

Ketogenic diet therapies for Neurological disorders

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In 400BC, Hippocrates wrote that he cured a man who had seizures through fasting. In an attempt to simulate fasting, the classic Ketogenic Diet (KD) was designed in 1921 at the Mayo Clinic. Although effective at controlling seizures, its restrictive nature limited widespread use. The discovery of several anti-seizure medications over many decades resulted in near extinction of the diet until 1994 when the parents of Charlie Abrahams started a foundation to advocate for the KD that completely arrested his seizures. Multiple randomized controlled trials and prospective studies have confirmed the response rate of approximately 50% in children and adults with medication-resistant epilepsy. A 2018 consensus guideline, "Optimal clinical management of children receiving dietary therapies for epilepsy", published in *Epilepsy Open*, advised that the KD be offered to patients after the failure of two anti-seizure medications. All KDs are high in fat, moderate in protein, and restricted in carbohydrate and are referred to as "ketogenic diet therapies" (KDTs) to highlight medical

management. Variations of the classic KD have been designed in recent years to make the diet more tolerable. In the absence of carbohydrate intake, mitochondrial beta-oxidation of fat in the liver generates ketone bodies which can be readily used as an energy source. Through a series of complex mechanisms, the diet has been found to have a powerful anti-inflammatory effect. Animal research has confirmed that mitochondrial, neuronal, and mammalian target of rapamycin (mTOR) pathways are positively affected, which may account for the anti-epileptic effect and improvement in brain function. New applications for KDTs have emerged in recent years including benefits in autism, diabetes, migraine headache, Parkinson's disease, early-onset Alzheimer's disease, Prader Willi syndrome, and traumatic brain injury. Use of KDTs for glioblastoma brain cancer has shown benefit in inhibiting cancer growth and improving tumour response to traditional cancer therapies.

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