Deficiency of Amino acids and their effects on the developing offspring

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Amino acids

- The body needs 20 different amino acids to maintain good health and normal functioning. People must obtain nine of these amino acids, called the essential amino acids, through food. Good dietary sources include meat, eggs, tofu, soy, buckwheat, quinoa, and dairy.
- Amino acids are compounds that combine to make proteins. When a person eats a food that contains protein, their digestive system breaks the protein down into amino acids. The body then combines the amino acids in various ways to carry out bodily functions.

Types and role of essential amino acids

- A healthy body can manufacture the other 11 amino acids, so these do not usually need to enter the body through the diet.
- Amino acids build muscles, cause chemical reactions in the body, transport nutrients, prevent illness, and carry out other functions. Amino acid deficiency can result in decreased immunity, digestive problems, depression, fertility issues, lower mental alertness, slowed growth in children, and many other health issues.
- Each of the essential amino acids plays a different role in the body, and the symptoms of deficiency vary accordingly.

Lysine

- Lysine plays a vital role in building muscle, maintaining bone strength, aiding recovery from injury or surgery, and regulating hormones, antibodies, and enzymes. It may also have antiviral effects.
- There is not a lot of research available on lysine deficiency, but a study on rats indicates that lysine deficiency can lead to stress-induced anxiety.

Histidine

- Histidine facilitates growth, the creation of blood cells, and tissue repair. It also helps maintain the special protective covering over nerve cells, which is called the myelin sheath.
- The body metabolizes histidine into histamine, which is crucial for immunity, reproductive health, and digestion. The results of a study that recruited women with obesity and metabolic syndrome suggest that histidine supplements may lower BMI and insulin resistance.
- Deficiency can cause anemia, and low blood levels appear to be more common among people with arthritis and kidney disease.

Threonine

- Threonine is necessary for healthy skin and teeth, as it is a component in tooth enamel, collagen, and elastin. It helps aid fat metabolism and may be beneficial for people with indigestion, anxiety, and mild depression.

Methionine

- Methionine and the nonessential amino acid cysteine play a role in the health and flexibility of skin and hair. Methionine also helps keep nails strong. It aids the proper absorption of selenium and zinc and the removal of heavy metals, such as lead and mercury.

Valine

- Valine is essential for mental focus, muscle coordination, and emotional calm. People may use valine supplements for muscle growth, tissue repair, and energy.
- Deficiency may cause insomnia and reduced mental function.

Isoleucine

- Isoleucine helps with wound healing, immunity, blood sugar regulation, and hormone production. It is primarily present in muscle tissue and regulates energy levels.
- Older adults may be more prone to isoleucine deficiency than younger people. This deficiency may cause muscle wasting and shaking.

Leucine

- Leucine helps regulate blood sugar levels and aids the growth and repair of muscle and bone. It is also necessary for wound healing and the production of growth hormone.
- Leucine deficiency can lead to skin rashes, hair loss, and fatigue.

Phenylalanine

- Some diet sodas contain sweeteners with phenylalanine.
- Phenylalanine helps the body use other amino acids as well as proteins and enzymes. The body converts phenylalanine to tyrosine, which is necessary for specific brain functions.
- Phenylalanine deficiency, though rare, can lead to poor weight gain in infants. It may also cause eczema, fatigue, and memory problems in adults.
- Phenylalanine is often in the artificial sweetener aspartame, which manufacturers use to make diet sodas. Large doses of aspartame can increase the levels of phenylalanine in the brain and may cause anxiety and jitteriness and affect sleep.
- People with a rare genetic disorder called phenylketonuria (PKU) are unable to metabolize phenylalanine. As a result, they should avoid consuming foods that contain high levels of this amino acid.

Tryptophan

- Tryptophan is necessary for proper growth in infants and is a precursor of serotonin and melatonin. Serotonin is a neurotransmitter that regulates appetite, sleep, mood, and pain. Melatonin also regulates sleep.
- Tryptophan is a sedative, and it is an ingredient in some sleep aids. One study indicates that tryptophan supplementation can improve mental energy and emotional processing in healthy women.
- Tryptophan deficiency can cause a condition called pellagra, which can lead to dementia, skin rashes, and digestive issues.

METABOLIC DEFECTS IN AMINO ACID METABOLISM

- Amino acids are the building blocks of proteins and have many functions in the body.
- Hereditary disorders of amino acid metabolism can be the result of defects either in the breakdown of amino acids or in the body's ability to get the amino acids into cells.
- Because these disorders produce symptoms early in life, newborns are routinely screened for several common ones.

Amino acids deficiency effects on the developing offspring

- Phenylketonuria
- Methyl melonic aciduria
- Alkaptonuria
- Maple syrup urine disease
- Parkinson’s disease
- Homocystinuria
- Hartnup’s disease

Phenylketonuria

Cause

- PKU is caused by a defect in the gene that helps create **phenylalanine hydroxylase**
- Unable to break down phenylalanine.
- This causes a buildup of phenylalanine in the body

Symptoms

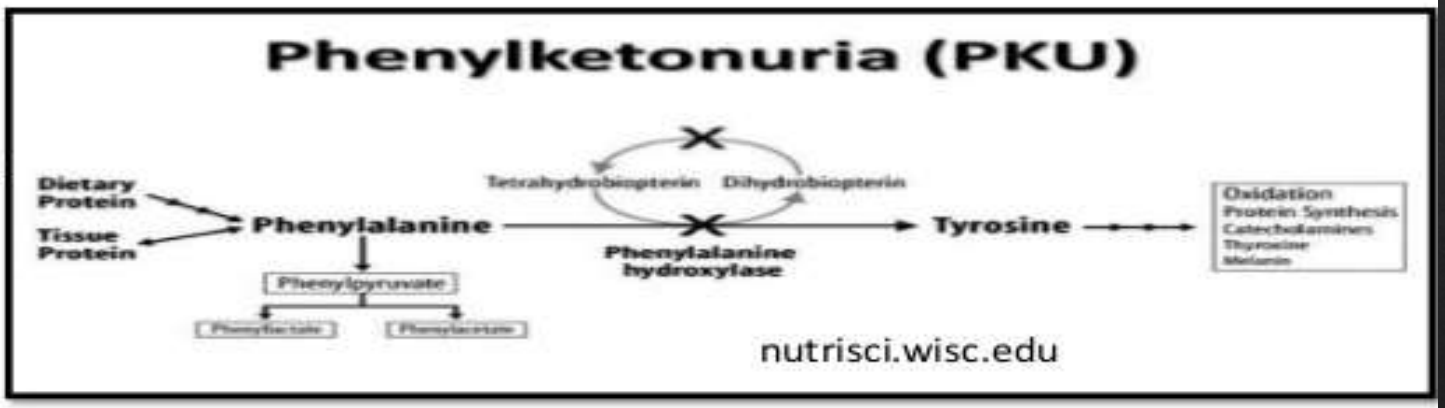
- Seizures
- Tremors, or trembling and shaking
- Stunted growth
- Hyperactivity
- A musty odor of their breath, skin, or urine

Treatment

Avoid foods high in protein

These include:

- eggs
- beans
- chicken
- beef
- pork
- fish



Medication- Sapropterin (Kuvan) for the treatment of PKU. Sapropterin helps lower phenylalanine levels.

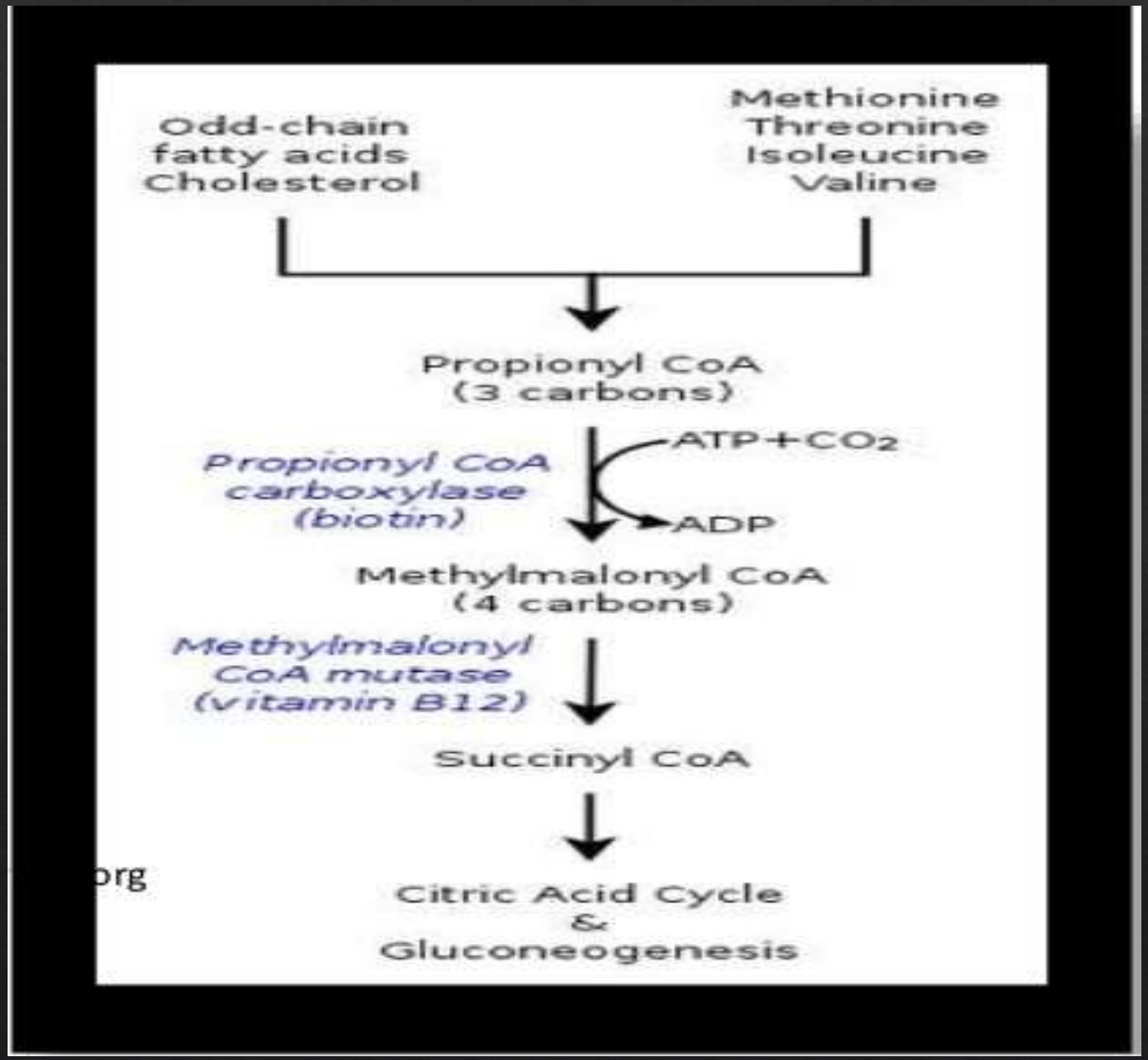
Methyl Malonic Aciduria

Cause

- Methylmalonic acidemia is an **autosomal recessive disorder of amino acid metabolism**, involving a defect in the conversion of methylmalonyl-coenzyme A (CoA) to succinyl-CoA

Symptom

- Neurologic manifestations, such as seizure, encephalopathy, and stroke
- Several cases have involved stroke


Odd-chain
fatty acids
Cholesterol
Methionine
Threonine
Isoleucine
Valine
Propionyl CoA
(3 carbons)
Propionyl CoA
carboxylase
(biotin)
ATP+CO2
ADP
Methylmalonyl CoA
(4 carbons)
Methylmalonyl
CoA mutase
(vitamin B12)
Succinyl CoA
Citric Acid Cycle
&
Gluconeogenesis

Treatment

- **Protein-restricted diet-** This modification decreases the key amino acids (eg, isoleucine, valine, threonine, methionine) that enter the metabolic pathway.
- **Cobalamin supplementation-** may help because cobalamin is a cofactor in the enzymatic conversion of methylmalonyl-coenzyme A (CoA) to succinyl-CoA.
- **L-carnitine**- an enzyme involved in the metabolism of long-chain fatty acids, buffers the acyl-CoA metabolites
- **Liver transplantation** alone or in conjunction with kidney transplantation has been attempted

Alkaptonuria

Cause

Homogentisic dioxygenase (HGD)

Mutation on your homogentisate 1,2-dioxygenase (HGD) gene

Used to break down a toxic substance called homogentisic acid

When you don't produce enough HGD, homogentisic acid builds up in your body

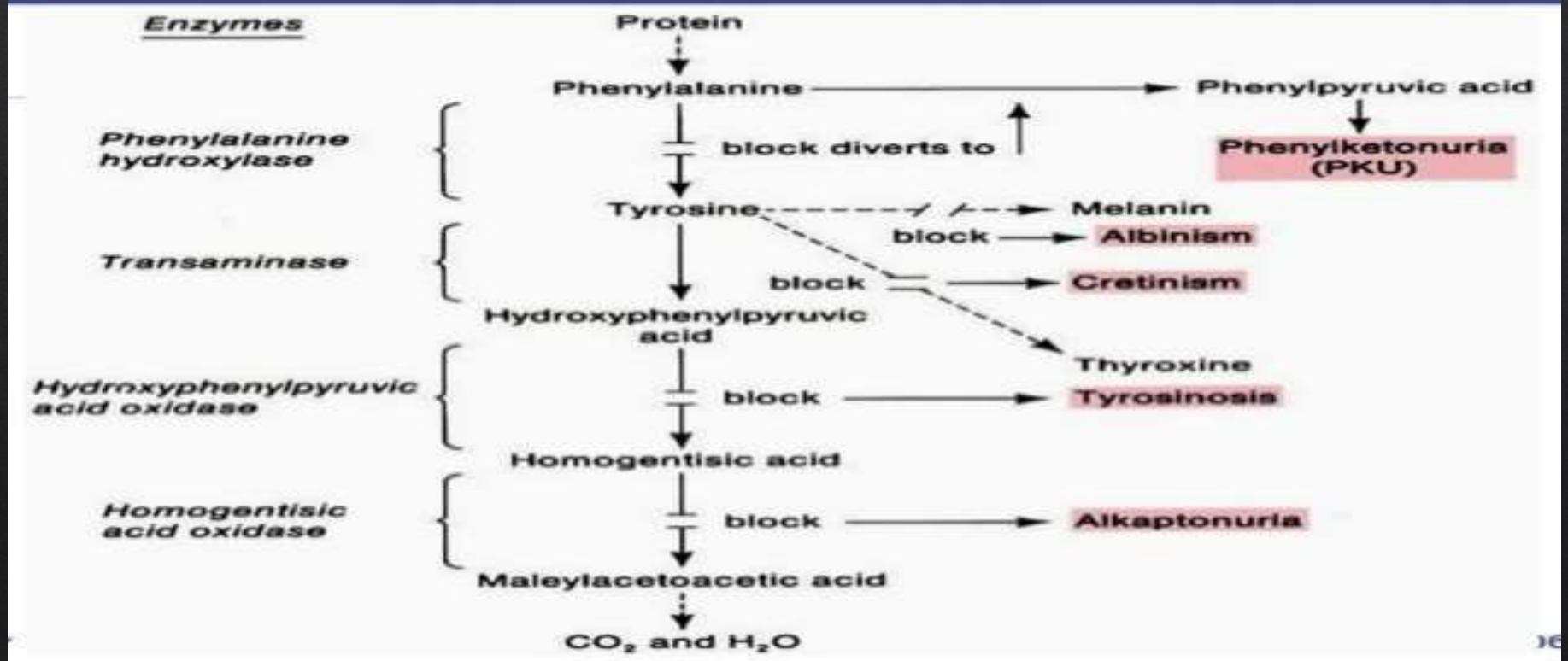
The buildup of homogentisic acid causes your bones and cartilage to become discolored and brittle.

Symptoms

- Dark spots in the sclera (white) of your eyes
- Thickened and darkened cartilage in your ears
- Blue speckled discoloration of your skin, particularly around sweat glands
- Black earwax
- kidney stones and prostate stones
- Arthritis (especially hip and knee joints)

Treatment

- A low-protein diet.
- large doses of ascorbic acid, or vitamin C, to slow down the accumulation of homogentisic acid in your cartilage.
- Physical and occupational therapy may help you maintain flexibility and strength in your muscles and joints.
- Use of the drug **nitisinone** as a possible treatment for alkaptonuria.



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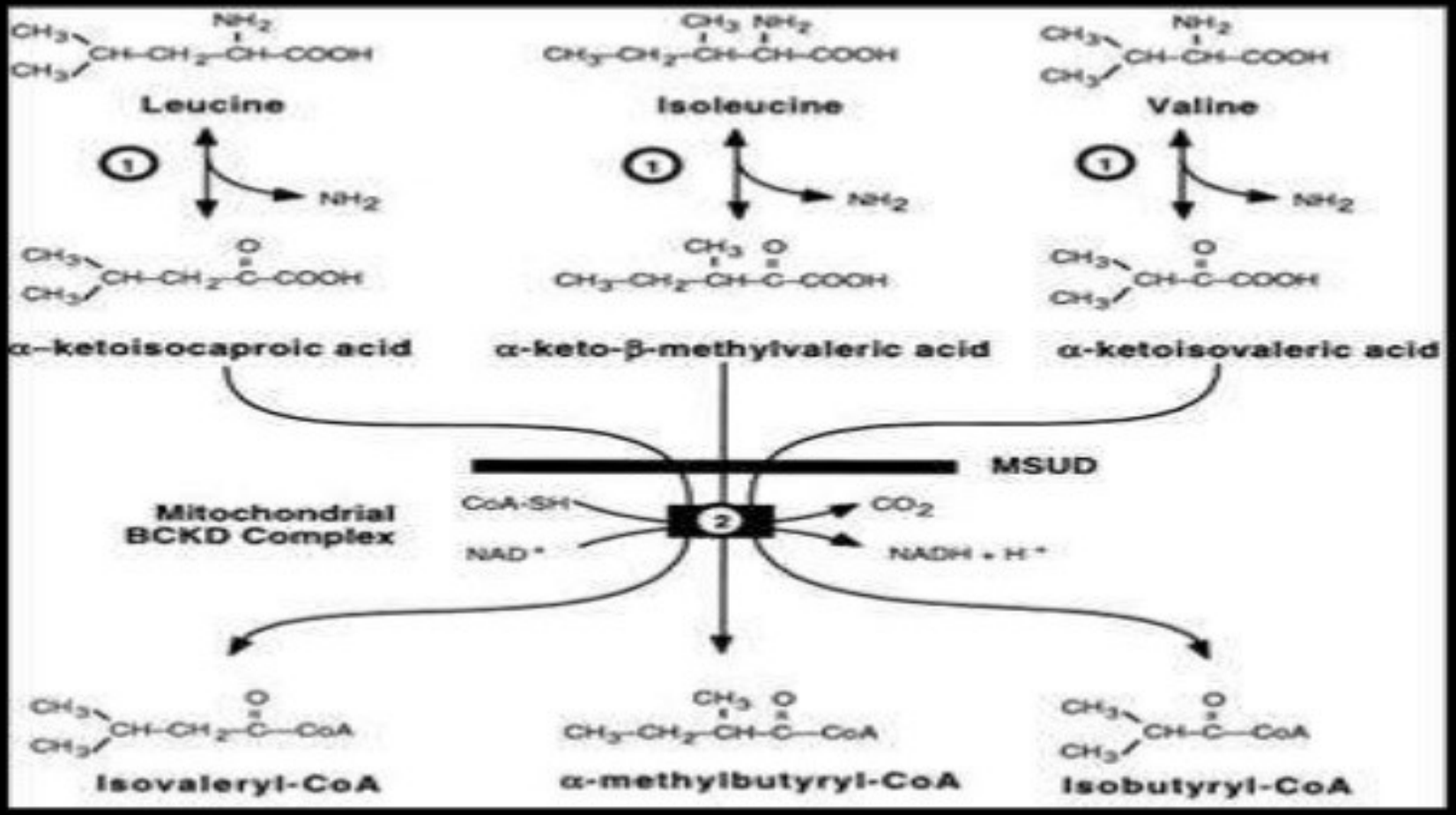
Maple syrup urine disease

Cause

Defects in any of the six subunits of the BCKD protein complex can cause MSUD. The most common defect is caused by a mutation in a gene on chromosome 19 that encodes the alpha subunit of the BCKD complex (BCKDHA).

Symptoms

- loss of appetite
- fussiness
- sweet-smelling urine


Leucine
Isoleucine
Valine
α-ketoisocaproic acid
α-keto-β-methylvaleric acid
α-ketoisovaleric acid
MSUD
Mitochondrial
BCKD Complex
CoA-SH
NAD+
CO2
NADH + H+
Isovaleryl-CoA
α-methylbutyryl-CoA
Isobutyryl-CoA

Treatment

- Treatment involved dietary restriction of the amino acids leucine, isoleucine, and valine.
- Patients can be treated with an intravenous (given through a vein) solution that helps the body use up excess leucine, isoleucine, and valine for protein synthesis.
- **Gene therapy** is also a potential future treatment for patients with MSUD. This treatment would involve replacing the mutated gene with a good copy, allowing the patient's cells to make a functional BCKD protein complex and break down the excess amino acids.

Parkinson's Disease

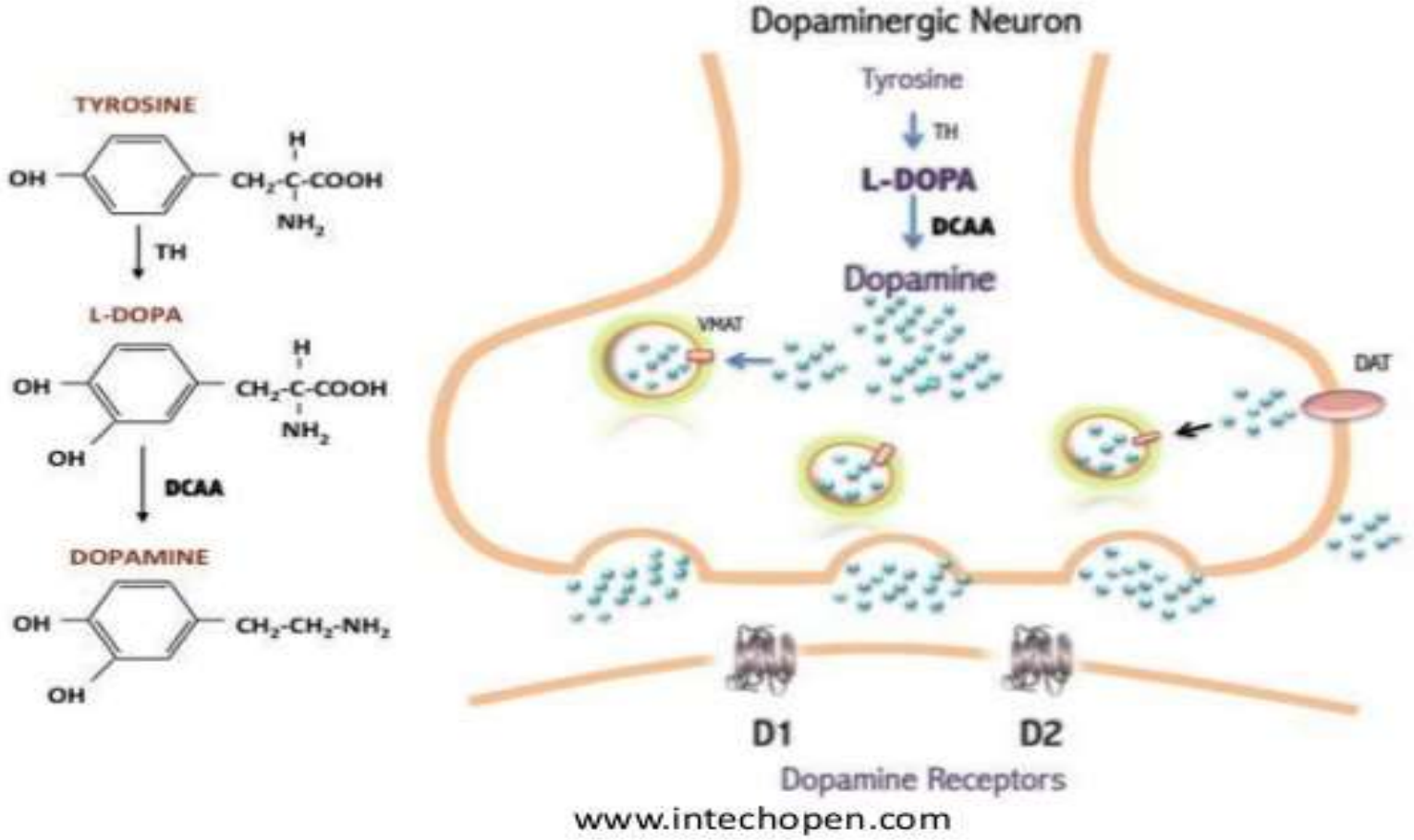
Cause

progressive neurological disorder that is caused by a degeneration of cells in the part of the brain that produces the neurotransmitter dopamine (chemical messenger)

Symptoms

Symptoms of Parkinson's disease differ from person to person

- lowness of voluntary movements, especially in the initiation of such movements as walking or rolling over in bed
- A shuffling gait with poor arm swing and stooped posture
- Unsteady balance; difficulty rising from a sitting position


TYROSINE
OH
CH2-C-COOH
H
NH2
TH
L-DOPA
OH
OH
DCAA
DOPAMINE
CH2-CH2-NH2
Dopaminergic Neuron
Tyrosine
TH
L-DOPA
DCAA
Dopamine
VMAT
DAT
D1
D2
Dopamine Receptors
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Treatment

- **Medicines**, such as levodopa and dopamine agonists.
- **Brain surgery**, for example deep brain stimulation (DBS), may be considered when medicine fails to control symptoms of Parkinson's disease or causes severe or disabling side effects.
- **Speech therapy:**Speech therapists use breathing and speech exercises to help you overcome the soft, imprecise speech and monotone voice that develop in advanced Parkinson's disease.
- **Physical therapy:**Therapists may help you improve your walking and reduce your risk of falling.
- **Occupational therapy**: Therapists can help you learn new ways to do things for yourself so you can stay independent longer.

Homocystinuria

Cause

Certain genetic mutations present at birth cause this disease.

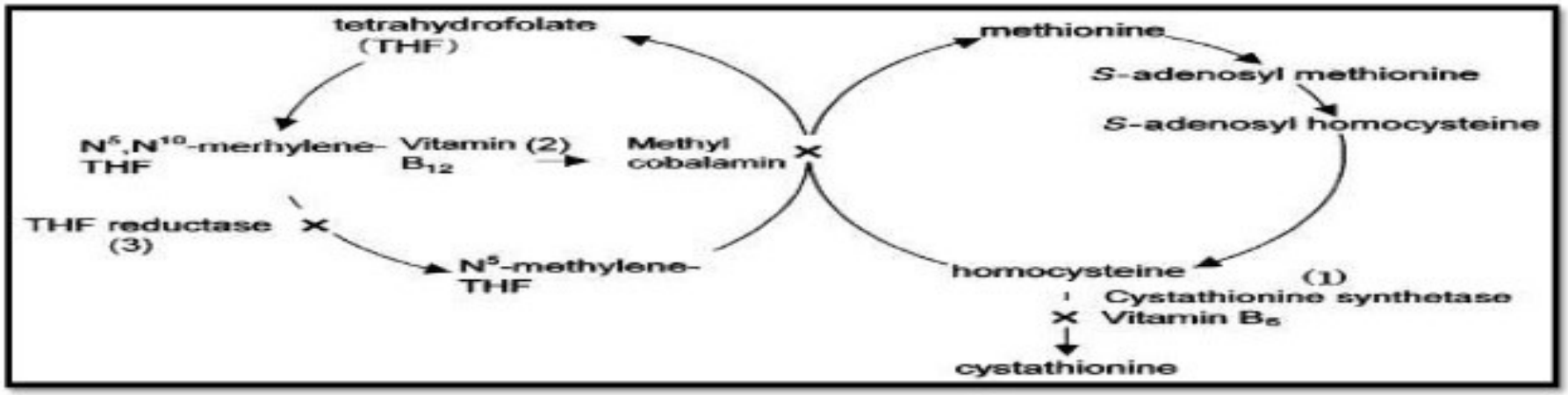
The CBS gene holds instructions for making an enzyme that uses vitamin B-6 to metabolize the amino acids homocysteine and serine.

The mutations prevent the normal functioning of the CBS gene.

This results in a buildup of homocysteine and other toxins that damage the nervous system, which includes the brain, and the vascular system

Symptoms

- dislocation of the lenses in the eyes
- nearsightedness
- abnormal blood clots
- osteoporosis, or weakening of the bones
- learning disabilities
- developmental problems
- chest deformities, such as a protrusion or a caved-in appearance of the breastbone
- long, spindly arms and legs
- scoliosis



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Treatment

- High doses of vitamin B-6 are a successful treatment for about half of the people with this disorder.
- Eating a diet low in foods containing the amino acid methionine
- **Betaine** is a nutrient that works to remove homocysteine from the blood. Taking a folic acid supplement and adding the amino acid cysteine to the diet are helpful.

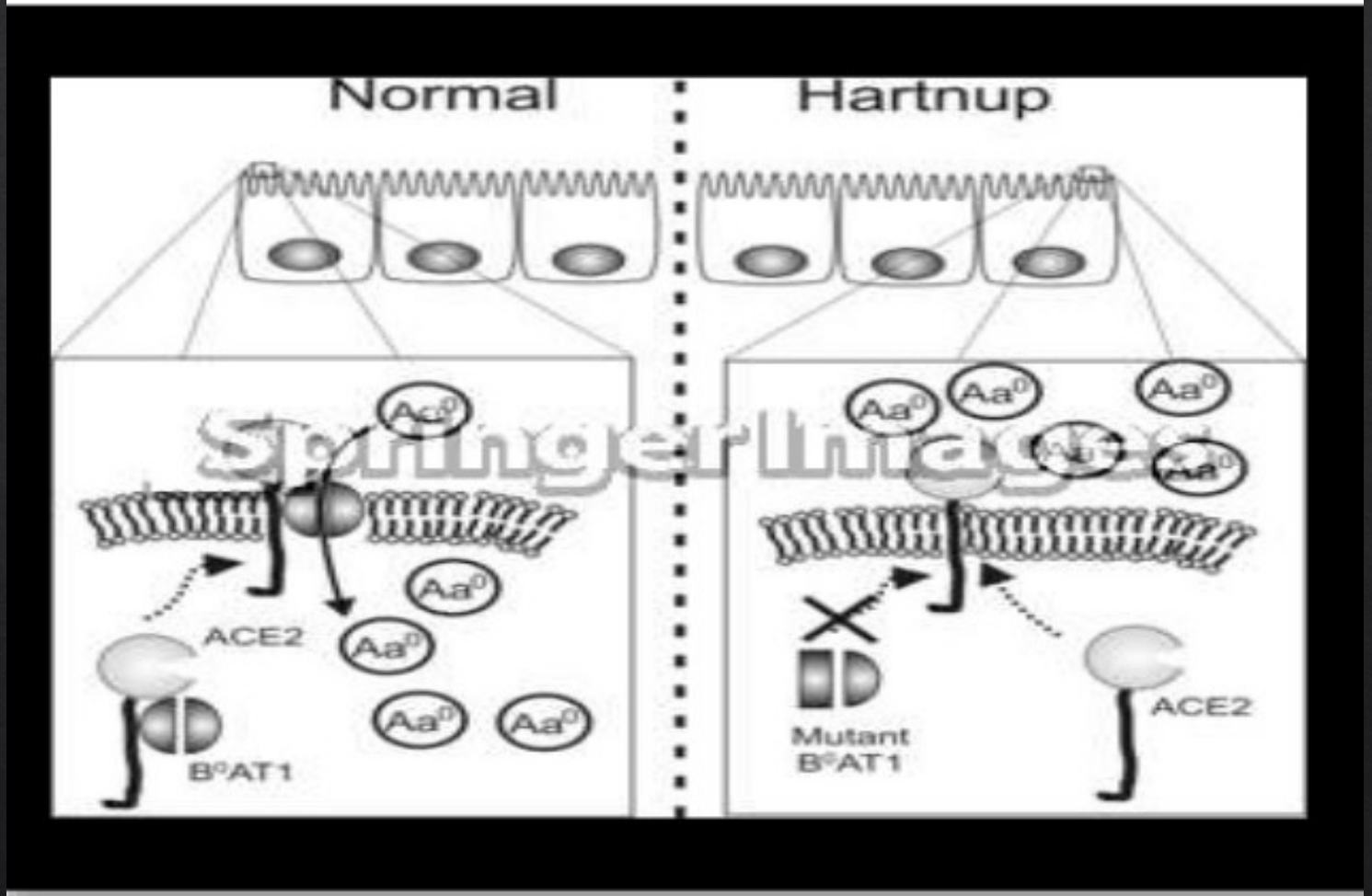
Hartnup's disease

Cause

disease is caused by a mutation(six mutations in SLC6A19) of the gene that controls the processes of amino acid absorption and reabsorption

Symptoms

- sensitivity to light
- anxiety
- rapid mood swings
- hallucinations
- delusions
- intention tremor
- speech difficulties
- abnormalities in muscle tone: either muscles can become more tight


Normal
Hartnup
ACE2
B°AT1
Mutant
B°AT1
ACE2

Treatment

- consists of a change in diet, avoidance of sunlight, and prescribing sulfonamide drugs
- Consuming foods that contain the B-complex vitamin niacin can significantly reduce your symptoms.
- Good sources of niacin include:
  - meat
  - poultry
  - fish
  - fortified and whole grains
  - peanut butter
  - potatoes

B-complex or niacin vitamin supplements (such as nicatonic acid)

DIAGNOSIS

- Blood Test
- Urine Test
- Prenatal Screening

Based On the Symptoms

Conclusion

Amino acid metabolism is very important for survival, any impairment will cause deadly disease most of them can't be treated