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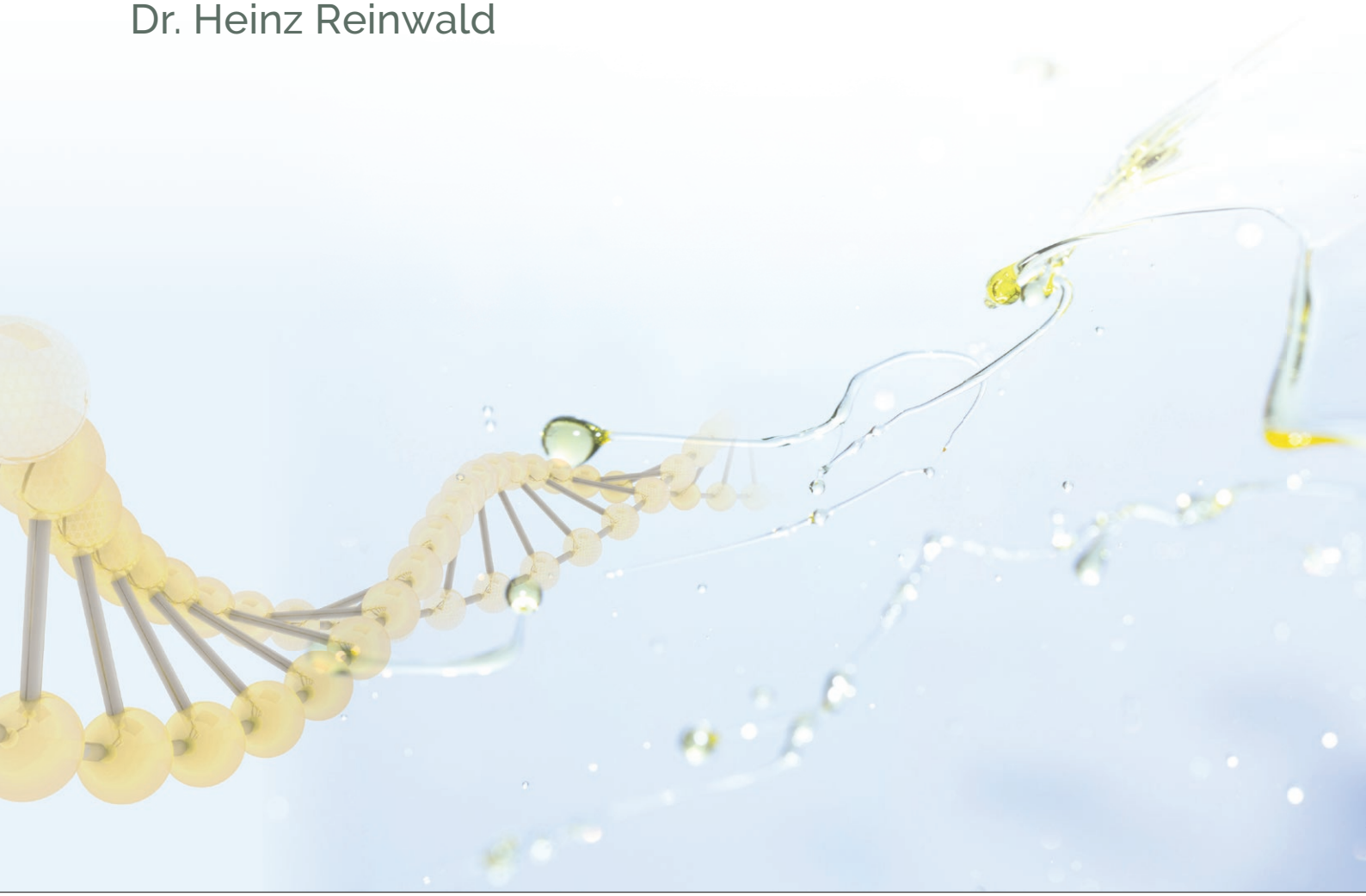
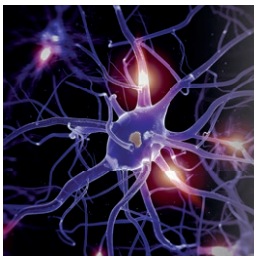
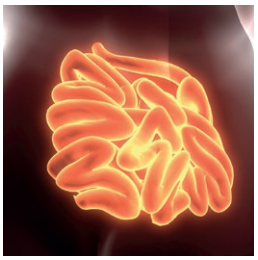
The Ketogenic Diet

Dr. Heinz Reinwald







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Index

The Ketogenic Diet (KD)

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Since the late 1990th the ketogenic diet (KD) as a therapeutic approach in the treatment of epilepsy experiences a renaissance. To better understand this developement of coming back to what some authors call our "Primal Blueprint" in nutrition, some basics are needed – so let's take a closer look. In mainstream medicine the KD is considered to be a non-pharmacological therapy to treat epilepsy. It can be also considered the treatment of choice for two other distinct disorders of the brain metabolism, i.e. the GLUT-1 deficiency syndrome and pyruvate dehydrogenase deficiency (PDHD). The KD has been developed to mimic a state of starvation or fasting, forcing the body to metabolize mainly fat instead of glucose – without the risk of depletion known from prolonged fasting. In the 1920s and 30s, the KD was very popular for the treatment of epileptic seizures but later largely abandoned in favor of the new anti-epileptic drugs developed by the emerging large-scale pharmaceutical industry. That, however, is only half of the story – and this is where most of today's misguided opinions and disorientation stems from. Fact is: It's the confused glucose metabolism caused by sugar and the effects it has on our highly excitable brain that is one of the main culprits for epilepsy – yet nobody dares to say it, thanks to the power of our food industry. As early as in the 1970s, Prof. Yudkin, founding Professor of the Department of Nutrition at Queen Elizabeth College in London, wrote in his seminal book about the toxicity of sugar with the title: *"Sugar: Pure, White, Deadly"*:

"If only a small fraction of what is already known about the effects of sugar were to be revealed in relation to any other material used as a food additive, that material would promptly be banned."

But it's better to start with a historical review of the disease. Ancient Greek and Roman physicians didn't know the scientific name or mechanism of action of the disease – but due to their brilliant observations they knew very well what todo. Therefore, before we go into more detail about the biochemistry of the KD and its implications on weight loss and chronic diseases, it makes sense to start with a historical review of the nutritional impact on epilepsy.

The History of the Ketogenic Diet

Epilepsy is, next to Diabetes mellitus for the fat and muscle tissue, one of the **first grain or sugar related brain diseases** described in history: it was the disease with 1,000 names, known amongst others as Falling Sickness or Speechless Spirit. It was considered "out of this world" – a belief perfectly expressed by the Italian Renaissance painter Raphael who, in the early 16th century, gave an eternal touch to his famous *"Transfiguration of Christ"* by depicting a boy with an epileptic seizure amongst the bystanders witnessing Jesus' ascent to heaven. The boy with the Sacred Disease clearly had a fit caused by deep religious feelings – would most likely have been the explanation given by the master painter. Many centuries before, in the Holy Bible (Mark, 9:18-29), an exact description of the major symptoms of epilepsy – and its treatment – was provided:

»And one of the multitude answered and said, Master, I have brought unto thee my son, which hath a ***dumb spirit****;«*

18: »And wheresoever he taketh him, ***he teareth him: and he foameth, and gnasheth with his teeth, and pineth away:*** *and I spoke to thy disciples that they should cast him out; and they could not.«*

19: »He answereth him, … bring him unto me.«

20: »And they brought him unto him: and when he saw him, straightway the ***spirit tare him; and he fell on the ground, and wallowed foaming****.«*

21: »And he asked his father, How long is it ago since this came unto him? And he said, ***of a child****.«*

29: »And he said unto them, ***This kind can come forth by nothing, but by prayer and fasting.****«*

But not only the Bible, which has its roots in the 6,000 year old Sumerian clay tablets, mentions the treatment of epilepsy with diet control. The Ancient Greek physicians also treated many diseases, including epi-

lepsy, by controlling their patients' nutrition intake. An early medical text in the Hippocratic Corpus, *"On the Sacred Disease"*, mentions and describes it very well. In fact: maybe Hippocrates (460–370 BC) was the first to recognize the rationale and physiological base of the disease, while the prevailing view gave it a rather supernatural origin. *"The brain is the cause of this affection … the patient loses his speech, and chokes, and foam issues by the mouth, the teeth are fixed, the hands are contracted, the eyes distorted, he becomes insensible, and in some case the bowels are evacuated. 'and these symptoms occur sometimes on the left side, sometimes on the right, and sometimes in both.*"

In the above-mentioned collection, the author then describes a man whose Sacred Disease is cured through complete abstinence from food and drink. One of Hippocrates' colleagues, Erasistratus (305–250 BC), one of the most important anatomists and physicians of his time, wrote about 100 years later: *"One inclining to epilepsy should be made to fast without mercy and be put on short rations."* Galen of Pergamon, also a Greek Physician (129–200 AD), and one of the most famous surgeons at his time, influencing medicine until the 18th century, wrote in his book *"De Sanitate Tuenda"*: *"I achieved to reduce a big fat guy in a very short time to a moderate corpulence, by letting him run every morning, until he had a strong perspiration; I rubbed him hard with a towel and sent him into a warm bath ... I allowed him plenty of required food but little extras, and finally, the rest of the day I let him do habitual work."*

Today we know that the switch to burn fat instead of sugar during exercise is flipped faster before breakfast, meaning: in a fasting state. Some modern doctors claim to have discovered this concept. But it was Galen who seems to have "known" about exercise on an empty stomach leading to immediate fat burning and ketosis as early as in the 2nd century. Fair enough, Galen may not have revealed the bio-molecular mechanism of action, just as Jesus didn't reveal exactly how fasting and praying could cure an epileptic boy. But their observations showed them what to do. By the way: Praying, as recommended by Jesus to treat epilepsy, has a meditative effect and calms down the oxidative stress and excitability in the epileptic brain. But that's not all: It is scientifically proven, that praying before a meal increases the flow of gastric acids, soothes the eater and puts the parasympathetic nerve in charge – all of which is crucial for digestion.

With the decline of the Roman Empire, the Mediterranean area forgot about the art of healing of the Ancient Greeks and Romans until the Islamic Golden Age brought the knowledge back to Europe via Moorish Spain. It was the Persian polymath Ibn Sina, better known under his Latin name Avicenna (980–1037 AD), and his Andalusian colleagues Al-Zahrawi, in Latin Abulcasis (936–1013 AD), as well as Ibn Rushd, in Latin Averroes (1126–1198 AD), who not only brought the philosophy of Aristotle back to Europe but also the ancient knowledge about medicine and the importance of diet. Thus, with their knowledgeable writings and the translation of the ancient canonical work in the famous school of Toledo (Spain), they formed the intellectual foundation for the Italian and later European Renaissance.

Abulcasis is considered the greatest medieval surgeon to have appeared from the Islamic World, and has been described as the father of surgery. His colleague Avicenna wrote more than 450 works, 40 of them on medicine. Two of his most famous works are the philosophical and scientific encyclopedia *"The Book of Healing"* and the medical encyclopedia *"The Canon of Medicine"*. The latter became a canonical medical text at many medieval universities and remained in use as late as 1650, thus influencing famous physicians in Europe like Paracelsus in the 16th century. By the way: Avicenna's *"The Canon Of Medicine"* was reprinted in New York as recently as 1973.

Lately, the Spanish researcher and physician Dr. R. Colomer discovered food-based treatments of cancer from as early as 1614 when studying the work of 17th century Italian writer Giacomo Castelvetro and his *"Sacred Law of Salads"* (i.e., "raw vegetables … plenty of generous [olive] oil") – as proposed in his book *"The Fruit, Herbs & Vegetables of Italy"*. According to Colomer, this may be considered the first (unintended) example of a customized high fat, low carb diet for breast cancer prevention, based on individual genetic makeup (i.e., nutraceuticals against human breast carcinomas bearing HER2 oncogene amplification/overexpression). The dietary pattern of salad vegetables (i.e., a large amount of raw vegetables and olive oil being low in carbohydrates and high in fat) appears to exert a protective effect mostly confined to the HER2-positive breast cancer subtype, with no significant influence on the occurrence of HER2-negative breast cancers. As reported by Colomer and others, the main olive oil constituents (i.e., the Omega-9 monounsaturated fatty acid and some polyphenolic compounds) dramatically reduce HER2 expression and apoptotic cell death in cultured HER2-positive breast cancer cells, with marginal effects on HER2-negative cells. And they specifically induce *"the reconstitution of the healthy human microbiome, which is equivalent to the reconstitution of the entire immune system ..."* apoptotic cell death in cultured HER2-positive breast cancer cells, with marginal effects on HER2-negative cells. Finally, a diet rich

in olive oil negatively influences experimental mammary tumorigenesis in rats, likewise decreasing HER2 expression levels, Colomer states. And, the author continues, *"… if in the early 1600s Castelvetro's salads (and fats, HR) could be used as dietary protocols capable to protecting women against biologically aggressive HER2-positive breast cancer subtypes, it is an intriguing prospect that warrants to be evaluated in human pilot studies in the future. Here, at least, we would like to recognize Giacomo Castelvetro as the father of modern nutritional genomics in oncology"*.[1]

But Castelvetro was not the only one recognizing the power of food and a low carb, high fat diet in the treatment of diseases. There were many more. In 1779, the Scottish military surgeon John Rollo became famous for his work on diabetic diets. In his book *"Two Cases of the Diabetes Mellitus: A General View of the Nature of the Disease and its Appropriate Treatment and Some Observations of the Nature of Sugar"*, he described a successful treatment of two diabetic patients on a diet low in carbohydrates and high in fat. While in 1825, the French lawyer and politician Jean Anthelme Brillat-Savarin, also known for being a gourmet and writer of several gastronomic essays, published his famous book on *"The Physiology of Taste"*, in which he described a solution to obesity. His recommendation was to limit the consumption of every kind of food containing starch or flour.

Probably the most famous book about diet ever written was published in 1863 by a man named William Banting from London. Banting was neither a dietician nor a doctor but a carpenter and undertaker, and he wrote possibly the first book on a ketogenic diet – without even knowing it. His *"Letter on Corpulence Addressed to the Public"* became one of the most famous works on obesity ever written and was published up until recently. Banting started to become obese in his thirties. He tried any slimming treatment the medical profession could devise – from heavy exercise to almost every form of weight loss diet such as calorie restriction and fasting – without success. By 1862, at the age of 65, Banting weighed 202 lbs at a body height of a mere 5 ft 5 inches. In his book he states: *"I could not stoop to tie my shoes, so to speak, nor to attend to the little offices humanity requires without considerable pain and difficulty which only the corpulent can understand, I have been compelled to go downstairs slowly backward to save the jar of increased weight on the knee and ankle joints and have been obliged to puff and blow over every slight exertion, particularly that of going upstairs."*

Meanwhile, his sight deteriorated, and he was becoming increasingly deaf – so in August 1862, Banting consulted a famous surgeon: the ear, nose and throat specialist Dr. William Harvey. Harvey had just returned from a symposium in Paris with one of the most noted scientists in medicine at his time, Professor Claude Bernard. Bernard was a renowned physiologist and father of the concept of the *milieu intérieur* – the underlying principle of what would later be called homeostasis, and what today could also be considered as the underlying concept of the *milieu intérieur* of the microbiota, which constitute the microbiome. His first important work was on the functions of the pancreas and its secretion, proving that it is of great significance in the process of digestion. An achievement that won him the prize for experimental physiology from the French Academy of Sciences. Perhaps his most famous finding, however, was on the glycogenic function of the liver, which, together with his work on the pancreatic juices, shed light on the causation of diabetes mellitus – although insulin still had to be discovered.

Harvey wisely connected Banting's multiple diseases to his obesity and put him on a diet – not a new one, as we now know, but one rather unknown to the majority of physicians at his time: a diet very low in carbohydrates and sugars, high in fat and optimized in protein. On this diet, Banting lost nearly 1 lb per week from August 1862 to August 1863. But the best part is that his joint problem, his failing sight and his deafness soon improved dramatically, as Dr. Harvey had supposed. In his own words Banting came to the conclusion, just like Galen 1600 years before: ***"I can confidently state that quantity of diet may safely be left to the natural appetite; and that it quality only which is essential to abate and cure corpulence."***

Modern-day doctors are still as far removed from the crucial insight that the effectiveness of a diet depends on the quality of food rather than on quantity and calorie counting, as most of the physicians were at Banting's time. Back then the public was impressed – and until today there is a British word for going on a diet: to "bant". Such was the success of the book, that Banting and Dr. Harvey were heavily attacked by the jealous medical community: While they had proved a functioning diet in reality they were accused of not having had a theory for it. The underlying theory yet had to be developed in the decades that followed – and was then suppressed for almost 100 years by the medical and pharmaceutical community and food industry in shoddy complicity with politics.

While obesity and diabetes were successfully treated with low carb, high fat and optimized protein diets prior to the discovery of insulin in the early 1920s, epilepsy was successfully treated with fasting. The me-

dical community started to make progress in seizure treatment with fasting, referring to more than 2,000 year old writings – but without linking it to the story of Jesus curing an epileptic boy. The Bible wasn't considered a medical textbook for illuminated doctors. It was in France in 1911, when two French Physicians – Guelpa and Marie – thought epilepsy was caused by an intoxication of the brain and started to "detox" with fasting and purging. They reported a 22 out of 26 children to be seizure free after a 10 day fast.[2] In 1920/21, two US-American pediatrics – Hugh Conklin and H. Rawle Geylin – reported the children in most instances seizure free after a water fast.[3] Although the efficacy in treating seizures with fasting led to a plethora of research activity, the metabolic mechanism of action still wasn't clear. Dehydration, ketosis and acidosis were possible explanations – in spite of the ketone bodies already having been known for half a century. Also, there was another crucial problem: the seizures returned sooner or later after reverting to a "normal" diet. And: **repeated fasting for children is impracticable** because it causes delayed growth and impaired bone health – and of course prolonged fasting is not healthy in adults either due to protein depletion and micronutrient deficiencies, which can lead to immune deficiency and other problems caused through malnutrition.

Ketones: The Metabolism's Ugly Duckling

In the mid-19th century, a new class of molecules entered somewhat clumsily the stage of our medical world, the ketones or ketone bodies: acetone, acetoacetate and beta-hydroxybutyrate. They were first discovered in the urine of Diabetic Type 1 patients – in combination with a disturbed glucose utilization and a life threatening state called ketoacidosis. Hence they were thought to be abnormal, undesirable byproducts of incomplete fat oxidation and thus considered *"Metabolism's Ugly Duckling",* as T. B. VanItallie called them in a seminal paper written in 2003: "… *only in the early 20th century, however, they were recognized as normal circulating metabolites produced by the liver and readily utilized by extrahepatic tissues".*

To be honest, our ignorant mainstream medicine never realized the scientific development that took place in this field in the past 100 years: They have simply been ignoring or even fighting it. So, to most, ketone bodies are still the ugly duckling, in spite of researchers having shown their health properties as early as in the 1920s. *"Doctors are afraid of ketosis. They always worry about ketoacidosis. But ketosis is a normal physiological stage. I would say the normal stage in humans. It´s not normal to have a McDonald or a delicatessen shop around the corner. It´s normal to have hunger"* writes Dr. Richard Veech, one of the late students of Nobel laureate Otto Warburg. Although Veech is wrong in believing that a person has to starve to get into ketosis (because he still thinks in the category of a starvation ketosis, instead of what we now call a nutritional ketosis induced by exercise or carbohydrate restriction), his general and correct complaints are still not heard in mainstream medicine. In Germany a physician even tried to sue a colleague because he recommended a cancer patient to follow a ketogenic diet. The patient did and showed up at the clinic with a ketone level of 3mM. His colleague was so scared he gave him a glucose infusion. There is nothing left to say if a doctor treats you inappropriately.

In 1921, while reviewing the research done on diet and diabetes, Rollin Woodywatt first reported a relationship between the production of ketone bodies and the low consumption of carbohydrates. He stated that "*acetone, acetic acid, and ß-hydroxybuturic acid appear … in a normal subject by starvation, or a diet containing too low a proportion of carbohydrates and too high a proportion of fat. It [ketoacidosis] appears to be the immediate result of the oxidation of certain fatty acids in the absence of a sufficient proportion of 'oxidizing' glucose …So why not shift the ratio of the diet in favor of fat, this way the diabetic would be able* ***to rest his pancreas,*** *remove the excess sugar from his bloodstream, and utilize fat instead as an energy source."*[4] This is the complete opposite to the official recommendation of eating five to seven meals rich in carbohydrates per day – as advocated by the American Department of Agriculture. A recommendation that turns us into cows: eating all day long and consuming the sugars the food industry produces. The funny thing about it: carbohydrates don't provide a filling meal. Insulin again and again forces the eater back into craving for even more sugar. It's the creation of the perfect, never satisfied and always corn-consuming human ruminant: no brain but (weight) gain. The result: generations of people with diabetes and pancreatitis. Meaning more business for the medical industry.

Dr. Russel Wilder, a physician at the Mayo Clinic treating a diabetic patient with a high fat diet, built upon Woodywatts research and was the first to coin the term "ketogenic diet" (KD) as used in the treatment of epileptic children. He wondered if *"the benefits of ... fasting ... could be obtained if ketonemia was produced by other means".* His aim was to **mimic the metabolic effects of fasting or starvation without starvation in an isocaloric diet which drastically reduces carbs and sugars. The KD replaces carbs with fat as primary fuel**, thus compensating for the obvious disadvantages of a prolonged fast. In one of his reports,

he described the dramatic improvement in seizure control of three patients with epilepsy, stating that without drawing final conclusions from the results of these few patients: *"… we have here a method of observing the effect of ketosis on the epileptic. If this is the mechanism responsible for the beneficial effect of fasting, it may be possible to substitute for that rather brutal procedure a dietary therapy (fasting, HR) which the patient can follow with little inconvenience and continue at home as long as seems necessary."*[5]

In a later seminal paper about *"The Threshold of Ketogenesis",* he described the required macronutrient ratio in which ketosis first appears, thus laying the cornerstone for the future concept of the ketogenic diet and for others to follow his calculations.[6] One of Wilder's colleagues, the pediatrician Mynie Peterman, suggested to customize the KD for children with a daily intake of one gram of protein per kilogram of body weight and 10–15 g of carbohydrates – while the remaining calories should be from fat. The classical ratio of 4:1 (fat:non-fat) was born. In severe cases of epilepsy, the ratio can be even lower (3:1 and 2:1) in order to avoid sugar uptake via protein and gluconeogenesis. This means even more protein depletion due to the fact that children in growth need more protein (≥1g/Kg body weight) . The KD of Wilder is identical to the KD used today in seizure treatment, although the nutritional approach in epileptic treatment was replaced by drug therapy in the 1930s for more than 70 years.[7]

It was in 1997, when Meryl Streep appeared in a stirring movie named "First Do No Harm". The movie tells the true story about an epileptic boy whose severe epilepsy – he didn't respond to medication, with terrible side effects – could be controlled by the KD within a short time. Since then, the nutritional concept of treating seizures has had a renaissance and scientific research has exploded in the field. One meta-analysis of studies done in 2003, ranging from 1925 to 1998, showed that 37% of patients on a KD have at least a 90% reduction in seizures, while 30% experience a 50-90% reduction.[8]

But in spite of the success, this is where the very problem starts. Although Wilder was far ahead of his time considering the research of ketones, and it was not until the late 1940s that science started to reveal a little more of the secrets of ketone bodies, he still was a child within the "Zeitgeist". Therefore, the KD in epilepsy is still **considered a "therapy"** and about some wrong basic assumptions it **has not been updated** or improved much since Wilder. Instead of finding solutions to crucial problems like delayed growth and impaired bone health due to protein reduction, little progress has been made. Even the emerging positive results in seizure treatment with MCT-oil, Ketone Ester or the Modified Atkins (MAD, calorie restricted) and the Low Glycemic Index Diet (LGID) **extrapolate the old errors** Wilder made as a scientist, following the calorimetric errors made by Atwater with protein. While using the calorie tables of Atwater (as authorities do until today to evaluate protein calories) – stating that calories are calories, no matter what their quality, and counting 4kcal per gram for carbs and proteins and 9 kcal per gram for fat – Wilder not only laid the cornerstone for the KD. He was also responsible for a false calculation of the macronutrients' energy percentage and – as a consequence – for an erroneous conception of the KD as a therapy.

In order to make progress, good science has to challenge basic assumptions if there are inconsistencies in the results – regardless of the admiration we have for the brilliant work of our precursors.

First: **the KD is NOT a therapy.** It's our primal blueprint and therefore natural human diet. It formed our nutritional foundation during the longest period in human history – namely the ice ages – until we made the *"worst mistake in the history of the human race"*: the invention of agriculture and the introduction of grain as staple food. (Diamond in *Discover Magazine*, May 1987). And: **therefore the KD is not an unpalatable, unhealthy high fat diet** to administer to sick people like the one with epilepsy only. If it is used as a therapeutic intervention with hyperketonemia from levels 3mmol/L and higher, as suggested by Prof. Seyfried to accompany cancer treatment, we may talk about a therapeutic approach. But not if we aim for nutritional ketosis, meaning the body's natural metabolic reaction to a low carbohydrate diet which forces it to metabolize fat, thus using fatty acids and ketones instead of sugar as the main source for fuel. In other words: our Primal Blueprint, like Mark Sission names it.

Second: The assumptions about protein and their caloric output are false. While the calories from carbs and fats are constant with 4 and 9kcal, the calories of proteins are not. Their energy outcome depends on the source of the protein, as I have shown in a paper about amino acids and MyAMINO. The Net Amino Acid Value (NAV) or the protein nutritional value (percentage of the amino acids following the anabolic pathway compared to amino acids following the catabolic pathway) determines the amount of nitrogen waste and energy (glucogenic or ketogenic) and thus the percentage of calories coming from the different sources of protein. With this new knowledge we have to put in question whether Wilder's KD, high in fat and

rather low, sometimes very low in protein, really is a diet "without starvation" as he asserted. It's not fasting, of course. But let´s face the whole picture:: although the KD drastically reduces the amount of seizures thanks to ketosis and reduced blood sugar levels, the long term **side effects** (due to the wrong notion of proteins and – sometimes – a lack of micronutrients) remain and undeniably lead to the known problems:

- delayed growth
- impaired bone health
- immune deficiency

To give a simple example: in 100 g of the usual formula drinks for the KD, you will normally find a whey protein, which is a very poor source for human protein nutrition. It has a NAV of 16% and releases up to 84% nitrogen waste and energy. If a drink claims to provide 14,5 g of whey protein per 100 g, this means that only 2,33 g of the digested protein will contribute to protein synthesis. On the other hand, 12,18 g of the whey protein digested will be catabolized and releases energy and nitrogen waste. This amount of protein will never nourish a growing child, so delayed growth, acidosis and impaired bone health can be the long term consequences. Even if you double the amount of protein to 29 g of whey with 200 g of formula drink, only 4,46 g of the amino acids follow the anabolic pathway – while you double the release of nitrogen waste and glucose coming from protein catabolism. This triggers the depletion of bicarbonate when detoxifying ammonia in the urea cycle – which in turn can lead to an acidotic situation in the child. It's a vicious circle – stemming from the confusion about the source of protein and wrong calorie measurements dating back to the 1890s and Atwater.

Meanwhile, it is scientifically proven that in breast-fed infants, high protein intake from meat as complementary food increases growth but not adiposity compared to formula-fed infants. Meat, fish and poultry have roughly double the amount of NAV compared to whey (still only about one third compared to MyAMINO®) – meaning a relatively lower nitrogen waste and energy outcome compared to whey protein. Using dairy protein instead of meat – which has about the same NAV as whey – has, according to the authors, a significant impact on weight gain (adiposity) but not on growth.[9] This is exactly what I am talking about: the quality of the protein source matters. Babies get fat thanks to the relatively high amount of sugar in formula milk while the lack of sufficient protein leads to water retention. They look healthy and fat, but they are malnourished and have edemas.

Let me tell you a story out of our daily clinical praxis to give you a clearer picture of what I am talking about. In the 2014 conference on Epilepsy and Cancer in Liverpool, UK, I met a therapist who asked me about our treatment protocol. She was treating an epileptic child, being on a traditional KD as well as on some anti-epileptic drugs since two years and still having several seizures a day as well as an acidotic state. I sent her the details about my ketogenic diet as well as some bottles of our amino acid formula. A short while later I received this email:

"Thank you, By the way, although the only thing we have changed is the patient´s protein/amino acid source, she had a seizure free day yesterday. That hasn't happened in two years, since she became acidotic. She generally has 6-12 generalized clonic tonic seizures daily, many of them lasting 15 minutes.
I will keep you posted! ... Rachelle"

The Metabolic Pathways of Digesting Food

After our *tour de force* through the history of the ketogenic diet, it makes sense to provide a few more basics on nutrition and how we metabolize food. The aim is to better understand the confusion about the so called "balanced" diet – and to recognize the fraud committed by the government, the agricultural industries and the medical profession when starting to advocate a cereal-based food pyramid and a low fat, low protein, high carb diet in the 1980s. This typically Western "balanced" diet, which turns us into human ruminants eating five to seven meals per day, suggests 10–15% of the daily caloric intake from protein, 10–25% from fat and 60–80% from carbohydrates. Instead of being "healthy", however, this officially imposed "balanced" diet has triggered chronic diseases to become an epidemic problem.

A British research, done by Professor Pritchard of Bournemouth University in 2013, revealed that the sharp rise of dementia and neurological deaths in people under 74 can't be put down to the fact of a longer lifespan. He showed that between 1979-2010, the increase in deaths due to brain disease in the USA increased up to 66% in men and up to a monstrous 92% in women. This is an "epidemic" development paralleling the epidemic rise in obesity, diabetes and cancer and thus clearly suggests the influence of environmental and societal changes – meaning a change in our lifestyle.

As early as in the early 1970s, Prof. John Yudkin predicted this development in the seminal book I've already mentioned, blaming processed food and sugar for the majority of chronic diseases. The book contained a breathtaking message, but was written for laymen – and was largely ignored by Yudkin's

colleagues. Those who did hear about it, like science cheater Ancel Keys, board member of the American Heart Association (AHA) and sponsored by Procter & Gamble (holding the patent on margarine) with 7 Million US $ a year in 1948 (equivalent to 70 Million US $ today), fought him militantly. In 1976, for instance, the „Sugar Association" won the „Silver Anvil Award", i.e., the Oscar for public relations. Misguiding the public, convincing them that sugar is a harmless substance and preventing doctors from complaining about it must indeed be based on excellent public relations practices! In the late 1960s, the New York Times made Ancel Keys and the AHA famous by putting them on the front page of the magazine with their Heart Lipid Hypothesis. In 2002, Gary Taubes, author for the same New York Times, started to dismantle this fraud with the article: *„What if It's All Been a Big Fat Lie?*". It was followed by a final stroke in the same magazine in 2014 by his colleague Bryan Welch: *"EAT BUTTER. Scientists labeled fat the enemy. Why they were wrong"*. A worldwide avalanche was triggered: There was no holding back the deconstruction of the paradigm based on so many scientific frauds. Still, mainstream medicine denies the facts.

In her seminal book, *"Death by Food Pyramid. How Shoddy Science, Sketchy Politics and Shady Special Interests Have Ruined our Health",* Denise Minger, a brilliant young US-writer working at the Weston Price Institute reveals a story of corruption in governmental institutions and among the big players in the food industry. So does Nina Teichholz who focuses on the corruption among medical professionals in her book *"The Big Fat Surprise: Why Butter, Meat and Cheese Belong in a Healthy Diet"*. Not to forget Gary Taubes and his bestselling book *"Good Calories – Bad Calories."* And there are more: Prof. Robert Lustig's *"Fat Chance: Beating the Odds Against Sugar, Processed Food, Obesity, and Disease"* and the American neurologist Dr. Perlmutter's bestselling books *"Grain Brain: The Surprising Truth about Wheat, Carbs, and Sugar – Your Brain's Silent Killers" and "Brain Maker: The Power of Gut Microbes to Heal and Protect Your Brain–for Life".* Or Dr. William David's *"Wheat Belly: Lose the Wheat, Lose the Weight, and Find Your Path Back to Health",* just to mention a few. All of them are must reads for anyone who wants to understand the going-ons around diet concepts in the medical and slimming business.

Proteins, Fats and Carbs – the Three Big Ones

Let's come back to the basics. The food we eat provides the fuel used by our bodies for reproduction, survival and regeneration. Just as hybrid cars that can run on two different types of fuel – electricity and gasoline – our body is designed to use three main fuels and their derivatives: **carbohydrates, fats and proteins.** Carbohydrates or starch are broken down into glucose and come mostly from plants. Fats, in general terms, come in two types: **saturated fats,** like butter, which comes from an animal source, and the likes of coconut or palm oil, which contain a lot of medium-chain triglycerides (MCTs), but come from plants. The second type, **unsaturated fats**, like corn, linseed or olive oil, mostly come from plants. Finally, there is protein. The main protein source for human consumption should be meat, fish, poultry or eggs. They have, as we know from the previous chapter, a higher Net Amino Acid Value (NAV), i.e., a higher protein nutritional value, compared to other dietary proteins like whey or plant proteins like soy or corn.

Carbohydrates, fats, and proteins all undergo the same type of chemical reaction with oxygen. Thus, our body breaks down the food into small substrates (catabolism) in order to build up new cells and get energy from it (anabolism). To serve as fuel for the body, carbohydrates are broken down into glucose, fats are catabolized into fatty acids (like PUFA, MCT and MUFA), and proteins into amino acids. The main difference is that carbohydrates and fats only produce water and carbon dioxide as waste products, while amino acids produce toxic waste (nitrogen catabolites) and energy – the latter being either glucose or ketones. Here we have it again! The question is: Are ketones only produced by amino acid break down? Not at all! On the contrary, protein catabolism is only a minor pathway to produce ketones from ketogenic amino acids. Their main source is fat metabolism.

So in the most general terms, **we call any diet that induces our metabolism to burn fat rather than sugar as the main fuel a ketogenic diet**. With an increase in fat burning there is an overproduction of Acetyl-CoA, one of the main intermediary substrates coming from the catabolization of fatty acids (and glucose) through oxygen. Acetyl-CoA enters the citric cycle, thus providing ATP as the body's general energy currency. If the oxidation occurs with fatty acids, it's called ß-oxidation. If it occurs with glucose, it's called pyruvate dehydrogenase (PDH). So what exactly happens with the excessive Acetyl-CoA from fat metabolism? Mitochondrial HMG-CoA synthase condenses it with acetoacetyl-CoA to HMG-CoA, from which it is turned into the ketone body Acetoacetate – which in turn is the common precursor for the other two ketone bodies: Acetone and ß-Hydroxybuturate. Ketone bodies are therefore three water-soluble compounds that are produced as by-products when fatty acids are broken down for energy. Now, most of the textbooks tell you

that ketones are only produced during prolonged fasting and that ketogenesis only takes place in the liver – but that's not true! As we've seen, ketones are also produced by simply restricting carbohydrates or going for more exercise. Plus: a major part of ketone bodies is produced in other organs, too – most of them in our gut. In fact, our gut's microbiome is not only constitutive for what Prof. Ruggiero calls in his recent findings our **Third Brain**, microbes also produce the biggest amount of the most important fuel we need for a healthy, so called **First Brain:** ketone bodies. But this happens only if the right microbes are there! The **Second Brain** is the enteric nervous system in our gut. Its mesh-like neurons govern the gastrointestinal system separately to our autonomic nervous system. The enteric nervous system consists of some 500 million neurons, outnumbers the neurons in the brain, and it has 5 times as many neurons as the one hundred million neurons in the spinal cord.

As early as in 1999, Fausto G. Hegardt, a molecular biologist and medical doctor like Dr. Ruggiero, wrote the following about ketone body synthesis in rat and human tissue: *"Ketogenesis in the small intestine of suckling rats ends at weaning. Simultaneously, the expression of mitochondrial HMG-CoA synthase is arrested. In contrast with the small intestine, the* ***colon and caecum are able to synthesize ketone bodies, mostly from the butyrate produced by the colonic bacteria.*** *In parallel, the colon mucosa expresses mitochondrial HMG-CoA synthase, this* ***expression being dependent on the bacterial status of the tissue. This effect is revealed by the low expression of mitochondrial HMG-CoA synthase in germ-free animals,*** *shown not only by the mRNA levels but also by the immunoprecipitable HMG-CoA synthase protein. … The expression of human mitochondrial HMG-CoA synthase mRNA in several adult tissues has been measured. It shows high values in liver and colon, low levels in testis, kidney, heart and skeletal muscle, and very low levels in the pancreas.* ***The colon shows 5-10-fold greater expression than the liver ... The significance of the very high expression in adult human colon mucosa*** *might be related, as in the rat, to* ***the occurrence of fermentative processes in the large intestine****, some of whose end- products, such as butyric acid and propionic acid, could be taken up by the mucosal cells to produce ketone bodies."*[10]

With this findings and right in the middle of a discussion around the ketogenic diet and its healthy properties we're back on the subject of our microbiome – our body's "software" – and its importance for almost all metabolic pathways. No proper immune response, no proper detox or digestion, no lipid or cholesterol synthesis or aromatase production, an enzyme important for our hormone balance. Without a healthy microbiome i.e. a healthy and high diversified microbiota, there is little defense and metabolism left in the body. Recent microbiome research has revealed that without these trillions of tiny helpers in our gut, not enough energy can be provided. This once again lets us realize the importance of the findings Dr. Ruggiero and his wife Dr. Pacini revealed in the last 30 years since they began studying the microbiome, the immune-boosting macrophages, the vitamin D-receptor and glycosaminoglycans, which are not mere sugars but contain important information just like our DNA or coded proteins: As Dr. Ruggiero and his colleagues discovered, the colonization of the gut with the right bacteria, i.e., bacteria that produce byturate and ß-OHB for a healthy brain development, occurs in a very complicated process during and after birth. With the colostrum and the mother's breast milk (containing important proteins and glycosaminoglycans) a **fermentation process starts, interacting with the fungi, yeast, bacteria, parasites** and unknown microbes that the baby picks up as it passes through the birth canal – thus forming a Th1 switch (basic immune response) to build up a proper immune system. Especially a group of approximately 40 bacterial strains, like those in BRAVO yoghurt, play a crucial and critical role in this process to create the microbiome during and after birth. If this process fails or is disturbed like it is with pre-, peri- and prenatal stress, C-section, anti-biotic treatment, early weaning, vaccines containing mercury or other toxins as a stabilizer, there is a much bigger risk for the newborn to develop a disease as has been shown in numerous studies.

To summarize our knowledge about the ketogenic diet: It mimics aspects of starvation by forcing the body to burn fat rather than carbarbohydrates, thus producing excessive Acetyl-CoA, which is turned into ketone bodies to be delivered to the tissue that can use them. Also, just like the middle-chained-triglycerides (MCTs), they don't need carrier proteins like the short- and long-chained-fatty acids, which need chylomikrones. This means that ketones can easily pass the blood-brain barrier to be oxidized there and to serve as fuel (as it has lately been assumed with the MCTs). Still, the textbooks keep telling us fairy tales. Like this one by Nelson & Cox: *"Some mammalian tissues and cell types (i.e. erythrozytes, medulla,* ***brain*** *and sperms) use the* ***glycolytic pathway*** *of glucose as the* ***sole source*** *of metabolic energy."* Also, the "German Bible for Biochemistry" – Löffler-Petrides – tells us similar stories: *"… only during prolonged fasting, the energy metabolism of the brain is switching. In the fasting state, the ketone bodies … can be oxidized by the CNS and largely replace glucose as an energy source but not complete. … During lactation the infant brain uses*

ketone bodies much more efficiently than the brain of an adult. After the birth, the activities of ketone bodies utilizing enzymes … rise significantly and thus allow optimal utilization of the high fat content of breast milk."
Meanwhile, on the homepage of the American College of Neuropsychopharmacology a ridiculous post around a similar factoid from September 25, 2015, can be read: ***"Under particular conditions,*** *such as* ***starvation, diabetes,*** *or in* ***breast-fed neonates****, plasma levels of the ketone bodies acetoacetate and D-3-hydroxybutyrate increase markedly."*

That's what doctors and biochemist learn at university: *"under particular conditions"*. Is a 10 mile walk without breakfast – causing a rise of ketone bodies – a particular condition? Definitely not! It's what our fathers and mothers experienced on their daily walk to school before WW II. It's the metabolic state every hunter faces when chasing his game. A particular condition? Maybe it is – in a society with a predominantly sedentary lifestyle that creates couch potatoes and digitally demented, soda-pop-fed-up kids. But to declare the degenerated state as normal is definitely the culmination of degeneration.

To be honest: all these statements made in textbooks about ketones are partly or completely wrong due to our gluco-centered imprinting: *"children produce and utilize ß-OHB more efficiently than adults…"* Of course, if they are still breast-fed they are in the hands of mother nature, not in the hands of ignorant doctors or misguided mothers administering formula-milk. Newman et al. write: *"a capability crucial in the days immediately after birth when the brain depends on ketone bodies as an energy source, and serum levels can reach 2–3mM…"* Indeed, as Stephen Cunnane revealed in his book *"The Survival of the Fattest"*: human babies are the fattest babies of all mammals – fatter even than sea lion or harp seal babies. Our capability to use ketones to fuel the brain is crucial for the development of our large brains, energetically as well as for lipid synthesis. *„Without ketones as an energy source,"* writes Dr. Mary Newport in her book "Stop Alzheimer", *„it would be highly unlikely that the human species would still exist, at least not with its modern large brains and high intelligence."* A few sentences later, the same authors Newman et al. write the opposite of what they wrote before: "*Similar 1–2mM levels of ßOHB can be reached after 90 minutes of intense exercise. Consistent levels above 2mM are also reached with a ketogenic diet that is almost devoid of carbohydrates"* … and: *"At the other end of life, the elderly generate ketone bodies after a fast or ketogenic meal to the* ***same extent as younger adults."*** [11] More confusion isn´t possible!

Now what? Why not name the real problem behind all this confusion? It's the sugar addiction and the lack of ketoadaption of the tissues. The adult body is no longer being able to produce the enzymes required to break down ketone bodies like a baby can do – if its mother doesn't follow the doctor's misguided recommendation of early weaning and milk formula. Thanks to a permanent overfeeding with carbs and sugars, we are highly degenerated. Couch potatoes who haven't exercised for years get sore muscles once they start moving again. What happens in our metabolically crippled brains isn't any different. After decades of running on sugar only, it's hard for our brains to switch between the different types of fuels, although they're originally designed to do so. The ability to quickly switch from one fuel to another represents good health, especially brain health. This was shown brilliantly by Dr. Colin Champ, author of the book "Misguided Medicine" on the 3rd World Congress on Ketogenic Diet and Cancer in Fulda, Germany 2015. He measured his blood sugar and ketone levels over a longer period of time and showed to be ketoatapted: His body was able to easily switch between glucose or ketones.

If you're not ketoadapted, plenty of symptoms may arise during the adaptation process – first and foremost energy shortage, due to the organs' fight for fuel: dizziness, a dry mouth, vision disorders, tachycardia, nausea, headaches, sweating … and a strong craving for sugar. Although our brain is the dominant tissue ruling the fuel distribution in our body, there is an overall energy shortage also for the brain until ketone bodies can once again be used properly. The symptoms are temporary until the enzyme production is back to a normal (i.e., not degenerated) level and our sugar and grain addicted brain has been weaned. When it comes to fuel supply, nature doesn't make a difference between low carb diets, fasting or starvation: In nature, a smooth switch between fuel sources is crucial for survival. Hence ketoadaption simply means a fast, unobstructed switch between all the different fuels our body can use for energy – not only proteins and carbs but also ketone bodies. That is a normal metabolic state – not the sick state for glucose addiction we currently consider as normal.

Is it surprising that – after all the rather mediocre knowledge taught about ketone metabolism in our biochemistry textbooks – physicians also confuse the dangerous state of ketoacidosis with nutritional ketosis or a managed therapeutic ketosis? I don't think it is. Let's summarize the most important points to differentiate between these two different metabolic states – one derailed, the other one a normal physiological metabolic state:

Ketoacidosis	Nutritional Ketosis	Therapeutic Ketosis
Diabetes Type 1 Alcoholics	Everybody being on a KD or prolonged exercise without carb loading	Everybody being on a strong KD, prolonged fasting and/or prolonged endurance exercise
Hyper-ketonemia **Abnormal** ketone levels 10-25mM	**Normal** keton levels 0,5–3mM	Therapeutic ketone levels 3–8mM (still healthy)
Hyperglycemia Abnormal high glucose levels 250-300 dg/ml and higher	**Normal** glucose levels 3,5–3,8 mM	Glucose levels under normal glucose levels, if needed like i.g. in cancer (between 1-3 mM without neurological disorders)
Hypoinsulinemia c Very low or even no insulin production like in T1D	**Normal** insulin levels 5-7 IU	**Normal** insulin levels 5-7 IU

As you can see in the table, the crucial difference is not only the mere height of the ketone levels, but also the extremely high glucose level and the lack of regulating insulin (and therefore glucagon) in the blood of a T1D patient with ketoacidosis. The complete opposite is the case in a normal person: all three levels – glucose, ketones and insulin (and thus glucagon) – are in a normal range with nutritional ketosis. Only during therapeutic use of ketosis, and if we wish to lower the normoglycemic level, the body normally holds it , there is a lower blood glucose level than normal (without neurological disorders due to ketosis) – but not a higher ketone level than in fasting. We use i.e. a therapeutic ketosis with 3mM and more in order to starve a tumor (especially the solid, high proliferating ones) from its most important fuel: sugar.

Let's repeat the important points: Nutritional Ketosis occurs under certain but **normal** nutritional and performance conditions when glucose is scarce and the insulin level consequently drops i.e. the fat metabolism gathers momentum to such an extent that it converts excess Acetyl-CoA into ketone bodies, which are then converted back for supply in the citrate cycle and create energy and building blocks for the tissue to supply. One of the fatal mistakes of a society with brains trapped in a ‚sugar-prison' is to eat most of a nutrient that we essentially need the least. John Brosnan, an expert in liver metabolism states: *"Strictly speaking, there is no dietary requirement for carbohydrate. Gluconeogenesis is able to supply the body with adequate amounts of glucose."*[12]

Glucose can be produced by converting three non-carbohydrate precursors: lactate, glycerol from fat metabolism, and glucogenic amino acids. It is possible to achieve nutritional ketosis without starving, namely by significantly or very significantly reducing carbohydrates and simple sugars and/or increasing our physical output (post-exercise ketosis). As glucose is normally also generated from dietary protein (glucogenic amino acids), sometimes we need to also restrict protein intake, as we've seen in the treatment of epilepsy. **However, protein restriction is certainly a walk along the razor's edge: Without proteins and amino acids as the building blocks for body protein synthesis, there is neither tissue repair nor cell renewal.** This is why the dietary concept *dr. reinwald metabolic regulation*® includes the use of a special amino acid formula that was described before (and in a separate paper) and supplies virtually zero nitrogen waste and almost no glucose (1% compared to up to 84% from e.g. vegetable or whey protein or an average of 68% from meat protein). This enables an optimal protein supply, even in the case of diseases where sugar and nitrogen waste should be restricted. The classic ketogenic diet according to Wilder or even the Modified Atkins Diet would be a suicide mission for patients with e.g. pancreatic or liver cancer, where there is no pancreatic juice to digest proteins or liver power to detox nitrogen waste in an adequate amount. MyAMINO neither requires peptidase, nor does it overstrain the liver or kidneys with nitrogen waste coming from nutritional protein. It virtually enables "fasting without fasting". An optimized supply of amino acids together with appropriate fat intake for energy needs accompanying cancer treatment can help to limit the dangers of tumor cachexia.

A key step towards a smooth use of ketones in tissues, we know now, is to pass through the process known as ketoadaption. In literature, it is generally assumed that this can last for up to three weeks among adults. In the 1980s, Cahill & Aoki[13] demonstrated – with the aid of insulin injections in the case of ketosis – that even among adults a blood sugar level of up to 25 mg/dl (1,4 mM) can be tolerated without any neurological deficits. Some of the tested subjects even tolerated up

to 20 mg/dl (1,1 mM) – if the ketone level is correspondingly high (4.5–5.0 mM/l) and there is the capability for ketolysis. The transition between metabolic states must run smoothly – something that is no longer given due to our inadequate diet. As described, ketoadaption is necessary due to the loss of ketolysis capacity in the tissues – especially the brain – which is in turn caused by an overload of sugar. The inability to metabolize ketones smoothly is due to the lack of enzymes required for the latter: mitochondrial 3-hydroxy-3-methylglutaryl-Coenzyme-A transferases (HMG-CoA).

Fact is: breast-fed infants are in a state of ketosis. As a responsible therapist, at this point one must take a deep breath when considering to what extent fat metabolism is in the fatal grip of established medicine and the foodstuff industry. The former tackles the production of cholesterol by inhibiting cytosolic HMG-CoA reductase using statins, while the latter helps to damage the brain's and other tissues' ability to enter ketolysis (inhibition of mitochondrial HMG-CoA) due to an overload of carbohydrates and simple sugars in our recommended, so-called "balanced" diet.

Neuroprotective and other Properties of Ketones[14,15]

According to a plethora of peer reviewed studies, ketones have various neuroprotective features and also improve mitochondrial function

- Ketone metabolism requires 3 enzymatic steps, glucose metabolism 11steps
- Increased antioxidant capacity by up to 50 %, reduction of reactive oxygen species (ROS) by 55 %
- Increase of noradrenergenic, inhibiting GABAergic neurotransmission
- In the hippocampus of rats: 4-fold increase in Glutathione peroxidase
- Switch in energy metabolism from glucose to ketones generates a general switch in the brain's excitability
- Uncoupling of cytochrome oxidase and shift to ATP instead of to heat via the Uncoupling Protein (UCP) by 55 %
- Increases the activity of the Na+/K+-pumps both in neurons and in glial cells – in turn this increases membrane potential and reduces excitability
- Ketone metabolism inhibits phosphofructokinase thus reducing the metabolic rate of glycolysis (fewer radicals with better O2 yields)
- Ketone metabolism inhibits pyruvate entering the citrate cycle and reduces the glucose oxidation rate

According to numerous scientific peer reviewed papers found in pubmed, the KD is now used as an essential nutritional approach in addition to standard therapy in a number of diseases, using the benefits of ketones:

- Leukodystrophy: degenerative breakdown of the brain's white substance
- Cognitive disruptions: in type I diabetes and basal insulin < 1 mM/l
- Parkinson: defects in mitochondrial NADH multienzyme complex can be eased (OxPhos I + II)
- Pyruvate Dehydrogenase Deficency: especially those in OxPhos complex I+II[16]
- Donohue syndrome and less pronounced forms of insulin resistance: bypass of GLUT transport paths, increase in MCT1 transport paths
- Cancer
- Polycystic ovarian syndrome
- Metabolic syndrome
- Multiple sclerosis, amyotrophic lateral sclerosis, head trauma, stroke, cardiovascular disease, type II diabetes, Alzheimer and other neurological diseases, depression, acne, etc.

In May 26, 2016, Science daily, an online science magazine posted: *"Fasting-like diet reduces multiple sclerosis symptoms. Evidence is mounting that a diet mimicking the effects of fasting has health benefits beyond weight loss, with a new USC-led study indicating that it may reduce symptoms of multiple sclerosis".* MS is a neurological disease like epilepsy and in my opinion also a sugar related brain disease, although co-factors like heavy metals also play a crucial role. At long last, 2.500 years after Jesus showed us how to heal an epileptic boy, science is coming up to discover the Mediterranean Sea, where Jesus was already fishing thousands of years ago. So, why not just go for a ketogenic lifestyle?

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