

Cryptopyrroluria –

The most common form of porphyria A typical example of a mitochondrial dysfunction



Kyra Hoffmann

„About 30% of the schizophrenic patients have Pyrroluria, and 11% of normal persons have it as well“
(Dr. Carl. C. Pfeiffer)

Cryptopyrroluria (CPU) is an almost unknown metabolic disorder. It is yet widespread. The general prevalence is estimated of about 10% of the Western population. I can confirm these estimated figures due to my long practical experience in the diagnosis and treatment of CPU-related disorders for many years.

Why is this disease so little known?

Obviously, diseases which are not designated or recognized by the ICD 10 code seem not to exist. For this reason, CPU patients are mostly treated wrongly, often for years, and the causal cause is not treated. They must therefore often lead a life with a variety of chronic diseases. The more astonishing fact is, that case reports show that patients after many previous years of torture often can fully recover through various practices, within a few months. The cause for this disease is the most common form of porphyria - namely cryptopyrroluria.

Background

In the 50s and 60s of the last century there was a dedicated group of psychiatrists and neurologists that had a high interest for the biochemical processes of so-called "mental diseases". Their main attention they spend on the major psychosis, such as schizophrenia. Through laboratory tests it was noted that patients with schizophrenia often had a certain, unknown chemical substance in their urine that was detected. This substance showed by staining a mauve-like color. This phenomenon was then initially named as Malverie/Malvaria.

In 1969 the laboratory doctor D.G. Irvine succeeded finally to identify the exact chemical structure of this "mauve factor". He found out that this component was cryptopyrrol (2,4-dimethyl-3-ethylpyrrol). The psychiatrist Dr. Carl Pfeiffer, a colleague of D.G. Irvine, called disease later simply pyrroluria because the pyrroles were excreted in the urine. The eight known acute and cutaneous porphyrias (ICD 10 E.80 ff) are described in detail in the literature.

CPU is a heme synthesis disorder caused by specific enzyme defects or enzyme deficiencies. Mainly known are the acute porphyrias, with their impressive and complex symptoms. The CPU is also one of these porphyrias. It runs only much more subtle, insidious and chronic. Its manifestations and symptoms are therefore varying extremely and the intensity of the symptoms is strongly fluctuating. Patients with CPU also have a heme synthesis disorder. This can be a genetically inherited disease or it can be acquired during the course of life.

The specific effect of the heme synthesis disorder is a noticeable degradation of heme. Physiologically, heme is degraded via the biliverdin-bilirubin cycle by so-called heme oxygenases and the metabolites are excreted via the biliary system with the feces.

In patients with CPU the heme is renal transported, this results in a complex formation with activated vitamin B6 (pyridoxal-5-phosphate), zinc and manganese. Via this mechanism patients with KPU are losing insidiously and unnoticed essential micronutrients with the urine.

This alone is already sufficient to greatly affect many physiological processes (see table, effects of zinc, manganese and vitamin B6). This defect can be proven by a special urine test. There are different test methods, either they measure the variation in the concentrated morning urine or in the 24-hour urine collection. A traditional urine test is not appropriate for this.

Conclusion 1

KPU can lead to chronic micronutrient deficiency of vitamin B6, manganese and zinc.

However, the micronutrient deficiency is only a secondary phenomenon.

The focus of the CPU is primarily the heme synthesis disorder.

This causes a deterioration of physiological processes, where heme is also involved, as for example the detoxification of the liver, Phase 1, in the area of cytochrome P450 enzymes.

Conclusion 2

CPU can lead to a limitation of the detoxification ability of the liver.

Heme plays also a crucial role in the mitochondrial cytochrome respiratory chain.

Conclusion 3

CPU can lead to a limitation of mitochondrial function.

In my opinion the analysis of the mitochondrial function is unfortunately often neglected for the diagnosis and treatment of CPU-associated diseases.

The supplementation of missing micronutrients alone is not an appropriate treatment of CPU and its symptoms.

However, micronutrient supplementation is necessary and important - but alone not sufficient - therapeutic pillar to successfully treat CPU (see therapy).

Mitochondrial function and CPU

For the better understanding of the pathological problems of CPU, I would now like to elaborate on the heme synthesis and the disruption. The heme synthesis takes place in the intermembrane space of the mitochondria and partially in the cytosol. Mitochondriopathies or mitochondrial dysfunctions are nowadays common diseases. Disturbed mitochondria function can also disturb heme synthesis and as a consequence cause CPU.

In the little literature that exists on CPU, the familial occurring, presumably genetic CPU is described exclusively. Here are - for as yet scientifically not clarified reasons - primarily the female members of a family affected. Sometimes in the family history a long disease pedigree of CPU is described. Since the findings of the environmental practitioner and internist Dr. Bodo Kuklinski, the acquired form of the CPU is known. This is due to a non-genetic disorder of mitochondrial function in which the heme synthesis is impaired. As pathological mechanisms that cause this disorder, reactive nitrogen and oxygen species (nitrosative and oxidative stress), in particular nitric oxide (NO gas) and peroxynitrite are discussed. Peroxynitrite blocked both the citric acid cycle in the mitochondrial matrix and the mitochondrial respiratory chain. Nitrosative and Oxidative Stress can be triggered by many causes including:

- Lack of antioxidant protection systems (for example, SOD deficiency)
- lack of micronutrients that act as antioxidants, for example, selenium, vitamin C
- Lack of vitamin B12 as the most important scavenger in nitrosative stress
- Toxic metal pollution (in this case I recognize more and more cases with heavy loads of aluminum and arsenic)
- Chronic, aseptic inflammation processes (eg chronic intestinal inflammation)
- cervical spine trauma with chronic irritation of vegetative nerve fibers

- various physical stressors (radioactive rays, electromagnetic fields)
- Various chemical stressors (herbicides, solvents)

However, psychosocial stressors (problems in partnership, conflicts at work) also can play a role. According to present knowledge thus can be said that patients with both the innate and the acquired form of the KPU may also have a mitochondrial dysfunction. This can be proven by laboratory tests.

The involvement of mitochondria in this special form of porphyria is a very important point in the diagnosis and therapy. A pure substitution therapy by administration of essential nutrients, such as pyridoxine (vitamin B6), zinc and manganese is a necessary, but alone not a sufficient treatment for the recovery of people suffering from CPU. The recovery and regeneration of the mitochondria in structure and function also have to be also treated simultaneously. The mixture of vital deficiency, disorder detoxification and mitochondrial impairment explains the various forms of this disease, which may be accompanied by CPU.

The most common diseases can be:

- osteoarthritis
- osteoporosis
- depression
- anxiety disorders
- CFS / chronic fatigue
- allergies
- fibromyalgia
- ADHD / ADD
- irritable bowel / irritable bowel syndrome
- thyroid disorders
- drug intolerance
- MCS (Multiple Chemical Sensitivity)

A typical symptom is a severe tiredness and exhaustion that can lead in the CNS to a noticeable concentration and memory disorder. Patients with KPU also often lack a regular dream recall.

Patients with these symptoms are often treated symptomatically or in the worst case - and that very often wrongly - are treated as mentally ill.

Figure 1 CPU - cycle according to Hoffmann / Kauffmann

The CPU is a metabolic disorder that can lead to vital substance deficiency diseases and detoxification disorders. Therefore, the sole administration of micronutrients is a necessary but not sufficient therapy for restoring health.

Patients that suffer from symptoms that are indicative for CPU, a CPU test should be performed in every case. Depending on kind of symptoms further laboratory tests are recommended.

These parameters can maybe give the explanation, which control loops and regulatory processes are out of balance due to the KPU. It should be remembered that this process of micronutrient deficiency and detoxification problems can already exist for months or even years.

Below I have shortly compiled the most important laboratory parameters:

- Micronutrient status: especially manganese, (B6), zinc, chromium, vitamin D3, vitamin B12 (methylmalonic acid, MMA), copper. The micronutrient status is needed to determine the individual dose of vital nutrients parenterally and orally.
- Neurostress profile of catecholamines and cortisol, DHEA, serotonin, GABA. In many KPU patients the catecholamine and the serotonin synthesis is disturbed. This must be treated in parallel.

- Thyroid profile: TSH , fT3 , fT4 , TPO, TAK , TRAK , selenium, zinc, iodine (24 urine collection). Many CPU sufferers have problems with thyroid disease. Notably, with the Hashimoto's thyroiditis, so in addition to the common thyroid profile, the antibody checking.
- Toxic metals: mercury, cadmium, aluminum, arsenic, lead.
We can find high levels of toxic metals in young CPU patients higher than average values.
- Mitochondrial parameters: ATP measurement, M2PK, LDH isoenzymes
Mitochondrial dysfunction is biochemically detectable in almost all cases. These can be quantified by the above-mentioned parameters. They are especially good for controlling the success of the course of the therapy.
- Food intolerances: fructose intolerance, Histadelia, IgG food reactions (often to gluten, cow's milk protein and eggs). CPU patients often have multiple food intolerances on. A targeted change of diet often results in relief of the organism and thus to a rapid symptom improvement.
- Stool diagnostics: Zonulin (leaky gut syndrome), Histamine in the feces, gut flora status. In many CPU patients gastrointestinal tract is chronically inflamed. Almost always increased histamine levels are found in the stool, often accompanied by a leaky gut syndrome. Increased histamine values alone can lead to a deterioration of CPU-related symptoms leading to a vicious circle that must be stopped by the therapy.
- Hormonal status in men and women in saliva - In many KPU patients hormone synthesis is disturbed. In women, we find often estrogen dominance, in men often a testosterone deficiency.

Vitamin B6 (pyridoxine)

Vitamin B6 is a vitamin of the B complex. The need for vitamin B6 is dependent on age, gender and protein intake and is indicated by an average of 1.6 mg per day. The more protein is taken, the more vitamin B6 is needed. Vitamin B6 is activated in the liver. Vitamin B6 is involved as a coenzyme in many biochemical processes:

- heme synthesis
- immuno competence
- neurotransmitter biosynthesis (serotonin, norepinephrine , dopamine, GABA)
- methyl group metabolism: homocysteine conversion to glutathione
- conversion of L -tryptophan to serotonin
- Synthesis of dopamine from L-Dopa
- cross-linking of collagen and elastin
- synthesis of niacin and picolinic acid from L- tryptophan
- synthesis of taurine and creatine
- synthesis of myelin lipids
- synthesis of phospholipids

Good vitamin B6 sources are whole grains, dairy products, potatoes, bananas, lentils, yeast and spinach.

Possible symptoms of vitamin B6 deficiency can be:

- Blood : anemia
- Blood Vessels: Because the total and LDL cholesterol in the blood increases and the healthy, protective form of cholesterol (HDL) is reduced, the risk of atherosclerosis may increase
- Skin : red, scaly , oily, painful and itchy spots on the skin (especially around the nose , mouth, ears , and genitals)
- immune system: impaired response of white blood cells to inflammation, decreased production of antibodies
- Mouth and throat: painful cracks and gaps at the corners of the mouth and lips. Smooth, purple, sore tongue, swollen, inflamed throat
- Kidney: can provoke the formation of gall stones composed of calcium oxalate
- Peripheral Nervous System: burning and tingling in the hands and feet, neuritis, impairment of the walk
- Central Nervous System: depression, irritability, anxiety, confusion, headache, insomnia

Zinc

Zinc is one of the essential trace elements in the body. Zinc is part of several hundred enzymes, it takes key roles and is involved in sugar, fat and protein metabolism with the construction of DNA. Both the immune system and many hormones require an adequate amount of zinc for its normal function. Latest research shows that zinc plays also an important role in brain metabolism. The daily demand is around 15 mg. Zinc deficiencies (if zinc is measured in whole blood), we find in our practices - even without kryptopyrroluria - often in vegetarians and vegans and those with chronic bowel disease. Zinc regulates as a cofactor various functions (regulatory, structural, catalytic) and over 200 enzymatic processes.

Other functions are:

- development, growth, regeneration processes (for example, wound healing, collagen synthesis)
- Antioxidant function (eg, stabilization of SH groups, antagonizing of iron and copper)
- health of skin, hair and nails
- Vitamin A metabolism
- There are a number of zinc- dependent enzymes, such as alkaline phosphatase, carbonic anhydrase, DNA / RNA polymerase, etc.)
- Cell proliferation / differentiation (eg, mucous membranes)
- Immuno competence (cellular)

- sensory functions (hearing, seeing, smelling, tasting)
- neurotransmitters (eg, dopamine, prostaglandin, hormone metabolism, insulin accumulation in the pancreas)
- thymic atrophy (decrease in T- lymphocytes)
- Hair loss
- disturbances in nail growth (white spots in fingernail)

Good sources of zinc are red meat, seafood, berries, sunflower seeds, corn, wheat bran, liver (pork, calf) and oysters.

Manganese

Manganese is like zinc an essential trace element and involved in over 100 enzymatic processes, and it is also involved in vitamin B1 metabolism.

Manganese is involved in the following processes in the body, among other things:

- Blood clotting (production of prothrombin)
- Antioxidant cell protection
- gluconeogenesis (glucose formation from organic non-carbohydrate precursors such as pyruvate)
- amino acid degradation (pancreatic enzymes: amino, carboxypeptidase)
- urea cycle (arginase: detoxification of ammonia)
- insulin synthesis and secretion
- Design of cartilage and bone tissue

Good sources of manganese include oatmeal, whole wheat, hazelnuts, wheat germ, walnuts, almonds, white beans, whole grains and cocoa.

Possible symptoms of manganese deficiency can be:

- Blood : decrease of HDL cholesterol , increased calcium - phosphorus and blood glucose values
- blood clotting disorder
- Endocrine system: reduced production of sex hormones, reduced fertility, growth disorders
- skin, bone, cartilage: disorders of the tissue structure, loss of hair pigmentation, osteopenia/osteoporosis/osteoarthritis
- Immune system: immune deficiency , decreased antibody formation
- Central nervous system : epilepsy , schizophrenia , disorders of neurotransmitter function (impaired nerve impulse transmissions to the muscle cells)

In any case it is useful to check the case history for any cervical spine trauma in the past. If there is evidence in this respect a check of the cervical spine by an experienced osteopath / physiotherapist makes sense.

Therapy of kryptopyrroluria

„For every drug that benefits a patient, there is a natural substance that can achieve the same effect“
Dr. Dr. Carl C. Pfeiffer

In my practice I use successfully the following steps as an approach to treat KPU patients.

It is a concept that considers the compensation of the micronutrient deficit, the treatment of detoxification disorder and of the mitochondrial dysfunction.

I. Compensation of micronutrient deficiencies

Step 1: change in diet

For mild forms of KPU, accompanied usually with slight symptoms indicated by correspondingly low kryptopyrrol values ("gray zone") a targeted change in diet can often be sufficient. We speak of a gray area, if the kryptopyrrol values lie on the border. Since the KPU is very stress-dependent, the value can differ depending on the stress level. Basically, we advise - and not just to our KPU patients - a varied, biological, histamine-poor and anti-inflammatory diet. This with respect to potential individual food intolerances. The diet for KPU patients should be rich in zinc, manganese and vitamin B6.

Step 2: Diet plus oral medication

In most cases, a change in diet alone is not sufficient. Here it may be necessary, in addition to optimized nutrition to use oral supplement products to give the body the missing micronutrients. The high-dosed "Krypto Oral " (Victoria Pharmacy Saarbrücken) is based on the original treatment recommendation by Dr. Carl Pfeiffer and can be used for rapid filling of the micronutrient depots at the beginning of the KPU therapy. Krypto Pro Balance of Tisso is suitable for long-term oral therapy because it takes into account not only the postulated micronutrient substitution, but contains also other substances that in addition support mitochondrial function.

Step 3: Diet plus oral medication plus infusion of a KPU-solution

In severe cases, including also some with significantly increased pyrrol excretion, the infusion of a KPU-solution is helpful. The infusion solution is used to fill up quickly the lacking micro-nutrients - independently of the status nature of the intestinal mucosa.

The infusion solution also supports the following processes the body:

- Antioxidant cell protection
- reduction of nitrosative stress
- heme synthesis
- glutathione synthesis
- detoxification of xenobiotics (drugs, pesticides, carcinogens, alcohols)
- neurotransmitter synthesis
- cell membrane stabilization
- anti-Inflammation
- mitochondrial energy metabolism
- homocysteine metabolism
- adrenaline synthesis
- carbohydrate metabolism

KPU-infusion solution for doctors and health practitioners	
Vitamin B6	200 mg
Magnesium chloride	200 mg
Taurine	1500 mg
Glycine	1000 mg
Niacin	100 mg
Riboflavin	50 mg
Vitamin B12 (Hydroxocobalamin)	1000 µg

Chromium (III) chloride	200 µg
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Additional the patient receives adrinking ampule with following composition:

Zinc	104,55 mg
Manganese	3,07 mg
Raspberry syrup	q. s.
Water	10 ml

Individual changes to the formulation (eg, enclosing of glutathione) are possible! References: Victoria Pharmacy Saarbrücken, www.internet-apotheke.de

II Comprehensive Mitochondrial relief and regeneration therapy

The Cell Symbiosis Therapy® by Dr. Heinrich Kremer (CST) is currently the only laboratory-documented, rational approach to the regeneration of mitochondrial functional and structural damage. In addition to mitochondrial laboratory diagnostics CST primarily includes the rational natural products therapy for the treatment of mitochondrial imbalances.

Particularly orally administered polyphenolic compounds are used, that can help to bridge the disorders of the mitochondrial respiratory chain.

Other key elements of the Cell Symbiosis Therapy® by Dr. Heinrich Kremer are:

- regeneration of the mucosa -associated immune system and the restoration of the intestinal mucosa as well as the physiological intestinal flora
- Individual allergen, organic diet therapy
- Infusion concepts
- detoxification therapies, especially excretion of cytotoxic metals
- Psychotherapeutic

So far, the latest knowledge is only benefitting a fraction of the affected KPU patients. This is a real tragedy said Carl C. Pfeiffer already more than 40 years ago. I strongly support his statement.

The Academy Cell Symbiosis Therapy offers special webinars / seminars for the diagnosis and treatment of mitochondrial illness and diseases, including the kryptopyrroluria.

More info at www.akademie-cst.de

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