

Ketogenic Diet and Immunotherapy in Cancer and Neurological Diseases. 4th International Congress on Integrative Medicine, 1, 2 April 2017, Fulda, Germany

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Abstract: In this Meeting Report, we review proceedings and comment on talks given at the 4th International Congress on Integrative Medicine held on April 1 and 2, 2017, in Fulda, Germany. The Theme this year was "Ketogenic Diet and Immunotherapy in Cancer and Neurological Diseases." Speakers came from Europe and the United States and the Congress was attended by more than 100 interested parties from all over the world.

Keywords: Ketogenic Diet, Immunotherapy, Integrative Medicine, Cancer, Autism, Lyme Disease

Introduction

The 4th International Congress on Integrative Medicine, was held on 1 and 2 April, 2017, in Fulda, Germany. The theme of this Congress was "Ketogenic Diet and Immunotherapy in Cancer and Neurological Diseases" (Ketogene Ernährung und Immuntherapie bei Krebs und Neurologischen Erkrankungen).

The Congress brought together researchers from all over the world to share their views and research on the role of nutritional ketosis and immunotherapy in a wide range of experimental and clinical conditions, from epilepsy and autism to cancer and Lyme disease.

The Congress was attended by over 100 Medical Doctors, Naturopathic Doctors (Heilpraktiker) and other interested parties and was an opportunity for stimulating interchange among researchers and attendees. The Congress was organized to allow each lecturer up to an hour to describe her/his findings. Most lectures were in English with simultaneous translation in German; a few lectures were in German with English translation.

In this report, we summarize and comment on the most relevant findings presented by each lecturer. Some lecturers gave permission to reproduce their slides and representative slides are shown in this paper as they were presented, without editing.

On Saturday, April 1st 2017, Dr. Reinwald, representing the organizers of this Congress, gave the introductory remarks and then introduced the first speaker, Dr. Angelika Poff, MD, from the Department of Molecular Pharmacology and Physiology of the University of South Florida, Tampa, USA. She presented

a talk entitled "Exploiting cancer metabolism with ketosis and hyperbaric oxygen". Dr. Poff lectured on the synergism between nutritional ketosis and hyperbaric oxygen in reducing tumor burden in experimental animals and offered insights on the mechanism of action of ketone bodies in a variety of conditions from seizures to cancer proliferation. The role of exogenous ketone bodies in counteracting cancer cell proliferation even in the absence of carbohydrate restriction was also discussed. Of particular relevance were the possible clinical applications in oncology.

The roles of ketone bodies in physiology and pathology was further elaborated by Prof. Dr. Ulrike Kämmerer, PhD, from the University Clinic of Würzburg, Germany. Her talk was entitled "Ketones: more effects than just energy". Of particular interest was the concept of ketone bodies as endogenous "drugs" produced by a ketogenic diet, "drugs" that preserve muscle mass, are endowed with anti-cachectic and anti-inflammatory properties and inhibit cancer cell proliferation (Fig. 1 and 2).

Prof. Dr. Adrienne Scheck, PhD, from the Neuro-Oncology Research of the Barrow Brain Tumor Research Center, Phoenix, AZ, USA presented a talk entitled "The Ketogenic diet as an adjuvant treatment for glioma". In her talk, Dr. Scheck reminded the audience how aggressive treatments that include surgery, chemo- and radiotherapy, are only partially effective in the management of malignant tumors of the brain and the prognosis for patients diagnosed with tumors such as glioblastoma remains very poor.

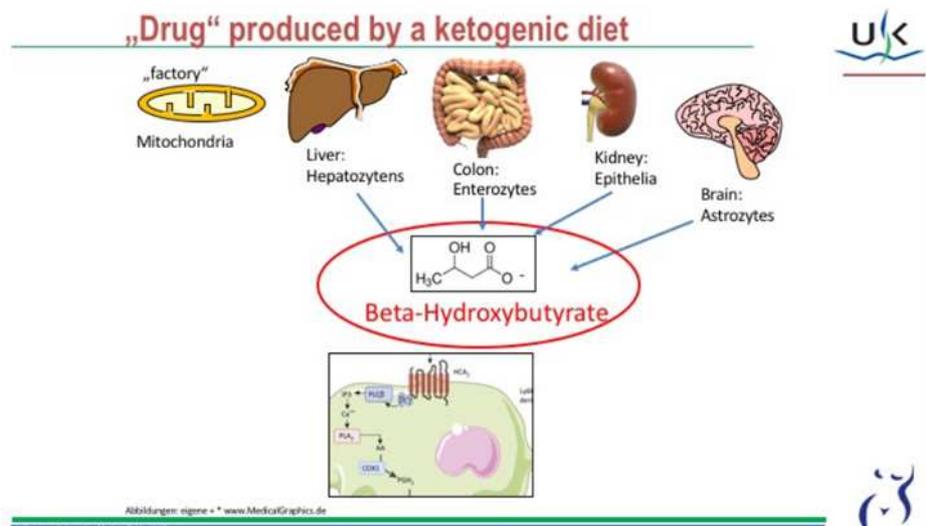


Fig. 1. Prof. Dr. Kämmerer; ketones as drugs produced by ketogenic diet

Conclusion

Ketones, especially 3-OHB have a wide variety of "modes of action" within cell signaling and metabolism.

Thus the ketosis as produced by starvation/fasting and/or a ketogenic diet supports the body with a physiological "drug" that has effects shown to:

- Downregulate inflammation via G coupled receptors (so far: GPR 109A and GRR 43)
- Inhibit (tumor) cell growth directly via acting as HDAC Inhibitor (and putative mTOR Inhibitor)
- Reduce muscle degradation via downregulation of Atrogin-1 and MuRF1
- Calm down excessive neuron activation by increasing GABA concentration

And ?????? (Research needed)

Fig. 2. Prof. Dr. Kämmerer; modes of action of ketones

She emphasized nutritional ketosis achieved through ketogenic diets may work in synergism with conventional therapies in improving the prognosis of patients with glioblastoma. Prof. Scheck offered an encouraging perspective in brain cancer treatment by mentioning that results emerged from clinical trials investigating the use of nutritional ketosis in patients with primary and recurrent brain tumors.

Prof. Dr. Thomas Seyfried, PhD, from the Biology Department of the Boston College, Chestnut Hill, MA, USA gave a talk entitled "The ketogenic diet as an adjuvant treatment for cancer" *via* videoconference from the USA. Prof. Seyfried opened his talk with a provocative question: "Is cancer a nuclear genetic disease

or is it a mitochondrial metabolic disease?" (Fig. 3) and proceeded to criticize what he defined as the current dogma that considers cancer a genetic disease originating in the nucleus of the cell. In his talk, Prof. Seyfried described the role of the nucleus and mitochondria in the origin of cancer and supported the hypothesis that the genesis of cancer is to be found in the cytoplasm and, more specifically, in the mitochondria, rather than in mutations occurring at the level of nuclear DNA (Fig. 4). He then proceeded to describe the role of nutritional ketosis in cancer management as a means to counteract the metabolic alterations associated with, or responsible for, cancer cell proliferation.

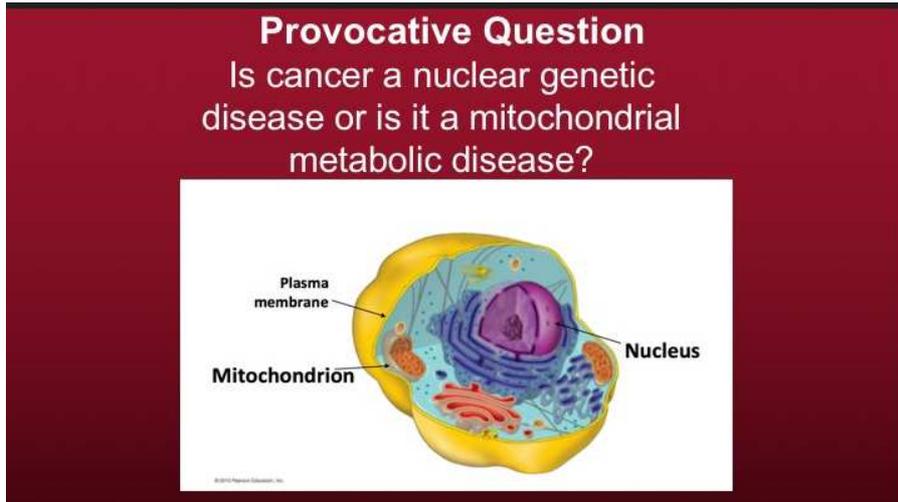


Fig. 3. Prof. Dr. Seyfried; is cancer a metabolic disease?

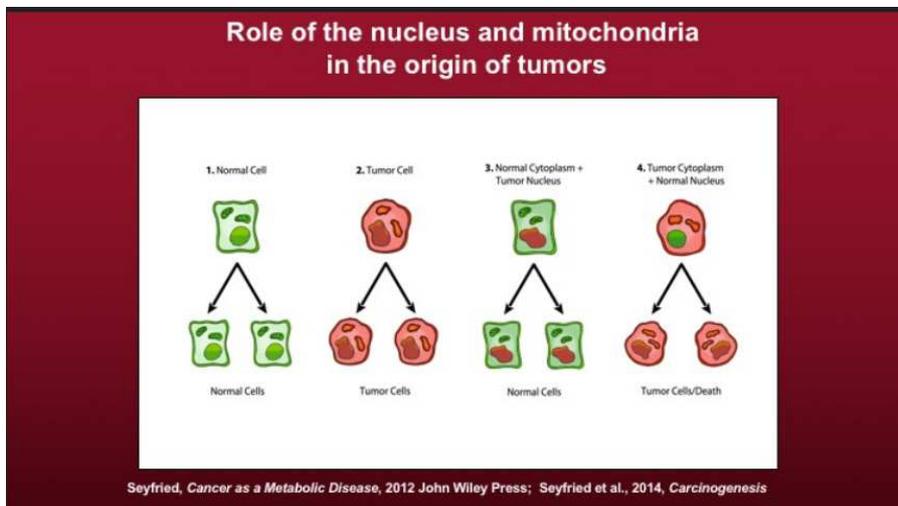


Fig. 4. Prof. Dr. Seyfried; the origin of cancer is in the cytoplasm

- ### The Cancer Code
1. Cancer is a mitochondrial metabolic disease where fermentation gradually replaces respiration for cellular energy.
 1. Glucose and glutamine are the major fermentable fuels for driving cancer growth.
 2. Ketone bodies can replace glucose in normal cells, but not in tumor cells.
 3. ROS production is greater in tumor cells than in normal cells.

Fig. 5. Prof. Dr. Seyfried; the cancer code I

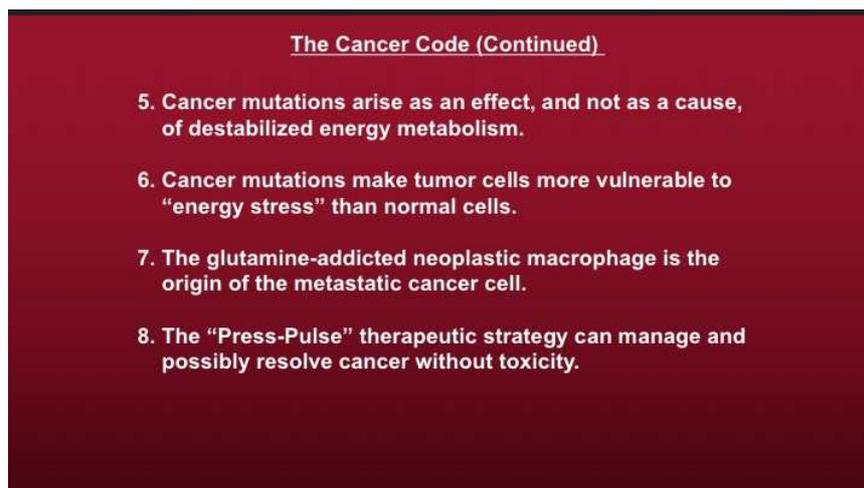


Fig. 6. Prof. Dr. Seyfried; the cancer code II

The conclusions of Prof. Seyfried's lecture - Cancer is a Mitochondrial Metabolic Disease - were as striking as the rest of his presentation as shown in Fig. 5 and 6.

A review on the role of nutritional ketosis in the treatment and management of cancer, authored by lecturers at this meeting and by others, was published in the June issue of Medical Oncology (Klement *et al.*, 2017).

Dr. Marco Ruggiero, MD, PhD, retired professor of molecular biology at the University of Firenze, Italy, gave a talk entitled "Novel concepts in the immunotherapy of chronic conditions". In his talk, he traced the history of immunotherapy from the times of Dr. William B. Coley and described his experience in the field of research related to macrophage activating factors. He elaborated on the role of glycosaminoglycans as immune modulators whose properties could be exploited in conditions as diverse as cancer, autism and Lyme disease (Ruggiero, 2017).

Dr. Judy Mikovits, PhD, spoke on the topic of "Human retroviruses, innate immunity and the development of immunotherapy". She reported her experience working in the field of human retroviruses that may be involved in chronic conditions where alterations of the immune system play a major role. Dr. Mikovits focused in particular on the role of retroviruses in the pathogenesis of neurologic conditions such as Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and autism. Dr. Mikovits also provided her views on the role of public health policy often deemed too technical and also shared personal experiences in this area. The experiences of Dr. Mikovits are described in further detail in a book entitled "Plague: One Scientist's Intrepid Search for the Truth about Human Retroviruses and Chronic Fatigue Syndrome (ME/CFS), Autism and Other Diseases" (Heckenlively and Mikovits, 2017)

The first day of the Congress concluded with a talk by Dr. Heinz Reinwald, PhD, Heilpraktiker, from the dr.

reinwald academy. The title of his talk "Ketogenic diet in cancer: mistakes you need to know" highlighted the practical approach to cancer management through nutritional intervention. Dr. Reinwald stressed the point that the so-called ketogenic diet is not to be interpreted as a "therapy," rather as the "normal" nutritional regime accompanying human evolution until the industrial revolution. He listed the most common mistakes that, in his experience, occur in the nutritional approach to cancer patients. He focused in particular on the role of proteins in the context of nutritional ketosis and reported his experience substituting dietary proteins with a proprietary amino acid formula that supports full protein anabolism in the context of ketogenic diets. He described a number of clinical cases that appeared to have benefitted from this integrative nutritional approach.

The second day of the Congress began with two presentations by researchers from the Department of Experimental Medicine of the University of Campania, Naples, Italy, Drs. Dario Siniscalco, PhD and Anna Lisa Brigida, PhD. Dr. Siniscalco's talk was entitled "Immune and inflammatory changes in autism: the potential application of a novel protocol". His talk described the role of neuro-inflammation in the pathogenesis of autism with particular reference to the role of glial cells. Dr. Siniscalco elaborated on the role of the endocannabinoid system in autism and how it relates to systemic and brain inflammation. He also described preliminary results obtained using a proprietary emulsion of chondroitin sulfate, vitamin D₃ and oleic acid that has proven effective in restoring signaling pathways altered in autism (Antonucci *et al.*, 2017).

Dr. Brigida further elaborated on the properties of this emulsion in her talk entitled "Effects of a specific vitamin-D₃ emulsion in *in vitro* models of cancer" describing the effects of such an emulsion on cancer cell proliferation, morphology and signaling related to apoptosis.

Autism Clinical Phenotypes

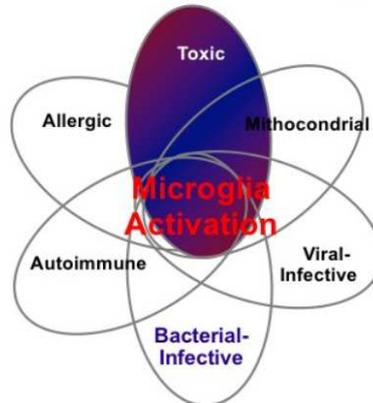


Fig. 7. Dr. Antonucci; microglia activation in autism

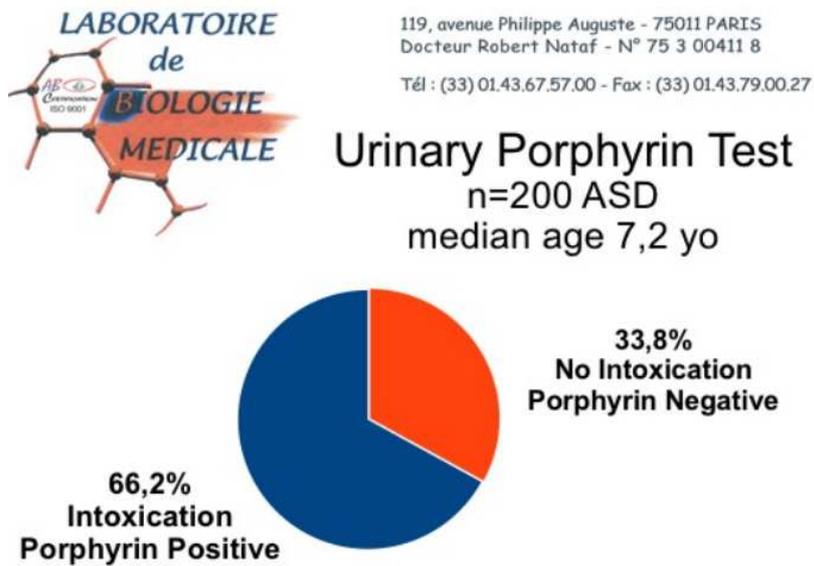


Fig. 8. Dr. Antonucci; results of porphyrinuria analysis in autism

Rerum pain study – set up and so far results

dr. reinwald partner (i.s.t.c.m.)

	Acute pain	Chronic pain
Number of patients treated	24	12
Number of injection per Patient (average)	1,3	3,8
Pain reduction in %	78%	55%
Duration of pain reduction (avarage) per injection	Different (some permanently, all at least 3 days)	4,4 days
Side effects (number of cases)	No	1 (fever)

Fig. 9. Dr. Peter; results of pain treatment

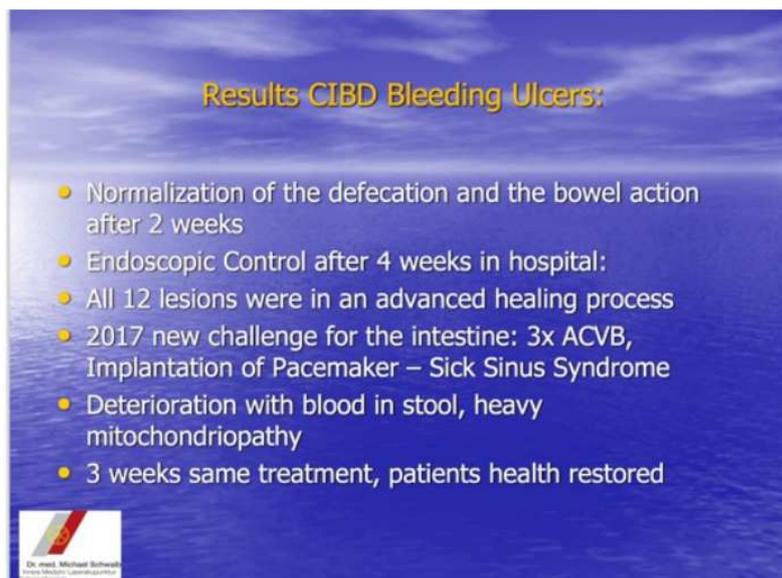


Fig. 10. Dr. Schwalb; results of chronic inflammatory bowel disease treatment

The results presented by Dr. Brigida suggest that this emulsion exerts a selective effect on cancer cells, inhibiting proliferation and inducing apoptosis of cancer cells, while at the same time, "protecting" normal, non-neoplastic, cells in culture. Dr. Brigida speculated that the effects observed *in vitro* may explain results previously reported in cancer patients to whom such an emulsion was administered as an integrative approach to cancer (see Schwalb *et al.*, 2016 and the presentation by Dr. Schwalb).

Dr. Nicola Antonucci, MD, founder of the Biomedical Centre for Autism Research and Treatment of Bari, Italy, gave a talk entitled "Integrated approaches to autism spectrum disorder treatment" where he presented preliminary results that were subsequently published in the American Journal of Immunology (Antonucci *et al.*, 2017). In his talk, Dr. Antonucci reported his clinical experience in autism treatment and how it relates to the concepts of neuro-inflammation and microglia involvement (Fig. 7). Of particular interest was his observation of porphyrinuria in a population of 200 autistic subjects (Fig. 8), a finding that confirms and supports the hypothesis of an involvement of environmental toxicants in the pathogenesis of autism.

Dr. Thomas Peter, MD, founder of the Therapy Center Anuvindati of Bensheim, Germany gave a talk entitled "Lack of adrenaline and mitochondrial disorder. Why capitulate?" where he explored the connections between chronic stress and adrenal hormones, with particular reference to adrenal fatigue and adrenaline deficiency and reported his experience treating acute and chronic pain (Fig. 9).

An original case report was presented by Dr. Daniel Beilin from California, USA. In his talk, he presented the case of a 23-year-old woman with Non-Hodgkin lymphoma, successfully treated with an integrative

immunotherapeutic approach (Schwalb *et al.*, 2017) following unsuccessful chemotherapy. Dr. Beilin also reported his experience with a proprietary system for diagnostic thermography and described how the results obtained by thermography compared with those of Positron Emission Tomography (PET)/Computed Tomography (CT).

The lecture by Dr. Dietrich Klinghardt, MD, PhD, founder of the Klinghardt Institute, the Klinghardt Academy, the Institut fuer Neurobiologie and the Sophia Health Institute of Seattle, WA, USA, presented a topic moment for the Congress. In his lecture entitled "Pain management with a novel integrated concept" Dr. Klinghardt reviewed his experience in a variety of fields ranging from neural therapy to Autonomic Response Test (ART) and persistent Lyme disease. He also presented the novel diagnostic protocol designated "Ruggiero-Klinghardt (RK) Protocol" for the diagnosis and treatment of chronic conditions (for details on the RK Protocol, please see Klinghardt and Ruggiero, 2017).

The final lecture was given by Dr. Michael Schwalb, MD, from Leverkusen, Germany. In his talk entitled "A novel integrated protocol in solid cancer, chronic bowel inflammation and arthritis" Dr. Schwalb described in detail, with numerous examples from his clinic, an immunotherapeutic protocol based on nutrition and immune system modulation (Schwalb *et al.*, 2016). Among the several cases successfully treated with this protocol, of particular interest was the case of a 76-year-old man suffering from Chronic Inflammatory Bowel Disease (CIBD) with recurrent bleeding after medical therapy and surgery. As shown in Fig. 10, implementation of the protocol described by Dr. Schwalb resulted in significant improvements in a relatively short time.

In addition to the schedule of medical scientific lectures, two "lay" members of the audience shared their personal experiences fighting cancer and autism, following approaches discussed at the Congress. A gentleman from Australia shared his experience involving metastatic sarcoma that had been diagnosed in 2014 and unsuccessfully treated with chemo- and radiotherapy. His talk was a most moving moment of the Congress, in particular when he concluded with these words: "And that brings me to today ... While I am the first to admit I'm still work in progress ... the facts are that my belly tumor has gone from 12 cm diameter last August to 2.5 cm x 2.5 cm x 0.9 cm and as the Radiologist stated in the last report ...'This has almost completely resolved with only a very small area of induration and soft tissue thickening remaining".

Equally moving was a second report by the mother of an autistic child from the United States; the child had followed the protocol described by Dr. Antonucci (see Antonucci *et al.*, 2017), with significant improvements.

Conclusion

The Congress concluded with remarks by Dr. Ruggiero who introduced the 5th International Congress on Ketogenic Diet and Immunotherapy in Cancer and Neurological Diseases to be held October 2018 in San Diego, CA, USA.

Acknowledgement

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Authors' Contributions

Both authors of the Meeting Report presented at the 4th International Congress on Integrative Medicine, 1, 2 April 2017, Fulda, Germany, wrote the editorial paper, provided critical input and assisted in revising and improving the Meeting Report.

Conflict of Interest

Thomas Peter is the founder of the Therapy Center Anuvindati (<http://www.anuvindati.de>), a private clinic in Bensheim, Germany.

Marco Ruggiero is the inventor of Rerum[®], the founder and CEO of Silver Spring Sagl, a company researching, developing and marketing probiotics and other supplements and consults for the company "dr. reinwald healthcare gmbh.". He had no prior knowledge of the results shown in the presentations herein reported.

Marco Ruggiero is member of the Editorial Board of The American Journal of Immunology and is waived from the Article Processing fee for this contribution; he receives no remuneration for his editorial work.

Ethics

This article is original and contains material that has not been published in any other scientific journal.

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