Phenylketonuria

Introductory information

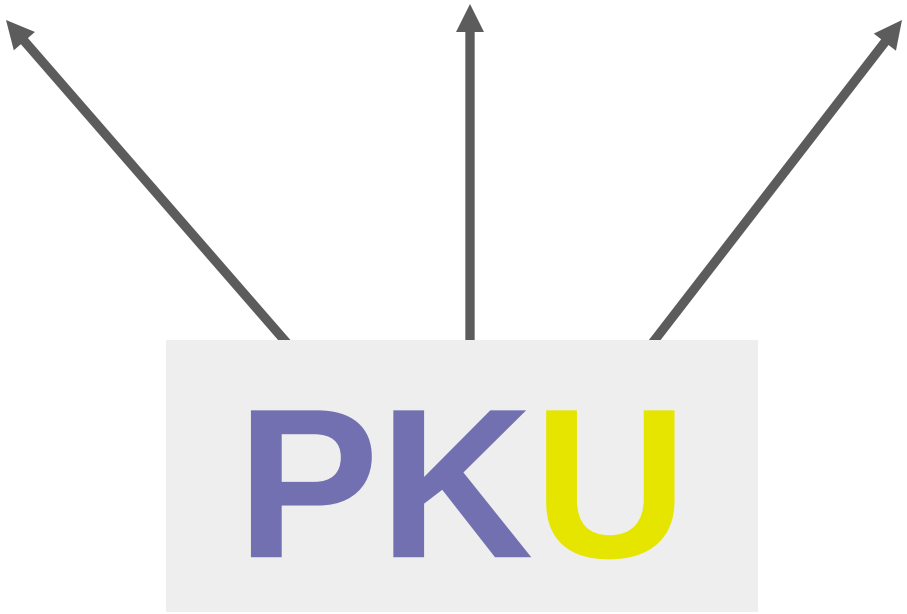
Written by:
P. Burgard & U. Wendel

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

Supported by NUTRICIA
as a service to metabolic medicine

TEMPLE
Tools Enabling Metabolic Parents LEarning

Phenylketonuria



Phenylketonuria

Phenylketones in urine

PKU

Hyperphenylalaninemia

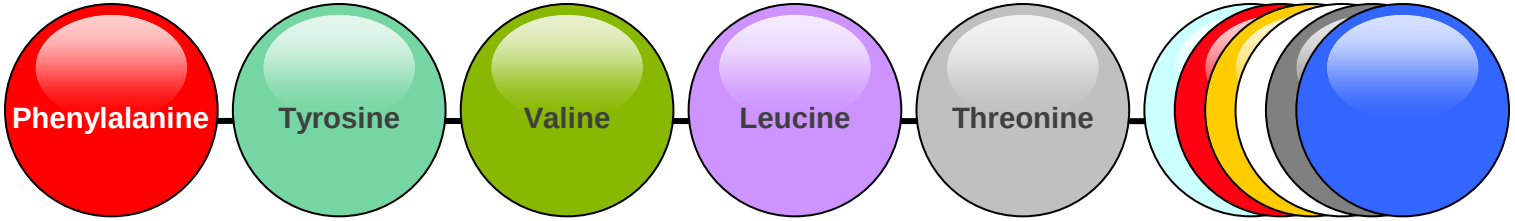
Too much **Phenylalanine** **in blood**

HPA

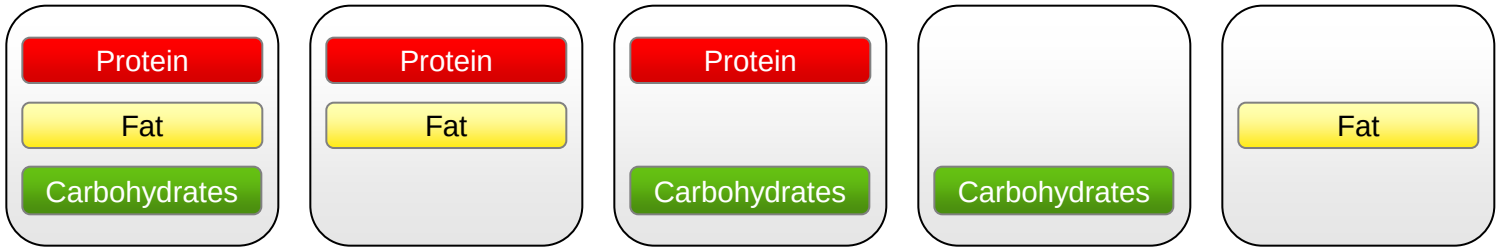
Food – Components of a normal diet

Protein | Fat | Carbohydrates

Protein consists of chains of amino acids



Natural Food



eg. milk, yogurt, nuts

eg. meat, poultry, fish, cheese, egg

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

eg. sugar, lemonade

eg. oil, margarine

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.

Phenyl**a**lanine **H**ydroxylase (PAH) is the enzyme that converts the amino acid phenylalanine to the amino acid tyrosine.

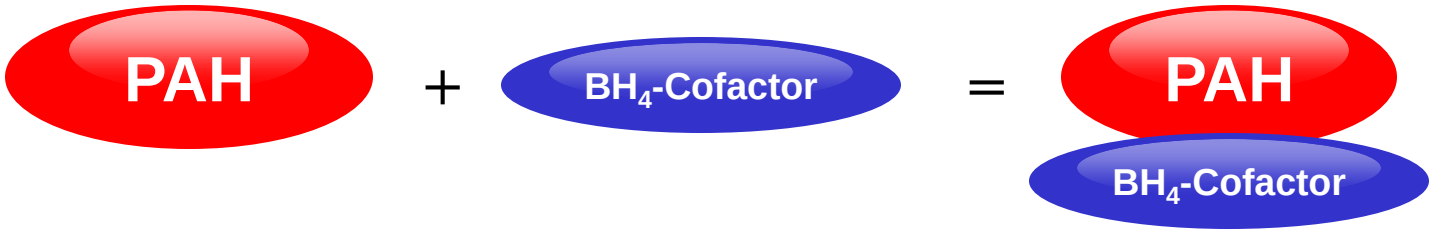
In HPA/PKU, the activity of the PAH enzyme is deficient.

Enzymes

In order to function correctly, some enzymes need the help of cofactors (= coenzymes).

PAH is such an enzyme and BH_4 is the cofactor.

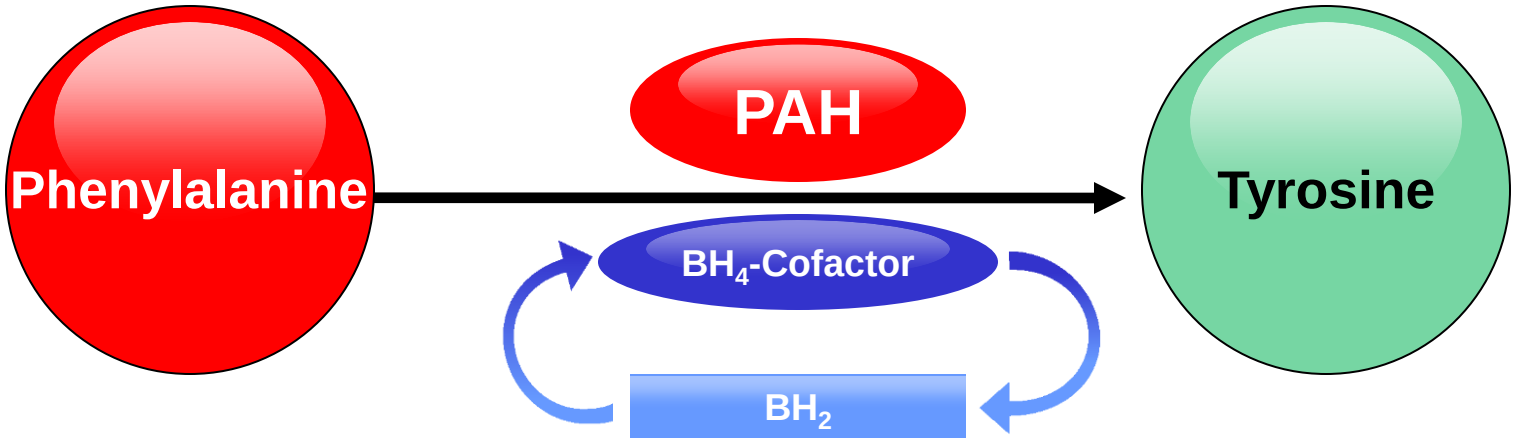
PAH requires BH_4 to become an active enzyme and function properly.



PAH inactive

PAH active

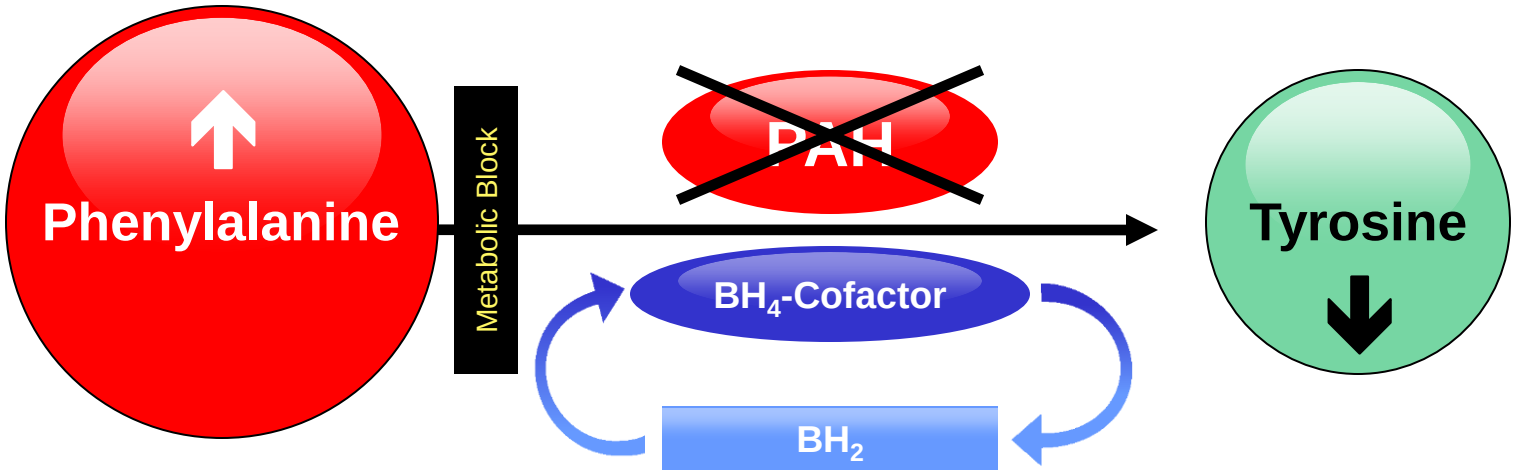
In a person without PKU – PAH works



PAH is functional

BH_4 supply is sufficient

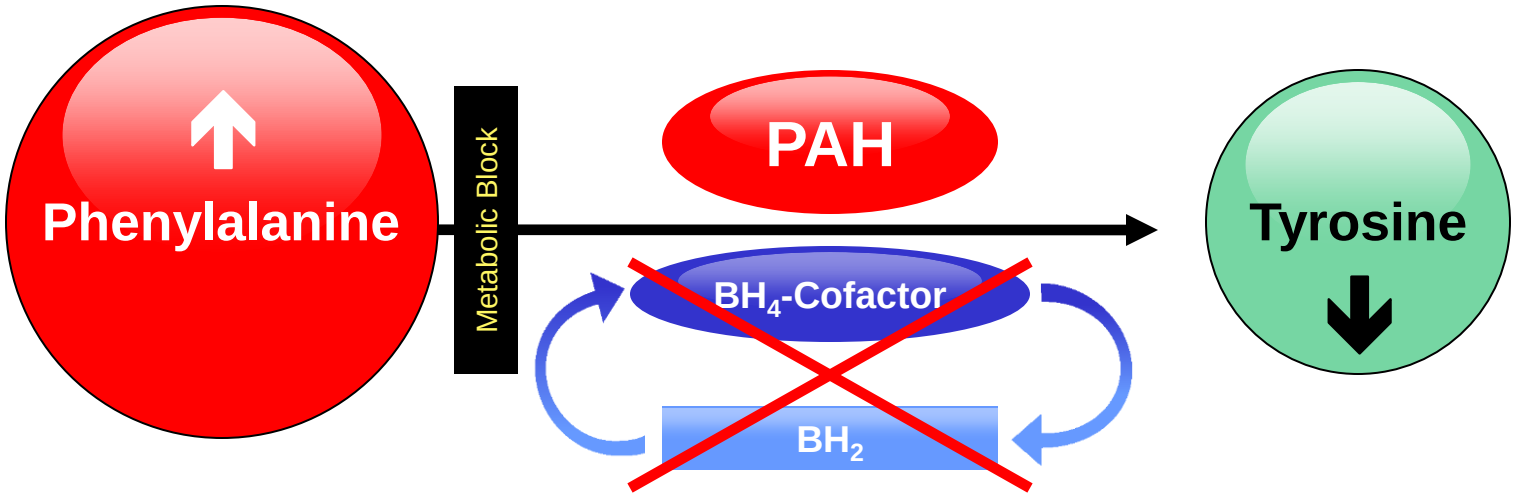
In a person with PKU or HPA – PAH is deficient



PAH is **not functional**

BH_4 supply is sufficient

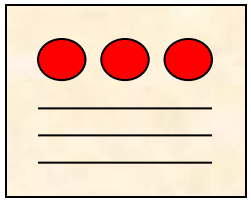
Hyperphenylalaninemias due to BH_4-deficiency



PAH is functional

BH_4 supply is **insufficient**

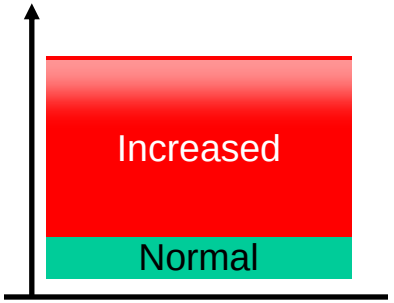
Diagnosis of PKU

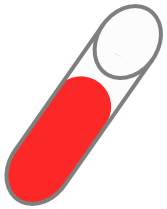


Dried blood spots

Newborn screening

Phenylalanine in dried blood spots

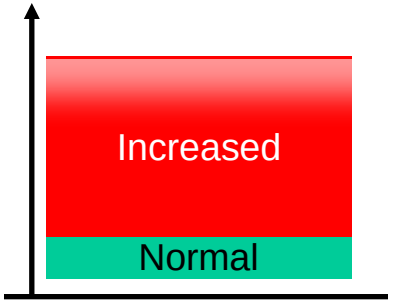




Venous blood

Confirmation of diagnosis

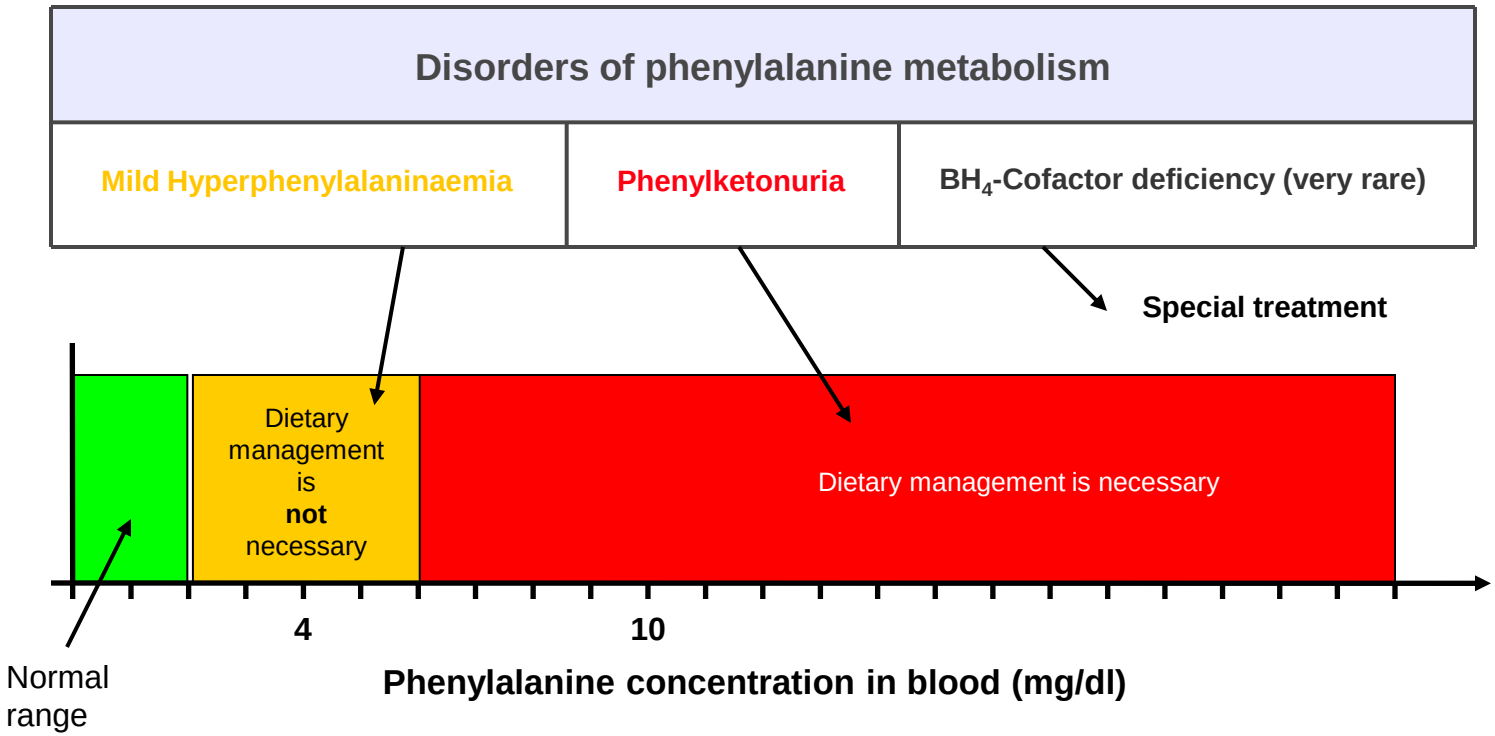
Phenylalanine in plasma



At confirmation of hyperphenylalaninaemia: plasma phenylalanine concentrations range from 2.0 mg/dl to > 20 mg/dl (120 µmol/L to > 1200 µmol/L)

Conversion of phenylalanine: 1 mg/dl ≈ 60 µmol/L

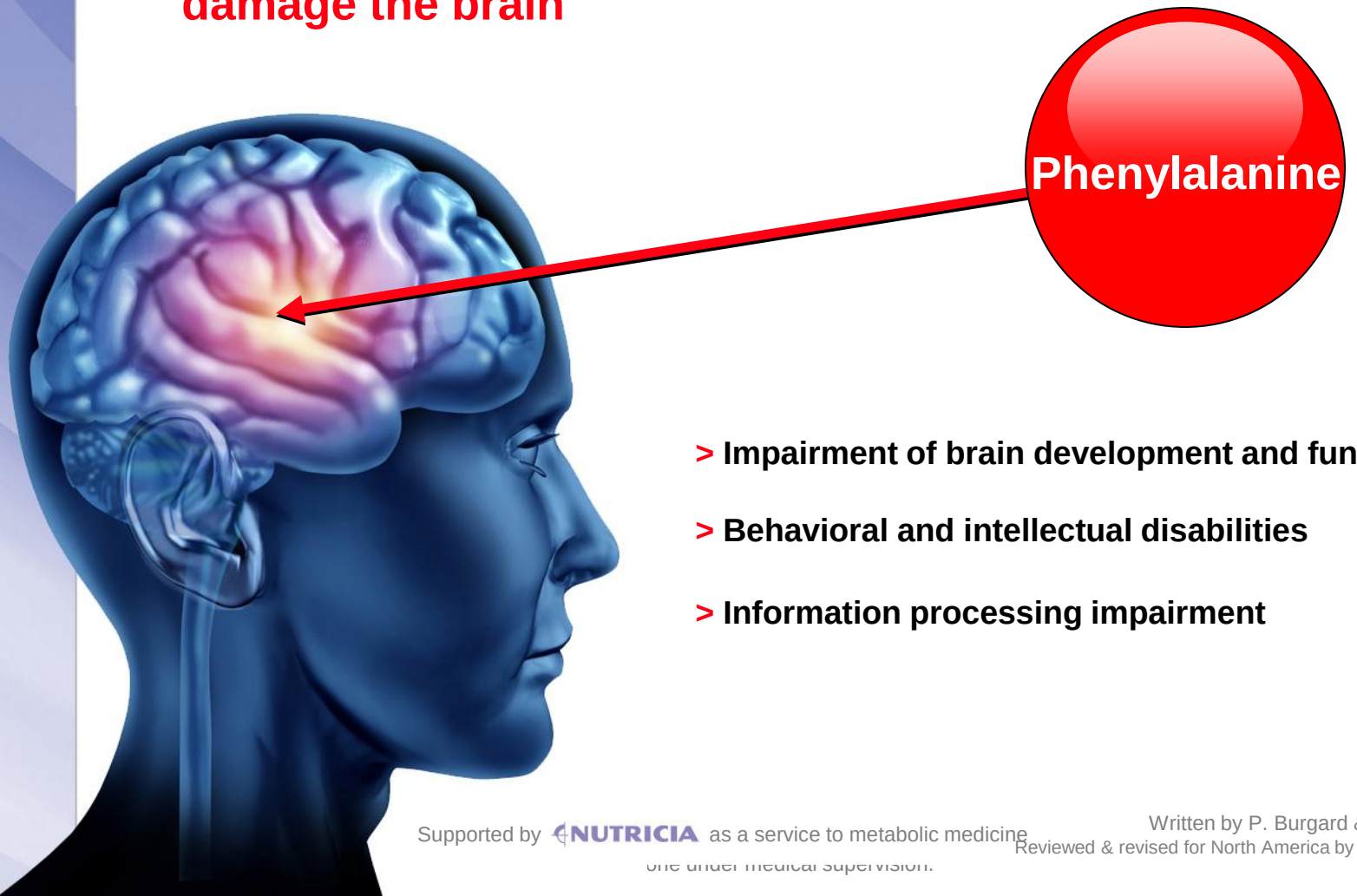
Diagnosis of PKU



Normal range in plasma:
Phenylalanine: ca. 60-120 µmol/L (1.0 - 2.0 mg/dl)

Pathogenesis

High concentrations of phenylalanine damage the brain

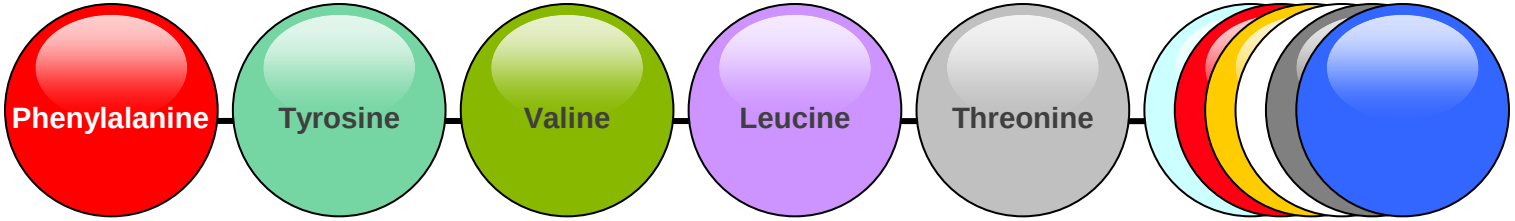


- **> Impairment of brain development and function**
- **> Behavioral and intellectual disabilities**
- **> Information processing impairment**

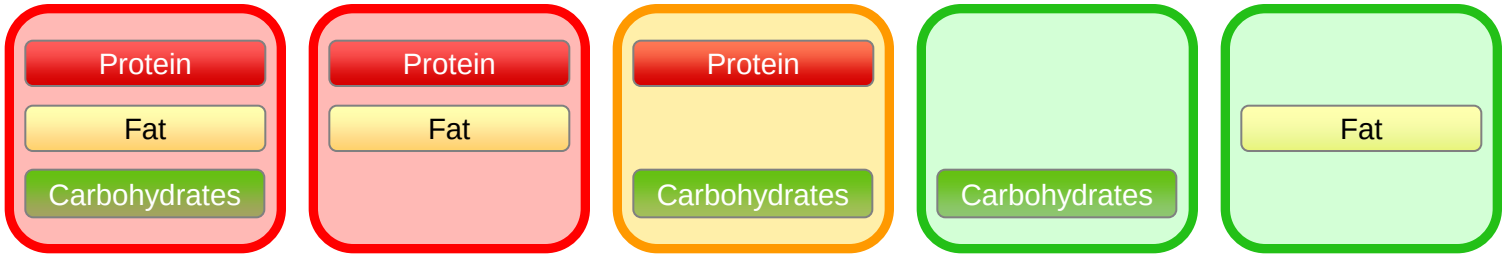
Food – Components of a normal diet

Protein | Fat | Carbohydrates

Protein consists of chains of amino acids



Natural Food



eg. milk, yogurt, nuts

eg. meat, poultry, fish, cheese, egg

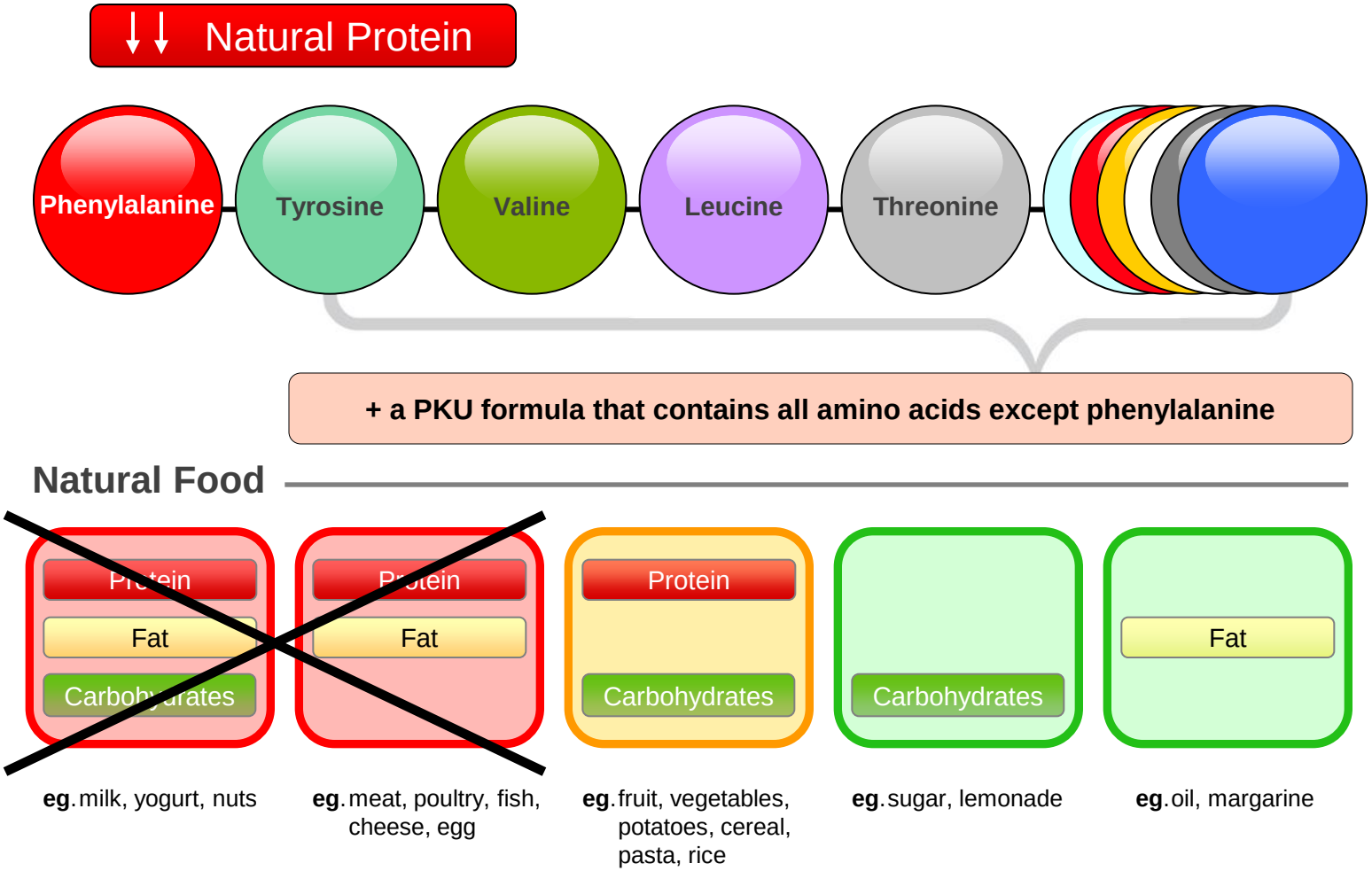
eg. fruit, vegetables, potatoes, cereal, rice, pasta

eg. sugar, lemonade

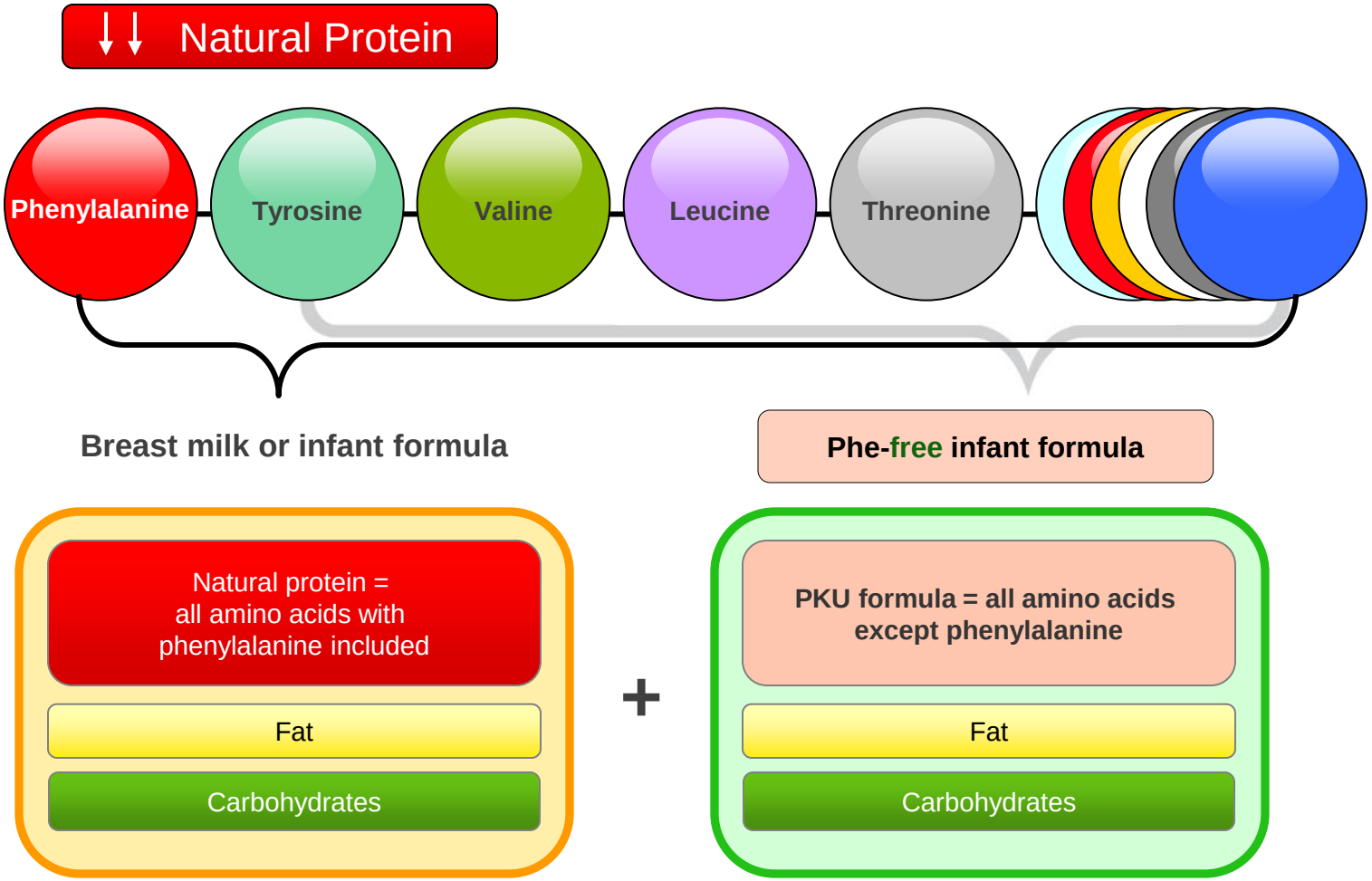
eg. oil, margarine

Principles of management

Diet is very low in natural protein + metabolic formula that does not contain phenylalanine

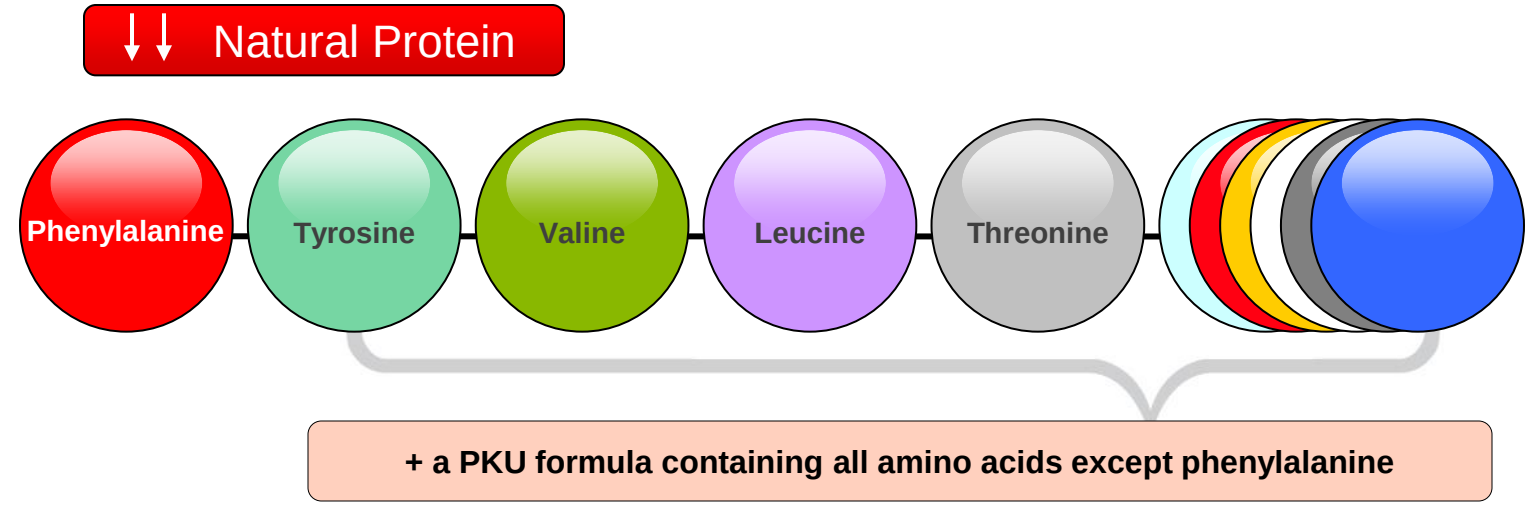


Dietary management during the first 4 to 6 months of life



Foods + special low-protein products + PKU formula

Nutritional components of the PKU diet once the baby is weaned and solids are introduced



Natural low-protein food	Special low protein products	PKU formula	Carbohydrates	Fat
eg. vegetables, fruits, potatoes, some cereals	**eg**. special breads, pasta and ready-made meals		**eg**. sugar, lemonade	**eg**. oil, margarine

Goals for management of PKU

PKU-diet
Very low-protein natural foods
+ special low-protein products
+ PKU formula

Management Goals for all ages

Long-term phenylalanine concentrations in blood should be:

2 to 6 mg/dl (120 to 360 µmol/L)

Blood phenylalanine levels need to be measured frequently!

Conversion of phenylalanine: 1 mg/dl ≈ 60 µmol/L

Monitoring the diet

Remember!

- Your child’s blood phenylalanine (phe) level needs to be checked frequently to prevent blood levels that are too high or too low.
- The metabolic team will check your child‘s clinical status and growth regularly.
- The metabolic dietitian will regularly assess the diet to assure that all nutrients (protein, fat, carbohydrates, vitamins and minerals) meet the recommendations for your child‘s age.

Treatment with BH_4

Pharmacological doses of BH_4 can reduce the blood phenylalanine levels in some individuals with PKU. This is called BH_4-responsive PKU. This may mean that the amount of phenylalanine in the diet can be increased, or for some, the PKU diet may not be needed at all.

With BH_4 treatment, the goals for blood phenylalanine levels remain the same as for those managed with diet only.

BH_4 is approved for infants, children and adults.

Chromosomes, Genes, Mutations

A **chromosome** is like a cookbook.

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

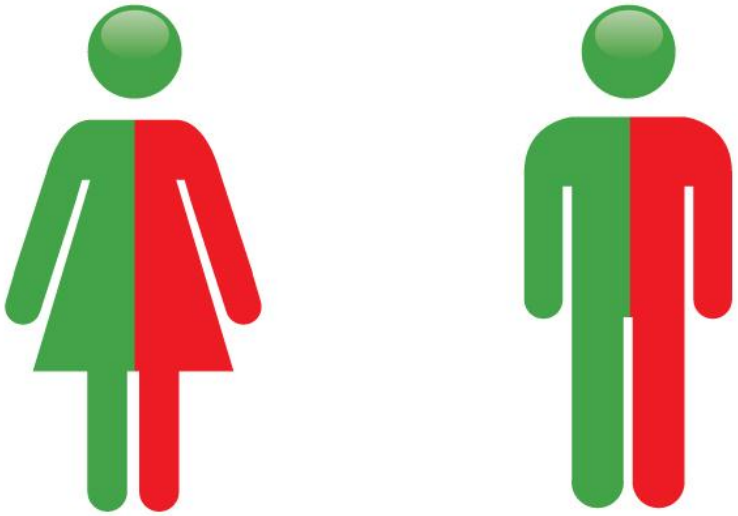
A **mutation** is like an error in the recipe or even a complete lack of a recipe.

The **enzyme** PAH 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.

Inheritance of HPA/PKU

Both parents are carriers in autosomal-recessive inheritance

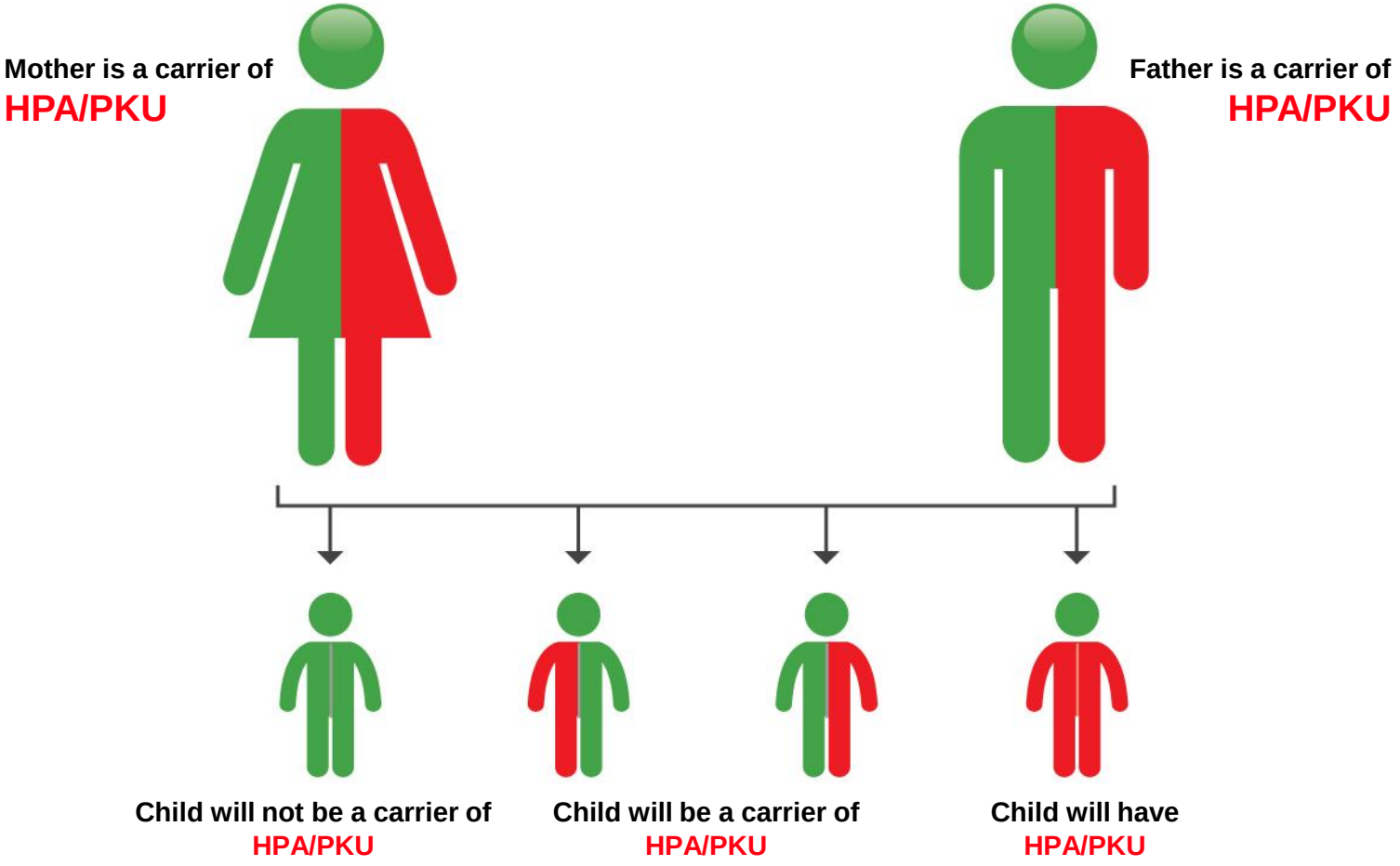
Mother is a carrier of
HPA/PKU



Father is a carrier of
HPA/PKU

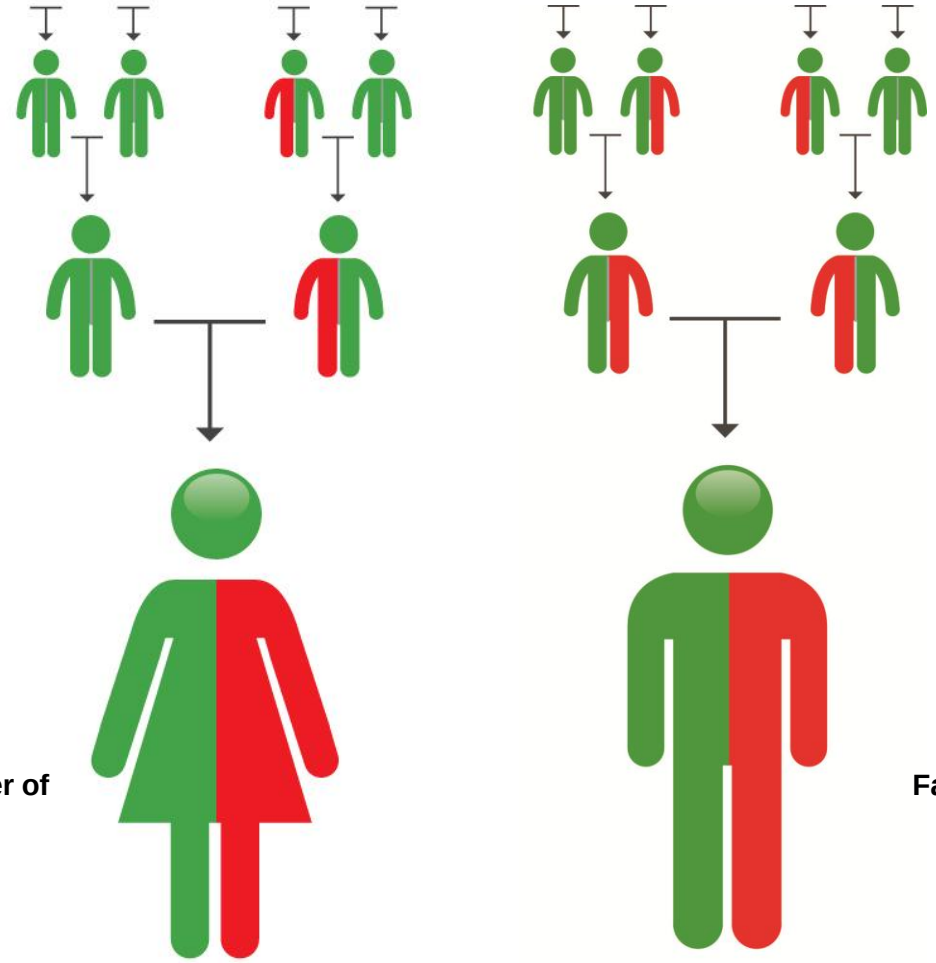
Inheritance of HPA/PKU

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



Inheritance of HPA/PKU

How HPA/PKU is inherited in families



Mother is a carrier of
HPA/PKU

Father is a carrier of
HPA/PKU

Summary

What is PKU?	An enzyme defect causing high phenylalanine levels in the blood
	⬆ Phenylalanine

Optimal Management

Dietary management reduces blood phe levels to the goal range

Result

Normal neurological and cognitive development

Monitoring

Lab
Frequent phenylalanine and other amino acids
Other routine lab tests

Physical development
Height, weight,
head circumference

Nutrition
Frequent adjustment of the diet

Development
Neuropsychology
Intelligence (IQ)

Insufficient Management

Poor dietary management increases blood phenylalanine concentrations above the goal range

Result

Impairment of neurological and intellectual development