



## Brief Communication

## History of dietary treatment: Guelpa &amp; Marie first report of intermittent fasting for epilepsy in 1911

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## ABSTRACT

We analyzed the article of Guelpa & Marie, published in 1911 and often quoted in the history of dietary treatment, as the basis for the use of ketogenic diet to mimic fasting. In this paper, the authors treated 21 patients with a diet consisting of daily administration of 30 g of sodium sulphate for 4 days, with unlimited aqueous beverage and no food, followed by a vegetarian diet restricted to half of the ordinary intake. This is the first report of intermittent fasting as treatment strategy for epilepsy. In this case series, 15 patients did not follow properly the diet while 2 improved temporarily before they quitted the diet and 4 presented an improvement.

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## 1. Introduction

It has long been believed that epilepsy was due to overeating [1]. Guelpa & Marie are usually recognized in the literature as the first modern authors to report on the value of fasting in epilepsy [2]. They are often reported to have successfully treated 20 patients with epilepsy, resulting in less severe seizures.

Ketogenic diet (KD) was introduced as a treatment for epilepsy to imitate the effects of fasting, with the advantage that it could be maintained for a much longer period. It is a low-carbohydrate, high-fat diet, used to treat drug-resistant seizures, especially in children. It was first formulated and used in 1921 by Dr. Wilder in Mayo Clinic [3]. Three patients with epilepsy saw their seizure control dramatically improved with KD. For two decades, KD was widely used to treat epilepsy, but with the appearance of the first antiepileptic drugs (e.g., the discovery of diphenylhydantoin by Merritt and Putnam in 1938), its use declined. In the late 20th century, the use of KD expanded again. Ketogenic diet therapies are now evidence-based treatments of epilepsy with several controlled and randomized studies [4]. An international consensus on the methodology to conduct such treatments has recently been published [5].

The history of dietary treatment is often tied to the article of Guelpa & Marie published in 1911 [2]. Since approximately 500 BC, fasting and dietary regimens have been suggested as a treatment for epilepsy. Fasting to treat seizures is recorded in the Hippocratic collection [6]: a man with seizures was cured by complete abstinence from food and

drink. Five centuries later, in King James version of the Bible, fasting is also reported to treat seizures when Jesus cured a boy with epilepsy by asking him to pray and fast [7,8].

We wrote this brief communication following an analytical reading of the original publication and evaluation of the contribution of this report towards the use of dietary treatment for epilepsy.

## 2. Materials and methods

The article of Guelpa & Marie “*La lutte contre l'épilepsie par la désintoxication et par la rééducation alimentaire*” (The fight against epilepsy by detoxification and dietary education), published in 1911 in *Revue de Thérapeutique Médico-Chirurgicale*, was found on the Bibliothèque nationale de France (BnF, or National Library of France) website, specifically its digital library known as Gallica: <https://gallica.bnf.fr/> (Fig. 1).

The article was read and analyzed by 3 fluent French speakers. We have reported in the results section below on how the authors conducted fasting, and we have summarized the patients' characteristics and the effects of the diet in Table 1.

## 3. Results

The diet applied by the authors consisted of daily administration of 30 g of sodium sulphate for 4 days, with unlimited aqueous beverage and no food, followed by a vegetarian diet restricted to half of the ordinary intake. This cycle was reproduced approximately every 8 days.

The patients reported in the article of Guelpa & Marie have been grouped in a table which summarizes all the information available on

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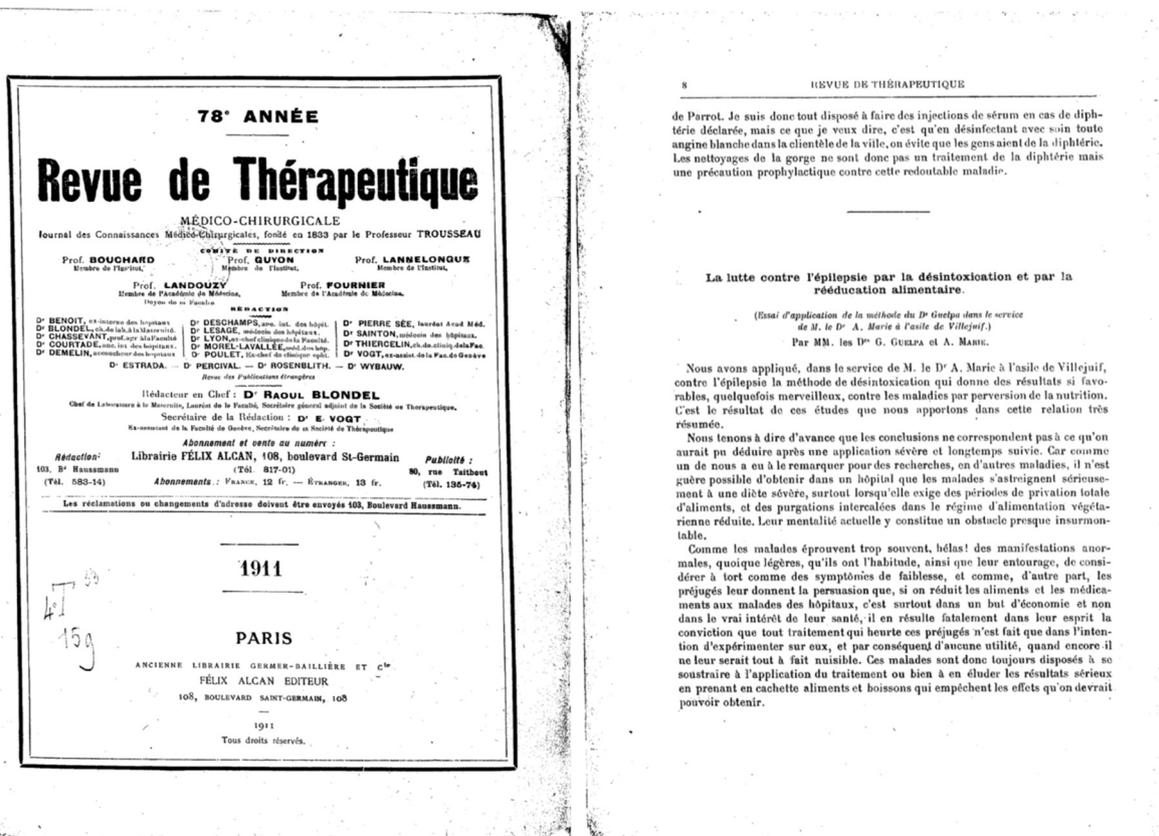


Fig. 1. Guelpa & Marie published their article "La lutte contre l'épilepsie par la désintoxication et par la rééducation alimentaire" in *Revue de Thérapeutique Médico-Chirurgicale* journal in 1911.

their description, the diet follow-up, and the impact of the diet (Table 1).

This diet was first applied to 2 patients with obesity in the Villejuif asylum (Mr. W and Mr. D). Only 1 of the patients, Mr. D, followed properly the diet. Meanwhile, Mr. W ate food in secret since the beginning of the diet. The results for Mr. W. had to be disregarded. Mr. D was obese (120 kg), and the authors described his medical condition as "senile prementia weakening, choking, and intense cough which were tiring him during the day and keeping him awake during the night". The authors observed that from the first days of the diet, his dyspnea totally disappeared, as well as his cough, which almost completely disappeared. Mr. D appeared more expressive and alert, with a steadier walk. This improvement progressed together with weight loss (the authors did not precise the exact amount of weight loss) for more than one month, until the patient decided to stop the diet as he was satisfied with the results obtained.

Following their study with the two patients with obesity, the authors decided to apply their dietary treatment to 21 patients with epilepsy from the Villejuif asylum, from which in the end only 6 patients were described. In total, 15 patients were not taken into account as they did not follow the diet for more than one cycle, either because the diet was too restrictive or because the patients did not observe any improvement. However, the authors stated that seizures were less intense and less frequent, and that patients were more alert, only after a couple of days of dietary modification. This claim of the authors was not associated with any quantitative data.

From the 6 patients with epilepsy who were described, 4 did not properly follow the dietary treatment. Mr. Don... ate food in secret since the beginning of the diet, and Mr. Mat... drank wine in secret. Two other patients, Mr. Meth... and Mr. Boul..., were also caught eating in secret. Mr. Meth... had frequent seizures and a complicated postictal state with mental clouding and delirium with homicidal impulses. At first, he seemed to seriously follow the diet, and the authors observed

a clear improvement with weight loss. However, after a while, seizures reappeared albeit with lower frequency and lower intensity. The authors hypothesized that the seizure reappearance might be because of irregular diet follow-up. Mr. Boul... had epilepsy with frequent seizures and dyspnea. He obtained good results with the diet with dyspnea disappearance, teguments color improvement, and seizure improvement, but after one month, seizures came back. The authors reported that seizure reappearance was linked to the fact that the patient was eating in secret. Overall, only 2 patients seemed to properly follow the diet. The authors observed a slight improvement in seizure duration associated with a fastest recovery in the case of Mr. Baud..., and the seizures of Mr. Dav... disappeared but he had to leave the asylum when he found a job. The authors claimed good results with their dietary treatment but they also stated that it was really difficult for patients to remain on diet.

Subsequently, the authors studied 2 additional patients from a private clinic. Patient no. 1 suffered from 5 to 6 seizures/day and tried to commit suicide twice. He was bruised from frequent falls, and the authors concluded that he coughed a lot because of partial paralysis of the vocal cords. He followed the diet, which was complemented with an 'electrical treatment' every two days for his vocal cords paralysis, in the Salpêtrière Hospital. The patient did not have any seizures for weeks. When seizures reappeared, they were a lot shorter, almost without falls nor mental clouding. The patient seemed to be more alert, less shy and afraid, and his suicidal thoughts disappeared. His voice became almost normal. Patient no. 2 was aged 20 and presented 1 seizure/week which was followed by mental clouding and depression. He followed seriously the dietary treatment for one and a half year, during which only 2 seizures were observed.

The authors also stated that their dietary treatment worked for a pregnant patient with eclampsia and for children, without giving further details.

**Table 1**

This table summarizes the patients' description, the diet follow-up, and the results of the diet described in the article of Guelpa & Marie published in 1911.

Patients	Description made by the authors	Diet follow-up described by the authors	Results described by the authors
Guelpa & Marie 1911: the diet consisted of daily administration of 30 g of sodium sulphate for 4 days, with unlimited aqueous beverage and no food, followed by a vegetarian diet restricted to half of the ordinary intake. This was reproduced approximately every 8 days.			
Mr. W., Villejuif asylum	Obesity.	Since the beginning, the patient ate food in secret.	Results could not be taken into account.
Mr. D., Villejuif asylum	Obesity (120 kg) with senile predementia weakening, choking, and intense cough which were tiring the patient during the day and keeping him awake during the night.	The patient followed the diet for one month.	Since the first days of the diet, the dyspnea totally disappeared, as well as the cough, which almost completely disappeared. The patient seemed more expressive and alert, with a steadier walk. This improvement progressed together with weight loss for more than one month until the patient decided to stop the diet.
Mr. Don..., Villejuif asylum	Epilepsy.	Since the beginning, the patient ate food in secret.	Results could not be taken into account.
Mr. Mat..., Villejuif asylum Mr. Baud..., Villejuif asylum	Epilepsy and alcoholism. Epilepsy.	The patient drank wine in secret. The patient seemed to follow properly the diet.	Results could not be taken into account. Slight improvement with seizure duration decrease and with a fastest recovery.
Mr. Meth..., Villejuif asylum	Epilepsy with frequent seizures and a complicated postictal state with mental clouding and delirium with homicidal impulses.	The patient seemed to follow seriously the diet but the authors realized that he ate food in secret.	Clear improvement with the diet and the weight loss. After a while, seizures reappeared with a lower frequency and intensity. Seizure reappearance might be because of diet infractions.
Mr. Boul..., Villejuif asylum	Epilepsy with frequent seizures and dyspnea.	The patient seemed to follow seriously the diet but the authors realized he ate food in secret.	Good results with dyspnea disappearance, teguments color improvement, and seizure improvement. After one month, seizures came back because the patient ate in secret.
Mr. Dav..., Villejuif asylum	Epilepsy.	The patient followed the diet but left the asylum.	Good results with seizure disappearance.
Patient no. 1 from a private clinic who followed the diet in Salpêtrière Hospital	Epilepsy: 5–6 seizures/day. The patient tried to commit suicide twice. He was bruised because of his frequent falls. He coughed a lot because of vocal cords partial paralysis.	The patient followed the diet which was completed by an electrical treatment every two days for his vocal cords paralysis.	The patient did not have any seizures for weeks. When seizures reappeared, they were a lot shorter, almost without falls nor mental clouding. The patient seemed to be more alert, less shy and afraid, and his suicidal thoughts had disappeared. Bronchial catarrh had also disappeared, and his voice was almost normal.
Patient no. 2 aged 20 years from a private clinic	Epilepsy: 1 seizure/week followed by mental clouding and depression.	The patient followed seriously the diet for one year and a half.	Only 2 seizures for one year and a half since the beginning of the diet. One seizure seemed to be due to overwork, and the other one did not seem to have a specific cause.
Pregnant patient	Eclampsia.	The patient followed the diet.	Success: end of seizures.

The authors did not comment on hunger or side effects, nor did they mention any laboratory analysis. The authors remarked that nurses dedicated to patients following this diet are required to seriously apply their dietary treatment which they called 'detoxification'. They also concluded that dietary education and hereditary preservation (syphilis, alcoholism, ...) are the key to cure epilepsy, and not drugs.

#### 4. Discussion

It is frequently stated that Guelpa & Marie treated some 20 patients with epilepsy with fasting, resulting in less severe and less frequent seizures [9]. Guelpa & Marie's article is not focused on fasting. Rather, it reports on the use of a dietary change in the treatment of epilepsy through an intermittent-fasting, reduced calorie vegetarian and laxative diet. Even if the authors initially meant to treat more patients, only a total of 6 patients with epilepsy followed this intermittent-fasting diet.

The first two patients who followed the diet were obese and did not have epilepsy. Among the 21 patients with epilepsy who were supposed to follow the treatment, the authors only analyzed the results of 6 patients because the other patients did not follow the diet for more than one cycle. Finally, among those 6 patients, only one of them was known to properly follow the treatment while another compliant patient with promising outcome was not followed-up upon his departure from the asylum.

The fasting diet consisted of daily administration of 30 g of sodium sulphate for 4 days, with unlimited aqueous beverage and no food.

Sodium sulphate was used as a laxative, and is still today found in some laxative drugs. In their article, the authors did not explain why they treated their patients with sodium sulphate but it may be hypothesized that it was given with the objective to empty the bowel in addition to stopping nutritional intake; this might be what the authors meant by 'body detoxification'. These 4 days of fasting were followed by approximately 4 days of vegetarian diet restricted to half of the ordinary intake. The cycle was then repeated. Nowadays, vegetarians usually have a balanced diet but in 1911, less information on a balanced vegetarian diet was available. It can thus be hypothesized that in the 20th century, a vegetarian diet was composed of a lot of vegetables and that the diet was hypoproteinic, with increased carbohydrates. We suggest that this dietary treatment should then be seen as an intermittent-fasting diet.

The two additional patients from a private clinic had dedicated nurse to ensure compliance of the dietary treatment which the authors had come to realize to be hard to follow without full-time support. For the first patient, confounding factors such as the electrical treatment limited the interpretation of the effects of the authors' dietary treatment. The impact of the dietary treatment on the second patient seemed interesting and long-lasting.

In conclusion, Guelpa & Marie did not report on the use of fasting but on a more complex dietary treatment for epilepsy using a 8-day cycle of intermittent-fasting, reduced-calorie vegetarian, laxative diet. The authors seemed to think that too much food could be toxic, as suggested by the wording of the title of the article, thus they aimed to restrict patients' food intake, and by the use of a laxative at the initiation of their

dietary treatment. In this case series, they claimed that the dietary treatment improved all patients that properly followed the dietary treatment. There is no evidence that research on this topic was continued until the KD emerged 10 years later [3]. As with any dietary treatment, the authors already mentioned in 1911 that the need of supervision and dedicated staff is crucial. Recent studies have suggested that intermittent fasting might be used for epilepsy [10,11]. It would be interesting to systematically study the effect of intermittent fasting which may become an efficient treatment option for epilepsy.

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#### Conflicts of interests

The authors report no conflicts of interest.

#### References

- [1] Kim JM. Ketogenic diet: old treatment, new beginning. *Clin Neurophysiol Pract* 2017;2:161–2.
- [2] Guelpa G, Marie A. La lutte contre l'épilepsie par la désintoxication et par la rééducation alimentaire. *Rev Ther Medico-Chirurgicale* 1911;78:8–13.
- [3] Wilder RM. High fat diets in epilepsy. *Mayo Clin Bull* 1921;2:308.
- [4] Dozières-Puyravel B, François L, de Lucia S, Goujon E, Danse M, Auvin S. Ketogenic diet therapies in France: state of the use in 2018. *Epilepsy Behav* 2018;86:204–6.
- [5] Kossoff EH, Zupec-Kania BA, Auvin S, Ballaban-Gil KR, Christina Bergqvist AG, Blackford R, et al. Optimal clinical management of children receiving dietary therapies for epilepsy: updated recommendations of the International Ketogenic Diet Study Group. *Epilepsia Open* 2018;3:175–92.
- [6] Temkin O. *The falling sickness: a history of epilepsy from the Greeks to the beginnings of modern neurology*. 2nd ed. Baltimore, MD: The Johns Hopkins University Press; 1971.
- [7] Mark. *The Bible New King James version*, vol. 9. Carmel, NY: Guideposts; 1982; 14–29.
- [8] Wheless JW. History and origin of the ketogenic diet. *Epilepsy Ketogenic Diet* 2004; 31–50.
- [9] Wheless JW. History of the ketogenic diet. *Epilepsia* 2008;49(Suppl. 8):3–5.
- [10] Hartman AL, Zheng X, Bergbower E, Kennedy M, Hardwick JM. Seizure tests distinguish intermittent fasting from the ketogenic diet. *Epilepsia* 2010;51:1395–402.
- [11] Hartman AL, Rubenstein JE, Kossoff EH. Intermittent fasting: a “new” historical strategy for controlling seizures? *Epilepsy Res* 2013;104:275–9.