TEMPLE

Tools Enabling Metabolic Parents LEarning

Medium-chain acyl-CoA dehydrogenase deficiency

Introductory information

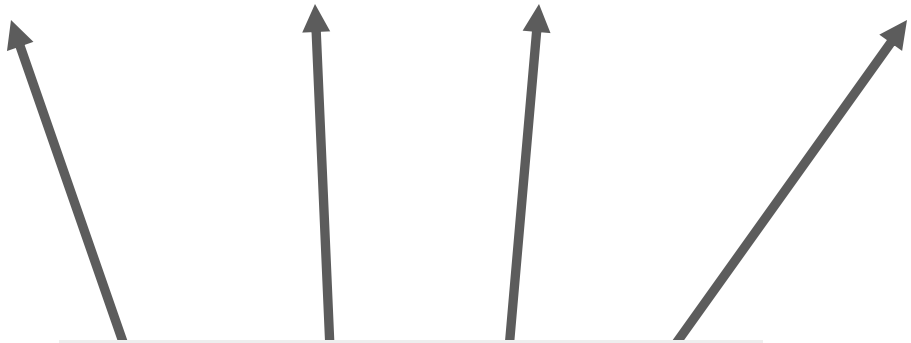
Written by:
V. Prietsch & P. Burgard

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

Supported by NUTRICIA
as a service to metabolic medicine

MU METABOLIC UNIVERSITY

Medium-chain acyl-CoA dehydrogenase

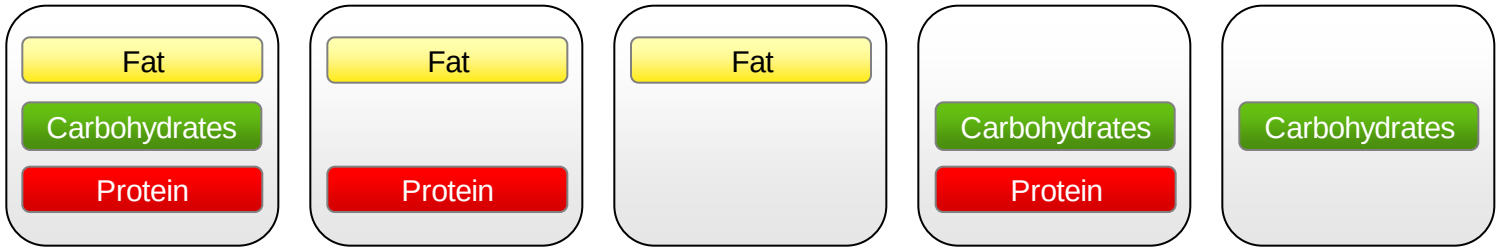


MCAD deficiency

Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

Food – Components of a typical diet

Natural Food



eg. milk, yogurt, nuts

eg. meat, poultry, fish, eggs, cheese

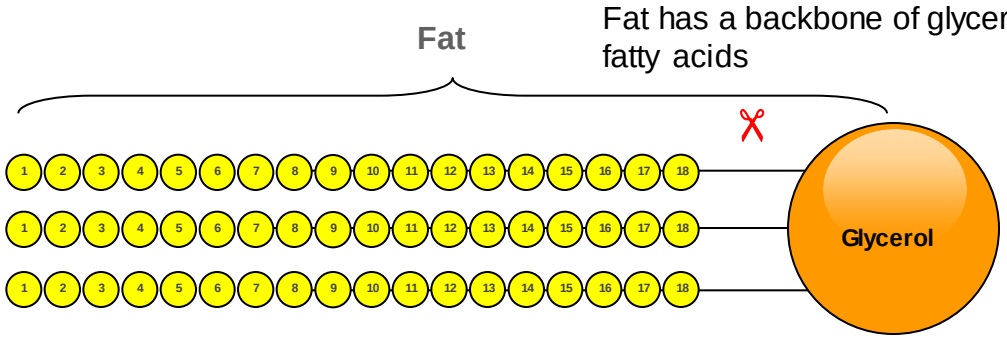
eg. oil, butter, margarine

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

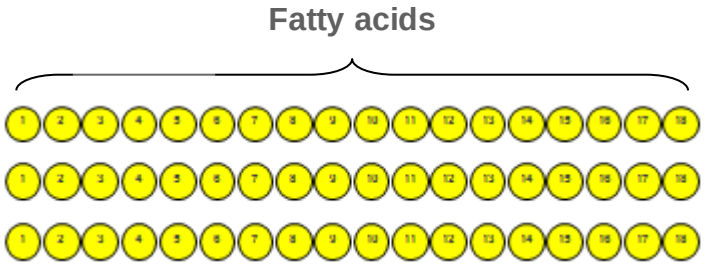
eg. sugar, lemonade

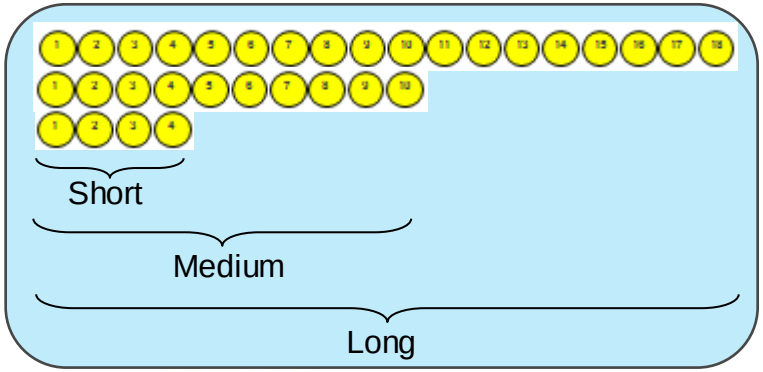
Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

Fat vs Fatty Acids



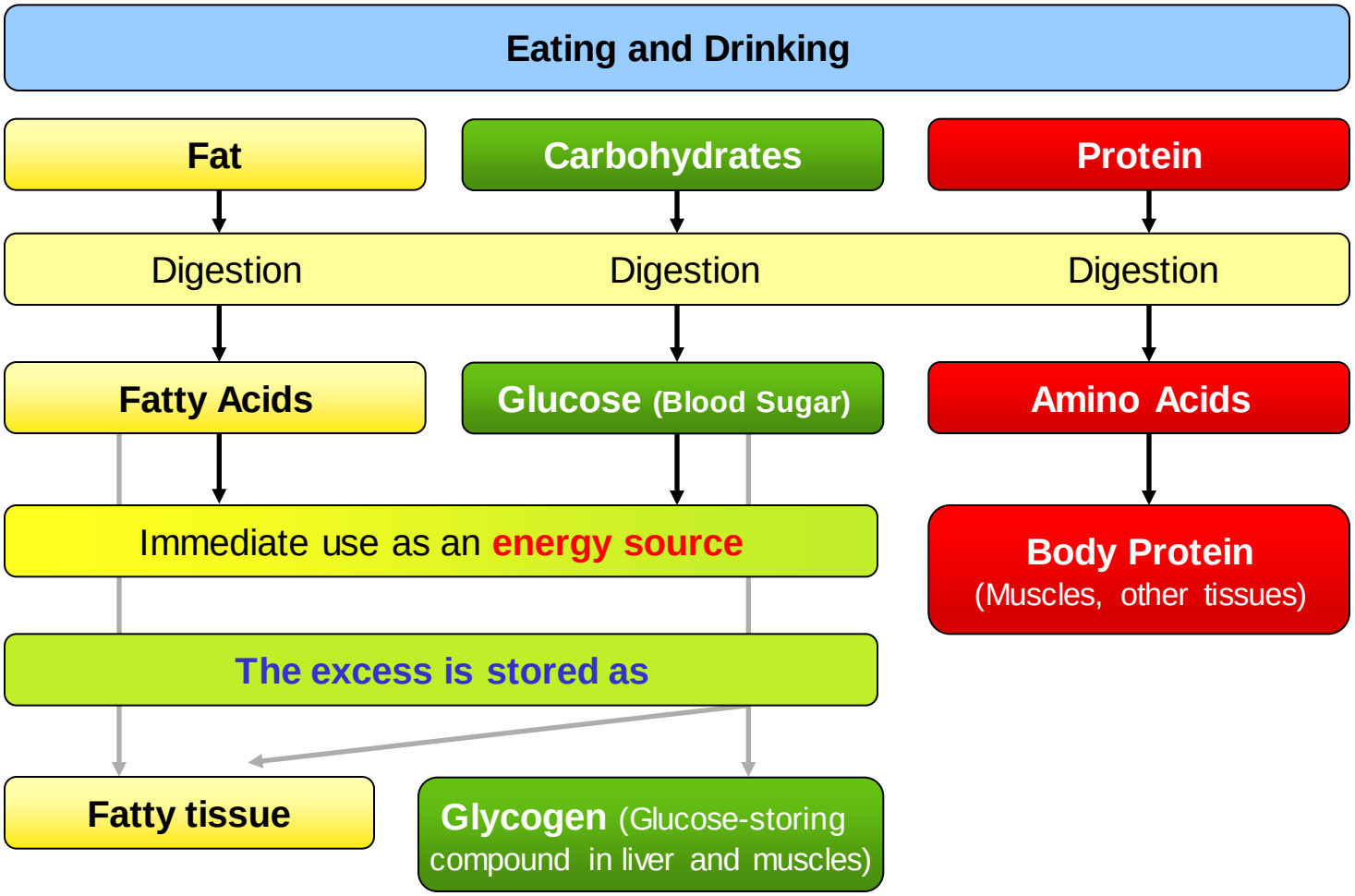
Fatty acids are made from chains of carbon atoms. There are different lengths of fatty acids; short-chain, medium-chain, and long-chain.





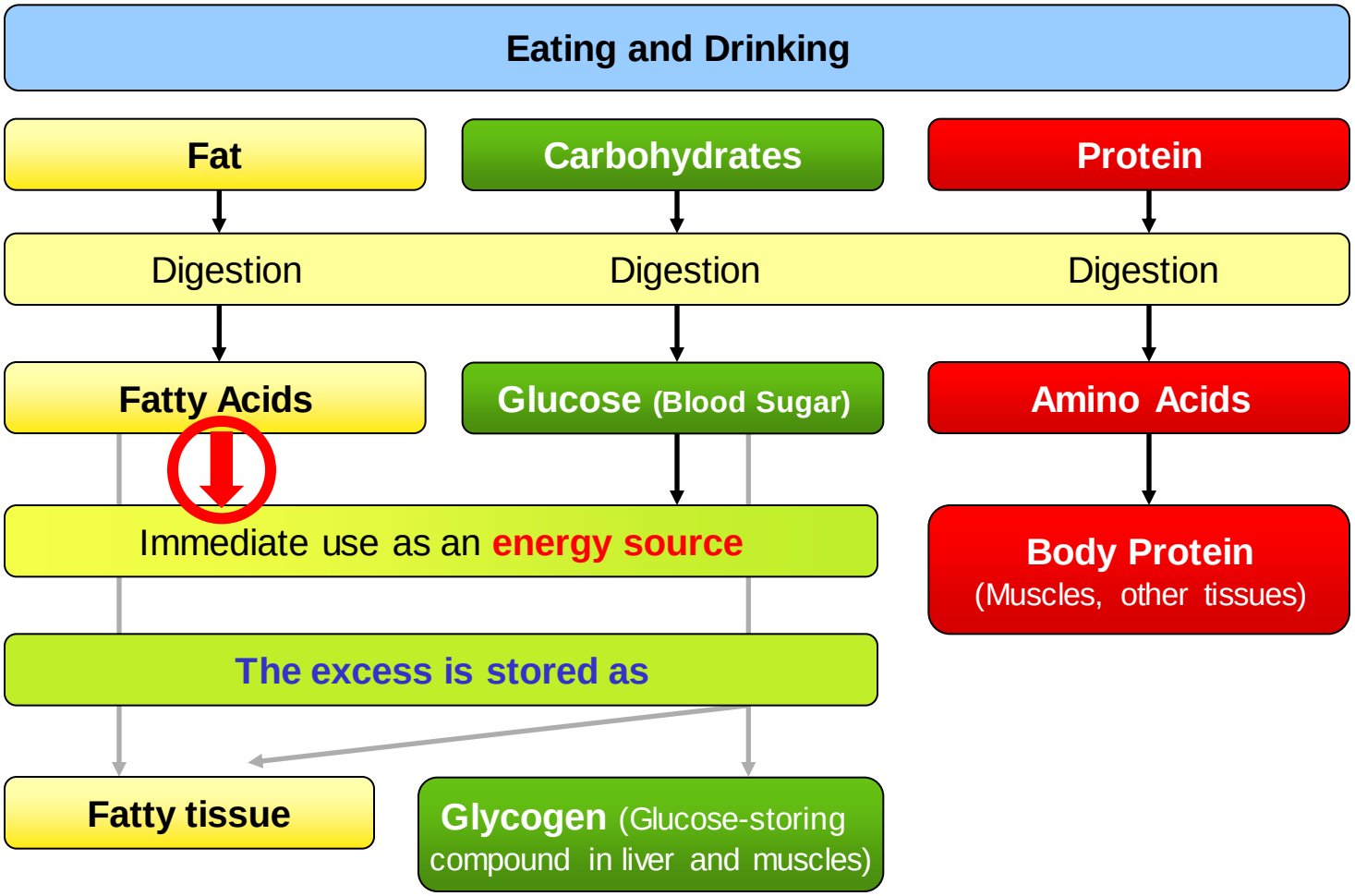
Long-chain fatty acids	> 12	carbon atoms
Medium-chain fatty acids	6-12	carbon atoms
Short-chain fatty acids	< 6	carbon atoms

How the body uses these nutrients



Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

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



Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

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**.

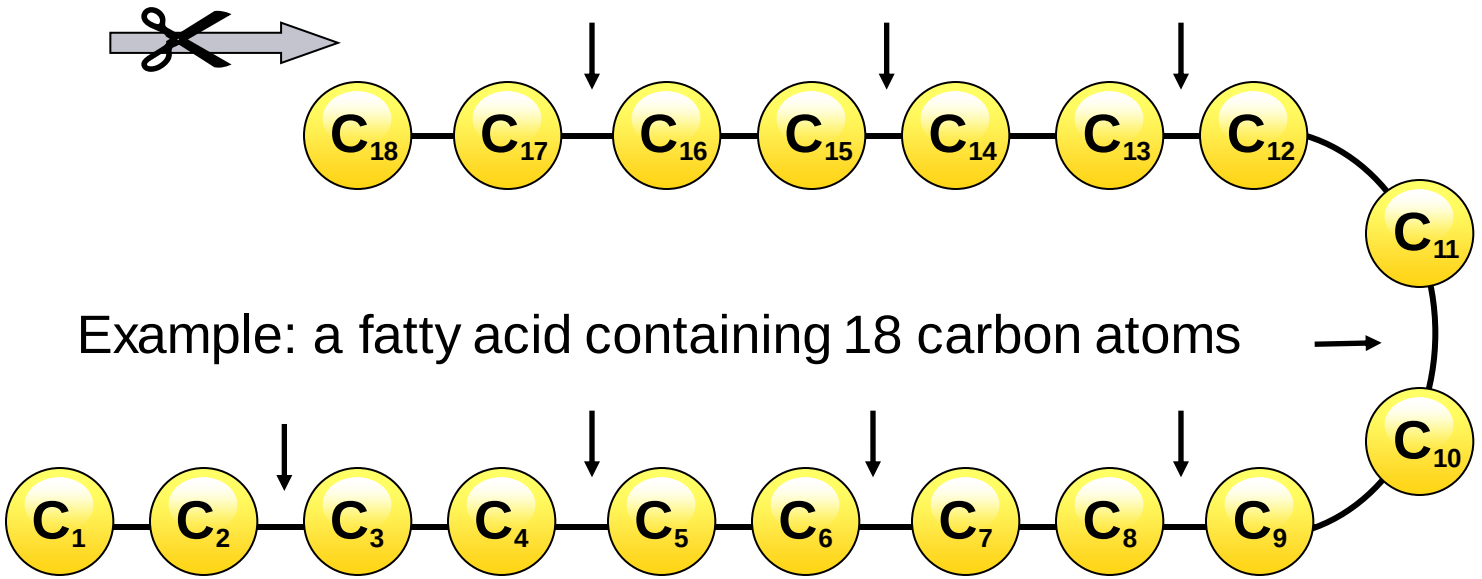
Acyl-CoA Dehydrogenases are enzymes required to break down fatty acids. The MCAD enzyme breaks down "**m**edium **c**hain" fatty acids.

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

Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

Fatty Acids

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



Example: a fatty acid containing 18 carbon atoms

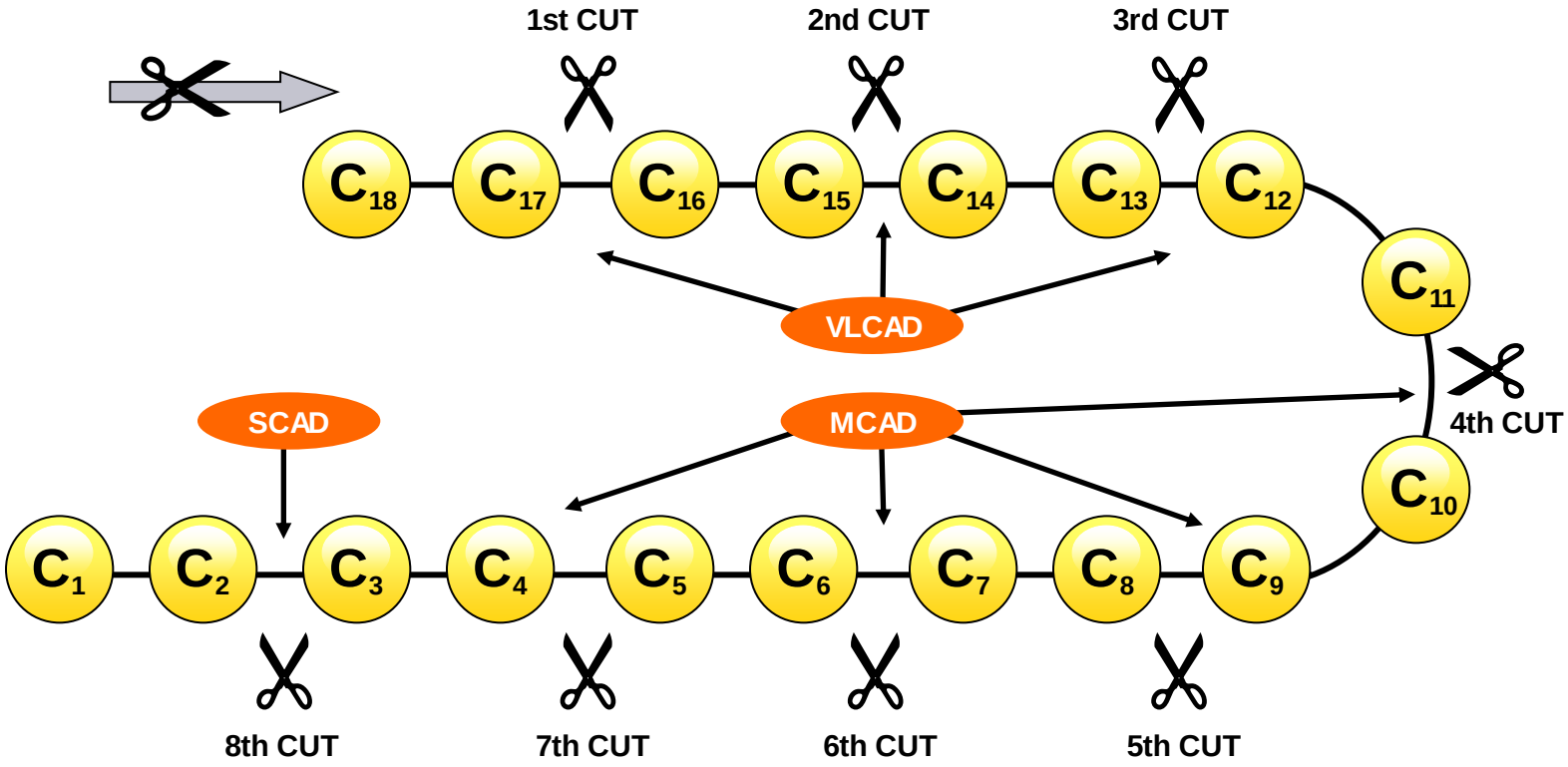
Long-chain fatty acids	> 12	carbon atoms
Medium-chain fatty acids	6-12	carbon atoms
Short-chain fatty acids	< 6	carbon atoms

Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

How enzymes break down a fatty acid

3 enzymes are needed for this process:

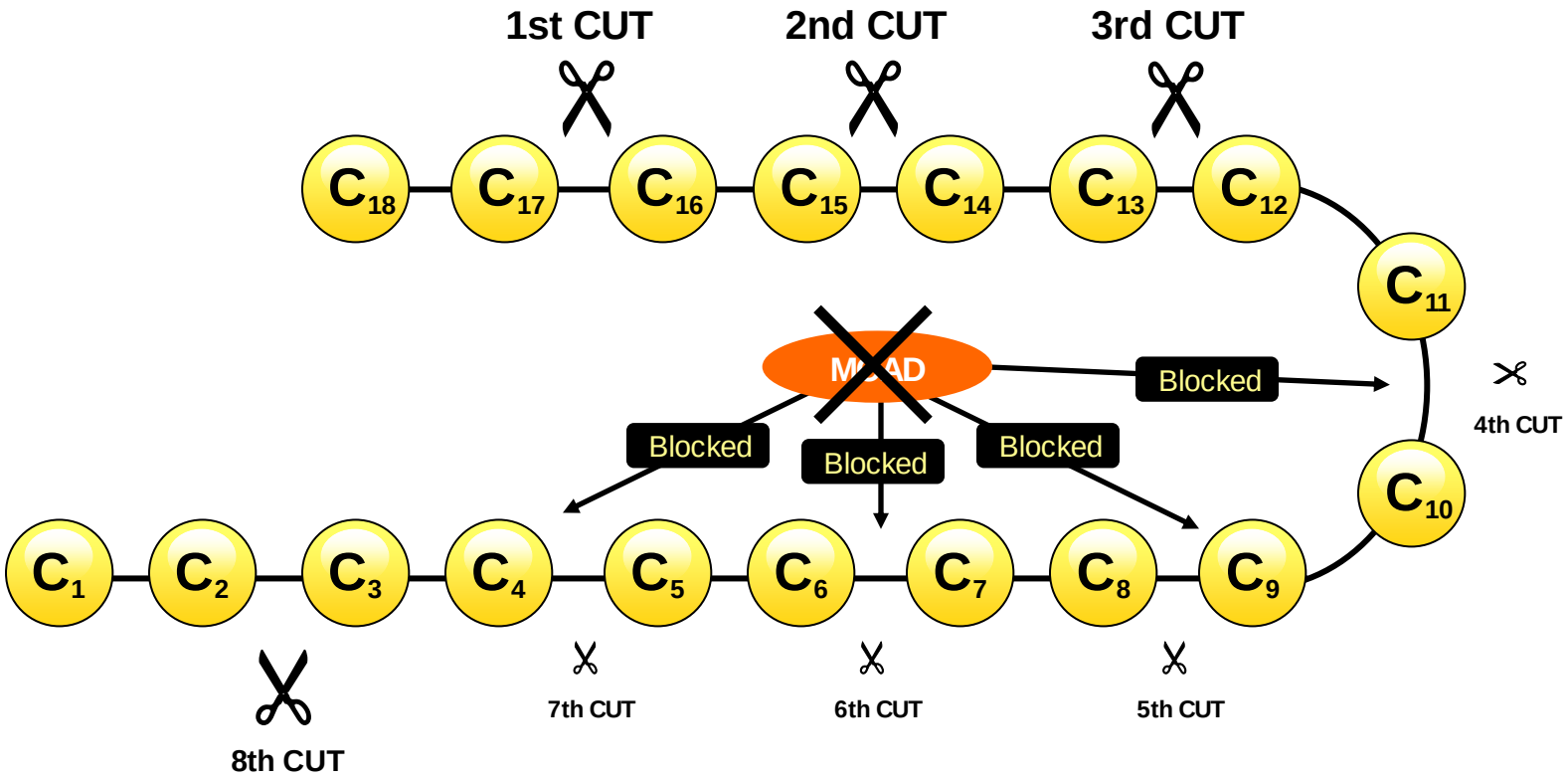
The enzyme VLCAD starts, the enzyme MCAD continues and the enzyme SCAD finishes



Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

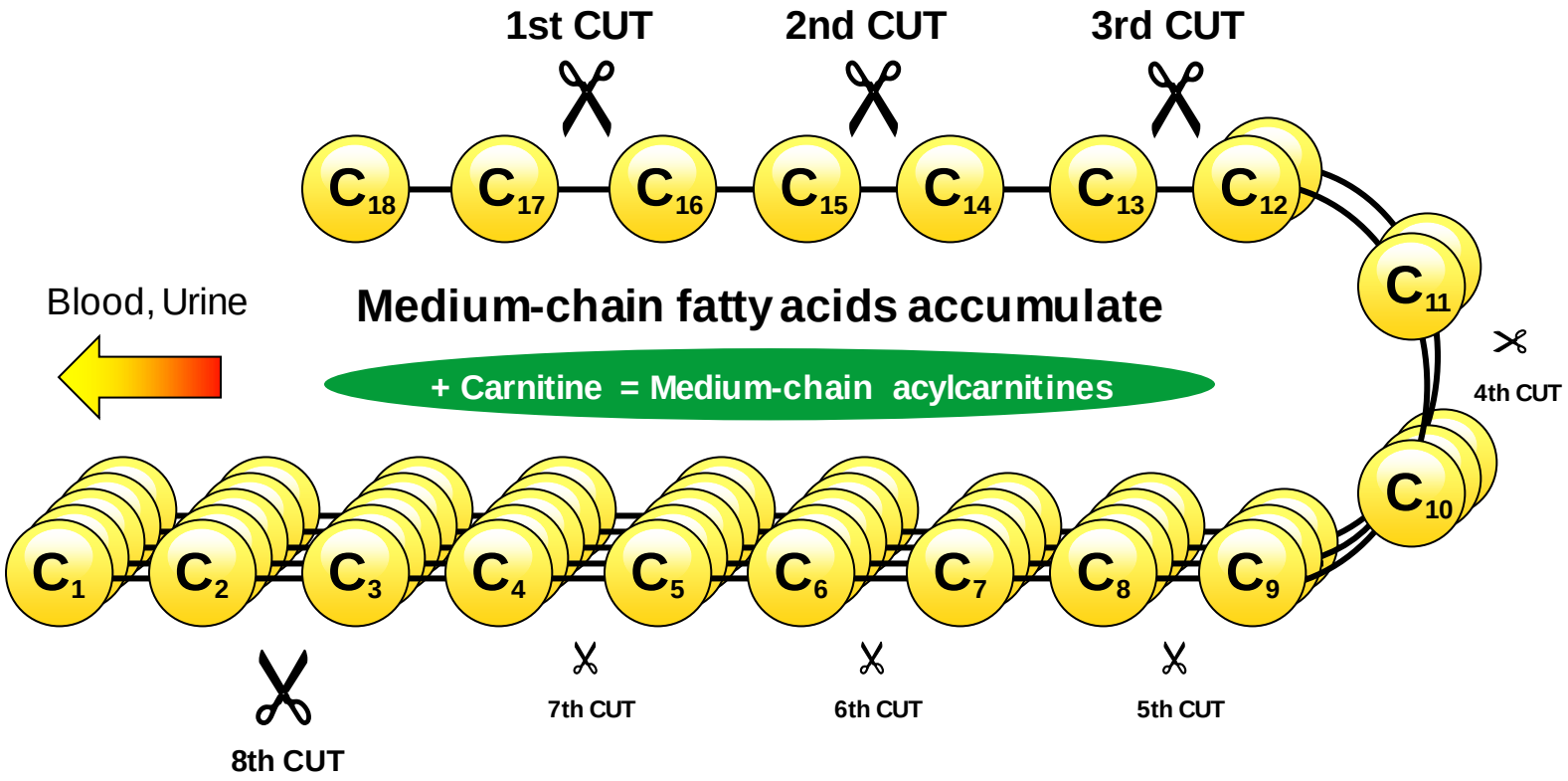
In MCAD deficiency, medium-chain fatty acids can not be broken down

Only the first three steps are possible



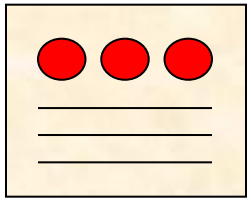
Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

In MCAD deficiency: Medium-chain fatty acids build-up and form medium-chain acylcarnitines



Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

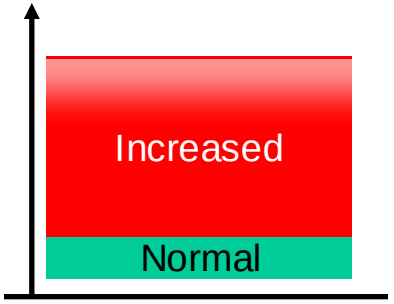
Diagnosis of MCAD deficiency

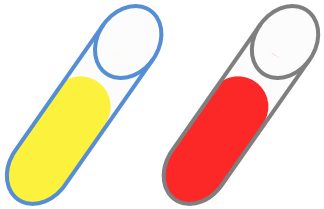


Dried blood spots

Newborn/Metabolic screening

Medium-chain acylcarnitines in blood



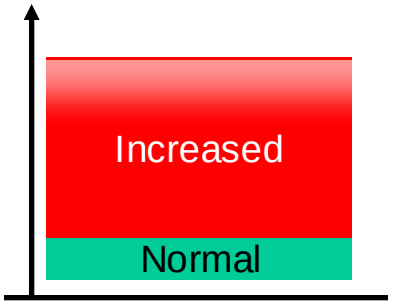


Urine sample

Blood sample

Confirmation of diagnosis

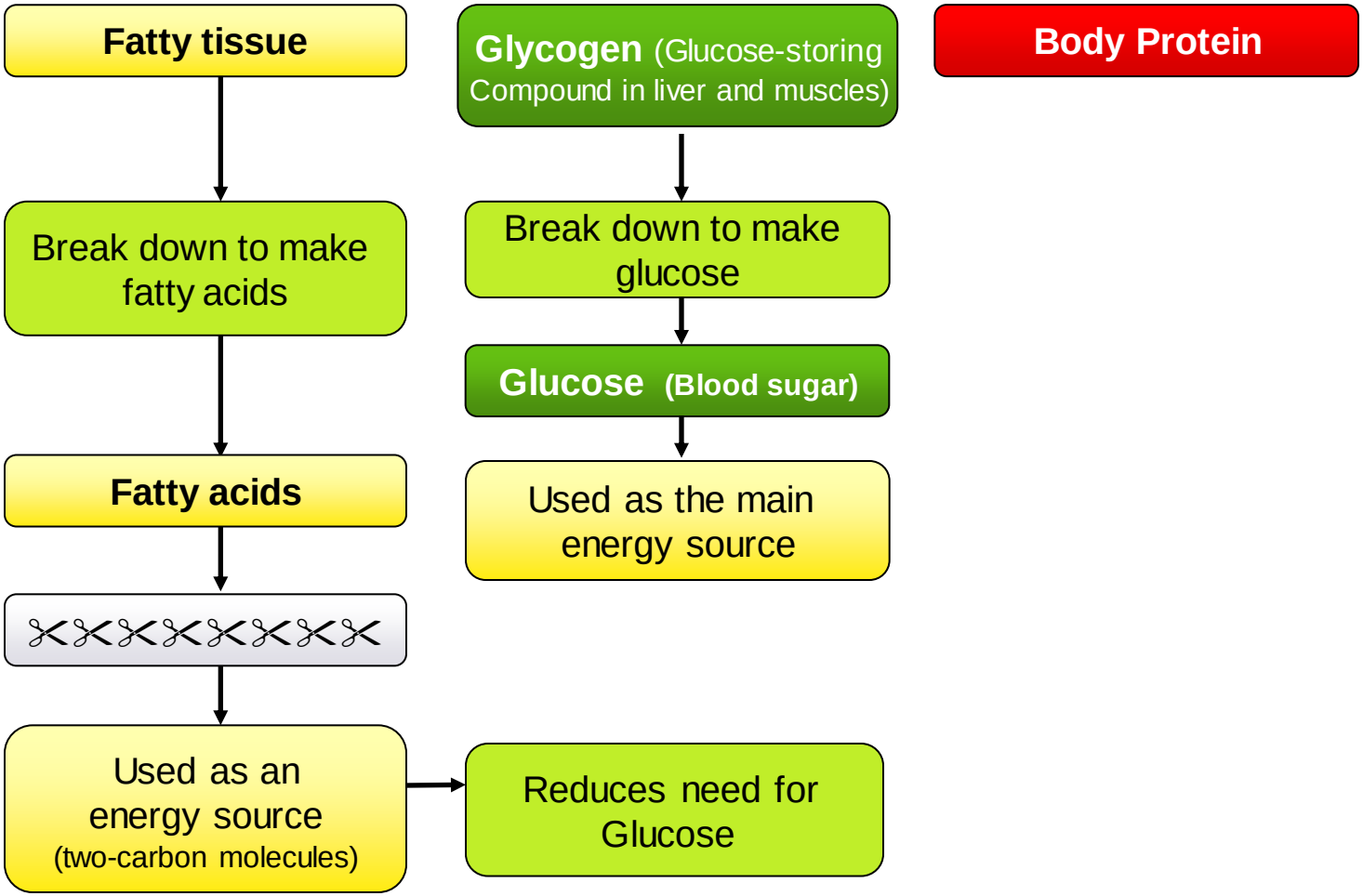
Abnormal compounds from medium-chain fatty acids in urine and blood



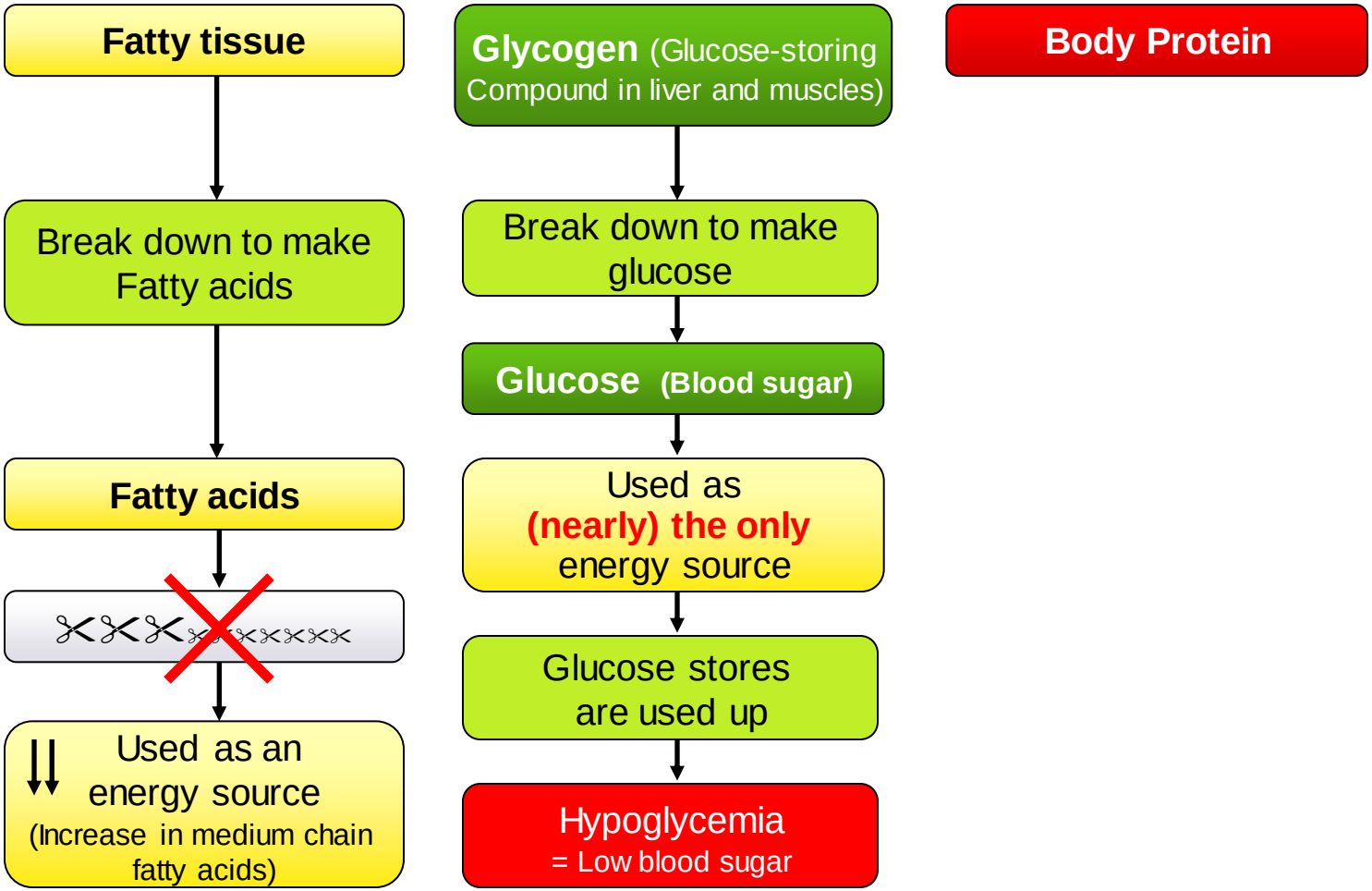
Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

What happens during Fasting?

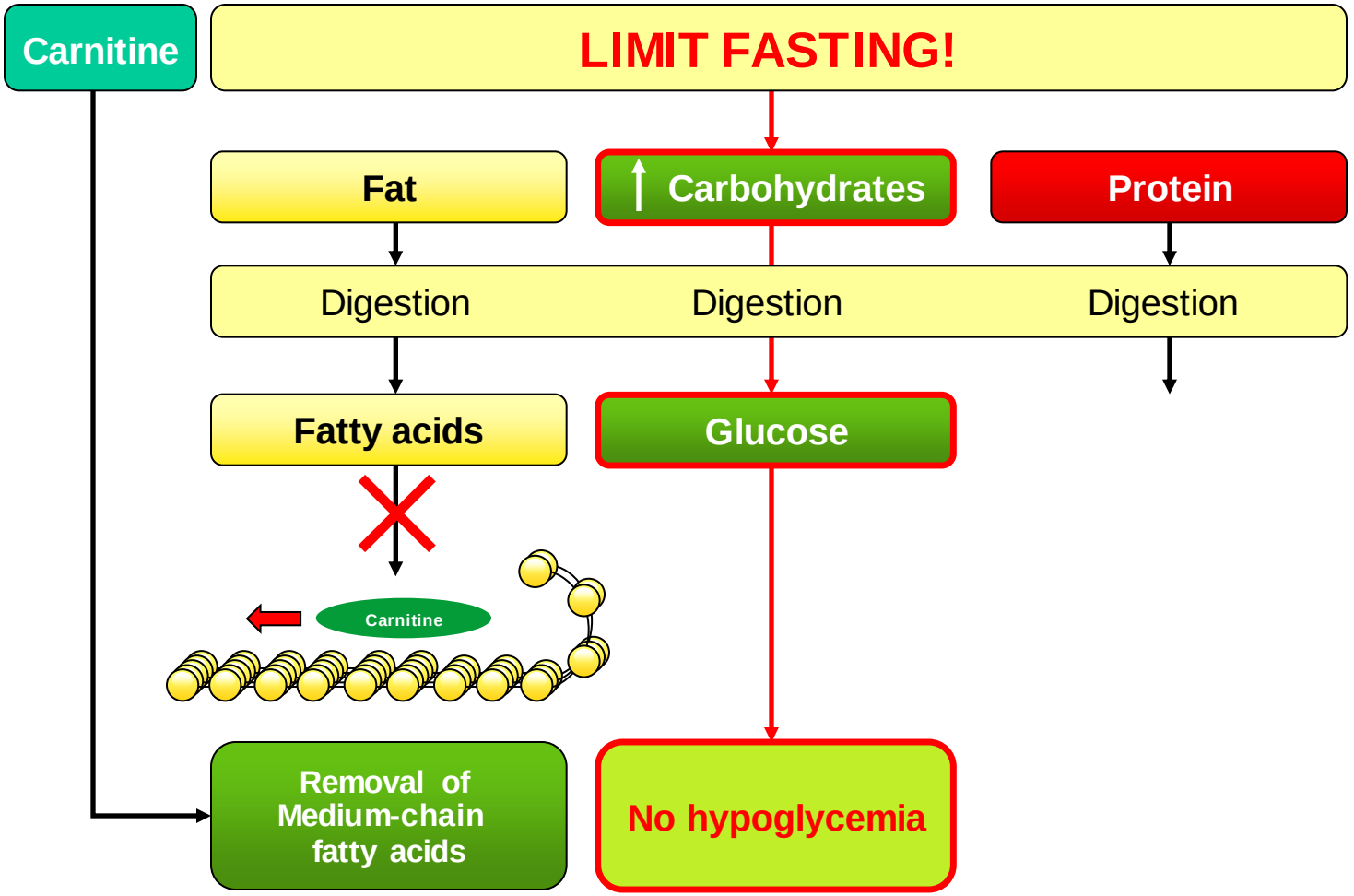
(Fasting is the time between meals when your child isn't drinking or eating anything)



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



Preventative measures for patients with MCAD deficiency



Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

Problems caused by increased medium-chain fatty acids and hypoglycemia in patients with MCAD deficiency

- **There is an increased risk for problems in the following situations:**

Febrile illness, especially with feeding problems (the child refused to eat or drink) or with vomiting.
General anesthesia and surgery.

- **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!**

- **Symptoms to watch out for:**

Vomiting
Increased sleepiness (lethargy)
Child is more difficult to wake up

Ask your clinic for an Emergency Protocol!

Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

Chromosomes, Genes, Mutations

A **chromosome** is like a cookbook.

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

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

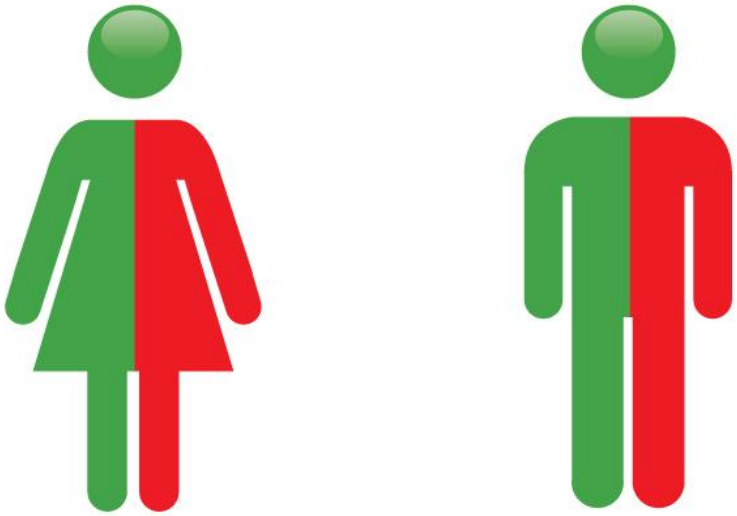
The **enzyme** MCAD is produced constantly in the body following a specific recipe (**gene**). If the gene contains abnormal **mutations,** the **enzyme** cannot function correctly or be properly produced.

Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

Inheritance of MCAD deficiency

Both parents are carriers in autosomal-recessive inheritance

Mother is carrier of
MCAD deficiency

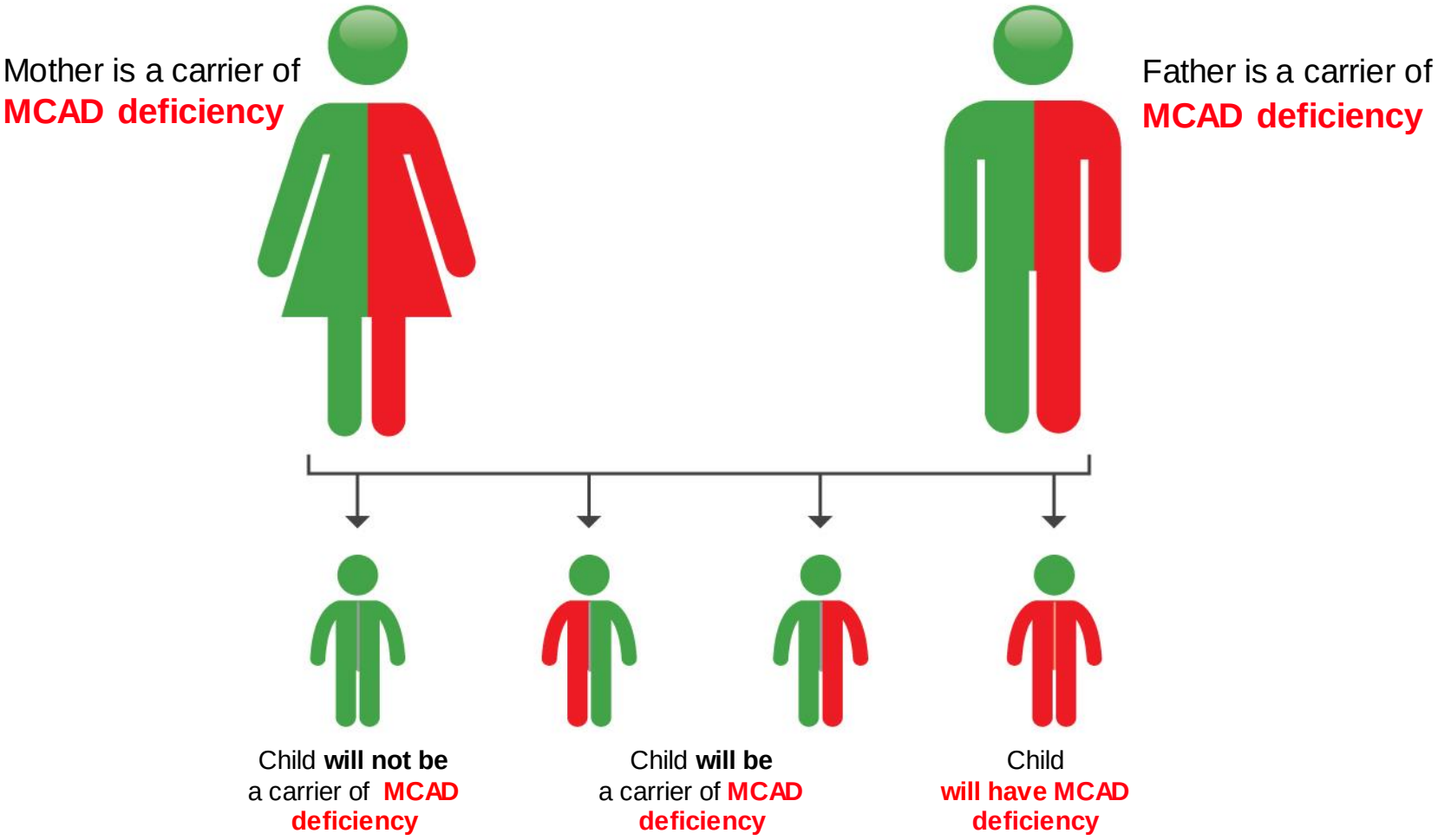


Father is a carrier of
MCAD deficiency

Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

Inheritance of MCAD deficiency

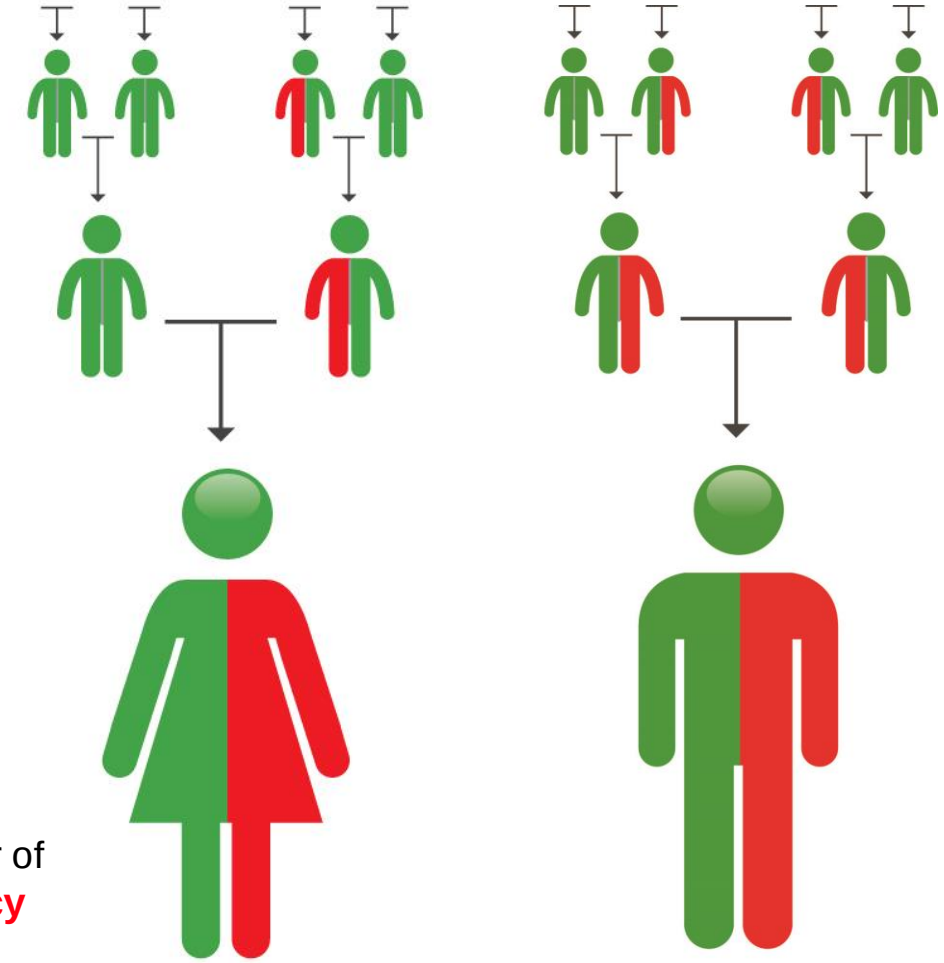
There are 4 possible combinations for any child born to parents who are carriers



Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

Inheritance of MCAD deficiency

How MCAD deficiency is inherited in families



Mother is a carrier of **MCAD deficiency**

Father is a carrier of **MCAD deficiency**

Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar

Prognosis of MCADD deficiency

Optimal management

Hypoglycemia is avoided during:

1. **Unusually long periods of fasting**
2. **Illnesses, especially with feeding problems and vomiting**

Insufficient management

Presence of hypoglycemia during:

1. **Unusually long periods of fasting**
2. **Illnesses, especially with feeding problems and vomiting**

Result

- **Completely normal development**
- **Prevention of any kind of brain damage that can cause neurological symptoms, seizures**

Result

- **Acute: life-threatening hypoglycemia with unconsciousness, brain edema and coma**

Sudden death

- **Chronic: severe brain damage, severe neurological symptoms, seizures**

Written by V. Prietsch & P. Burgard
Reviewed & revised for North America by S. van Calcar