

THE CHARLIE FOUNDATION TO HELP CURE PEDIATRIC EPILEPSY



Third International Symposium

Diet therapies for epilepsy & other neurological disorders

ABSTRACTS

Hilton Indian Lakes, Bloomingdale, IL

9/19/2012

An abstract is a brief summary of an author's experience in patient care or in scientific research. The intent of an abstract is to share evidence that will further evolve or improve use of diet therapies for epilepsy and other neurological disorders. The following abstracts were submitted in advance of the meeting by symposium attendees, reviewed and accepted by the Steering Committee of the symposium. Authors displayed their abstracts in a special session during the Symposium.

Prepared by Beth Zupec-Kania, RD, CD

Author's last name: Abstract title

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<p>1. Title HOW DO PARENTS FIND OUT ABOUT THE KETOGENIC DIET?</p> <p>Sarah Doerrer PNP Co-authors Eric Kossoff MD, Zahava Turner RD Johns Hopkins University Hospital, Meyer 2-147; 600 North Wolfe Street Baltimore, MD21287</p> <p>Keyword 1 ketogenic Keyword 2 internet Keyword 3 diet Keyword 4 children Keyword 5 perception</p> <p>Parents of children with epilepsy are often faced with myriad treatment options to choose from. It has been previously reported that child neurologists often view the ketogenic diet (KD) as a treatment of last resort and therefore may not recommend it. An anonymous survey was provided to parents of 107 children about to start the KD at our institution regarding their family's path to the KD. The average time from epilepsy to KD onset was 2.8 years, but the average wait time for KD onset was only 1.7 months after referral. The most common reason for starting the KD was seizure reduction, followed by less intense seizures, medication reduction, and cognitive improvement. The majority (72%) obtained information from their neurologist; however, more than half also had viewed related websites. The mean rank of neurologist supportiveness was 7.9/10; 53% reporting their neurologist as maximally supportive (score of 10).</p>	<p>2. Title A GENETIC BASIS FOR RESPONSE TO THE KETOGENIC DIET IN DRUG-RESISTANT EPILEPSY</p> <p>Natasha Schoeler</p> <p>Co-authors J. Helen Cross, Josemir W. Sander, and Sanjay M. Sisodiya 54 Balin House, London, UK 12345</p> <p>Keyword 1 ketogenic diet Keyword 2 genetics</p> <p>The Ketogenic Diet (KD) is a high-fat, low-carbohydrate diet used to treat people with difficult-to-treat epilepsy. Class I evidence has shown the KD to be effective in children, but it is resource-intensive and predictors of response are limited. This project is concerned with genetic markers of response: whether there is an over-representation of specific gene variants in responders to the KD, compared to non-responders. Changes to DNA methylation and gene expression will also be investigated. Further understanding of the mechanisms behind the effects of the KD could lead to ways to provide individuals with the benefits of dietary treatment without the side effects that impair compliance. Half of participants achieved ≥50% seizure reduction at 3-months. Gender, age at seizure onset and diet onset, and serum beta-hydroxybutyrate (BHB) do not predict diet effectiveness. One quarter of non-responders reported other beneficial effects from dietary treatment on seizures; over half reported other beneficial effects, such as improved cognition and behaviour. Three-quarters of participants reported adverse side effects. A genome wide association study (GWAS) will be carried out on all cases, and exome sequencing on extreme responders and non-responders. Gene expression changes pre-, during and post-diet will be measured by microarray. This work was undertaken at UCLH/UCL who received a proportion of funding from the Department of Health's NIHR Biomedical Research Centres' funding scheme. NS is supported by a UCL Impact Studentship. Professor JH Cross has received funding from HSA, Smiths Charity, SHS, Matthews Friends, and the Milk Development Council for Ketogenic Diet study.</p>
<p>3. Title The effect and Long-term retention rate of ketogenic diet in Chinese patients</p> <p>Author: DENG Yu Hong Co-authors ZHOU Jin-Hua, LI Bing-Mei, LIU Xiao-Rong, LIAO Wei-Ping</p> <p>Changgang Dong road 250, haiZhu, Guangzhou, GuangDong, P.R China,510260</p> <p>Keyword 1 ketogenic diet Keyword 2 refractory epilepsy Keyword 3 effect Keyword 4 retention rate</p> <p>Objective: To evaluate the effect and long-term retention of ketogenic diet (KD) in add-on therapy for refractory epilepsy patients with Chinese eating habits.</p> <p>Methods: 28 Chinese patients with refractory epilepsy were recruited in one and half a year. In the first three months, there were no changes of the anti-epilepsy drug. All patients were hospitalized and started with fat / (protein + carbohydrates) = 4:1 diet, then maintained the 4:1 diet after discharged. According to the recruiting day, the follow-up period persist from 3 months to 12 months. The retention rate, the efficacy and the incidence of side effects on specific follow-up time point were observed.</p> <p>Results: On the third month, 68% of patients reduced >50% seizures, 43% (12/28) of patients reduced >90% seizures, 11% were seizure-free. The retention rate was 68% (19/28) at the third month, while it was 43% (10/23) at the sixth month and 28% (5 /18) at the twelfth year. The major side effects in the first two weeks included gastrointestinal reactions, ketoacidosis and low glucose; the major side effects in the persistence period were constipation, hyperlipidemia, and hypoalbuminemia. Only one patient withdrew the diet due to side effects.</p> <p>Conclusions: KD in Chinese refractory epilepsy patients is highly effective, but the long-term retention rate is low probably related to the Chinese eating habits. Better implementation needs to be further studied.</p>	<p>4. Title Ketogenic Diet in Patients with Tuberous Sclerosis – A German-French Study with Respect to a Possible Tumour Growth</p> <p>Author: Adelheid WiemerKruel Co-authors Anne de Saint Martin, Thomas Bast Sandsteinweg 7, Kehl, BW77694, Germany</p> <p>Keyword 1 tuberous sclerosis complex Keyword 2 ketogenic diet Keyword 3 tumor growth Keyword 4 epilepsy treatment</p> <p>Introduction: The ketogenic diet (KD) is an alternative treatment for therapy resistant epilepsies, leading to seizure reduction of more than 50% in about 50 - 60% of patients in general. Responder rates are even higher in patients with tuberous sclerosis complex (TSC) (at least 50% reduction in more than 90%; at least 90% seizure reduction in more than 60%). However, with regard to a study of Chu-Shore, facilitation of tumour growth in TSC by KD has to be considered. Methods: Six patients with TSC were treated with KD in both centres and followed up continuously for 5 months to 7 years. In addition, a questionnaire was sent by the German TS Alliance in October 2010. Four families answered. The data were actualized in February 2012 with regard to development of subependymal giant cell astrocytomas (SEGA) and angiomyolipomas (AML). Results: Nine in our ten patients had a seizure reduction of > 50% after 3 months, three a seizure reduction > 90%, two were seizure-free. We observed no TSC-related tumor development and tumor growth, neither in SEGA, nor in AML. We found the same incidence of SEGA (20%) and AML (40%) as seen in the general TSC population. Summary: KD is an effective and safe option to treat therapy resistant epilepsies in TSC children, leading to more quality of life, if regular follow-up examinations are done (ultrasound/MRI of the kidneys, cerebral MRI).</p> <p>The authors disclose any source of contributed support.</p>

5.

Title: Resting energy expenditure should be taken into account when calculating diet composition in children (0-18 y) with KD for intractable epilepsy
Author: E J T M van der Louw
Co-authors D.N. Lagerwerf, M.Verhagen, K.F.M Joosten, C.E Catsman-Berrevoets

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Keywords: Ketogenic Diet, Diet composition, Resting energy expenditure, Food diary

Introduction: The nutritional need of children on ketogenic diet (KD) may conflict with factors e.g. protein amount, diet ratio, total energy expenditure (TEE) which influence efficacy of KD. Severe psychomotor retardation (PMR) is frequently seen in children with intractable epilepsy. PMR may influence Resting Energy Expenditure (REE) based on deviated bodycomposition¹.

Purpose: To identify deviant REE characteristics which influence calculations of TEE in children with severe PMR.

Methods: At diet initiation TEE is calculated with Schofield method, which is based on data of healthy children, compared with outcome of patient's 3-day food diary (FD)¹. REE measurement by Deltatrac[®] was used in the Sophia Children Hospital incidentally from 2001-2008 and structurally from 2008 as baseline for diet energy calculation. From 2001-2011 100 children started the KD.

Results: Evaluation of outcome in 54 children with severe PMR shows that in 66.6% the diet needed to be adjusted based on the finding that Deltatrac[®] REE kcal/kg differed from Schofield REE kcal/kg. In one subgroup 48% (n=26) Schofield overestimated Deltatrac[®]. In this subgroup TEE/kcal/kg based on Deltatrac[®] sign correlated (p=0.023) with TEE kcal/kg of Food Diary. In contrast no correlation was found with TEE/kcal/kg based on RDA and Schofield.

¹ Sullivan P.B. (2009) Feeding and Nutrition in children with neurodevelopmental disability, Mac Keith Press, London UK.

² Hurk van den, T. and E. Louw van der (2011). Dietary treatment guideline for the ketogenic diet in children with refractory epilepsy. Evidence based manual for multidisciplinary treatment. Utrecht, University Medical Center Utrecht, department of Nutritional Sciences and dietetics.

6.

Title: AN AUDIT OF THE USE OF ELECTROENCEPHALOGRAM (EEG) IN THE KETOGENIC DIET (KD)
Author: Dr Katharine Buchanan Liverpool UK, UK15
Keyword: Ketogenic Diet, EEG, electroencephalogram

The Ketogenic Diet (KD) is used in drug-resistant epilepsy and has been shown to be effective at seizure reduction in recent trials. Limited evidence is available about the use of EEG in the KD.

Aim: Survey to determine the value of follow-up EEG's in patients who responded to the KD.

Method: Patient details were recorded including baseline and follow-up treatment EEG results.

Follow-up: EEG's were arranged after 3 months if a clinical improvement in seizures was noted.

Method: Twenty-four (71%) children tolerated the diet for more than three months (most commonly (47%) discontinued due to lack of effect). Eleven (46%) had a follow-up EEG with a median (range) time of 12 (3- 48) months. Twelve (93%) patients didn't have an EEG (no clinical improvement). One child clinically improved, but did not have a follow-up EEG. Four (57%) children had normal EEG's compared to 1 (3%) at baseline

Results: Thirty-four patients were available for analysis. From baseline EEGs 24 (70%), had generalised epilepsy; 9 (26%) had focal epilepsy; one had a normal EEG. Fourteen (43%) had a seizure during the EEG.

Conclusion: Follow-up EEG's were done appropriately in 46% of the 24 patients. Improvement in the follow-up EEG was seen, which may be reassuring for parents. Follow-up EEG's may not be necessary, as it did not alter management and cost could be saved. Those without a follow-up EEG usually stopped the diet shortly after due to lack of effect.

7.

Title: SUCCESSFUL EMERGENT UTILIZATION OF THE KETOGENIC DIET IN A PATIENT PRESENTING WITH PHARMACORESISTANT EPILEPSIA PARTIALIS CONTINUA: A CASE STUDY

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Co-authors Jennifer L. Richards, MSN, ARNP, and Ronald Davis, MD, FAAP Arnold Palmer Hospital for Children, 92 West Miller Street, MP 317

Keywords: Epilepsia Partialis Continua, Ketogenic Diet, Pharmacoresistant focal status epilepticus

OBJECTIVE/METHODS: We report the case of a previously well 9 month old Caucasian male presenting with pharmacoresistant focal status epilepticus. Focal left temporoparietal spikes, correlated with twitching of the body and head were noted on EEG, consistent with epilepsy partialis continua (EPC). Due to continued seizures which were resistant to multiple treatments, the patient was acutely initiated on the ketogenic diet (KD).

RESULTS: Ketosis was achieved and maintained via enteral nutrition. The patient experienced an improvement and eventual resolution of clinical seizures as blood ketone measurements stabilized. An EEG performed eleven days post diet initiation demonstrated focal posterior slowing, a marked improvement compared to previous studies. This was followed by a normal routine and 24 hour prolonged study fourteen and nineteen days post diet initiation respectively. Final diagnosis for etiology of his resistant EPC was confirmed one month later as POLG-1 mutation (Alpers Disease).

CONCLUSION: Literature examining cases of EPC in pediatrics is limited. No protocol exists which directs successful treatment of

f this population that tends to be resistant to multiple antiepileptic agents. With failure of multiple treatment options, the KD was initialized in hopes of attaining seizure control. This case demonstrates a patient with EPC who achieved control of seizures and improved electroencephalogram pattern following KD initiation. It remains unclear when the diet should be introduced, and how many trials of antiepileptic agents should be utilized prior to its consideration. It is also unclear if POLG-1 patients should be treated early with the KD.

Disclosure: No contributed support for this case study

8.

Title: OPEN TRIAL OF THE MODIFIED ATKINS' DIET FOR CHILDREN WITH UNCONTROLLED EPILEPSY

Author: Ritu Sudhakar
Co-authors Dr. Gagandeep Singh, Dr. Jatinder Singh Goraya
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Keyword: modified Atkins' diet, intractable epilepsy, ketogenic diet

Purpose: Like the ketogenic diet, the modified Atkins' diet [MAD] is a high fat, low carbohydrate diet used in intractable epilepsy. It does not require rigid weighing of foods and there is no restriction on recommended daily calories according to patient age (1).

Objective: To evaluate the efficacy of modified Atkins' diet

Methods: 20 children with epilepsy were treated with a modified Atkins diet. Of this 13 remain on the diet till today. Patients were in the age group of 1.4 to 11 years, with mean age of 4.6 years. Infants, children and adolescents were allowed 5, 10 and 15gm carbohydrate per day respectively. Following the start of the diet all patients went through a week of carbohydrate wash out so as to attain a ketone of 160mg/dL (4+). Throughout the diet treatment urine ketones were checked four times daily and seizure control recorded.

Results: All the patients achieved greater than 50% improvement in seizure control within 3 months of starting on the diet. Of this, 15% became seizure free, 50% achieved more than 90% control and 25% achieved more than 75% control.

Conclusion: The results of the modified Atkins diet are encouraging and it can be used as a substitute for the ketogenic diet in intractable epilepsy.

REFERENCES:

1. A modified Atkins Diet Is effective for the treatment of Intractable Pediatric Epilepsies Kossoff EH, Mc Grogan JR, Bluml RM, Pillas DJ, Rubenstein JE, and Vining EP ; Epilepsia, 2006; 47 : 421 – 424.

2. A prospective study of the modified Atkins Diet for Intractable Epilepsy in Adults Kossoff EH, Rowley H, Sinha SR and Vining EPG; Epilepsia, 2008; 49:316 – 319.

9.

Title: IMPROVED LIPID PROFILES WITH USE OF KETOCAL® 4:1 LIQUID

Author: Rebecca Randall MS RD LDN
Co-authors Cagla Fenton, RD Christina Bergqvist, MD Claire Chee RN
Children's Hospital of Pittsburgh, PA
Keywords: Ketogenic diet, lipid level, enteral formula

Objective: The ketogenic diet (KD) can result in hyperlipidemias. There are few options for children who need commercially available KD enteral formulas. Nutricia North America has recently modified the lipid content in their new KetoCal® 4:1 Liquid formula by removing the trans fatty acids and reducing saturated fats to 15%. We report improvements in the lipid profiles of 3 children who were switched from KetoCal® 4:1 powder to KetoCal® 4:1 Liquid formula.

Methods: A retrospective chart review revealed 3 patients in our KD program with elevated lipid profiles while receiving 100% of their nutritional needs from KetoCal® 4:1 powder. Patients were switched to KetoCal® 4:1 Liquid and treated for > 3 months. Fasting lipid profiles were obtained before and 2-3 months after the formula switch. All patients were on ≥ 4:1 ratio KD and had no other dietary changes during this time.

Results: Three patients identified, baseline mean ± standard deviations (SD) levels: CHL: 257 ± 49 mg/dL, LDL: 172 ± 61 mg/dL, HDL: 44 ± 1 mg/dL, TGA: 201 ± 92 mg/dL. Mean time from KetoCal® 4:1 Liquid switch to post labs = 3.4 ± 0.8 months. Post intervention means CHL: 182 ± 9 mg/dL, LDL: 116 ± 5 mg/dL, HDL: 48 ± 3 mg/dL, TGA: 85 ± 17 mg/dL. The average decrease: CHL: 29%, LDL: 33%, TGA: 58%, while HDL increased 10%.

Conclusion: A significant decrease in lipid levels was seen with transition to KetoCal® 4:1 Liquid in an average of 2.1 months. Clinicians should consider KetoCal® 4:1 Liquid for patients with elevated lipid levels.

10.

Title EXPRESSED BREAST MILK WITH THE KETOGENIC DIET

Author: Cagla Fenton RD LDN
Co-authors Rebecca Randall, RD, LDN, Christina Bergqvist, MD, Claire Chee, RN
Children's Hospital of Pittsburgh, PA

Keyword 1 Ketogenic diet
Keyword 2 breast milk
Keyword 3 ketosis

Introduction: World Health Organization recommends exclusive breastfeeding for the first 6 months of life and continued breastfeeding with complementary foods for 2 years or beyond. Breast milk's (BM) digestibility, composition and immune functions are unique and unmatched by formula. The ketogenic diet (KD) is an effective treatment for infants and children with treatment resistant epilepsy (TRE). We report our experience using expressed BM as the carbohydrate source for the KD treatment in infants.

Case Descriptions: A retrospective chart review (1999-2012) of patients enrolled at our KD program identified 4 patients. Inclusion criteria were < 2 years of age and use of BM before KD initiation. All patients achieved ketosis within 1-6 days of initiation at lower (2:1 to 3:1) ratios. All maintained ketosis while using BM (Average beta-hydroxybutyrate 2.4 ± 1.1 mmol/L). The average amount of BM was 139 ± 50 ml/day. Average carbohydrate intake was 11 ± 4.5 grams/day. Three out of four patients showed improvement in seizures activity within first 2 months of treatment. Patients continued on BM for an average of 105 ± 50 days and all discontinued BM due to maternal preference.

Discussion: We found that BM is a viable, perhaps preferred, dietary carbohydrate source for the KD treatment. Although the amount of BM used was small, all mothers felt it was important for them to provide BM as a source of their child's nutrition. Ketosis was achieved and maintained with controlled amounts of expressed BM.

11.

Title TRANSITION FROM MODIFIED ATKINS DIET TO MCT KETOGENIC DIET

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Keyword 1 MCT Ketogenic Diet
Keyword 2 Modified Atkins Diet
Keyword 3 Pediatric Epilepsy

Objective : Our case report documents on the outcome of a patient who was successfully transitioned from the Modified Atkins Diet (MAD) to the MCT Ketogenic Diet (KD).

Methodology : Our patient, a male aged 9.75 yrs, started the MAD as an outpatient. After 5 months, there was no improvement in seizure frequency (averaging 4 seizure per day), even though he had urine ketones of 3+, and he was reluctant to continue the diet.

Results : Patient was transitioned from the MAD to the MCT ketogenic diet in 2 phases. Firstly, up to 10% MCT was added to his home diet, in 5ml per week increments to test tolerance. Then, he was admitted for the MCT KD. A 40% MCT KD was planned; however, patient developed frequent watery stools, which resolved when the MCT amount was reduced to 30%. Upon discharge, patient was able to consume some of his usual carbohydrate-containing foods and urine ketones were maintained at 2-3+ throughout. He has been seizure-free for 4 months since transitioning to the MCT KD

Conclusion : Patients with epilepsy are usually recommended to stay on the KD for about 2-7 years. Our case shows that we can use the MAD, which is easier to initiate, to test tolerance and compliance, after which we can transition to the MCT KD, which is easier to sustain.

12.

Title A Research Protocol: Cost-Effectiveness of a Ketogenic Diet in Children with Intractable Epilepsy

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D Department of Behavioral Sciences, Epilepsy Centre Kempenhaeghe, Heeze, The Netherlands

Keywords: Ketogenic diet, epilepsy, cost-effectiveness, randomized controlled trial, design

Methods: In a randomized controlled trial (RCT) we will compare the ketogenic diet (KD) with usual care. Embedded in this RCT will be a trial-based and model-based economic evaluation, looking from a societal perspective at the cost-effectiveness and cost-utility of the KD versus usual care. Fifty children and adolescents (aged 1-18) with intractable epilepsy will be screened for eligibility before randomization into the intervention or the usual care group (Fig. 1). The primary outcome measure is the proportion of children with a 50% or more reduction in seizure frequency. Secondary outcomes include seizure severity, side effects/complaints, neurocognitive, socio-emotional functioning, and quality of life. Costs and productivity losses will be assessed continuously by a prospective diary and a retrospective questionnaire. Measurements will take place during consults at baseline, at 6 weeks, at 4 months after the baseline period, at 3, 6, 9 and 12 months follow-up after the 4 months consult (Fig. 2). Website: Compliance with a KD is difficult due to its restrictive nature. Unfortunately, non-compliance limits the intended effect and increases the costs, resulting in a less favorable cost-effectiveness ratio. In order to overcome this problem, patients will be monitored according to a strict standardized protocol.

In order to help those parents preparing meals, a website was developed on which tasteful recipes can be found. Our master-chef encourages menu plans that can be shared by the entire family. These tasty menus can be found at www.ketogenmenu.nl. Figure 2: Timeline of the study Figure 1: Flowchart of the study. References: De Kinderen R.J.A., Lambrechts D.A.J.E., Postular D., Kessels A.G.H., Hendriksen J.G.M., Aldenkamp A.P., Evers S.M.A.A., Majoie M.H.J.M. Research into the (Cost-)Effectiveness of the Ketogenic Diet among Children and Adolescents with Intractable Epilepsy: Design of a Randomized Controlled Trial. BMC Neurology 2011 11(1): 10. Acknowledgements: This study is being performed at epilepsy centre Kempenhaeghe and is funded by ZonMw.

13.

Title Successful control of status epilepticus with a ketogenic diet in patients who needed a continuous administration of anaesthetic drugs

Author: Ikuko Hiejima

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Keywords: ketogenic diet, status epilepticus, anaesthetic drugs

Purpose: We report good responses to a ketogenic diet in two patients with refractory status epilepticus (SE).

Patient 1: A 7-year-old girl with symptomatic frontal lobe epilepsy caused by a leukodystrophy presented with convulsive SE consisting of the clusters of brief tonic seizures. The SE was refractory to intravenous administration of high doses of phenobarbital, midazolam, and lidocaine. The SE could be controlled by a continuous infusion of propofol. However, the SE recurred when the propofol infusion was tapered. The 3:1 ketogenic diet was introduced with Meiji Ketonformula, a ketogenic milk available in Japan, via a gastrostomy tube. Four days after the initiation of the diet, the seizures decreased dramatically in frequency and the continuous infusion of propofol could be tapered off.

Patient 2: A 20-year-old woman with symptomatic frontal lobe epilepsy due to severe birth asphyxia developed SE consisting of clusters of loss of consciousness with mild stiffness in the face and extremities. The seizures could be controlled by continuous administration of midazolam. However, the SE recurred as the midazolam was tapered. The 3:1 ketogenic diet with Meiji Ketonformula via a gastrostomy tube was not effective, either. Fourteen days after the initiation of the 3:1 ketogenic diet, the ketogenic ratio from 3 : 1 to 3.5 : 1. Seven days later, the midazolam infusion could be tapered off successfully.

Conclusions: Ketogenic diet can control refractory SE which cannot be controlled without a continuous administration of anesthetic drugs.

14.

Title Experience of successful low glycemic index treatment using Japanese ethnic foods in a girl with Lennox-Gastaut syndrome

Author: Tomohiro Kumada

Co-authors Tomohiro Kumada, Ikuko Hiejima, Tomoko Miyajima, Fumihito Nozaki, Anri Hayashi, Tatsuya Fujii.
Moriyama, Japan

Keywords: Low glycemic index treatment, Japanese ethnic foods, Lennox-Gastaut syndrome, tuberous sclerosis

Objective: We designed a low glycemic index treatment (LGIT) using Japanese ethnic foods for a patient who could not continue modified Atkins diet (MAD) because of its restrictiveness.

Methods and patients: We introduced the LGIT to a 15-year-old girl with Lennox-Gastaut syndrome associated with tuberous sclerosis, who had refused MAD containing 10g per day of carbohydrate within 2 weeks 2 years previously. The LGIT was implemented at 7:2 calories of fat : protein by limiting a daily carbohydrate intake to 50 g, thus making a glycemic index of less than 50 relative to that of glucose. The useful carbohydrates included 'udon' (thick white noodles made of wheat), 'soba' (buckwheat noodles), and Japanese unpolished rice with 'natto' (fermented soybeans).

Results: At the time of introduction of LGIT, the patient was on valproate, ethosuximide and topiramate, and suffered from 30-minute tonic seizures twice or three times per week during sleep, frequent myoclonic seizures daily, as well as daytime somnolence. By one month after the initiation of the LGIT, the tonic seizures during sleep had reduced to once or twice per month, the myoclonic seizures during awake disappeared, and the daytime somnolence also improved. She has been on the LGIT for more than one year now, and the efficacy of the diet has remained sustained.

Conclusions: LGIT should be considered for patients with medication-resistant epilepsy who cannot be on more restrictive diet therapies. Japanese ethnic foods could be used for LGIT.

15.

Title KETOGENIC DIET AS A SUCCESSFUL TREATMENT FOR NEW ONSET REFRACTORY STATUS EPILEPTICUS SYNDROME (NORSE)

Author: Candy Richardson

Co-authors Candy Richardson, Mohamad Mikati, Beth Zupc-Kania

Keywords: ketogenic diet, status epilepticus, pentobarbital, oral diet, NORSE

Abstract Text RATIONALE: Status epilepticus is associated with a high risk of morbidity and mortality despite the availability of anti-epileptic drugs (AEDs). The role of the ketogenic diet (KD) in refractory status epilepticus is not well established.

METHODS: Chart review identified successful use of KD in treating a nine year-old male with new onset refractory status epilepticus syndrome (NORSE).

RESULTS: A previously healthy, male displayed headache, abdominal pain, left arm extension and stiffness, and subsequently had a cluster of clinical seizures with posturing, apnea and desaturations. The patient then became lethargic and noncommunicative. EEG showed electrographic seizures from bilateral temporal lobes with generalization. Despite multiple AEDs, including pentobarbital to achieve burst suppression and minimal stimulation, electrographic seizures persisted.

After transfer to this facility, patient was started on KD at 4:1 ratio via nasoduodenal tube after which he experienced significant improvement in seizure control. The patient later entered a rehabilitation facility maintained on BiPAP, AEDs and KD at a 4:1 ratio via PEG. The patient transitioned from tube feeding to oral diet after discharge from rehabilitation. Approximately one year after symptom onset, current regimen includes KD at 3:1 ratio and AEDs with recent seizure activity characterized as 1 to 2 focal seizures per month. The patient's status is described as post-NORSE

CONCLUSIONS: After achieving seizure control with concurrent use of KD and AEDs, the patient has continued to make progress in motor and cognitive function. NORSE patients may benefit from the inclusion of KD in their treatment regimen

16.

Title: Ketogenic Diet for Amphiphysin Antibody Related Refractory Status Epilepticus

Author: KuangLin Lin

Co-authors Jainn-Jim Lin, Huei-Shyong Wang, I-Jun Chou, Shao-Hsuan Hsia

Keywords: Amphiphysin Antibody, Limbic Encephalitis, Refractory Status Epilepticus

Abstract Text Objective: Limbic encephalitis is characterized by a triad of signs, including rapidly progressive short term memory deficit, limbic seizures, cognitive dysfunction and psychiatric symptoms. Limbic encephalitis is rare in people less than 18 years of age and is usually considered to be paraneoplastic. Refractory status epilepticus caused by amphiphysin antibody associated nonparaneoplastic limbic encephalitis was rarely reported.

Method: We report a 12-year-old boy with partial refractory status epilepticus who diagnosed as acute limbic encephalitis was refractory to conventional anticonvulsants and was only suppressed by high-dose intravenous suppressive agent. Serum amphiphysin-antibody was detected on day 3. High dose methylprednisolone pulse therapy and intravenous immunoglobulin were used, but was not effective. Result: Difficult to wean the high-dose intravenous suppressive agent was noted after 6 weeks treatment. However, it exhibited a favorable response about 7 days after introduction of a ketogenic diet. Then it was successful to wean the high-dose intravenous suppressive agents.

Discussion: Although there are few data regarding the use of the ketogenic diet in the treatment of nonparaneoplastic limbic encephalitis with refractory status epilepticus in children, our observation suggests induction of ketosis may be a novel strategy to effectively treat amphiphysin antibody related nonparaneoplastic limbic encephalitis with status epilepticus even after weeks to months of refractory seizures.

<p>17. Title PANCREATIC ENZYME THERAPY REDUCES HIGH TRIGLYCERIDES IN KETOGENIC DIET PATIENT Author: Lisa Vanatta Co-authors Beth Zupiec-Kania RD, CD Randa Jarrar MD, Micah Olson MD, Jeffrey Buchhalter MD Keywords: Triglyceride, Pancreatic enzyme, Lipid</p> <p>Abstract Text We present a case of a 4 yo male with a diagnosis of myoclonic astatic epilepsy or Doose syndrome. Because of medical intractability of his seizures, he was started on the ketogenic diet resulting in excellent seizure control. His ketogenic diet included one meal of KetoCal 4:1 powder mixed with water (240 mL) through a gastric feeding tube and two 4:1 ketogenic meals consumed orally. After 6 weeks on this therapy, his fasting triglycerides (TGY) were 1415 mg/dL and were subsequently 1988 mg/dL when drawn 1 month later. In an attempt to remedy this lipid abnormality, his diet was augmented with MCT oil (18 gm daily), KetoCal was changed to 4:1 Liquid (better fat profile) and he was treated with a pharmaceutical grade omega-3 fatty acid supplement (Lovaza). A repeat fasting TGY on this regimen was 2770 mg/dL. A pancreatic enzyme was initiated (Pancreatic Enzyme Formula) providing 1 capsule with each feeding. After three weeks, a repeat fasting blood analysis revealed a TGY of 105. On routine follow ups, normal TGY levels have been maintained. Although he did not exhibit any signs of malabsorption of fat such as flatulence or abnormal stooling prior to initiating the enzyme, we conclude that this enzyme is a harmless therapy that could potentially prevent discontinuation of the ketogenic diet and return of uncontrolled seizures.</p>	<p>18. Title: WHAT ARE THE SAFETY, EFFICACY AND PROCEDURES FOR INITIATING THE KETOGENIC DIET TO PATIENTS WITH ENTERAL FEEDING TUBES AS OUTPATIENTS? Author: Beth Chatfield MS RD CDN Co-authors Jamie Cubanski RN, BSN, CPN, Deborah Johnson RN, BSN, CPN, Jennifer Madan Cohen, MD Keywords: Epilepsy, ketogenic diet, outpatient, enteral feeding tubes</p> <p>The ketogenic diet center at Connecticut Children’s Medical Center has been initiating the ketogenic diet for inpatients since 1995. The established Ketogenic Diet pathway requires a three day admission for the initiation to monitor for potential side effects. Over the past couple of years, there have been circumstances inhibiting the admission of patients wanting to initiate the ketogenic diet which include: flu season and patient immune compromised status, other dependent child care issues and self pay financial issues. The literature cites a couple of references to outpatient initiation of the diet at home; however, safety guidelines, transition procedures, and follow up protocols have not been identified. The ketogenic team developed an outpatient transition plan to gradually wean patients with gastrostomy tubes from a standard formula over to Ketocal®. The standard pre-keto diet evaluation and follow up protocol were followed. Observational case! studies of two patients were reviewed and there were no medical complications or side effects observed in either of the patients with the transition to the ketogenic diet via enteral feeding tubes. Efficacy results indicated a >90% seizure improvement in one patient and 50-75% improvement in the other patient.</p> <p>CONCLUSION: Our observational findings demonstrated that the ketogenic diet can be initiated for outpatients with enteral feeding tubes using Ketocal®, along with a standardized transition procedure and guidelines at an established keto center. The enteral feeding transition protocol can be shared with other keto centers to improve quality of care. The efficacy results remain comparable to initiating as inpatients.</p>
<p>19. Title: Parent Perceptions of Health-Related Quality of Life Following Ketogenic Diet Therapy for Treatment of Refractory Epilepsy Author: Katie Barwick Co-authors Nicole Murphy, Michael Leveritt Katie Barwick 1, Nicole Murphy 2, Dr Michael Leveritt 3 1 Department of Nutrition & Dietetics, Mater Children’s Hospital, Brisbane Qld, Australia 2,3 School of Public Health, Griffith University Qld, Gold Coast Campus Qld Australia Keywords: Ketogenic, Quality-of-life, Epilepsy, Diet, Perceptions</p> <p>Introduction: Health-related quality of life (HRQoL) measures are widely utilized for evaluating therapies in populations where seizures are resistant to medications. Domains measured in epilepsy-specific HRQoL tools include cognition, behavior, social, relationships, physical and health changes. Children following ketogenic diet (KD) therapies have characteristics that differ from the general epilepsy population meaning these tools are not appropriate to assess HRQoL. This research aimed to explore parental perceptions of 1.change in the HRQoL domains of their child’s life while on the KD, and 2.impacts of the KD treatment on their child’s life and their own life to guide the development of a relevant HRQoL tool.</p> <p>Methods: A qualitative study, using semi-structured telephone interviews with parents, explored the impact on the child and adaptations to the family routine imposed by the KD. Questions were informed by domains from generic and epilepsy-specific HRQoL tools. Thematically analysis produced emerging themes and relationships.</p> <p>Results: Thirteen carers were interviewed (average time on KD 1.5 years). HRQoL-domains perceived as most improved were physical and cognitive. Profound changes reported included enhancements in children’s energy and physical abilities, awareness and focus. Other domains of impact were social, behavioural and emotional. Families had an positive attitude towards the regimented KD and readily adapted. There were no perceived additional negative impacts to the HRQoL-domains posed by the KD.</p> <p>Conclusion: This study demonstrates the potential for improvement within the HRQoL domains for children and families experiencing success on the KD. Detection of this improvement is currently not possible with available HRQoL tools due to concurrent severe cognitive and physical impairments. These findings provide a theoretical base for formulation of a HRQoL tool specific to this population of children and their families.</p>	<p>20. Title MODIFIED ATKINS DIET IN CHILDREN WITH DRUG RESISTANT EPILEPSY IN NORWAY – A PILOT STUDY Author: Kathrine C Haavardsholm Co-authors Merete Lillevand Hem, Magnhild Kverneland, Anette Ramm-Pettersen, Morten Lossius, Knut Risberg Keywords: Modified Atkins diet, ketogenic diet, epilepsy, children, adolescents</p> <p>Abstract Text Background: The modified Atkins diet is an alternative to the traditional ketogenic diet for children and adolescents with epilepsy.</p> <p>Methods: A pilot study was conducted to evaluate the modified Atkins diet as a treatment for drug resistant epilepsy. 21 patients aged 5-18 years were included in an observational study with 6 months follow-up. They were instructed to restrict carbohydrates to 10 grams per day and have a high fat intake.</p> <p>Results: After one month, 15 patients (71 %) were still adhering to the diet. Nine were responders (>50% seizure reduction), and two of these had more than 90 % seizure reduction. Six patients quit treatment before the first follow-up (3 because of difficulties adhering to the diet, 3 due to lack of effect). Seven patients (33 %) were still on the diet after six months, of which five continued the treatment after the project period. Two of these experienced more than 90 % seizure reduction.</p> <p>Conclusion: The modified Atkins diet had a very good effect for the patients who were able to follow the treatment. In the majority a fast response to treatment was noted, with 60 % being classified as responders after 1 month. Our results illustrates that a strict diet is demanding for the patient and the family. Important issues for future applicability of this treatment are identifying patients who can adhere to the diet, as well as identifying individuals that have a high probability for experiencing a positive effect.</p>

21.

Title: Neurocognitive function and psychological profile in Pediatric epilepsy on ketogenic diet

Author: Soyong Eom

Co-authors Hoon-Chul Kang, Joon Soo Lee, Heung Dong Kim

Keywords: neurocognitive function, behavioral problems, parenting stress pediatric epilepsy, ketogenic diet

Purpose: This study investigated the neurocognitive functions, emotional/behavioral problems in children with epilepsy on ketogenic diet(KD), and parenting stress of their parents.

Methods: Neurocognitive and general adaptive function of 14 school age children with pediatric epilepsy(boys=7, girls=7) on KD, aged 6 to 14 years(M=9.43, SD=2.68) were included, at the time of pre-diet and follow up about 13 months on average. Their parents provided the information of behavioral and emotional problems and parenting stress. EEG findings, seizure frequency, seizure duration, and seizure type were evaluated.

Results: The level of neurocognitive and general adaptive function were sustained by similar level at post-KD evaluation compared to pre-KD state. Internalizing and externalizing behavioral problems were reduced, and, especially, thought, attention problems and aggressive behaviors were shown to be reduced among them. Total parenting stress was decreased in all subdomains. The longer duration of KD seemed to improve full scale IQ and verbal IQ in Intelligence, and the decrease of attention problems and aggressive behaviors.

Conclusions: Adequate, well-designed KD program in pediatric epilepsy showed benefits in neurocognitive, psycho-behavioral function and parenting stress.

22.

Title: Ketogenic diet in children with pharmaco-resistant epilepsy

Author: Christiane Elpers

Co-authors Fiedler, Schwartz, Linden, Omran Germany

Keywords: ketogenic diet, pharmaco-resistant epilepsy, efficacy, safety

Some epilepsy syndromes in childhood show a distinct pharmaco-resistance. Possibly in these cases the ketogenic diet [KD] is a therapeutic option. Furthermore KD is first line therapy in children with specific metabolic diseases [e.g. Glut-1-Deficiency]. We present our results of a retrospective study of patients with KD regarding efficacy, safety and adverse events.

Retrospective analysis of 16 patients aged 1 to 19 years [7♀, 9♂] with pharmaco-resistant epilepsy [n = 13] or metabolic disease [n = 3] and initiation of KD between the years 2000 – 2011.

In all patients KD was induced after unsuccessful therapy with at least three antiepileptic drugs. 9 of 16 patients received eight or more antiepileptic drugs before KD was started. After introduction a ketogenic metabolism was achieved in mean after three days. Generally KD was well tolerated, typical adverse events [hypoglycemia, gastrointestinal problems, reduced appetite] occurred only in 4 of 16 patients and no life-threatening metabolic conditions appeared. During KD, 11 of 16 patients showed positive effects regarding mental development and seizure frequency; in one patient a stable disease course was observed. In EEG one patient showed seizure-free period under KD, however 4 of 16 patients had no changes in EEG. After initial improvement of seizure frequency an increase of seizures occurred during follow-up. In our study population this problem was the most frequent cause for completion the KD [8/16].

Based on results of our retrospective study the KD is a safe therapy option for patients with pharmaco-resistant epilepsy in childhood. Further studies are needed to estimate the efficacy of KD towards new antiepileptic drugs.

23.

Title Dietary therapy for Juvenile Myoclonic Epilepsy

Author: Mackenzie Cervenka

Co-authors Bobbie J. Henry, Eric H. Kossoff

Keywords: JME, Ketogenic, Atkins, epilepsy

INTRODUCTION: Juvenile myoclonic epilepsy (JME) is often successfully treated with anticonvulsants; however some cases may be medically resistant. The modified Atkins diet (MAD) has been reported as effective for idiopathic generalized epilepsy (absence) and is increasingly being selected for use in adolescents and adults over the ketogenic diet due to the greater flexibility in its administration. We reviewed our experience in using the MAD for JME.

METHODS: Since 2006, 9 adolescents and adults were started on the MAD for JME at the Johns Hopkins Hospital. Seven patients were followed prospectively and records were retrospectively reviewed for two patients to ascertain efficacy, diet duration, and adverse effects.

RESULTS: Of these 9 patients, 7 (78%) were female, with a mean age of seizure onset of 11 years (range: 6-15 years) and MAD initiation at 24.2 years (range: 15-44 years). Patients had tried a mean of 4.3 anticonvulsants before dietary therapy with the exception of a 15-year-old female who attempted the MAD as first-line therapy. Eight achieved at least moderate ketosis; the mean diet duration to date is 11.2 months (range: 0.5-36 months). After 1 month, 7/9 (78%) had >50% seizure reduction. Side effects included weight loss in 5 patients and a temporary increase in cholesterol in one. Most patients found the MAD difficult to adhere to, with 3 reporting temporarily increased seizures during periods of noncompliance.

CONCLUSIONS: In this limited experience, the modified Atkins diet was efficacious adjunctive therapy for young adults with typically very medically resistant juvenile myoclonic epilepsy, as long as patients remained motivated and compliant. It may be also helpful for patients with juvenile myoclonic epilepsy and comorbid obesity and females who wish to avoid valproate. Prospective clinical trials are warranted.

24.

Title: THE MAGIC OF THE DIET: THE KETOGENIC DIET AT A SINGLE CENTRE DURING 2010-2012

Author Natalie Rowe

Co-authors Michael Cardamone, Erin Beavis, Helen Kepreotes, Anne Connolly, Dr John Lawson

Keywords: seizure frequency, retrospective chart review, Tuberous Sclerosis

The ketogenic diet (KD) is a high fat, adequate protein, low carbohydrate diet to help control seizures in epilepsy. A single centre hospital has been providing the ketogenic diet to patients since the mid 1990s. The objective of this study was to evaluate our patient cohort and review patient outcomes.

Aim: To review a cohort of patients over the past 24 months focusing on the type of ketogenic diet seizure control and seizure cessation.

Methods: This is a retrospective review of patients enrolled in the KD program between 2010 to 2012. We identified the epilepsy syndrome diagnosis of patients enrolled, diet type and seizure frequency. A 2 year program was offered and patients were commenced on either the classical, MCT or the modified atkins diets. We aimed for 4:1 ratio of fat to protein and carbohydrate.

Results: A total of 31 patients were started on the KD since 2010. There were 23 patients on classical diet, 5 patients on MCT diet and 3 patients on MAD diet. The average duration was 17 months. Four patients achieved seizure freedom (13%), of these, the tuberous sclerosis patients (3) all had seizure freedom, 21 patients reported a decrease in seizures (70%) and 6 patients (17%) had ceased the program after 3 months. Cessation of diet was due to either poor seizure control (5), poor compliance (1) and aspiration pneumonia (2).

Conclusion: The ketogenic diet is generally well tolerated in our cohort. Patients with tuberous sclerosis responded well to the ketogenic diet.

25.

Title: TWO YEARS ON KETOGENIC DIET: EFFECT ON SERUM LIPID LEVELS IN CHILDREN WITH EPILEPSY

Author: Emily Samuels

Co-author: Rebecca J. Schultz

Keywords: ketogenic, hyperlipidemia, cholesterol, triglycerides, dyslipidemia

Dyslipidemia is a potential adverse effect of ketogenic diet therapy. Serum lipid levels have been reported to increase after ketogenic diet initiation and may gradually increase or stabilize over the first year of treatment. However, there are limited studies that assess lipid levels after treatment with the ketogenic diet for two years. The purpose of this study is to determine the differences in serum levels of cholesterol, triglycerides, low-density lipoprotein (LDL) and high density lipoprotein (HDL) at baseline, 12 months and 24 months of ketogenic diet therapy. This is a retrospective chart review of serum lipid levels of 15 children (mean age 4.9 years) with refractory epilepsy maintained on the ketogenic diet for two years. Children were fed with either KetoCal® formula, RCF®-based formula, ketogenic foods or combination of ketogenic foods and formula. Serum lipid levels were drawn at baseline, 12 months and 24 months. Data were analyzed using one-way, repeated measures analysis of variance (ANOVA). The Greenhouse-Geisser method was used to adjust degrees of freedom. Demographic characteristics were summarized using descriptive statistics. The mean baseline levels of cholesterol (170.87 ± 38.728) were borderline while mean baseline levels of triglycerides (122.40 ± 81.709), HDL (48 ± 13.232), LDL (100.75 ± 25.680) were in acceptable ranges. There were no significant differences in mean cholesterol, triglyceride, HDL and LDL levels at 12 months and 24 months. These findings suggest that dyslipidemia does not occur in children who are on ketogenic diet therapy for 24 months.

27.

Title: Parents experience of having a child on the Ketogenic diet

Author: Vibeke Stubbings

Keywords: Ketogenic nursing, Lived experience, Contexts of diets Home treatment

International studies indicate that parents responsible for their child's treatment often carry an emotional burden. So far no broader studies seem to have shown the parental perspective of the ketogenic diet (KD). Therefore this study from the Danish Epilepsy Centre proves to elucidate parent's experience of having a child on KD in the homely context. The study is based on a literature research and a semi-structured interview with 3 families. Methodologically the study is based upon Kvaales phenomenological interview theory and was carried out as a part of a Master piece with the purpose of obtaining a deeper introduction to the lived experience on the KD.

Findings: By a phenomenological approach themes like; Social togetherness at mealtimes, Treatment in the home, Want to stop the diet and Context of the surrounding world, appeared. These themes seem to demonstrate emotional implications and one could emphasize that greater nursing attention should be provided during the diet, in order to prevent failure and emotional conflicts in the context of everyday life.

Follow up: As a result, The Danish Epilepsy Centre has now (since 2011) introduced independent nurse consultations prior to the visit at doctors out-patient clinic for the children treated with KD. In this setting, KD nurses are now focused upon, and able to follow up on aspects regarding the lived experience of having a child on KD. This enables the family along with their nurse, to pay early attention towards difficult issues which otherwise might have led to conflicts and tension.

26.

Title: Treatment of Non-Ketotic Hyperglycinemia with ketogenic diet

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Keywords: Non-ketotic, hyperglycinemia, ketogenic, diet

Abstract Text Non-ketotic hyperglycinemia (NKH) is an autosomal recessive disorder of the glycine cleavage system. Patients usually present with severe encephalopathy, seizures and respiratory failure during the first week of life. For surviving children outcome is poor and most patients suffer from pharmaco-resistant epilepsy. In a recent paper, three children with NKH were reported to be successfully treated with a ketogenic diet.

A boy, now 2 years and 4 months of age, was admitted to the hospital three days postnatally with severe encephalopathy and respiratory failure. EEG showed burst-suppression and MRI revealed thalamic cytotoxic edema. The cerebrospinal fluid to plasma glycine ratio was highly elevated and the diagnosis NKH was later confirmed genetically. Treatment was started with ventilatory support, sodium benzoate, dextrometorphan and antiepileptic drugs (AEDs). He could be discharged from the hospital at 2 months of age.

(Despite normalization of plasma glycine using high levels of sodium benzoate) The patient developed severe mental retardation, dystonic cerebral palsy and pharmaco-resistant epilepsy with frequent daily seizures including spasms and tonic seizures. At 23 months of age ketogenic diet was introduced and administered as total enteral nutrition via a nasogastric tube. As a result the seizure frequency declined dramatically. The patient however remains severely encephalopathic.

The hypothesis of an indirect neuroprotective effect of the ketogenic diet as well as the dramatic reduction of seizures using this diet raises the question whether early dietary intervention may preserve brain function and lead to a better outcome.

28.

Title Adverse events from the co-administration of ketogenic diet and valproic acid

Author: Athanasios Evangeliou

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Keyword 1 Ketogenic diet

Keyword 2 Valproic acid

Keyword 3 adverse events

This study reports on co-administration of the ketogenic diet and valproate in four patients and the appearance of undesirable side effects after the increase or decrease of pharmaceutical valproate levels. Specifically, in two patients we saw that higher valproate levels resulted in seizure increase without any change in ketosis. Decreasing the valproate dose achieved effective seizure reduction. In two other patients, removal of valproate treatment resulted in increased ketosis with respective clinical signs. The conversion of the diet from 4:1 to 1:1 and 2,5: 1 respectively resulted in the reduction of ketosis and clinical improvement without repetition of convulsions. Apart from these 4 patients, during last five years 75 others have been on the ketogenic diet without us seeing any interaction between diet and valproic acid.

Conclusion. In the majority of patients, co-administration of valproate and the ketogenic diet appears safe. Despite this, we have to be aware that in a few cases fine tuning is required in order to avoid undesirable effects.

29.

Title: Camp experience of intractable childhood epilepsy with the ketogenic diet

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Co-authors: Min Jung Lee, Hoon-Chul Kang, Joon Soo Lee, Heung Dong Kim 50 Yonsei-ro Seodaemun-gu, Seoul, aa11111 , South Korea

Keyword 1 ketogenic diet Keyword 2 camp Keyword 3 questionnaire survey

Purpose: Since there are lots of limitations on food for children who are continuing the ketogenic diet(KD) therapy, whole meal should be prepared in advance for going out. So lots of things should be considered before leaving their home which leads to reducing the chance of travel. The camp was arranged in order to lighten the burden of parents for meal preparation, and dispel fear of emergency situation.

Method: Total 27 family members of 18 children in the age of 17months to 13years old participated in the camp. On the last day of the camp, 18 questionnaires were distributed and collected. The questionnaire is composed of items regarding satisfaction level of the camp and the KD therapy, most memorable things and things which needs improvement.

Results: Total 18 families participated in the camp and all of them answered to the questionnaire. There were five different programs for parents. In the meantime, play therapy were held for children. The satisfaction levels were (very satisfied, satisfied, moderate, unsatisfied, very unsatisfied, respectively); orientation (55%, 30%, 15%, NA, NA), introduction to the KD therapy (60%, 30%, 10%, NA, NA), talking about the KD therapy with dietitian (60%, 25%, 15%, NA, NA), discussion with doctor (81%, 9%,10%, NA, NA), time for harmony (67%, 24%, 9%, NA, NA), play therapy-1 (62%, 19%, 14%, 5%, NA), play therapy-2 (66%, 24%, 5%, 5%, NA).

For the two days and one night camp, all the KD meal were supplied with same calories and ratio. The mealtime was separated from parents and children for the KD therapy. The KD meals were selected from recently developed menu which rated top preference from the children and the difference of the calories were supplemented with Ketonia.

The satisfaction levels were (very satisfied, satisfied, moderate, unsatisfied, respectively); dinner (62%, 24%, 14%, NA, NA), breakfast (67%, 24%, 9%, NA, NA). We couldn't evaluate the lunch which was last meal just before leaving the camp.

The most memorable items were discussion time for disease with doctor and Q&A time with dietitian. Participants had nice time with sharing information about their experiences and they encouraged each other. They were thankful to the staffs for playing with their kids happily.

There were some opinion that duration of programs and the camp were short. They also wanted to participate in the camp in continuous and periodical manner.

Conclusions: The participants of the camp had helpful time with understanding more about the KD therapy, being relieved from meal preparation, gaining confidence and courage through deep conversation with medical team.

What we learned from the camp were; we should hold the camp in continuous and periodical manner, we should survey the quality of life before and after the camp programs.

30.

Title: The contribution of the nurse practitioner in succeeding the ketogenic diet

Author: Marion van Ool

Co-authors Carly Jansen Netherlands

Keyword 1 ketogenic diet Keyword 2 multidisciplinary Keyword 3 nurse practitioner

To optimise the effect of the ketogenic diet (KD), multidisciplinary treatment is essential (Kossoff et al., 2009). Integration of nursing, dietary and medical care is the specific contribution of the nurse practitioner (NP). These interventions are presumed to have a positive effect on the patient's well-being, the efficacy of patients' self-management and efficacy of the diet. It is therefore that the role of the NP in the dietary treatment can be seen as crucial.

Before the start the NP informs the child/parents about the diet, investigates the competentions, motivation and contra-indications. When on KD, the NP communicates weekly with the patient, provides succeeding information, helps to navigate through the multidisciplinary treatment and educates how to solve problems by implementing protocols and directives. When a patient is having a difficulty the NP will troubleshoot with the patient to determine whether the problem is medical, dietary or nursing. The NP serves as the coordinator and liaison for the clinical nursing team, giving education and directives and evaluating the given care. The patient is seen in a multidisciplinary visit and on indication separately. To improve the commitment of the child/parents the NP uses innovative instruments like cooking classes for children, parents and nurses, a KD website and mobile phone application on which they can find an individualized menu of the day.

The results of this intensified counseling will be assessed in a randomized controlled trial (De kinderen et al., 2011).

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31.

Title: Parental perspective, of the department's learning environment, in relation to their education in managing the children's Ketogenic diet treatment.

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Keywords, Parental perspective, Learning environment, Ketogenic

The Danish epilepsy Centre's core service, in a Danish context, is to diagnose and treat people with difficult to treat epilepsy. This places a great importance on the nursing, in terms of education and training of the majority of the persons, who might benefit from the Ketogenic Diet (KD). According to Illery's theory of learning, the process of learning is a very broad concept.

The KD treatment is a multidisciplinary structured patient process, across the ambulatory and the children's department. The families are admitted to the hospital, when the child is to start on the diet. The diet imposes requirements on the parents and their family. It is the personnel's job to create a learning environment, where the families are being educated in handling these requirements. Currently, no valid user perspective on the parent's experience of this learning environment exists.

In this qualitative nursing study, two mothers have participated in a semi-structured focus group interview, inspired by Kvale. The interviewees represent families, with children treated respectively 6 months and one year.

Findings: This study has exposed the following themes: comprehensive information prior to diet initiation; psychosocial consequences for the family; the importance of the relationship with the personnel. These themes seem to demonstrate implications of the KD and the importance of nursing care.

Follow-up: As a result of this study, the structured patient process will be revised regarding the initiation of the KD. By conducting a further quality studies, the evaluation of these initiatives will be clarified.

32.

Title: Factors influencing the efficacy of ketogenic diet on childhood epilepsy

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Keywords: ketogenic diet, childhood epilepsy, efficacy, age, idiopathic generalised epilepsy

Objective: To investigate the efficacy of the ketogenic diet (KD) treatment of childhood epilepsy and determine which children are more likely to respond.

Methods: We conducted a retrospective study on 48 children who started on the KD between 2009 and 2011. We obtained their starting age, underlying conditions, reported seizure frequencies before and after the diet.

Results: Analysis showed that starting age has influenced efficacy. After 3 months, 18 out of 37 children in age group 0-10 achieved >50% seizure reduction, whereas 1 out of 11 in the 11-16 age group had >50% reduction ($p < 0.05$). The difference is maintained after 24 months and could not be explained by difference in dropout rate or level of ketosis i.e. tolerance of the diet. Severity of epilepsy did not affect the children's response. We separately analysed children with Lennox-Gastaut Syndrome and those with idiopathic generalised epilepsy (IGE). The former showed a similar response to the overall study, whereas 4 out of 5 in the latter group exhibited >90% seizure reduction at 3 months, a result significantly better ($p < 0.01$) than the rest of the children. The IGE group continued to perform much better than the other children up to 24 months.

Conclusions: Children should be started on the diet at the earliest appropriate opportunity; delay may correlate with a poorer prognosis. Severity of epilepsy should not affect patient selection. The better response in the small number of children with IGE suggests further studies into the effect in this population.

33.

Title: USE OF AN ACIDOSIS SPARING KETOGENIC DIET IN A MALE CHILD WITH LISSENCEPHALY-SUBCORTICAL BAND HETEROTOPIA AND REFRACTORY SEIZURES

Author: Alan Yuen
Co-authors Dr Alma Bicknese

Keywords: refractory epilepsy, ketogenic diet, acidosis sparing

Classical ketogenic diet, the modified Atkins diet and other variants generally produce hyperketonemia and a metabolic acidotic state. Acidosis is associated with negative health consequences. As a correlation between the extent of hyperketonemia and clinical efficacy has not been demonstrated, might a ketogenic diet modified to limit ketosis and acidosis be better tolerated and exhibit improved efficacy?

SH is a 30 months old male diagnosed with lissencephaly-subcortical band heterotopia with DCX gene mutation. SH had seizures from birth and his first tonic seizures at 1 month. He has had multiple seizure types including partial, myoclonus and infantile spasms. He was treated with multiple drugs but continued to have seizures. At 8 months old, he was having multiple seizures a day and was started on the classical ketogenic diet. There was no initial change in his seizure frequency, however he became more alert. At 11 months he developed renal stones and Polycitra was started. At 18 months he was still experiencing multiple seizures daily and was transitioned over to an acidosis sparing ketogenic diet, whilst continuing on his antiepileptic drugs. Since then he has experienced a marked reduction in partial seizure frequency and severity. SH also derived other benefits from the diet: significantly less gastro-eosophageal reflux and constipation, and no longer have frequent episodes of intractable crying and head banging. He has also shown significant improvement in visual tracking, can support his head when upright and has even learned to target and activate simple switch toys.

34.

Title: Frequency of diet-related problems in tube-fed and oral-feed patients on Ketogenic Diet

Author: Helle Nielsen Denmark
Co-author: Kathrine May Holmslykke

Keywords: Ketogenic Diet, Tube-feed, Oral-feed

Purpose; To represent results from Ketogenic Diet (KD) treatment in groups of patients who are tube-feed compared with group of oral-feed patients. This by study frequency of hunger, nausea/not eating up, dietbreak and mood.

Methods: Review of week-reports for patients (age 0 to 25 years), starting KD in the period November 1st 2006 to June 1st 2012. Week-reports shows several parameters. "Hunger" (if hungry 30 minutes or more before a meal), "nausea /not eaten up", "dietbreak" and "mood" (rated by number 1-5, 1 is best) are selected, and compared by frequency in the two groups. If patients have dietbreak or nausea/not eaten up its noted.

Hunger and mood is typically estimated by patient's relatives.
Patients receiving KD in a combination of tube- and oral-feed is withdrawn.

Results: 94 patients treated with KD. 29 patients tube-feed, 28 patients oral-feed. 39 patients feed in a combination and are excluded. Duration of treatment is 3 to 182 weeks. Received week-reports 2369 (73.78%). Oral-feed: received week-report 813 (72.09%). Frequency of hunger: 803 (0.96/week). Nausea/not eaten up: 1382 (1.70/week). Dietbreak: 197 (0.24 /week). Mood: average 2.15 /week. Tube-feed: received week-report 1556 (75.46%). Frequency of hunger: 423 (0,27 /week). Nausea/not eaten up: 776 (0,5 /week). Dietbreak: 187 (0.12 /week). Mood: average 2.40 /week

Discussion: Received week-report seems similar in the two groups. Incidence of hunger and nausea/not eaten up is more than 3 times as often in oral-feed group. Dietbreak occurs twice as often in oral-feed group. The oral-feed group gets better mood-rate in average.

35.

Title: PARTNERING WITH PARENTS; A RECIPE FOR SUCCESS

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Keywords: collaboration, parents, hospitals, education

Keto families are bonded by the common goal of seizure freedom and optimal quality of life. These families are also a neglected resource that can fill the gap between hospital and home management.

At the Children's Hospital of Philadelphia, we have a full day educational program on the ketogenic diet before families commit to this effective but demanding treatment. Initially, we approached parents to take an adjunctive role supporting the professional lectures. However, the enthusiastic response was so overwhelming that it quickly became apparent that parent presenters were more important, effective and convincing than staff. Telling their personal stories translated science to actual practice. Trials, tribulations, successes and achievements allowed prospective parents to better appreciate living with the diet. Evaluations frequently commented on instant connection with peers who fully understood their journey of hope.

It was not long before family involvement took on a life of its own as parents began requesting involvement in family-to-family support projects. Suddenly we had a keto webpage and a newsletter highlighting favorite recipes with a parent/child corner. Peer mentors now visit during admission for diet initiation. Many bring care packages at their own expense; from small plastic bowls with secure lids to small rubber spatulas, toothpaste and sweetener. Some bring flowers and gifts.

Collaborative partnership with parents builds trusting relationships, is a win-win situation for families and is an inspiration for the entire medical community.

36.

Title: Hypoglycemia is common during non-fasting ketogenic diet initiation

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Keywords, ketogenic diet initiation, hypoglycemia, ketosis, oral feed tube feed

Introduction: Surveillance laboratory testing is recommended for safe ketogenic diet treatment. Understanding the incidence of clinically significant laboratory values and the timing of their occurrence is essential to refine clinical practice. We aimed to quantify the risk of hypoglycemia during gradual ketogenic diet initiation (without fasting), and to determine whether there was a difference in risk among children who receive tube feeds, compared with those who eat orally.

Methods: We retrospectively reviewed the trajectory of serum glucose and beta-hydroxybutyrate levels among tube fed and orally fed patients initiating treatment with the ketogenic diet to quantify and compare the risk for hypoglycemia among the two groups.

Results: Thirty-seven patients were admitted for gradual initiation of the ketogenic diet over a three year period (n=24 male). The majority had generalized epilepsy syndromes (n=23, 62%) or infantile spasms (n=8, 22%). All but two had been prescribed multiple antiepileptic medications prior to diet initiation (median= 4). Most were oral feeders (n=26, 70%). Hypoglycemia (serum glucose <50mg/dL) occurred in 10 patients (27%), half within the first 24 hours of initiation. Hypoglycemia did not vary significantly between patients fed orally or by gastrostomy tube (p=0.26, Fisher's exact). Ketosis (serum beta-hydroxybutyrate >1.5mMOL/L) was achieved on average within 2 days of diet initiation, with no difference between those with and without hypoglycemia.

Conclusion: During inpatient non-fasting initiation of the ketogenic diet for treatment-resistant epilepsy, the risk of hypoglycemia is significant, regardless of route of feed. Serum glucose should be monitored regularly, beginning the day of initiation.

37.

Title: CHARACTERIZATION OF LIPID PROFILE AND NUTRITIONAL STATUS OF PATIENTS WITH REFRACTORY EPILEPSY IN A REFERENCE CENTER IN BRAZIL

Author: Patricia Azevedo de Lima

Co-authors Leticia Pereira de Brito Sampaio, Daniela Murakami, Mariana Baldini Prudêncio, Nágila Raquel Teixeira Damasceno, Brazil

Keywords: refractory epilepsy, status nutricional, lipid profile

The aim of study was to characterize the lipid profile and nutritional status of children and adolescents with refractory epilepsy that will be part of a ketogenic diet program. It was measured weight, height, subscapular and triceps skinfolds and fat mass and lean mass by bioimpedance. Biochemical profile included analysis of total cholesterol (CT), LDL, HDL, and triglycerides in patients screened. The types of seizures were evaluated and classified by structured questions. The program included seven patients, 5 children and 2 adolescents. The mean age and standard deviation (SD) was 7.5 years (4.4). The types of seizures observed were myoclonic atonic, myoclonic tonic, tonic, focal seizures with altered consciousness and seizures is not sorted.

According to BMI, 42.85% of the patients were normal, 42.85% with risk of overweight or overweight and 14.3% had severe obesity (WHO 2006, 2007). The sum of skinfolds showed that 57.14 % of the patients are p50-85 and 28.57% are above p95. The average lean mass and fat mass in children and adolescents was 80.24 % (11.36), 19.76% (11.36); 65.85% (0.07), 34.15% (0.07), respectively. Mean values of lipid profile were CT 153 mg/dL (20), LDL 81 mg/dL (7), HDL 53 mg/dL (12), VLDL 11 mg/dL (4), TG 57 mg/dL (22).

The results showed that the CT is above desirable levels for children and adolescents and that most children and adolescents present risk of overweight or obese. The values of fat mass and lean mass can be considered within the normal standard for age.

38.

Title: Correction of acidosis in an enterally fed child receiving a ketogenic blenderized formula in combination with zonisamide

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1.Private RN, BSN 2. Consultant Nutritionist 3. Consultant Nutritionist

Key Words: Acidosis, Buffering, Bicarbonate, Baking soda, Potassium

Case Report: We report on an 11 year old female with a novel chromosomal abnormality, diffuse encephalopathy, sensorimotor and communication difficulties, and medication resistant seizures. Medical history includes one severe episode of rash and eosinophilia secondary to Lamictal intolerance. Nutritional history includes 100% nutritional intake via gastric feedings and multiple food allergies including dairy products and soy. Ketogenic diet was added to the regimen of zonisamide therapy.

Method: A ketogenic diet of blenderized meat, vegetables and oils was implemented while maintaining 12mg/kg of zonisamide. The diet ratio was increased from 3.5:1 to 4:1 in efforts to improve ketosis and seizure control. Seizures were absent for 2 days after 4:1 ratio initiation, but increased over baseline in number and intensity on day 3 of the diet.

Symptoms of acidosis developed with lethargy, complaints of hunger, tachypnea, and Kussmaul respirations. Serum electrolytes revealed initial CO2 levels consistently below 20mEq/L. Bicarbonate therapy was initiated using baking soda (2mEq/kg) diluted in water, administered between feedings 5 times daily. An additional buffer of potassium chloride salt (30% of Dietary Reference Intake for potassium) was added to the formula.

Results: Respiratory rate and energy level improved dramatically within minutes of receiving each dose of bicarbonate but deteriorated in 3 hours. Three subsequent increases in bicarbonate, with a final dose of 5mEq/kg were necessary to improve CO2 to greater than 20mEq/L which alleviated symptoms of acidosis. Potassium levels remained normal throughout. Zonisamide therapy was tapered during this process resulting in improved seizure control after each reduction. Bicarbonate was reduced and hopefully not be necessary after discontinuation of zonisamide.

Conclusion: Bicarbonate therapy with the use of baking soda (bicarbonate) in combination with potassium chloride (Morton Lite Salt) is a carbohydrate-free and effective buffering therapy for ketogenic diet related acidosis.

39.

Title: Two adult case reports of improved neurological status with the removal of gluten from diet

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1. Dietitian, Matthews Friends Clinics 2. Nutrition Consultant

Key words: 1. Gluten-free 2. Gluten sensitivity 3. Epilepsy 4. Neurological dysfunction

Introduction: Gluten sensitivity is a systemic autoimmune or immune mediated disease with diverse manifestations¹. Coeliac disease (CD) is the most commonly recognized of these and estimated to occur in at least 1% of the population. There has been conflicting data provided by studies of the association between epilepsy and coeliac disease. However, a recent review concluded with the recommendation that routine screening for CD be performed on all patients with intractable epilepsy, particularly those with temporal lobe epilepsy and hippocampal sclerosis^{2,3}. We present two adult cases of intractable epilepsy where gluten exclusion has led to an improvement in seizures and/ or neurological symptoms. Ketogenic diet regimes are readily gluten free and this may carry more significance, particularly in the management of adult cases of intractable epilepsy, than previously thought.

Case 1: A 62 year old female with a long standing history of gastro-intestinal disturbance and a 7 year history of intractable temporal lobe epilepsy with hippocampal sclerosis (negative TTG and jejunal biopsy) was started on a strict gluten free diet trial prior to consideration of ketogenic therapy. Within three months, the absence seizures resolved and this has now been maintained for sixteen months. Infrequent seizure incidences have been traced back to accidental exposure to gluten and generally occur within one to two hours of eating.

Case 2: A 47 year old female with medication resistant epilepsy was initiated on a modified ketogenic diet restricted to 30 grams of carbohydrate daily resulting in strong ketosis. Her tonic-clonic seizures reduced to greater than 50% after 3 months and she was able to return to activities of daily living. In attempts to improve the selection of carbohydrate in her diet, gluten-containing foods were removed (breads and cereals) and were replaced with equivalent carbohydrate from vegetables. Her husband noticed a dramatic improvement in her cognition and balance however no change in seizure-control. The gluten-free diet restriction was maintained due to these neurological benefits.

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M Hadjivassiliou, D Sanders, R Grünewald, et al.

40.

Title: Classic ketogenic diet: comparison study between paediatric patients with or without gastric tube feeding

Author: Maria Vaccarezza
Co-authors: Alejandra Gonzalez, Clarisa Maxit, Delfina Marchione, Guillermo Agosta

Keywords: classic ketogenic diet, hypokalemia, tube feeding

Objective: To evaluate the efficacy and complications of the classic ketogenic diet in a group of patients with a diagnosis of refractory epilepsy.

Design: Retrospective comparison cohort study.

Method: A retrospective review of clinical charts was performed in patients with the classic ketogenic diet treatment followed in our institution between the years 2006 and 2011. The patients were divided into two groups: those fed by gastric tube (group I) and those with no gastric tube feeding (group II). Efficacy, follow through and adverse effects were compared in both groups, six months after the diet was initiated. Results: Forty-seven patients were analyzed (18 patients in group I and 29 in group II). No significant difference was observed in treatment efficacy or follow through. Over 50% seizure control was achieved in more than 70% of both populations. Some complications were seen in more than 80% of the patients in both groups, most of them mild. Hypokalemia was statistically significant and was found in 77.7% of the patients within group I ($p < 0.0001$, RR 6.78).

Conclusion: There were no significant differences between patients with or without gastric tube feeding in our series in terms of efficacy or follow through with the classic ketogenic diet, in comparison to previously reported studies. Hypokalemia, noticed in patients fed with gastric tube is outlined as a statistically significant finding, which must be considered in managing this particular group of patients.

41.

Title: DEVELOPMENT AND MANAGEMENT OF A TEAM-BASED KETOGENIC DIET PROGRAM

Author: Emily Danna
Co-authors Bridget Stone, Michelle Oliva, Liu Lin Thio

Keywords: ketogenic ,children, families, teach, team

BACKGROUND: The Ketogenic Diet has gained popularity in the treatment of pediatric epilepsy. To be effective, this diet requires significant education and training prior to initiation along with committed, compliant families. Training on the diet, its intricacies and challenges can be overwhelming to both medical providers and caregivers. Current SLCH ketogenic families encouraged our team to develop a more formalized, team-based ketogenic diet initiation process to better prepare families for the diet.

OBJECTIVE: Determine efficacy and benefits of classroom-based educational programming prior to ketogenic diet initiation.

METHODS: Potential candidates for the diet were referred to the Ketogenic Diet Class. A physician, dietitian, pharmacist, and nurse provided comprehensive classroom-based education. This course reviewed eligibility, side effects, medication management, hospitalization expectations, diet / lifestyle considerations and defined ketogenic diet differences. After attending class, families were eligible to move forward with ketogenic clinic and diet initiation. We assessed the efficacy of this classroom-based education via two surveys: one provided at the conclusion of class (n=26) and another following diet initiation (n=10).

RESULTS: Most families (90%) confirmed a better understanding of the diet upon initiation after attending this class. Families reported they were less overwhelmed (90%) and were well prepared for changes and requirements associated with diet initiation. The most beneficial aspects of the class were identified as hearing from a ketogenic diet parent, reviewing what to expect during hospitalization and the open question & answer session.

CONCLUSION: Classroom-based, multidisciplinary education benefits families with children being initiated on the ketogenic diet.

42.

Title: Follow up on children previously treated with classical ketogenic diet, with at least 50% seizure reduction.

Author: Miranda MJ
Coauthors: Nielsen H; Povlsen JH; Stubbings V
Danish Epilepsy Centre (all) & Herlev University Hospital, Copenhagen University, Denmark (MJM).

Purpose: The Ketogenic diet is an established treatment for severe medically intractable epilepsy in children; 50% of children achieve $\geq 50\%$ seizure reduction. The purpose of this study is a follow-up on children previously treated with KD and considered responders ($\geq 50\%$ seizure reduction at 6 months)

Methods: 21 patients with a median current age of 9 years (24- 4 years), who were considered responders to the ketogenic diet between November 2005- Marts 2009, and who has been off the diet at least 1 year, were invited to complete a questionnaire. All 21 participated.

Results: 9/21 (43%) of children are actually seizure-free and 15/21 (71%) mean their children's epilepsy is the same or better now as compared with the time they were on diet. 17/ 21 (81%) would have wished- and said yes to the diet earlier, if they had been offered it. However, only 7/21 (33%) would say yes to the diet now. 18/21 (86%) would recommend the diet to others. Regarding side effects, 2/21 (9%) has had kidney stones and 3/21 (14%) has had one bone fracture. None has had cardio-circulatory problems. 6/21 (28%) complains of tiredness.

Conclusion: Despite the small numbers, our study shows that children who responded to the ketogenic diet, continue doing well after the diet is discontinued, regarding their epilepsy (43% seizure-free, 71% improved) and without experiencing severe health problems.

43. Basic Science

Title: INTRAGASTRIC KETONE ESTER ADMINISTRATION PREVENTS CENTRAL NERVOUS SYSTEM OXYGEN TOXICITY VIA TIDAL VOLUME AND RESPIRATORY FREQUENCY MODULATION IN RATS

Author: Raffaele Pilla Tampa, FL33617

Co-authors Dominic P. D'Agostino, Carol S. Landon, Jay B. Dean

Keywords: Ketone Ester, Respiration, Respiratory Frequency, Tidal Volume Radio Telemetry

In clinical and military procedures, hyperbaric oxygen (HBO2) can lead to central nervous system oxygen toxicity (seizures) via CO2-chemoreceptors stimulation and hyperventilation. In a previous study, we demonstrated that the intragastric administration of ketone ester (KE), a non-ionized ketone bodies precursor, has a prominent anti-seizure effect. In this follow-up study, we test the anticonvulsant properties of multiple KEs, and their effects on respiration. 60 male rats were surgically implanted with radio-telemetry devices in order to record electroencephalogram, diaphragmatic electromyogram (dEMG) and electrocardiogram. Rats were orally administered with four KEs: beta hydroxybutyrate, R,S-1,3-butanediol, acetoacetate monoester (AcAc), and acetoacetate diester (AcAc2). 30 min later, rats were exposed to HBO2 at 5 atmosphere absolute, until the onset of neurological and behavioral convulsions, and the latency to seizure (LS) was calculated. Our results! showed that: a) AcAc2 was found to be the most potent anticonvulsant ester, as it increased the LS of 574%, compared to controls; b) HBO2 significantly increased dEMG, that peaked <2-8 min before seizures; c) AcAc and AcAc2 administration caused a significant increase in tidal volume (VT) and d) stabilized the respiratory frequency (fresp) in a period comprised between 15 min before and after seizure, compared to controls. In summary, we report that HBO2 affects neural plasticity and respiration patterns (\uparrow dEMG before seizures), that ketone esters (notably AcAc and AcAc2) increase the animals' resistance to seizures, and that the resulting effect on the ventilatory response (VT and fresp) may occur via CO2-chemosensitive neurons in the solitary complex, a cardio-respiratory integration center.

44. Basic Science

Title NEUROMETABOLIC PHOSPHOLIPID INTERVENTION FOR NEUROLOGICAL DISEASE

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Keywords: Phosphatidylcholine, Specific Ratio 3 (SR3) oil, Butyrate, Peroxisome, Cardiolipin

Accumulating evidence suggests that even subtle perturbations in the lipid content of neurons and myelin can disrupt their function. The membrane and organelles within the cell are the primary focus of electrical discharge within the central nervous system and may be stabilized with phospholipid therapy and a Phospholipase A2 (PLA2) suppressive diet. Dietary intervention includes a balanced essential fatty acid and phospholipid nutrient dense diet with low carbohydrate and moderate protein. Recent research has revealed that in the brain myelin acts as one enormous mitochondrion. Stabilization of myelin, neuropilids, and mitochondria may be achieved with lipid support of the phospholipid cardiolipin, located exclusively in the inner membrane of mitochondria and myelin. Cardiolipin may serve as a primary consideration as a therapeutic target in seizure disorders. Examination of red cell lipids at Johns Hopkins Peroxisomal Diseases Laboratory in subjects with epilepsy and other neurological diseases has revealed a characteristic accumulation of very long chain fatty acids (VLCFAs) revealing cell membrane derangement per disturbance in peroxisomal respiration, interrupting cell membrane integrity and function. In our current study we have captured visual images of distorted phospholipid membranes and have linked the impact of the DNA adducts (toxins) altering gene expression to aberrations in lipid metabolism, cellular dysfunction and alteration of the structure of phospholipids in the cell membrane characteristic to the presenting diagnosis and symptoms. We have documented significant clinical neurological improvement in our patients, including cessation of seizures, along with marked normalization of cellular architecture and function following six months of a targeted phospholipid dietary regime.

45. Basic Science

Title DECANOIC ACID MAY MIMIC AND SUBSTITUTE FOR THE MITOCHONDRIAL PROLIFERATING EFFECT OF THE KETOGENIC DIET

Author: Sean David Hughes

Co-authors Simon Eaton, Glenn Anderson, Marta Kanabus, Trisha Rutherford, Maura O'Donnell, Shamima Rahman, Helen Cross, Simon Heales

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Keywords: Ketogenic Diet, Fatty Acid

Objective: The ketogenic diet (KD) is complex to implement and presents a challenge for patients and their families. Currently, the mechanism whereby the diet exerts its beneficial effects is not known. However, there is a growing body of evidence to implicate enhanced mitochondrial function as a potential mechanism. Since there appears to be little correlation between ketosis and seizure control, other factors are likely to be responsible for the efficacy of the diet. In this study we have evaluated the effect of medium chain fatty acids (octanoic [C8] and decanoic [C10] acid) on mitochondrial function.

Methods: SH-SY5Y neuroblastoma cells and human fibroblasts were exposed to 250 μ mol/L C8 or C10 for 6 days. Mitochondrial enrichment was assessed by determination of citrate synthase activity and electron microscopy (EM). Respiratory chain complex I activity was also measured.

Results: When normalised to protein, C10, but not C8, exposure resulted in a 30% increase ($p < 0.01$) in citrate synthase activity in the SH-SY5Y cells; a comparable increase was also observed in fibroblasts. For the SH-SY5Y cells exposed to C10, EM revealed a two-fold ($p < 0.05$) increase in the number of mitochondria per cell. Also normalised to protein, complex I activity was significantly ($p < 0.01$) increased by 42% in the C10-treated SHSY5Y cells.

Conclusions: C10 may stimulate mitochondrial biogenesis and enhance mitochondrial function. This may provide insight into the mechanism by which the KD induces mitochondrial proliferation and acts as an anticonvulsant.

46. Basic Science

Title: Ketone esters induce sustained ketosis and delay central nervous system oxygen toxicity seizures in rats

Author: Dominic D'Agostino Tampa, FL 33617

Co-authors: Dominic P. D'Agostino, Raffaele Pilla, Heather E. Held, Michelle Puchowicz, Henri Brunengraber, Csilla Ari. Patrick Arnold, Jay Dean

Keywords: seizures, ketone ester, ketogenic diet, oxygen toxicity neuroprotection

Central nervous system oxygen toxicity (CNS-OT) seizures occur with little or no warning, and no effective mitigation strategy has been identified. Ketogenic diets elevate blood ketones and have successfully treated drug-resistant epilepsy. We hypothesized that a ketone ester (KE) given orally as a non-ionized precursor of acetoacetate, would delay seizures in rats breathing hyperbaric oxygen (HBO2) at 5 atmospheres absolute (ATA). Adult male rats ($n = 60$) were implanted with radio-telemetry units to measure diaphragmatic electromyogram (dEMG), electrocardiogram (ECG), electroencephalogram (EEG), core body temperature and physical activity. Rats were administered a single dose (3 ml) via oral gavage of KE, R,S-1,3-butanediol (BD) or water before being pressurized to 5 ATA O2. Latency to seizure (LS) was measured from the time maximum HBO2 was reached until the onset of increased EEG activity and tonic-clonic contractions. Blood was drawn from rats and levels of glucose, pH, pO2, pCO2, β -hydroxybutyrate (BHB), acetoacetate (AcAc) and acetone were analyzed. KE caused a rapid and sustained (>4 h) elevation of BHB (>3 mM) and AcAc (>3 mM), which exceeded values reported with a ketogenic diet or starvation. KE increased LS by $574 \pm 116\%$ compared to control (water), and was due to the effect of AcAc and acetone, but not BHB. BD produced ketosis in rats by elevating BHB (>5mM), but did not increase LS. In conclusion, KEs produced sustained ketosis and significantly delayed CNS-OT by elevating AcAc and acetone. KEs represent a promising mitigation strategy against CNS-OT and seizure disorders, especially drug-resistant seizures.

47. Basic Science

Title KETOGENIC DIET IMPROVES MOTOR PERFORMANCE BUT NOT COGNITION IN TWO MOUSE MODELS OF ALZHEIMER'S DISEASE

Author: Milene Lara Brownlow

Co-authors Leif Benner, Dominic D'Agostino, Aurelie Joly-Amado, Marcia Gordon, Dave Morgan

Keywords: Alzheimer's Disease, Ketogenic Diet, amyloid, tau

Abstract Text Dietary manipulations are increasingly viewed as possible approaches to treating neurodegenerative diseases. Recent studies suggest that Alzheimer's disease (AD) patients present brain hypometabolism and mitochondrial deficits. Ketogenic diets (KD) have been suggested to bypass these metabolic deficits by providing ketone bodies as an alternative fuel. We investigated the effects of a ketogenic diet on two AD mouse models. Five months old APP/PS1 and Tg4510 mice were kept on either a KD or a control (NIH-31) diet for 3 months and then submitted to behavioral testing. Body weight and food intake were monitored and blood was collected for ketone and glucose assessments. Both APP/PS1 and Tg4510 mice weigh less than nontransgenic mice despite elevated food intake. The ketogenic diet didn't affect these differences. We found that both models presented hyperactivity, measured by open field and the y-maze tests, compared to nontransgenic controls and this effect was not prevented by KD. Mice kept on KD performed significantly better on an endurance trial in the rotarod compared to the control diet independent of genotype. Only a genotype effect was observed in the radial arm water maze test with no significant differences between diets. Tissue was collected at the end of behavioral testing and analysis of amyloid, tau and microglial markers were performed. No significant differences between diets were observed. These initial data suggest that the metabolic rate of the transgenic mice is considerably greater than the nontransgenic mice. Additionally, the ketogenic diet may play an important role in enhancing motor performance in mice.

48. Basic Science

Title INFLUENCE OF DIETARY INTAKE ON PLASMA METABOLITES IN MICE

Author: Joshua Meidenbauer Boston College, MA

Co-authors: Nathan Ta, Thomas N. Seyfried

Keywords: Calorie restriction, Ketogenic diet, Fish oil, Glucose, Ketones

Abstract Text Dietary therapy, which includes calorie restriction, ketogenic diets, and diets high in omega-3 fatty acids, has been used to improve health and to treat a variety of neurological and non-neurological diseases, including cancer. It is not clear if the therapeutic effects of these diets arise from their composition or from the amount of calories consumed. We evaluated the influence of a standard mouse chow diet (SD), a lard-based ketogenic diet (KD), and a standard mouse chow diet supplemented with fish oil (FO) on circulating energy metabolites (glucose and beta-hydroxybutyrate) and lipids in C57JBL/6 mice over a period of 30 days. Each diet was administered in either unrestricted (UR) or restricted amounts (R) to reduce bodyweight by 20% (n = 4 mice/group). The KD-UR increased glucose, beta-hydroxybutyrate, triglycerides, and cholesterol compared to SD-UR. The FO-UR diet increased beta-hydroxybutyrate while decreasing glucose and triglyceride levels. When given in restricted amounts, all three diets yielded a similar plasma metabolite profile, which included decreased glucose and triglycerides along with increased beta-hydroxybutyrate compared to SD-UR. We also performed linear regression analysis to analyze the predictors of bodyweight, glucose, beta-hydroxybutyrate, triglyceride, and cholesterol levels. We found 1) circulating glucose strongly predicted bodyweight (R² = 0.850) and triglyceride levels (R² = 0.883); 2) Calorie intake moderately predicted glucose levels (R² = 0.500), but strongly predicted beta-hydroxybutyrate levels (R² = 0.771); 3) Dietary fat intake strongly predicted total cholesterol levels (R² = 0.701). These findings have implications for the role of diet therapy for disease states.

This work was supported by grants from the NIH, AICR, and Boston College Research Expense Fund.

49. Basic Science

Title: TRIHEPTANOIN COUNTERACTS CHANGES IN CITRIC ACID CYCLE METABOLITE LEVELS IN AN EXPERIMENTAL EPILEPSY MODEL

Author: Karin Borges Australia

Co-authors: Tanya McDonald, Mussie Ghezu Hadera, Olav Smeland, Ursula Sonnewald

Keyword 1 citric acid cycle

Keyword 2 glutamate

Keyword 3 pyruvate dehydrogenation

We compared the brain levels of citric acid cycle (CAC) metabolites in the chronic pilocarpine epilepsy mouse model treated with anticonvulsant triheptanoin (Neurobiol Dis 40: 555f). After pilocarpine-induced status epilepticus (SE) CD1 mice were fed standard diet or 35% triheptanoin (caloric value) for 3 weeks. [1,2-13C]glucose (i.p) was administered before 5KW microwave irradiation of the head. Cortex and hippocampal metabolites were quantified through HPLC and CNMR and compared using One-Way ANOVA and Bonferroni tests (n=9-10 mice per group). SE mice fed standard diet showed reduced hippocampal levels of glutathione (by 20%), glutamate (28%) and alanine (35%) and increased levels of lysine (20%) and threonine (21%) compared to mice without SE, consistent with reduced CAC activity (p<0.05-0.001). Triheptanoin feeding attenuated the changes in glutathione, lysine and threonine levels. Cortical [4,5-13C] glutamate (37%) and [3,4-13C] aspartate (39%) concentrations, markers of pyruvate dehydrogenation and subsequent CAC activity, were reduced in SE mice on the control diet (p<0.05-0.01), but not those on triheptanoin. These results suggest the pyruvate dehydrogenation pathway is deficient in chronically epileptic mice, resulting in suboptimal NAD reduction and subsequently ATP synthesis. Triheptanoin improved the activity of this pathway, which is likely to underlie its anticonvulsant activity in mice.

50. Basic Science

Title: Leucine: an amino acid that protects against seizures in mice

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Co-authors: P. Santos, J.M. Hardwick

Key words: Leucine, Amino acid, Anticonvulsant

Rationale. One underutilized option for patients whose seizures are not controlled by medicines is metabolism-based therapy. The most widely recognized form of metabolism-based therapy is the high-fat, low-carbohydrate ketogenic diet, which for logistical reasons, is used only in a few centers worldwide. Treatments with similar effects that are more easily implemented could be used in more centers. Leucine is a ketogenic amino acid but it is unknown whether leucine has an anticonvulsant mechanism similar to the ketogenic diet. We investigated the anticonvulsant effects of leucine using acute seizure tests in normal mice.

Methods. Cohort #1: NIH Swiss mice aged 3 weeks received leucine via drinking water (1.5% w/v) for 12 days (control mice received water without leucine). Seizures were induced using a panel of acute seizure tests. Blood ketones were measured prior to seizure testing. Cohort #2: mice aged 5 weeks were injected intraperitoneally with leucine (300 mg/kg in PBS) either 3 hours before or 15 minutes after kainic acid injection.

Results. Cohort #1: leucine-treated mice were protected against 6 Hz-induced seizures (P=0.02). In the pentylentetrazol test, leucine-treated mice had a prolonged latency to first tail twitch (P=0.04). In the kainic acid test, leucine-treated mice had lower overall seizure scores (P=0.0009). Blood ketone levels were similar between leucine-treated and control mice. Cohort #2: mice treated with leucine 3 hours prior to kainic acid had significantly lower overall seizure scores (P<0.0001) and a shorter duration of convulsions (P=0.003). Mice treated with leucine 15 min after kainic acid treatment had lower maximum seizure scores (P=0.01).

Conclusions: Leucine is protective in acute seizure tests with a profile that is distinct from current anticonvulsants and the ketogenic diet. Anticonvulsant effects could not be attributed to differences in blood ketone levels.

51. Basic Science

Title: DISSOCIATION OF THERMAL HYPOALGESIA, KETOSIS, AND HYPOGLYCEMIA WITH TWO KETOGENIC DIETS IN RATS

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Keyword 1 pain
Keyword 2 analgesia
Keyword 3 glucose
Keyword 4 ketones
Keyword 5 time course

Abstract Text Ketogenic diets are high-fat, low-carbohydrate formulations highly effective in treating epilepsy; we demonstrated lower sensitivity to thermal pain in rats fed a ketogenic diet (Ruskin et al. 2009, PLoS One). Regarding anticonvulsant and hypoalgesic mechanisms, theories are divided regarding the importance of direct effects of elevated blood ketones (ketosis) and/or mild hypoglycemia, metabolic hallmarks of these diets. To characterize the relationship between thermal hypoalgesia, ketones and hypoglycemia, we quantified the time courses of ketogenic diet-induced hypoalgesia, ketosis, and hypoglycemia. Recently-weaned rats were fed ad libitum normal chow or one of two ketogenic diets: with either a 6.8:1 ratio of fat:(protein+carbohydrate) or a more moderate 3.1:1 ratio. The 6.8:1 diet produced ketosis and mild hypoglycemia significantly and maximally after 2 days of feeding, whereas thermal hypoalgesia was not found before 10 days of feeding. Thus, the hypoalgesic effect of this diet was delayed by several days compared to ketosis and hypoglycemia. Hypoalgesia was absent one day after return to control chow. Feeding the 3.1:1 diet for 2 or 10 weeks also produced significant hypoalgesia, but at 10 weeks hypoglycemia was no longer present. Thus, ketogenic diet-related hypoalgesia can occur in the absence of hypoglycemia. These findings demonstrate a consistent hypoalgesic effect of ketogenic diets, dissociate changes in thermal nociception from direct actions of elevated ketones or reduced glucose, and suggest mechanisms with a slow onset in this paradigm. These data provide further support that metabolic approaches can relieve pain.

52.

Title A PET AND MRI APPROACH TO STUDY BRAIN GLUCOSE AND KETONE METABOLISM DURING AGING AND ALZHEIMER'S DISEASE.

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Key words: PET, ketone, Alzheimer's

Background: Lower brain glucose uptake can be present before the onset of aging-associated cognitive deterioration and may increase the risk of Alzheimer's disease (AD). Ketones are the brain's main alternative energy substrates to glucose. We have developed the positron emission tomography (PET) tracer – [11C]-acetoacetate ([11C]-AcAc) – to study brain ketone metabolism in humans. Our goal was to assess whether deteriorating brain fuel uptake affects uptake of any brain fuel or is specific to glucose. This approach might also be informative about how ketogenic treatments improve cognition in AD and mild cognitive impairment.

Methods: Healthy elderly (65-85 y; n=15) and young adults (18-30 y; n=15), and 8 patients with mild AD underwent a dual tracer brain PET protocol with [11C]-AcAc followed by [18F]-FDG. Cerebral metabolic rates of AcAc (CMR_{AcAc}) and glucose (CMR_g) were calculated using an image-derived input function with correction for brain atrophy.

Results: Compared to young adults, CMR_{AcAc} in the healthy elderly was 20-25% lower in specific brain regions, notably the superior frontal cortex and cingulate (p<0.01); CMR_g in the elderly was also 15-20% lower in the caudate, thalamus and frontal cortex (p<0.01). Different brain regions had lower CMR_g and CMR_{AcAc} in AD than in the elderly.

Conclusion: Both major brain fuels are affected in aging and in AD but differently depending on the brain regions. We are developing protocols with ketogenic pharmaceuticals/nutraceuticals in order to sustainably induce mild ketonemia to determine whether it can correct or bypass deteriorating brain glucose uptake, thereby hopefully reducing the risk of cognitive decline. Financial support from CRC, CIHR, CFI, FRQS, CFQCU and the Université de Sherbrooke.

53. Basic Science

Title: ADJUVANT USE OF THE KETOGENIC DIET FOR THE TREATMENT OF MALIGNANT BRAIN TUMORS INHIBITS CYCLOOXYGENASE-2 EXPRESSION AND REDUCES TUMOR-ASSOCIATED EDEMA

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Keywords: glioma, edema, cyclooxygenase 2, mouse model

Malignant gliomas are uniformly fatal despite treatment including surgery, chemotherapy and radiation. One source of morbidity is brain edema caused by tumor growth and/or treatment. This can have a variety of sequelae including headaches, seizures and steroid dependence. We previously used a bioluminescent intracranial mouse model of malignant glioma to demonstrate that a ketogenic diet (KD) extends survival following tumor implantation, and potentiates the therapeutic effects of radiation and chemotherapy. The KD also prevents the increased expression of Cyclooxygenase 2 (COX2) seen in tumors from animals fed standard rodent chow (SD). COX2 is a mediator of inflammation and we hypothesize that KD is reducing tumor-associated edema through its inhibition and concomitant downstream effects. Bioluminescence is a quantitative measure of live tumor cells and we have found that animals maintained on KD have more tumor-associated bioluminescence when they succumb! to their disease than do animals maintained on SD. Survival is a function of overall tumor burden consisting of the tumor and peritumoral edema. The increased bioluminescence in tumor from animals fed KD suggests that the diet may be reducing the contribution of peritumoral edema to the overall tumor burden. Taken together, our data demonstrates that metabolic alteration not only affects tumor bioenergetics, it alters the expression of genes involved in other aspects of tumor growth and therapy response. The adjuvant use of KD for brain tumor therapy may improve the patients' quality of life in addition to extending survival.

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