

Ketogenic Diet Following its 100th Anniversary

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The ketogenic diet (KD) has gained significant attention in recent years among health care professionals and the general population. The KD primarily consists of a high proportion of fat, moderate protein and a very low proportion of carbohydrates intake.^{1,2} The standard KD regimen has approximately 55–60% of total caloric intake from fat, 30–35% from protein, and 5–10% from carbohydrates. This macronutrient distribution induces a metabolic shift from glucose dependence to fatty acid utilization, resulting in the production of ketone bodies and establish a state of sustained nutritional ketosis, while maintaining adequate protein intake for lean body mass preservation and tissue repair.^{1,2} Nutritional ketosis is generally considered safe since it involves the production of ketone bodies in moderate concentrations without significantly impacting blood pH. Nutritional ketosis differs from the life-threatening condition, ketoacidosis, where excessively high levels of ketone bodies are produced leading to acidosis in the blood.³

The year 2021 marked the 100-year anniversary of the ketogenic diet (KD). As a therapeutic strategy KD was first proposed in 1921 by Dr. Russell M. Wilder at the Mayo Clinic as a dietary alternative to fasting for patients with epilepsy.⁴ Wilder noticed the KD diet reduced the frequency and intensity of seizures in a subset of his patients who followed this dietary approach. For almost a decade, the ketogenic diet was viewed as a therapeutic option for paediatric epilepsy, but its prominence diminished with the advent of antiepileptic drugs. Even though over a century KD has evolved as a useful intervention for refractory

seizures, obesity, type 2 diabetes mellitus, metabolic syndrome, and even certain cancers; it was not yet unanimously accepted in medicine whether it would be presented as one of the most studied and debated dietary approaches.

In 1940s and afterward, the advent of phenytoin and other modern antiepileptic drugs, as well as a lack of publications by epilepsy centres, KD was ignored by the mainstream medicine surviving only in specialized paediatric neurology centres. Vining et al in 1998, in their first multicentre prospective study on KD in children with refractory epilepsy found that more than half of patients had a greater than 50% reduction in seizure frequency after 6 months.⁵ Interestingly a new focus was thrown on KD in the late 20th century when Neal et al. re-established it as an effective therapy for refractory epilepsy by a multicentre study, and Martin-McGill et al. supported their results in a systematic reviews and Cochrane analyses.^{6,7} Besides these, the International Ketogenic Diet Study Group, has given evidence based recommendation that dietary therapies be strongly considered in patients of any age who had failed two antiepileptic medications.^{8,9}

During the last two decades a remarkable expansion of KD research has been done. Beyond epilepsy, KD has been found as a therapeutic intervention in obesity, type 2 diabetes mellitus, polycystic ovarian syndrome, neurodegenerative diseases, cardiovascular disease, and certain forms of cancer. Studies reveal that ketosis exerts profound effects on energy metabolism, mitochondrial function, and inflammatory pathways.¹⁰ These findings underscore its therapeutic potential but also

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raise questions regarding long-term safety, cardiovascular risk, renal complications and sustainability.¹¹

In 2021, during its 100-year anniversary, the ketogenic diet (KD) has reached an interest level which was not previously seen. One hundred years on, KD exemplifies how an old therapy can be rediscovered and redefined, bridging the fields of neurology, endocrinology, and nutrition science. Its centenary offers not only a moment of celebration but also an opportunity for renewed a scientific inquiry. So large-scale, long-term clinical trials are needed to determine the comparative efficacy and safety of KD. Furthermore, personalized approaches may help to identify the patients who could get the greatest benefit with minimum adverse effects from ketogenic diet.

Outstanding questions at the centenary concern long term cardiovascular outcomes, head to head comparative effectiveness with other evidence based dietary patterns, durability and quality of life impacts, and precision nutrition predictors of response; addressing these through adequately powered, longer duration trials and translational studies will determine how a rediscovered therapy integrates across neurology, endocrinology, and nutrition in its second century.

References

1. O'Neill B, Raggi P. The ketogenic diet: Pros and cons. *Atherosclerosis*. 2020 Jan; 292:119-126. [PubMed]
2. Kim JM. Ketogenic diet: Old treatment, new beginning. *Clin Neurophysiol Pract*. 2017; 2:161-162. [PMC free article] [PubMed]
3. Hernández F. Glycolysis and gluconeogenesis: A teaching view. *J Biol Chem*. 2021 Jan-Jun; 296:100016. [PMC free article] [PubMed]
4. Wilder RM. The effects of ketonemia on the course of epilepsy. *Mayo Clin Bull*. 1921; 2:307-308.
5. Vining EP, Freeman JM, Ballaban-Gil K, Camfield CS, Camfield PR, Holmes GL, Shinnar S, Shuman R, Trevathan E, Wheless JW, Ketogenic Diet Multi-Center Study Group. A multicenter study of the efficacy of the ketogenic diet. *Archives of neurology*. 1998 Nov 1;55(11):1433-7.
6. Neal EG, Chaffe H, Schwartz RH, Lawson MS, Edwards N, Fitzsimmons G, Whitney A, Cross JH. The ketogenic diet for the treatment of childhood epilepsy: a randomised controlled trial. *The Lancet Neurology*. 2008 Jun 1;7(6):500-6.
7. Martin-McGill KJ, Bresnahan R, Levy RG, Cooper PN. Ketogenic diets for drug - resistant epilepsy. *Cochrane Database of Systematic Reviews*. 2020(6):CD001903. doi: org/10.1002/14651858.CD001903.pub5
8. Kossoff EH, Zupec - Kania BA, Amark PE, Ballaban - Gil KR, Christina Bergqvist AG, Blackford R, Buchhalter JR, Caraballo RH, Helen Cross J, Dahlin MG, Donner EJ. Optimal clinical management of children receiving the ketogenic diet: recommendations of the International Ketogenic Diet Study Group. *Epilepsia*. 2009 Feb;50(2):304-17.
9. Kossoff EH, Zupec - Kania BA, Auvin S, Ballaban - Gil KR, Christina Bergqvist AG, Blackford R, Buchhalter JR, Caraballo RH, Cross JH, Dahlin MG, Donner EJ. Optimal clinical management of children receiving dietary therapies for epilepsy: Updated recommendations of the International Ketogenic Diet Study Group. *Epilepsia open*. 2018 Jun;3(2):175-92.
10. Masino SA, Rho JM. Mechanisms of ketogenic diet action. *Epilepsia*. 2019;60(8):1602-1614.
11. Paoli A, Rubini A, Volek JS, Grimaldi KA. Beyond weight loss: a review of the therapeutic uses of very-low-carbohydrate (ketogenic) diets. *European journal of clinical nutrition*. 2013 Aug;67(8):789-96.