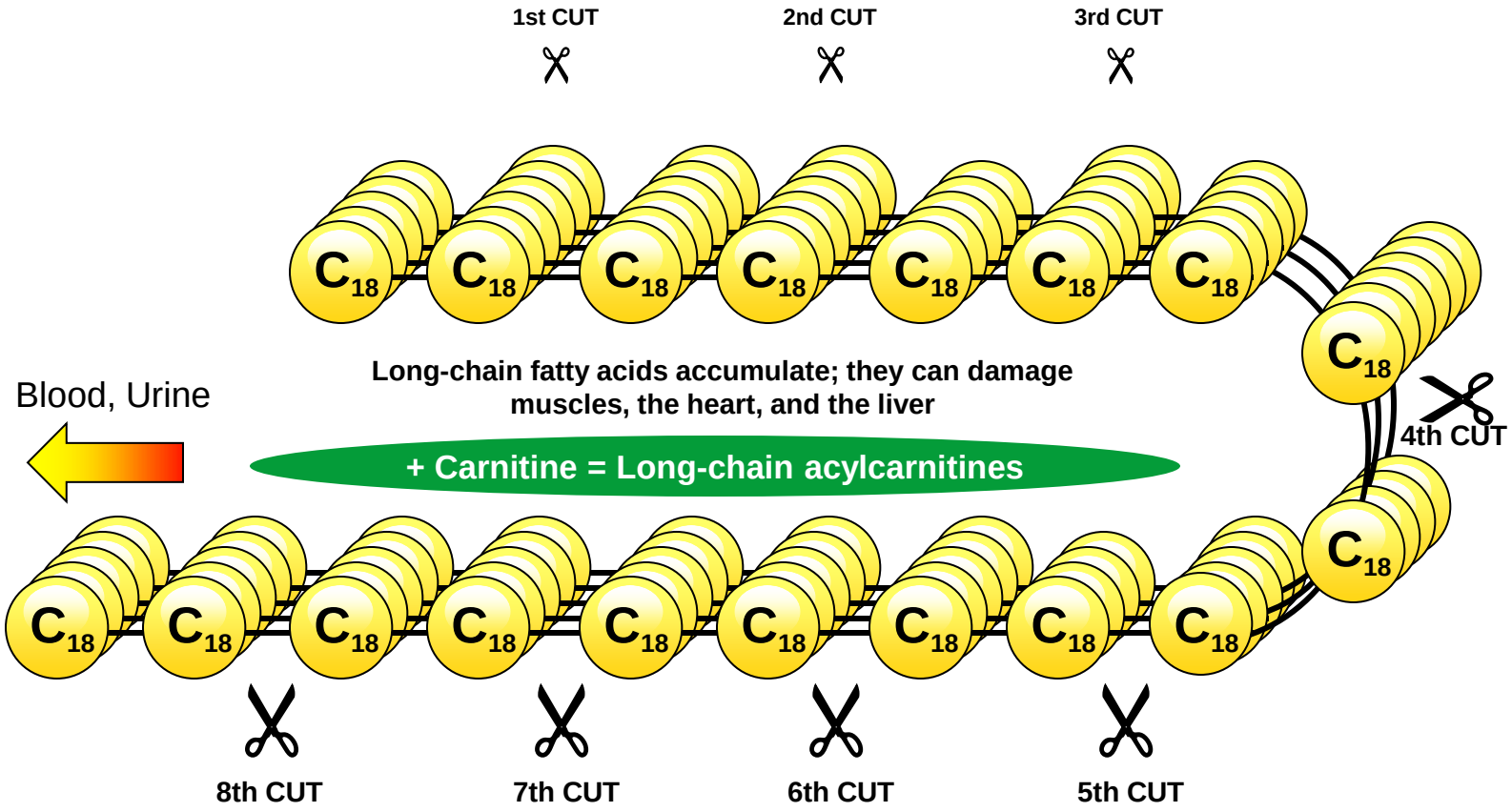
In VLCAD deficiency, long-chain fatty acids build-up and form long-chain acylcarnitines



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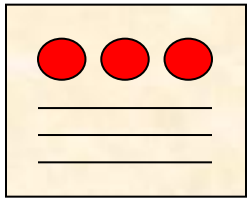
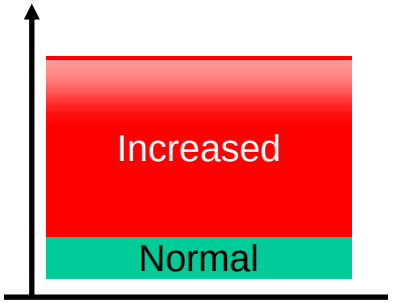
Diagnosis of VLCAD deficiency

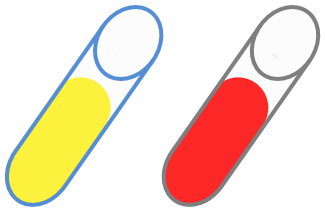


Dried blood spots

Newborn/Metabolic screening

Long-chain acylcarnitines in blood



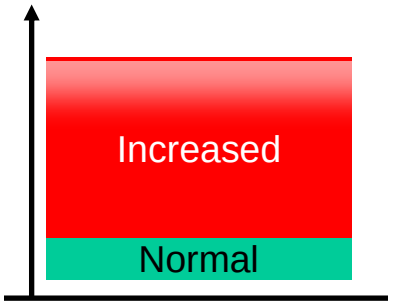


Urine sample

Blood sample

Confirmation of diagnosis

Abnormal compounds from long-chain fatty acids + long-chain acylcarnitines in urine and in blood



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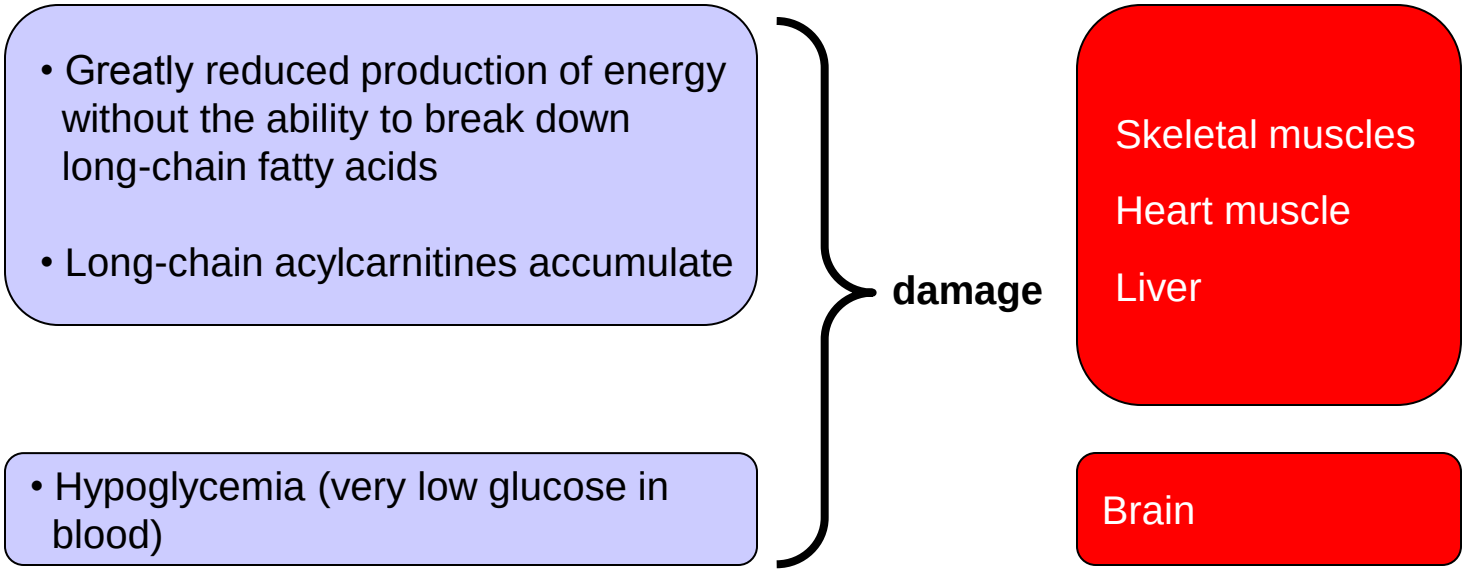
Pathogenesis of VLCAD deficiency



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The principles of dietary management for VLCAD deficiency

Avoid the need to use long-chain fatty acids as "fuel" for energy production.

by means of

1. **Avoid fasting too long**
   Fasting is the time when your child isn't drinking or eating anything
2. **Limit fat from the diet (fat in the diet is all long chain fat)**
3. **Replace long-chain fatty acids in the food with medium-chain fatty acids (MCT-supplements)**
4. **Consume sources of glucose before, during and after exercise**

Energy production from long-chain fatty acids is defective.

Energy production from medium-chain fatty acids is intact.

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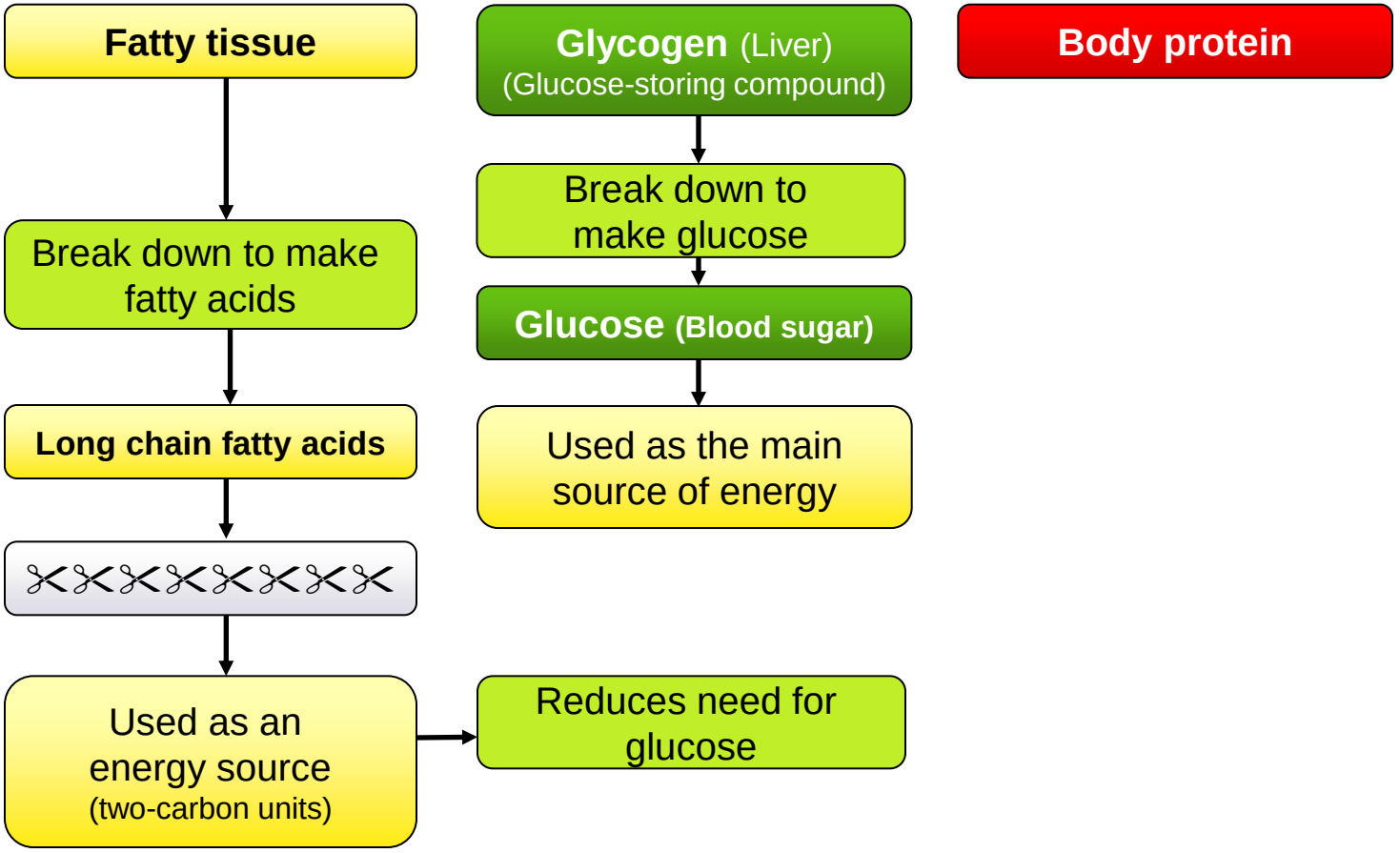
What happens during Fasting?



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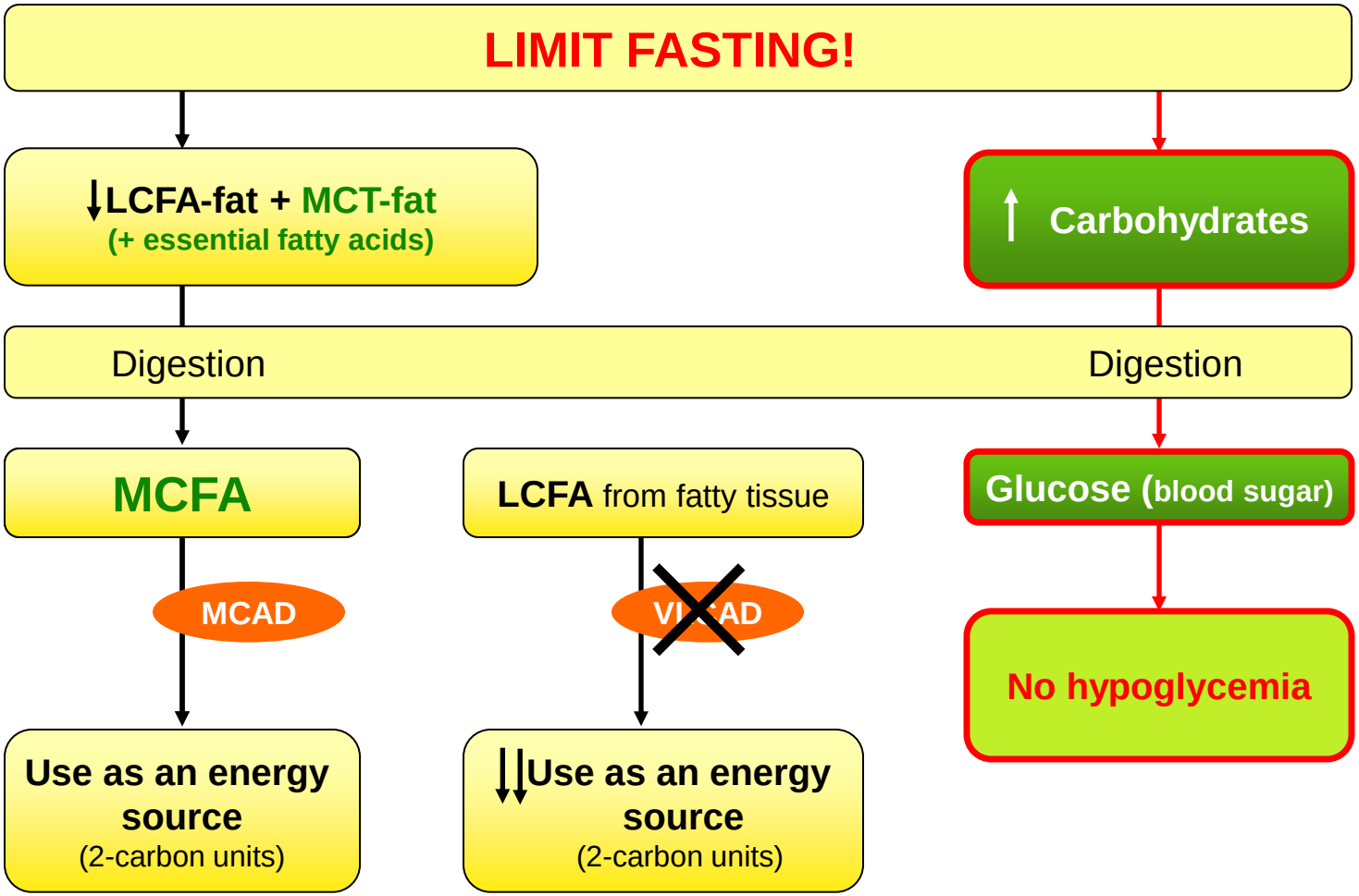
Management: Avoid Fasting Too Long



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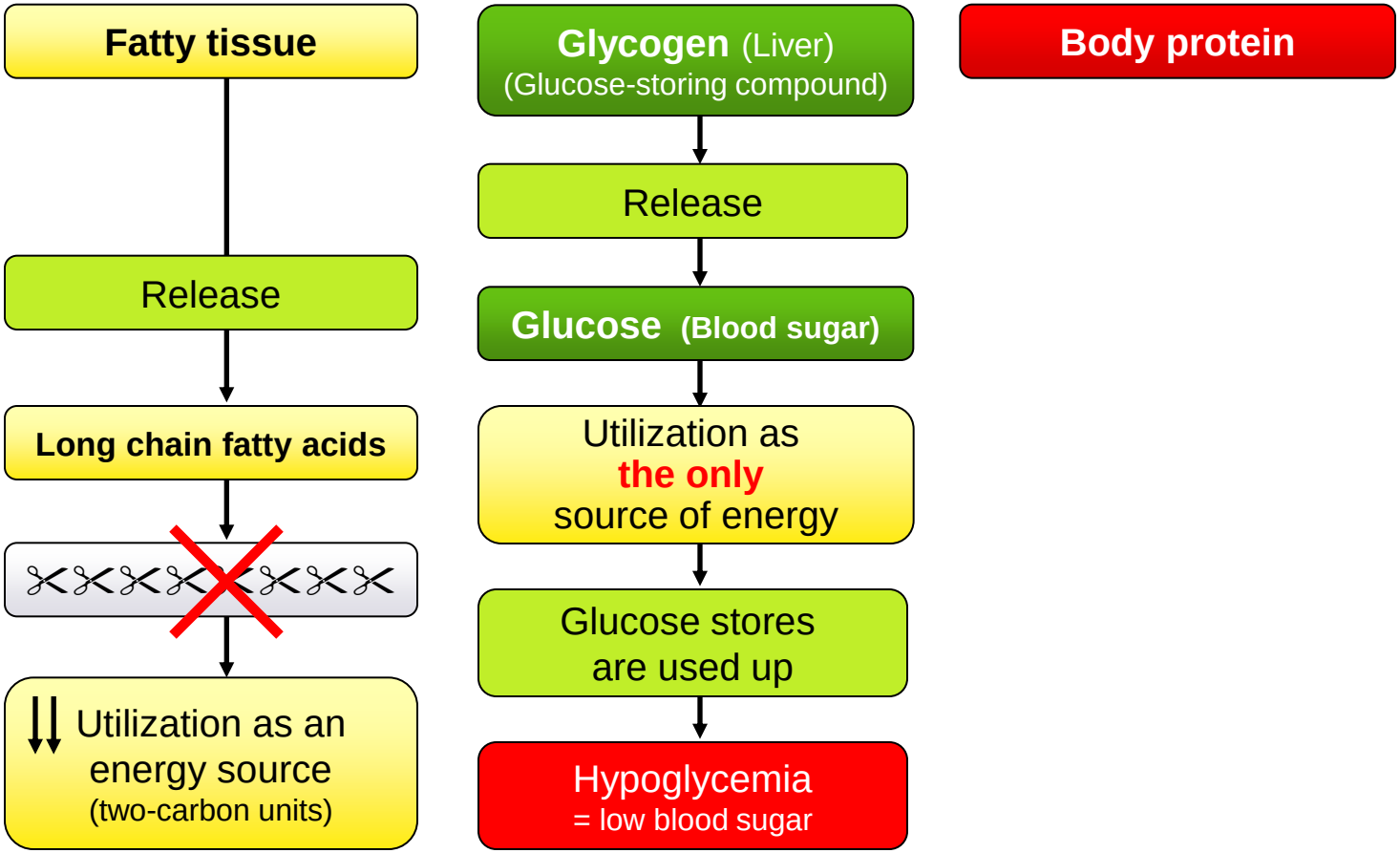
VLCAD deficiency: Problems can develop if your child fasts too long



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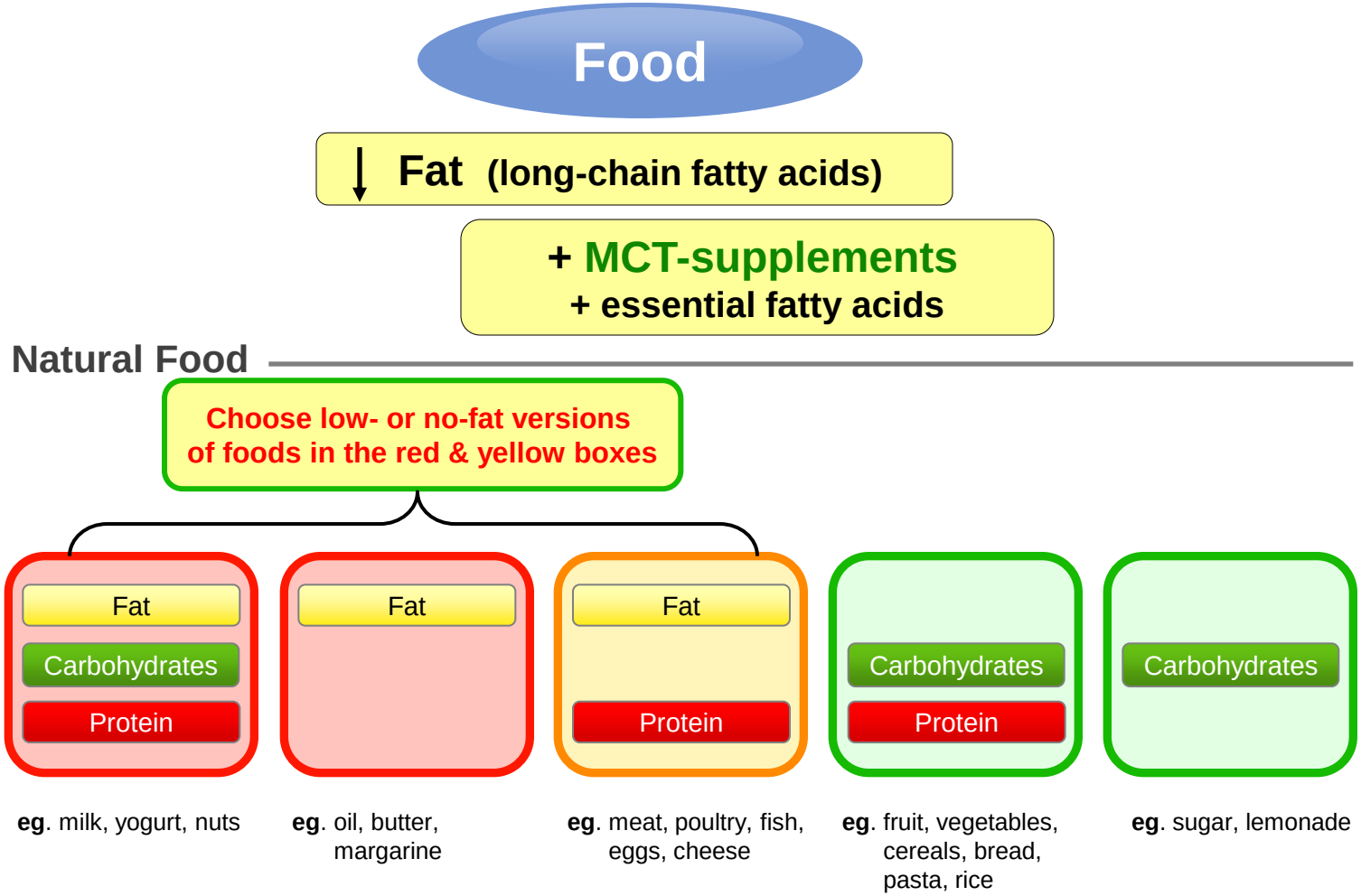
Dietary Management: very-low-fat diet + MCT-supplements



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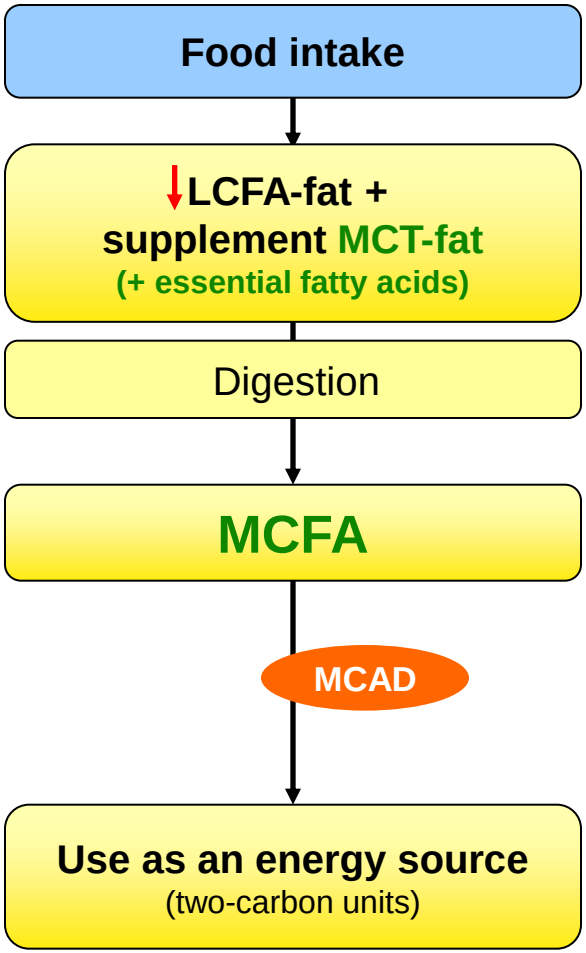
Dietary Management: very low-fat diet + MCT-supplements



Abbreviations:

LCFA-fat = Fat from long-chain fatty acids (LCFA)

MCT-fat = Fat from medium-chain fatty acids (MCFA)

MCAD = enzyme that breaks down medium chain fatty acids

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Illness and other stresses can cause problems for patients with VLCAD deficiency

- **What causes problems?**

Decreased energy production from long chain fatty acids
Toxicity of long chain acylcarnitines and other metabolites
Hypoglycemia (low blood sugar)

- **When can problems occur?**

Illness, especially with vomiting and poor food intake
Infections
Prolonged fasting
Excessive exercise (when older)
Surgery and anesthesia

- **What can happen?**

Heart problems – enlarged heart (cardiomyopathy), abnormal beats (arrhythmia)
Liver problems
Muscle breakdown – muscle pain, blood in urine
Problems with consciousness – coma is possible

The severity of the disease varies between individuals with VLCAD deficiency

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Illness and other stressors can cause problems for patients with VLCAD deficiency

- **Symptoms to watch out for**

Vomiting

Increased sleepiness (lethargy)

Child is more difficult to wake up

Complains that muscles ache

- **Necessary measures**

Reduce fasting time.

Offer a maltodextrin solution, juice or other food or beverage that will provide glucose.

An emergency room visit to start an intravenous glucose infusion may be necessary.

During fasting periods before anesthesia/surgery - always initiate an intravenous glucose infusion.

→ **Intravenous fat emulsions should NEVER be used!**

Ask your clinic for an Emergency Protocol!

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Chromosomes, Genes, Mutations

A **chromosome** is like a cookbook.

A **gene** is like a recipe in the cookbook.

A **mutation** is like an error in the recipe or even a complete lack of a recipe.

The **enzyme** VLCAD is produced constantly in the body following a specific recipe (**gene**). If the gene contains abnormal **mutations,** the **enzyme** cannot be properly produced or function correctly.

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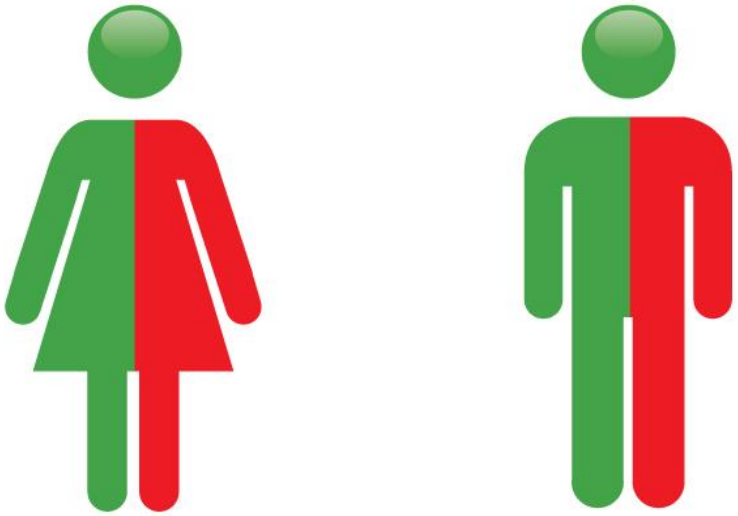
Inheritance of VLCAD deficiency

Both parents are carriers in autosomal-recessive inheritance

Mother is a carrier of
VLCAD deficiency



Father is a carrier of
VLCAD deficiency

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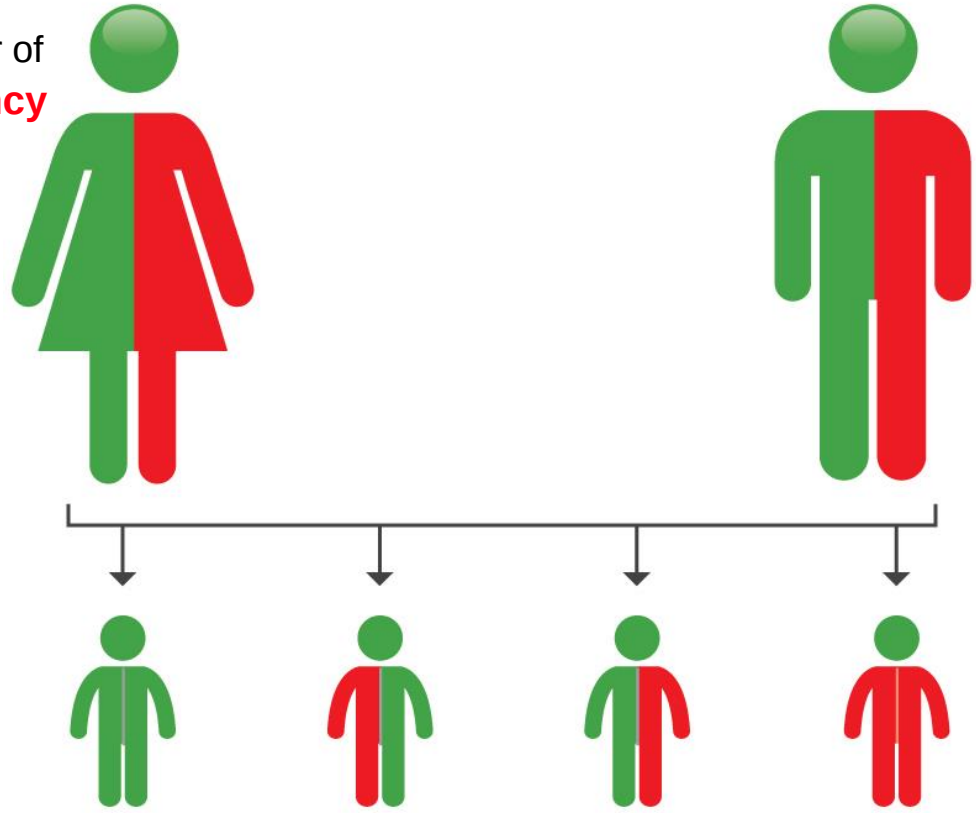
Inheritance of VLCAD deficiency

There are 4 possible combinations for any child born to parents who are carriers

Mother is a carrier of **VLCAD deficiency**

Father is a carrier of **VLCAD deficiency**



Child **will not be** a carrier of **VLCAD deficiency**

Child **will be** a carrier of **VLCAD deficiency**

Child **will have VLCAD deficiency**

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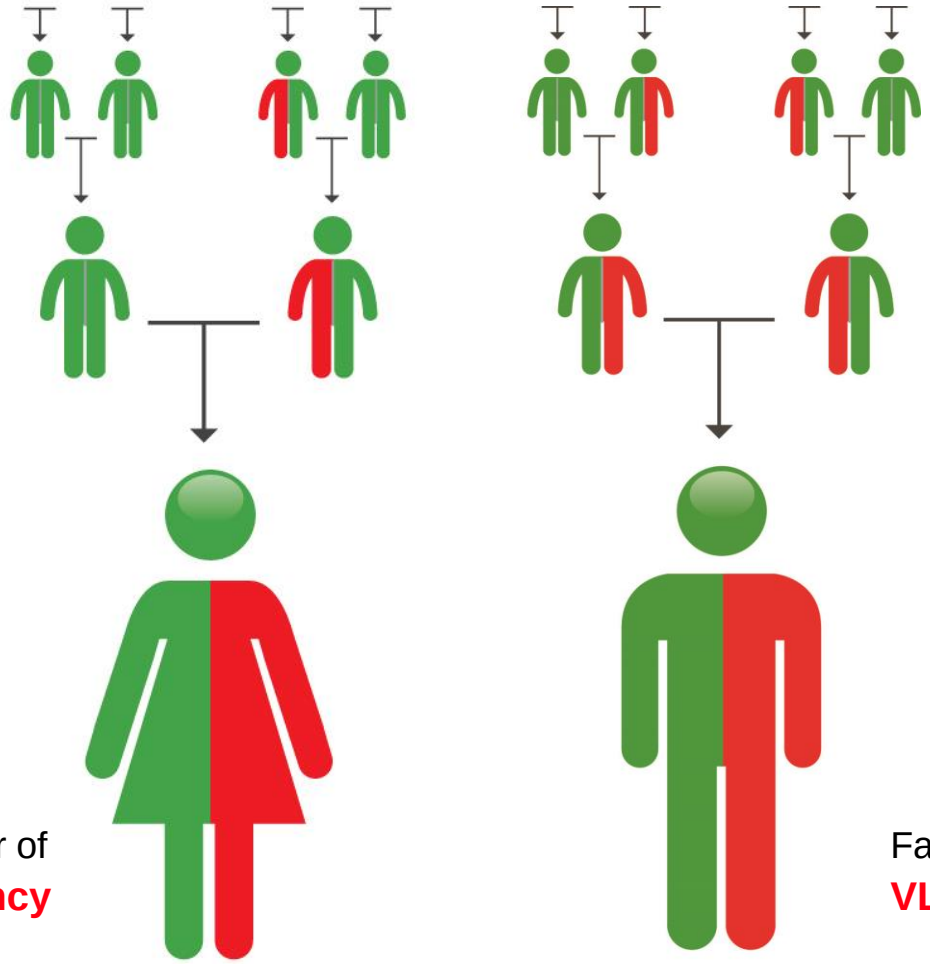
Inheritance of VLCAD deficiency

How VLCAD deficiency is inherited in families



Mother is a carrier of **VLCAD deficiency**

Father is a carrier of **VLCAD deficiency**

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Prognosis of VLCAD deficiency

Optimal management

1. **Reduction of long-chain fatty acids in diet and supplement MCT-fat**
2. **Plus essential fatty acids**
3. **Avoid fasting too long**
4. **Caution with illness, especially if child refuses to eat or is vomiting**

Result

- **Normal development**
- **No cardiomyopathy**
- **Muscle weakness and muscle pain associated with excessive exercise can still occur**

Follow-up

Laboratory tests
• Special tests
- Acylcarnitines
- Carnitine
- Essential fatty acids

• Routine tests
- Muscle enzymes
- Liver tests

Physical development
- Height and weight, head circumference

Cardiology consultations

Monitoring motor and developmental skills

Insufficient management

1. **Insufficient reduction in dietary fat and MCT supplementation**
2. **Fasting too long**
3. **Insufficient preventive measures during illness or other stresses.**

Result

- **Life-threatening hypoglycemic episodes with unconsciousness, brain edema, coma, permanent brain damage**

Sudden death

- **Cardiomyopathy**
- **Skeletal muscle weakness**

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