BRAIN AND MALNUTRITION
Chronic Diseases Association ONLUS

VI Congresso Nazionale B&M
Nutrizione e Neurodegenerazione

SESSIONE IV: RELATORI

•Dieta chetogenica nell'epilessia

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MILANO | 11-12 MAGGIO | 2017

Dieta chetogenica nell'epilessia

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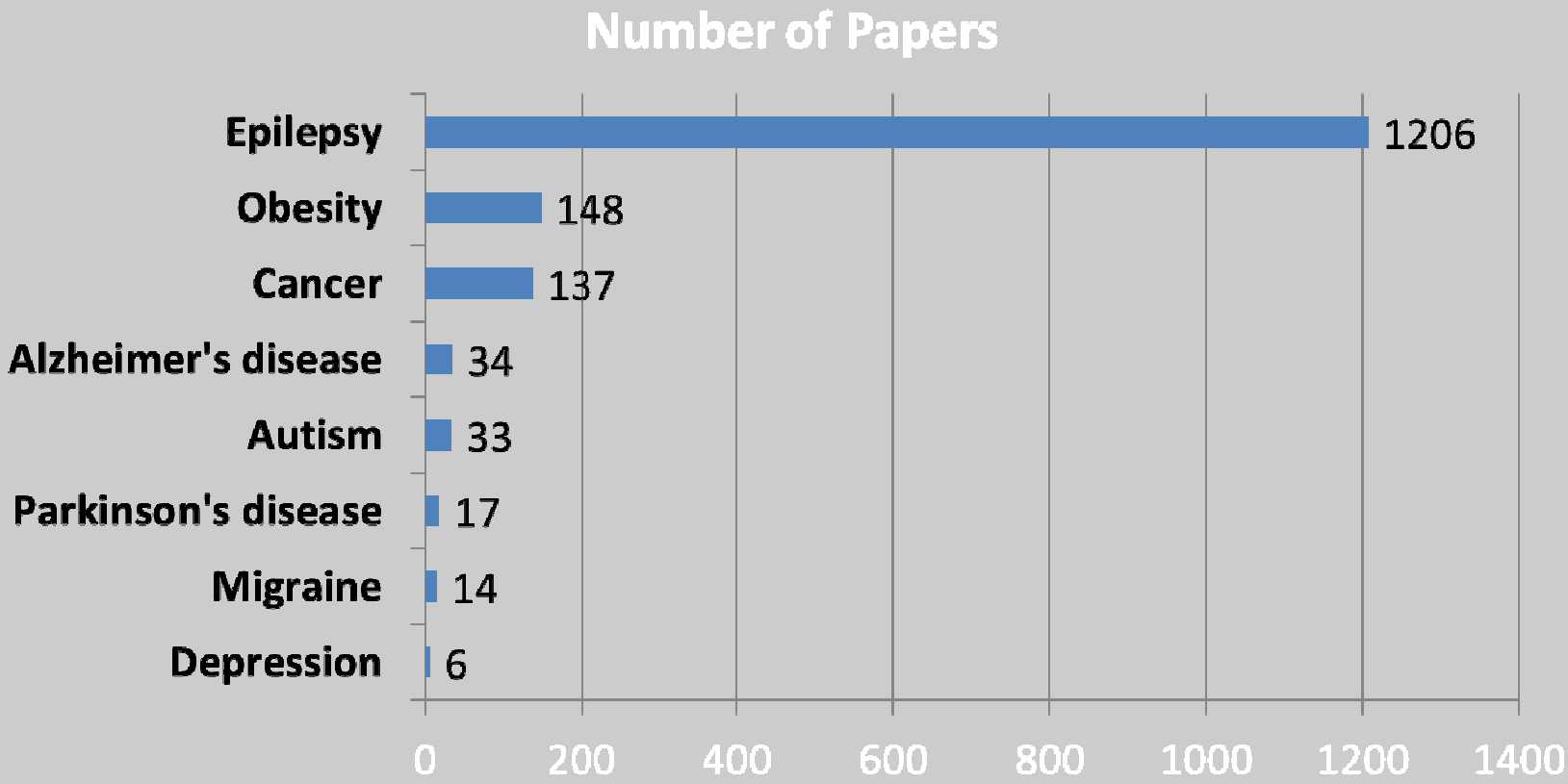
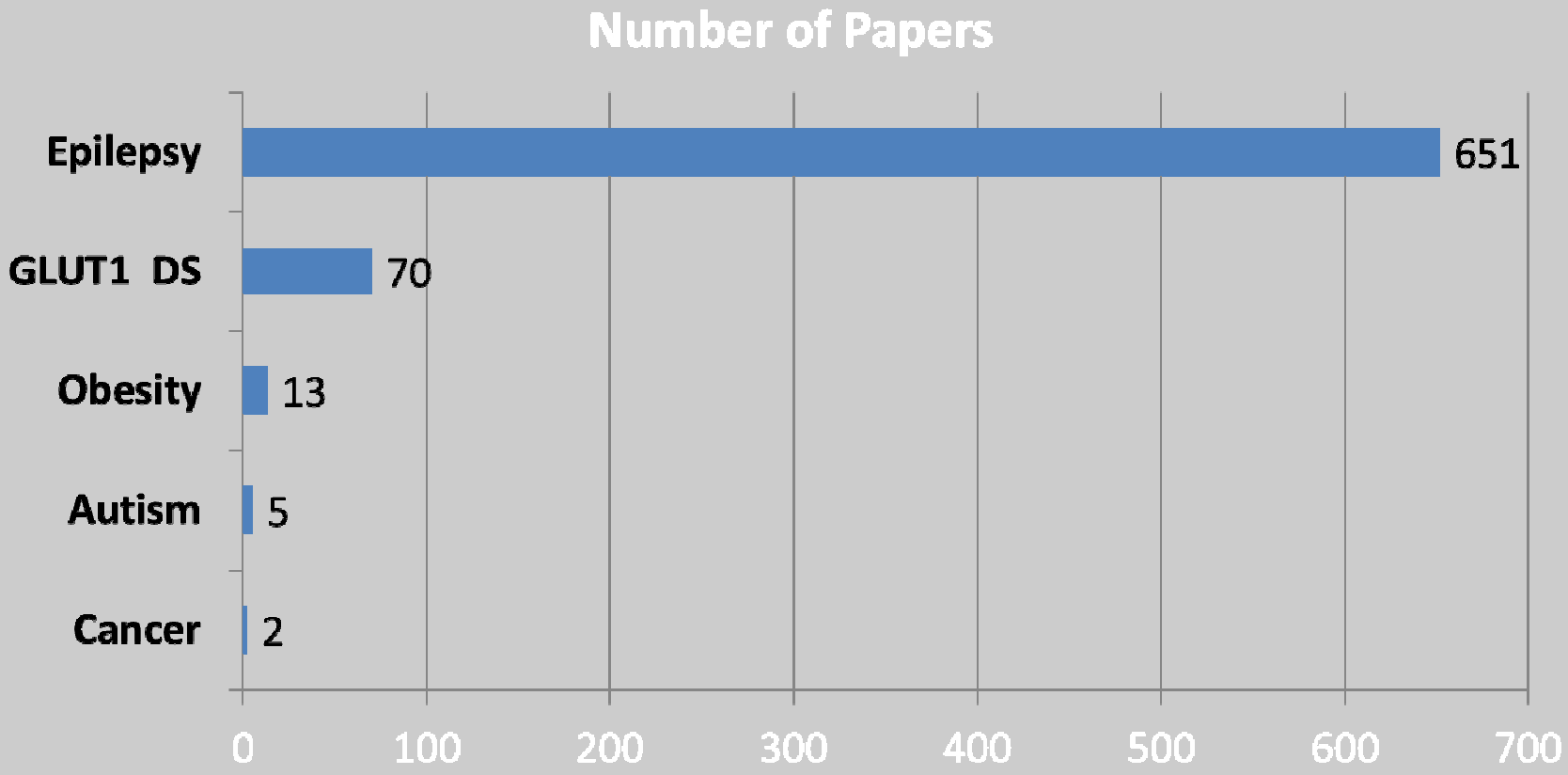
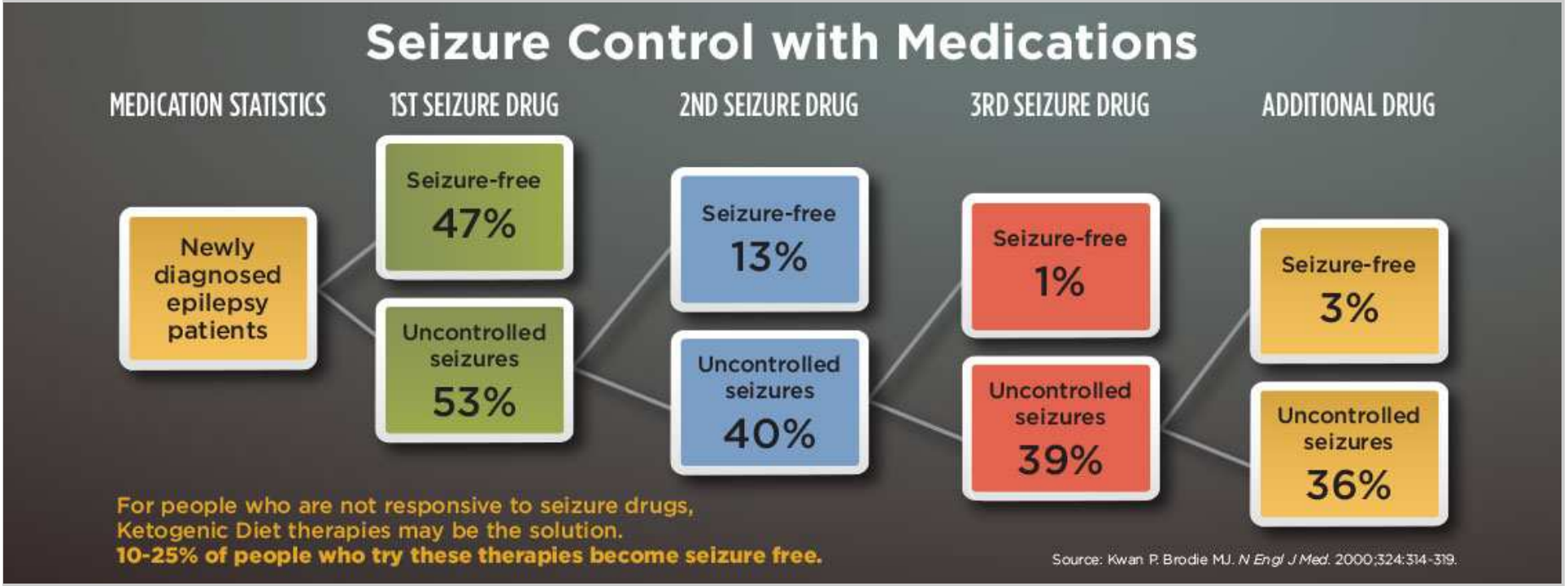
Università of Pavia

Medline : Ketogenic diet and ……



Medline : Ketogenic diet and …… humans; age range 0 - 18




Seizure Control with Medications
MEDICATION STATISTICS
1ST SEIZURE DRUG
2ND SEIZURE DRUG
3RD SEIZURE DRUG
ADDITIONAL DRUG
Newly diagnosed epilepsy patients
Seizure-free 47%
Uncontrolled seizures 53%
Seizure-free 13%
Uncontrolled seizures 40%
Seizure-free 1%
Uncontrolled seizures 39%
Seizure-free 3%
Uncontrolled seizures 36%
For people who are not responsive to seizure drugs, Ketogenic Diet therapies may be the solution.
10-25% of people who try these therapies become seizure free.
Source: Kwan P. Brodie MJ. N Engl J Med. 2000;324:314-319.

Epilepsia, 33(6):1132–1136, 1992
Raven Press, Ltd., New York
© International League Against Epilepsy

Efficacy of the Ketogenic Diet for Intractable Seizure Disorders: Review of 58 Cases

†‡Stephen L. Kinsman, *‡§Eileen P. G. Vining, ‡Shirley A. Quaskey, ‡§David Mellits, and *‡§John M. Freeman

**Pediatric Epilepsy Center, †The Kennedy Krieger Institute, and the Departments of ‡Neurology and §Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland*

Summary: The ketogenic diet was developed in the 1920s as a treatment for intractable childhood seizures when few antiepileptic drugs (AEDs) were available. There are still children whose seizures are refractory even to modern therapy, but use of the ketogenic diet appears to be waning. At Johns Hopkins, we continue to believe that the diet is very effective and well accepted by patients and families. To reevaluate our opinion of the efficacy and acceptability of this form of therapy in patients cared for in the 1980s with the newer AEDs, we analyzed the records of 58 consecutive patients who had been started on the diet. Before using the diet, 80% of the patients had multiple seizure types and 88% were treated with multiple AEDs; these children were among our most intractable patients. Despite this, seizure control improved in 67% of patients with the ketogenic diet, and actuarial analysis indicated that 75% of these improved patients continued the diet for at least 18 months. Sixty-four percent had AEDs reduced, 36% became more alert, and 23% had improved behavior. The improvement in these patients with intractable seizures and the length of time that families maintained the regimen indicate that the ketogenic diet continues to have a very useful therapeutic role in selected patients and their families. **Key Words:** Epilepsy—Diet therapy—Dietary fats—Ketone bodies—Blood—Child.

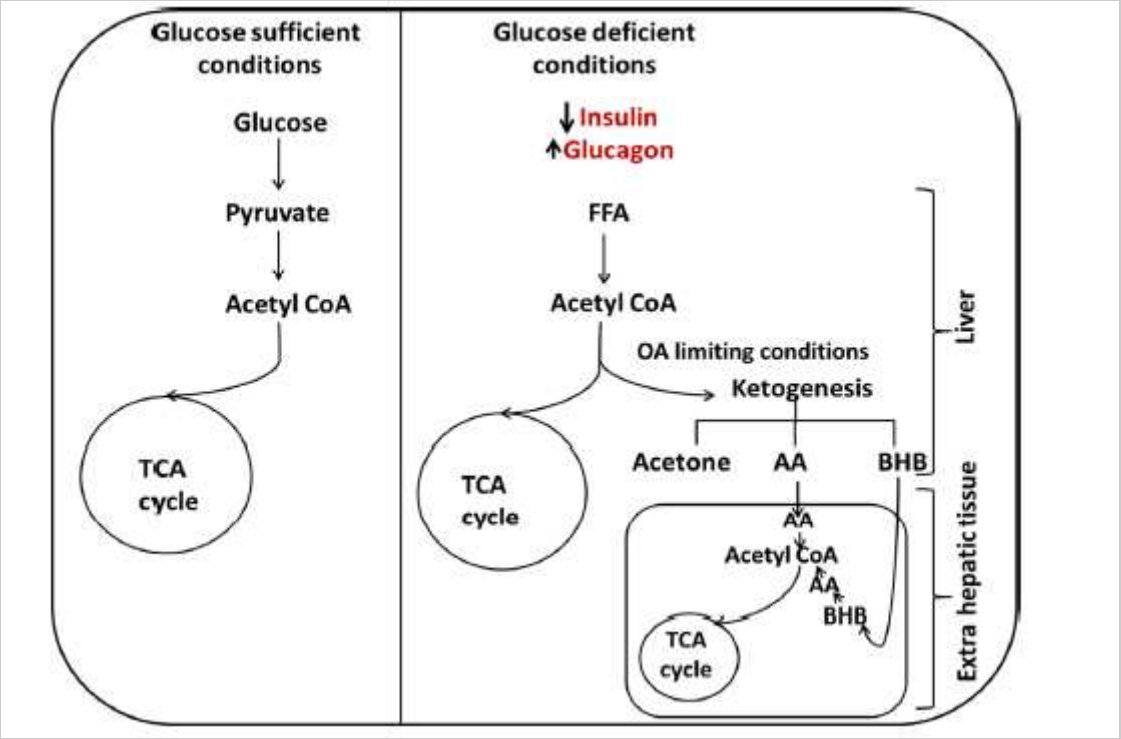
Quale dieta chetogenica per epilessia?

- Un regime terapeutico che mantenga l'organismo in uno stato metabolico di chetosi a lungo termine
- La chetosi è dovuta all'aumento in circolo dei *corpi chetonici* derivanti dall'aumento dell'ossidazione dei grassi

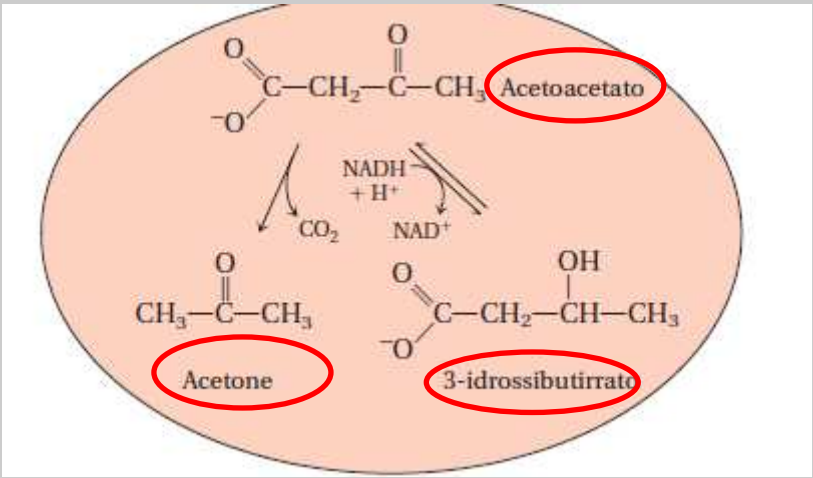
In condizioni fisiologiche:

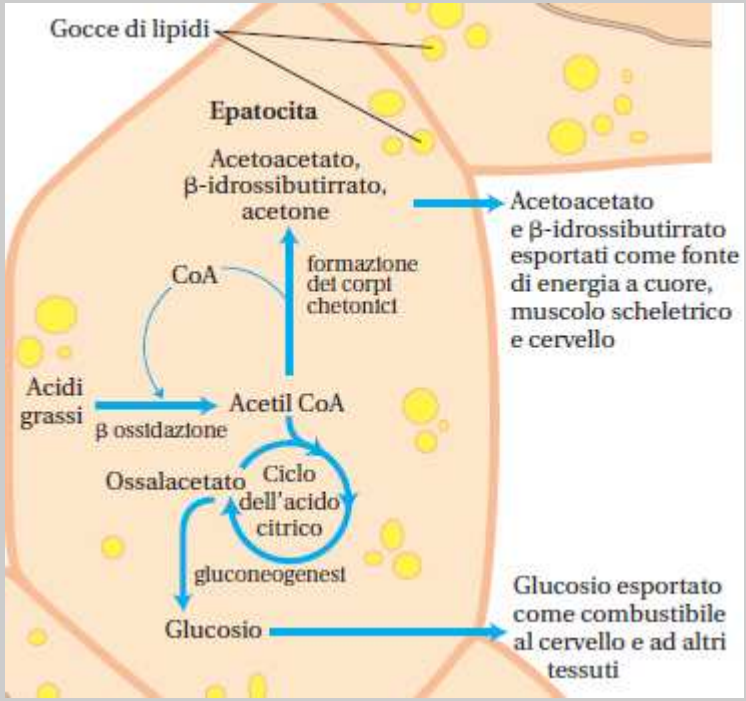
- il livello di chetoni in circolo è trascurabile
- la produzione di corpi chetonici aumenta in situazioni di carenza di glucosio (digiuno o semidigiuno o diete fortemente ipoglucidiche normoproteiche)

ketogenesis



Corpi chetonici





Valori normalità nel sangue fino a 0.5 mmol/L (2.7 mg /dl) dopo digiuno notturno come *beta-idrossibutirrato*

Chetosi dietetica e patologica

Table 2: Comparison of Dietary Ketosis and Diabetic Ketoacidosis (DKA)

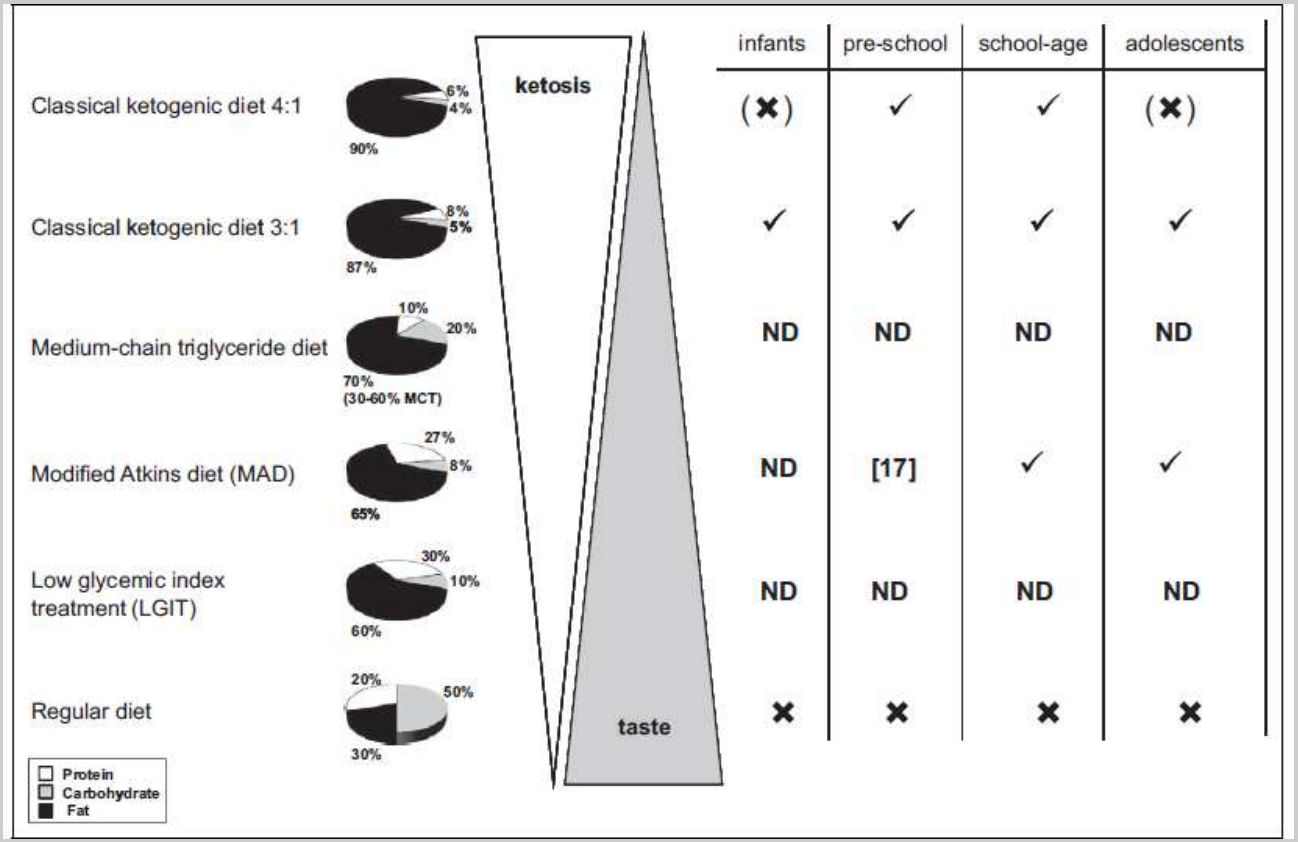
	Normal diet	Dietary ketosis	DKA
Blood glucose (mg/dl)	80-120	~ 65-80	300+
Insulin	Moderate	Low	Absent
Glucagon	Low	High	High
Ketones production (g/day)	Low	115-180	400
Ketone concentrations (mmol/L)	0.1	4-10	20+
Blood pH			

Mc Donald L, 1998

Andamento chetosi in risposta a vari protocollo dietetici

Il livello di chetosi dipende dal rapporto tra nutrienti grassi e non grassi

Rapporto chetogenico



	infants	pre-school	school-age	adolescents
Classical ketogenic diet 4:1	(✖)	✓	✓	(✖)
Classical ketogenic diet 3:1	✓	✓	✓	✓
Medium-chain triglyceride diet	ND	ND	ND	ND
Modified Atkins diet (MAD)	ND	[17]	✓	✓
Low glycemic index treatment (LGIT)	ND	ND	ND	ND
Regular diet	✖	✖	✖	✖

Klepper & Leiendecker *J Child Neurol* 2013

Chetosi in corso di digiuno

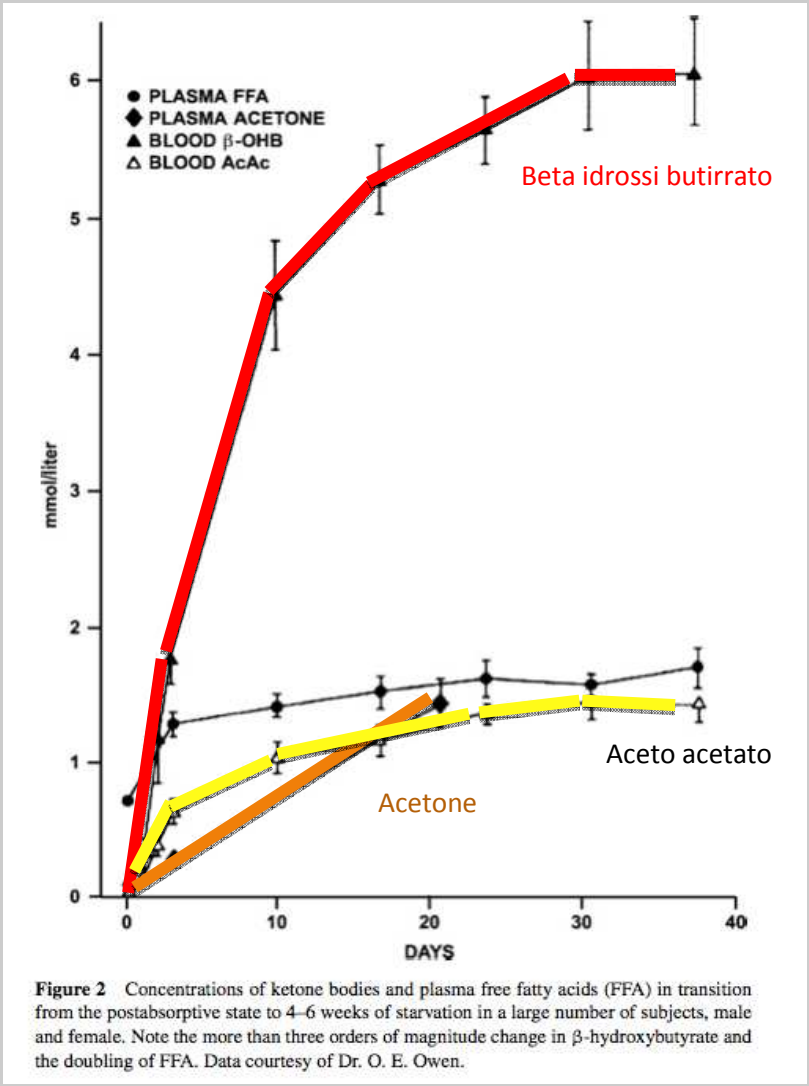
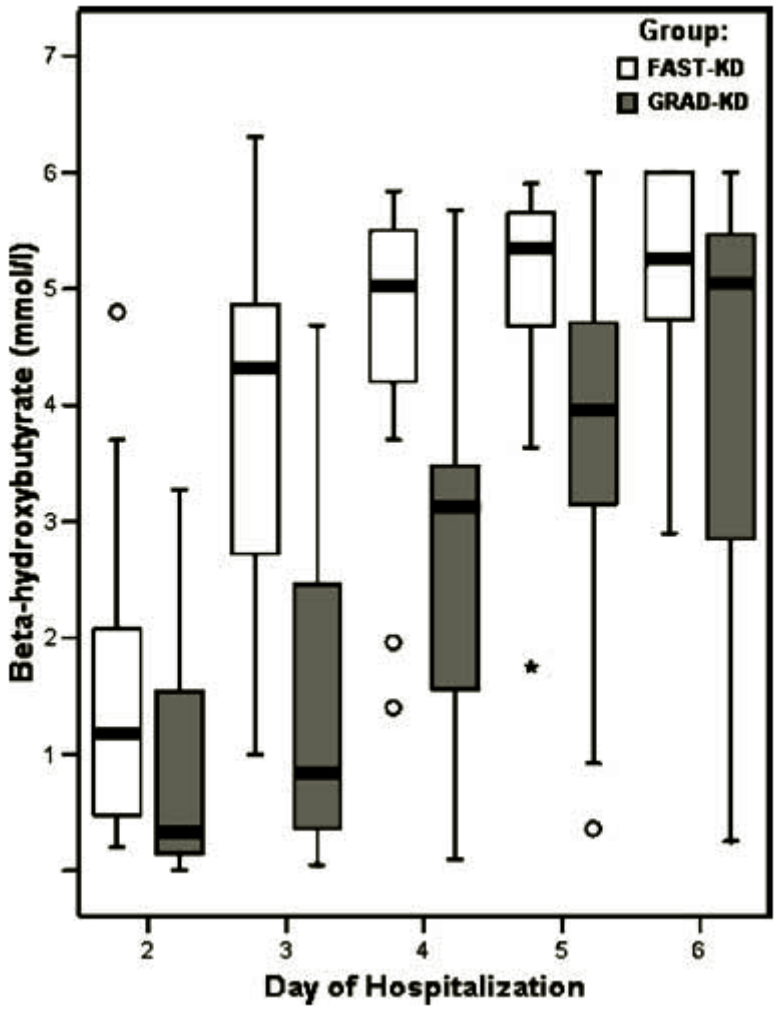


Figure 2 Concentrations of ketone bodies and plasma free fatty acids (FFA) in transition from the postabsorptive state to 4–6 weeks of starvation in a large number of subjects, male and female. Note the more than three orders of magnitude change in β-hydroxybutyrate and the doubling of FFA. Data courtesy of Dr. O. E. Owen.

GF Cahil Annu. Rev. Nutr. 2006. 26:1–22

Chetosi in corso di dieta chetogenica classica (rapporto lipidi/non lipidi 4:1)



Epilepsia, 49(11):1810–1815, 2008

Fasting versus Gradual Initiation of the Ketogenic Diet: A Prospective, Randomized Clinical Trial of Efficacy

*A. G. Christina Bergqvist, †Joan I. Schall, ‡Paul R. Gallagher, ‡Avital Cnaan, and †Virginia A. Stallings

*Divisions of Neurology, †Gastroenterology and Nutrition, ‡Biostatistics and Epidemiology, The Children's Hospital of Philadelphia, and Departments of Pediatrics and Neurology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, U.S.A.

Dieta chetogenica nell' epilessia: note storiche

Nel 1920 il figlio epilettico di un notaio di New York fu affidato alle cure di un medico osteopata del Michigan, Hugh Conklin che ritenendo

"l'epilessia conseguenza di un'intossicazione cerebrale da parte di sostanze provenienti dall'intestino."

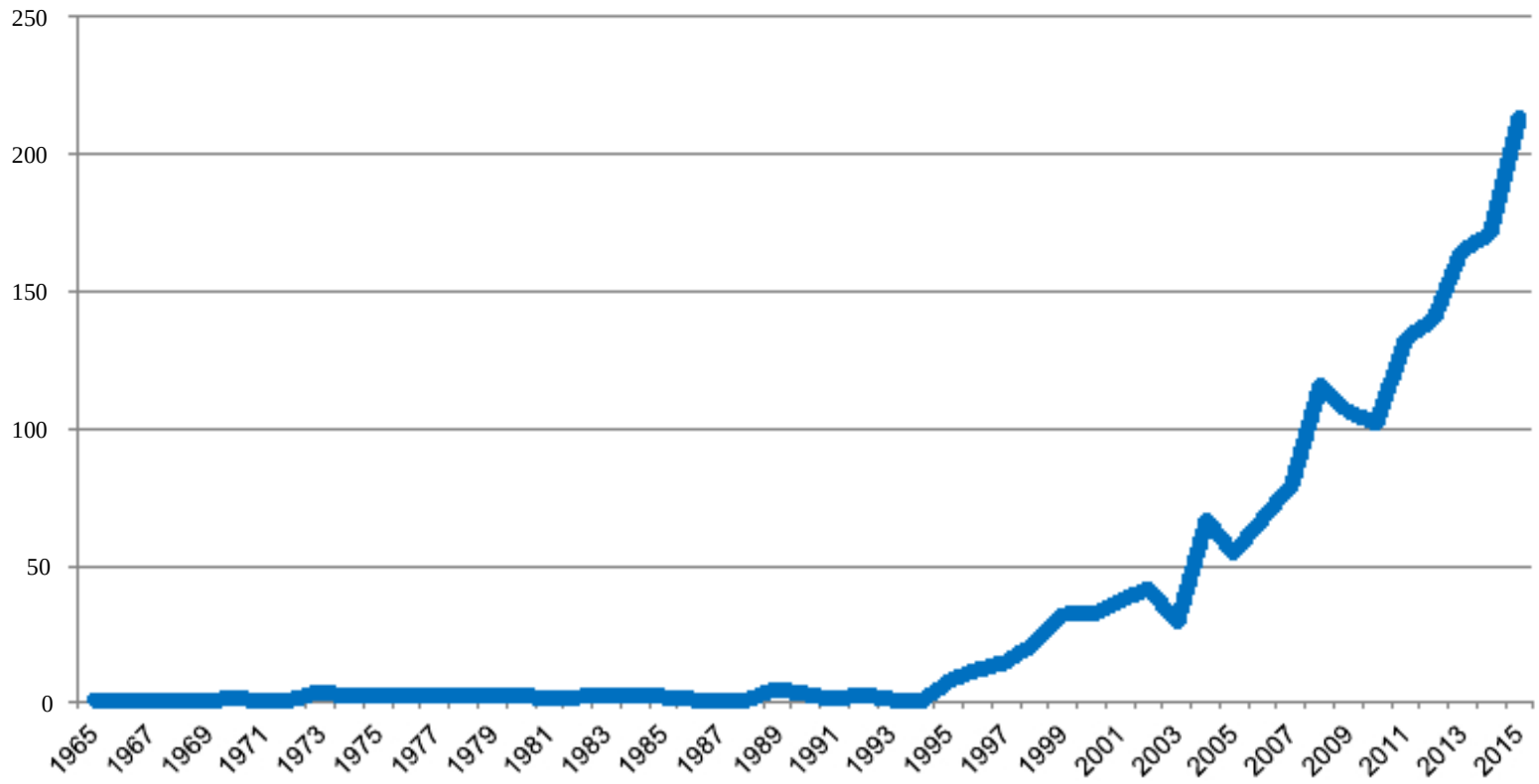
sottopose a preghiere e dieta liquida (acqua) per qualche settimana e ottenne buoni risultati

In seguito al Presbiterian Hospital di New York iniziarono le prime sperimentazioni che confermarono l'efficacia del ***digiuno*** nel controllo delle crisi

Dieta chetogenica nell' epilessia: note storiche

- Per ovvie ragioni questo approccio basato sul digiuno ebbe un limitato sviluppo finchè Wilder (1921) alla Mayo Clinic mise a punto una **dieta che mirava a mimare l'effetto del digiuno**
- Per ottenere una chetosi sovrapponibile a quella indotta dal digiuno è necessario **ridurre drasticamente la quota glucidica e controllare anche la quota proteica**.
- Tale risultato si ottiene calcolando la dieta secondo un **rapporto prefissato tra i nutrienti definito *chetogenico*** (termine coniato da Peterman nel 1925) ancora utilizzato.

Ketogenic Diet Studies Published



First Do No Harm (1997)

Prodotto e diretto da Jim Abrahams, racconta la storia di un ragazzo epilettico farmacoresistente che migliora con la dieta. Il film è ispirato alla storia vera del figlio Charlie del regista e fu seguito dalla creazione della ***Charlie Foundation*** , associazione di pazienti mirata alla diffusione delle conoscenze sull'uso della dieta. Fu seguito da un rinnovato interesse nell'uso e nello studio dell'efficacia della dieta

The ketogenic diet for the treatment of childhood epilepsy: a randomised controlled trial

Elizabeth G Neal, Hannah Chaffe, Ruby H Schwartz, Margaret S Lawson, Nicole Edwards, Geogianna Fitzsimmons, Andrea Whitney, J Helen Cross

Children randomly assigned to receive a ketogenic diet, either immediately or after a 3-month delay with no other changes to treatment. There was no significant difference in the efficacy of the treatment between symptomatic generalised or symptomatic focal syndromes

	Patients who achieved cut-off points		p value
	Diet group (n=73)	Control group (n=72)	
>90% reduction in seizures	5 (7%)	0 (0%)	0·0582
>50% reduction in seizures*	28 (38%)	4 (6%)	<0·0001
<50% reduction in seizures†	45 (62%)	68 (94%)	<0·0001

Percentages based on numbers allocated to each intervention. *Includes patients who reported >90% reduction. †Includes 71 patients with data and 42 unknown (16 did not recieve treatment, 10 discontinued treatment, 16 with no data).

Table 4: **Number of children in each group who achieved 50% and 90% seizure reduction at 3 months**

The results from this trial of the ketogenic diet support its use in children with <u>treatment-intractable epilepsy</u>

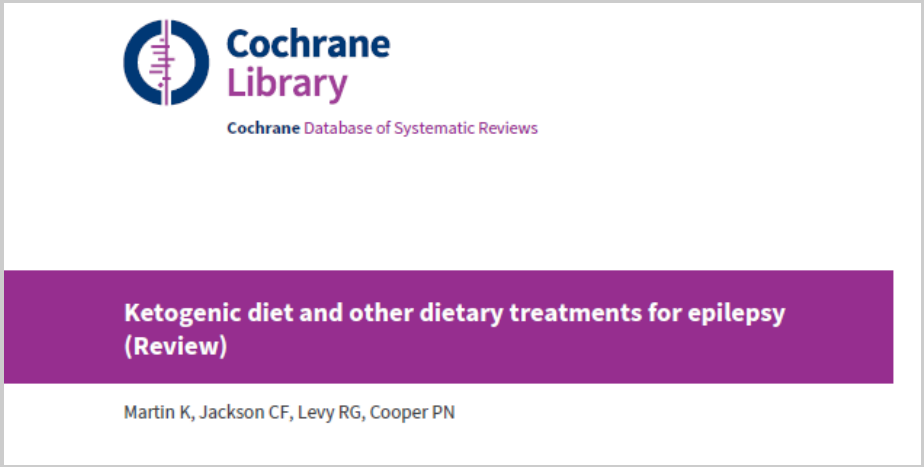
Lancet Neurol 2008; 7: 500–06

Ketogenic diet and other dietary treatments for epilepsy (Review)

Levy RG, Cooper PN, Giri P, Pulman J

2012

"These studies suggest that in children, the ketogenic diet results in short to medium term benefits in seizure control, the effects of which are *comparable to modern antiepileptic drugs*" ……
"For those with medically intractable epilepsy or those in whom surgery is unsuitable, a ketogenic diet could improve seizure control,
but tolerability is poor"



Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD001903

Main results

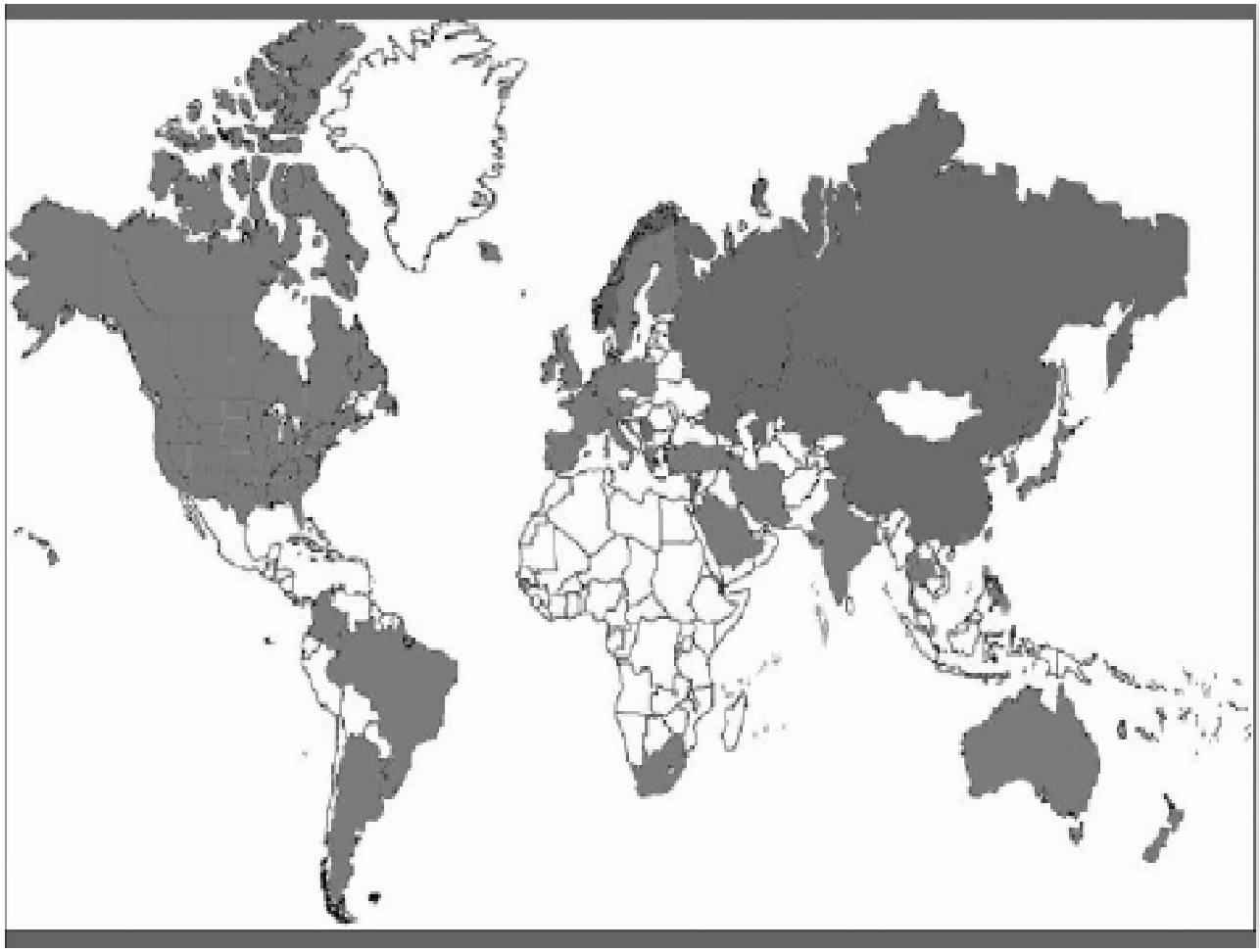
S*even* RCT on ***427 children and adolescents.***

Reported rates of seizure *freedom* reached as high as 55% in a 4 : 1 KD group after three months

Reported rates of seizure *reduction* reached as high as 85% in a 4 : 1 KD group after three months.

For people who have medically intractable epilepsy or people who are not suitable for surgical intervention, a KD remains a valid option; however, further research is required

La dieta chetogenica oggi: diffusione nel mondo



Selezione dei pazienti

Valutazioni pre-dieta

Scelta protocollo dietetico

Modalità di induzione chetosi

Integrazioni nutrizionali

Monitoraggio

Follow-up

Durata e interruzione

Linee guida esistenti

- Optimal clinical management of children receiving the ketogenic diet: Recommendations of the International Ketogenic Diet Study Group. *Epilepsia, 50:304–317, 2009*
- The ketogenic diet for Dravet syndrome and other epileptic encephalopathies: An Italian consensus. *Epilepsia, 52(Suppl. 2):83–89, 2011*
- What are the minimum requirements for ketogenic diet services in resource-limited regions? Recommendationsfrom the International League Against Epilepsy Task Forcefor Dietary Therapy *Epilepsia, 56:1337–1342, 2015*
- Ketogenic diet guidelines for infants with refractory epilepsy *Eur J Paediatr Neurol, 20:798-809, 2016*
- *Ketogenic dietary therapies in adults with epilepsy: a practical guide Pract Neurol, 16: 208 – 214, 2016*

22

Controindicazioni

Box 1 Disorders that contraindicate the use of ketogenic dietary therapy, taken from the International Ketogenic Diet Study Group consensus statement[31]

Disorders
- Carnitine deficiency (primary)
- Carnitine palmitoyltransferase I or II deficiency
- Carnitine translocase deficiency
- β-Oxidation defects
- Medium-chain acyl dehydrogenase deficiency
- Long-chain acyl dehydrogenase deficiency
- Short-chain acyl dehydrogenase deficiency
- Long-chain 3-hydroxyacyl-coenzyme A deficiency
- Medium-chain 3-hydroxyacyl-coenzyme A deficiency.
- Pyruvate carboxylase deficiency
- Porphyria

Da valutare caso per caso
- Reflusso gastroesofageo
- Calcolosi renale
- Osteopenia
- Dislipidemia familiare
- Difficoltà gestione dieta

Schoeler NE, Cross JH. Pract Neurol 2016;16:208–214

Scelta protocollo dietetico

Deve essere fatta in funzione:

- Obiettivo terapeutico (livello di chetosi)
- Miglior rapporto rischio-beneficio
- Risorse disponibili

Comprende

- Tipo somministrazione
- Scelta rapporto chetogenico e dieta
- Modalità induzione chetosi
- Setting ospedaliero o ambulatoriale

Four Different Diets Today

1. Classic ketogenic diet 1921
2. Medium chain triglyceride diet 1970
3. *Modified Atkins Diet* 2003
4. Low Glycemic Index Treatment 2005

Table 1: Comparison of the four major ketogenic diets in clinical use (1000 kcal/day provided)

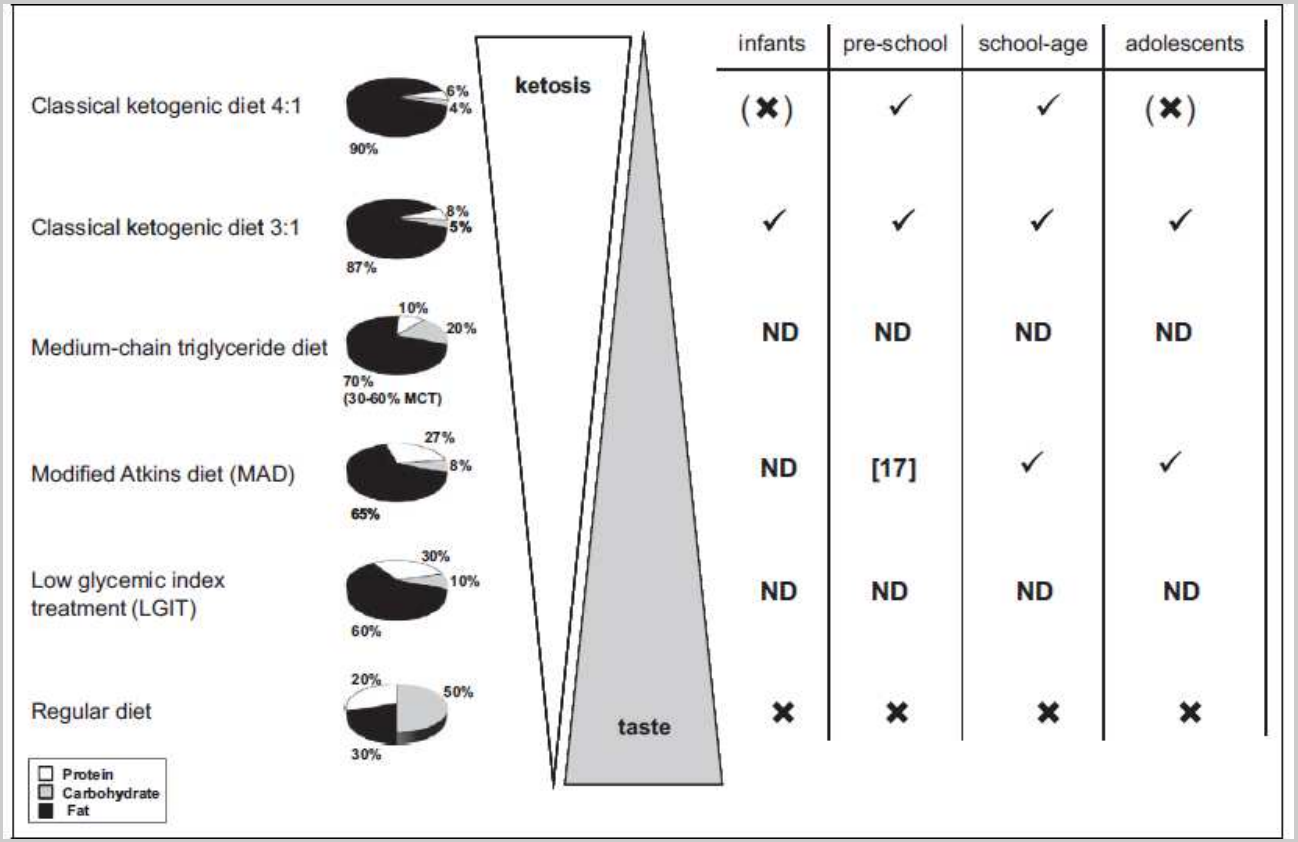
Diet	Fat (g), % calories	Protein (g), % calories	Carbohydrate (g), % calories
Classic long chain triglyceride			
4:1	100 (90%)	17 (7%)	8 (3%)
3:1	96	18	14
2:1	92	20	26
1:1	77	37	40
Medium chain triglyceride oil diet	78 (70%)	25 (10%)	50 (20%)
Low glycemic index treatment	67* (45%)	40-60* (28%)	40–60 (27%)
Modified Atkins diet	70* (70%)	60* (25%)	10–20 (5%)

*Values are approximate

Andamento chetosi in risposta a vari protocollo dietetici

Il livello di chetosi dipende dal rapporto tra nutrienti grassi e non grassi

Rapporto chetogenico



	infants	pre-school	school-age	adolescents
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Medium-chain triglyceride diet	ND	ND	ND	ND
Modified Atkins diet (MAD)	ND	[17]	✓	✓
Low glycemic index treatment (LGIT)	ND	ND	ND	ND
Regular diet	✖	✖	✖	✖

Klepper & Leiendecker *J Child Neurol* 2013

Livelli di chetosi e controllo crisi

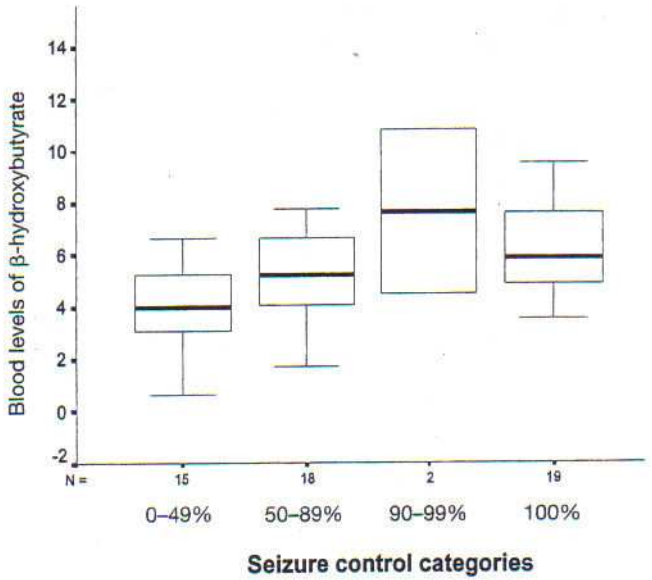


Figure 1. Box plot of range of values of blood β-hydroxybutyrate measurements. Boxes contain median, interquartile range (the middle 50% of values by category of seizure control), and the extreme values of β-hydroxybutyrate in each seizure control category for children presenting to follow-up at 3 to 6 months after diet onset.

The Ketogenic Diet: Seizure Control Correlates Better With Serum β-Hydroxybutyrate Than With Urine Ketones

Donald L. Gilbert, MD; Paula L. Pyzik, BA; John M. Freeman, MD

Journal of Child Neurology / Volume 15, Number 12, December 2000

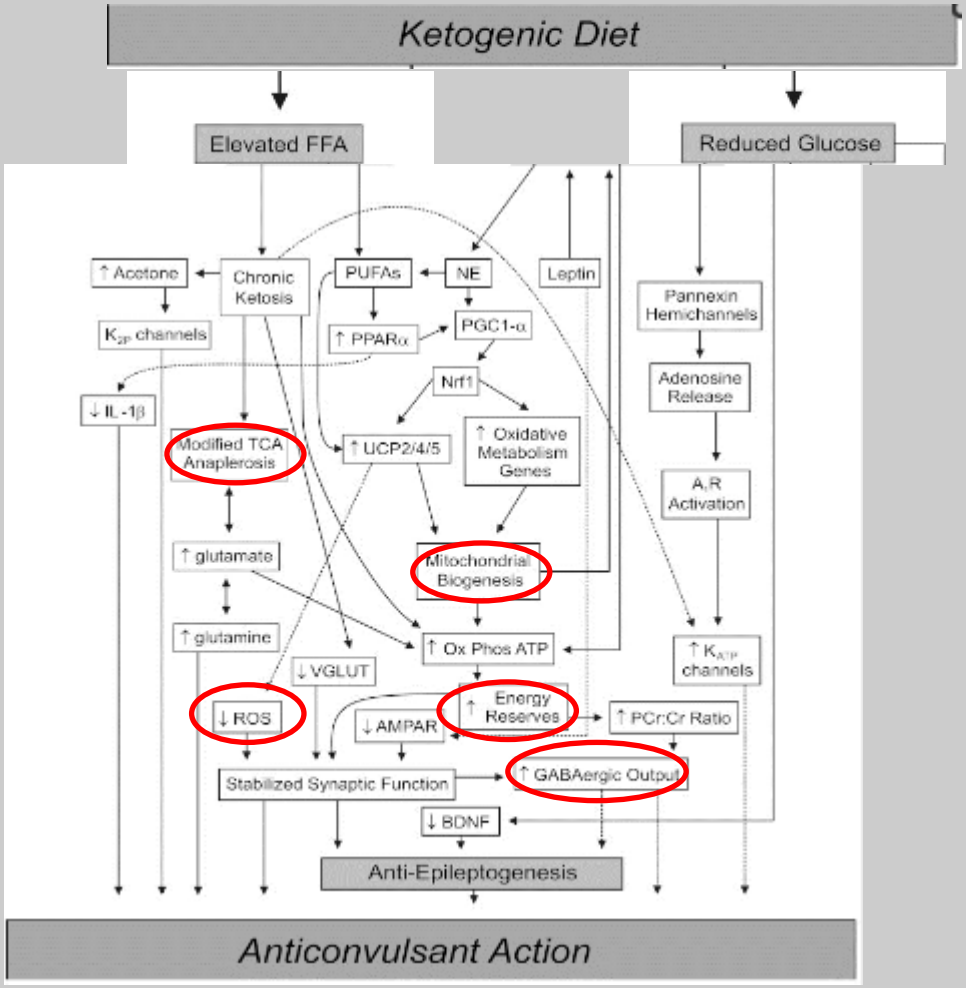
Mechanisms of Ketogenic Diet Action

Susan A. Masino[1] and Jong M. Rho[2,*]

[1] Neuroscience Program and Psychology Department, Trinity College, Hartford, CT (USA)

[2] Departments of Pediatrics and Clinical Neurosciences, Alberta Children's Hospital, University of Calgary Faculty of Medicine, Calgary, Alberta (Canada)

[*] *For correspondence:* Susan A. Masino, PhD, Life Sciences Center, Trinity College, 300 Summit St., Hartford, CT 06106, Phone: 860-297-2557, Fax: 860-297-2538, Email: susan.masino@trincoll.edu



Long-term side effects in drug-resistant epileptic children on KD

Author, year	Patients, Diet	Mean duration	Side effetcs
Dressler et al 2010, retrospecitve	50 pts on classic KD 2.5:1 – 4:1	1,2 yrs (6 mos - 3,8 yrs)	Adverse effects 28% carnitine deficiency moderate growth impairment one case of kidney stones
Caraballo et al 2011, retrospective	216 pts on classic KD 2.5:1 – 4:1	3,5 yrs (1 -12 yrs)	gastrointestinal disorders 33% hypercalciuria or hyperlipidemia 12% ; kidney stones 3%
Wibisono et al 2015, retrospective	48 pts on classic, MCT or MAD	Median of 16 mos	constipation 65% dislipidemia 40% growth retardation 30%
Lambrechts et al , 2015 prospective	48 pts on MCT diet	10 mos	constipation 65%; growth retardation 30% dislipidemia 40%

Prevention of long-term side effects

Table 2. Pre-KD evaluation

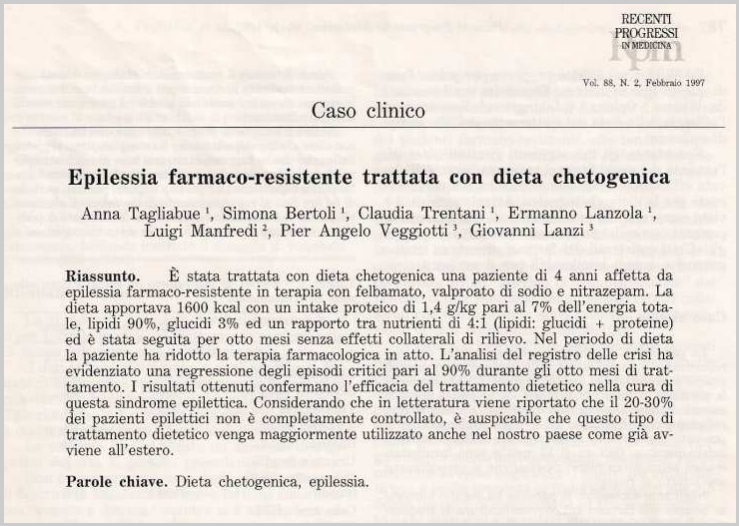
Neurologic evaluation
Etiology
Seizure type
Seizure frequency
AEDs and other medication review
EEG/Holter EEG
MRI
Cognitive/development assessment
Full serum and urine metabolic evaluation
Pediatric evaluation
ECG if history of heart disease
Abdomen ultrasound
Laboratory analysis
Nutritional evaluation
Baseline weight, height, and ideal weight for stature
Body mass index (BMI)
Skinfold thickness measurement
Dietary history
Bioelectrical impedance analysis
Indirect calorimetry[a]
Dual energy x-ray absorptiometry (DEXA)[a]
Counseling

[a]If these last two tests are not available, the use of predictive equations of basal metabolic rate and wrist x-ray could be performed

Table 4. Follow-up KD management

Neurologic assessment
Neurologic evaluation (at 1–3–6–12 months)
Electroencephalography (at 1–3–6–12 months)
Review efficacy of the diet
Cognitive/development evaluation (at 6–12 months)
Pediatric assessment
Electrocardiography (every 6 months)
Abdominal echo (every 6 months)
Laboratory evaluation (at 1–3–6–12 months)
Complete blood count with plates
Serum liver and kidney tests
Blood sugar level
Electrolytes
Blood gas analysis
Laboratory evaluation (at 3–6–12 months)
Fasting lipid profile
Parathormone and vitamin D
Osteocalcin (if osteopenia)
Urinalysis and 24 h urine calcium and creatinine (only if previously altered)
Anticonvulsant drug levels
Nutritional assessment
Assess compliance to therapy
Height and body mass index (BMI)
Skinfold thickness measurements
Bioelectrical impedance analysis
Indirect calorimetry (each 3 months)
Dual energy x-ray absorptiometry or wrist x-ray (every 6–12 months)
Review appropriateness of diet prescription (calories, protein, and fluid)
Review vitamin and mineral supplementation

Our experience



RECENTI PROGRESSI IN MEDICINA

Vol. 88, N. 2, Febbraio 1997

Caso clinico

Epilessia farmaco-resistente trattata con dieta chetogenica

Anna Tagliabue [1], Simona Bertoli [1], Claudia Trentani [1], Ermanno Lanzola [1], Luigi Manfredi [2], Pier Angelo Veggiotti [3], Giovanni Lanzi [3]

Riassunto. È stata trattata con dieta chetogenica una paziente di 4 anni affetta da epilessia farmaco-resistente in terapia con felbamato, valproato di sodio e nitrazepam. La dieta apportava 1600 kcal con un intake proteico di 1,4 g/kg pari al 7% dell'energia totale, lipidi 90%, glucidi 3% ed un rapporto tra nutrienti di 4:1 (lipidi: glucidi + proteine) ed è stata seguita per otto mesi senza effetti collaterali di rilievo. Nel periodo di dieta la paziente ha ridotto la terapia farmacologica in atto. L'analisi del registro delle crisi ha evidenziato una regressione degli episodi critici pari al 90% durante gli otto mesi di trattamento. I risultati ottenuti confermano l'efficacia del trattamento dietetico nella cura di questa sindrome epilettica. Considerando che in letteratura viene riportato che il 20-30% dei pazienti epilettici non è completamente controllato, è auspicabile che questo tipo di trattamento dietetico venga maggiormente utilizzato anche nel nostro paese come già avviene all'estero.

Parole chiave. Dieta chetogenica, epilessia.

Since1994: classic KD according to the John Hopkins Hospital protocol

Since 2008 :

- At home initiation
- Without fasting
- No calorie or fluid restriction
- Gradual increase in ketogenic ratio

ELSEVIER Epilepsy Research 48 (2002) 221–227
www.elsevier.com/locate/epilepsyres

Short Communication

The ketogenic diet in children, adolescents and young adults with refractory epilepsy: an Italian multicentric experience

Giangennaro Coppola [a,*], Pierangelo Veggiotti [c], Raffaella Cusmai [b], Simona Bertoli [c], Simonetta Cardinali [c], Carlo Dionisi-Vici [b], Mirella Elia [b], Maria Luisa Lispi [b], Chiara Sarnelli [a], Anna Tagliabue [d], Caterina Toraldo [a], Antonio Pascotto [a]

[a] *Clinic of Child Neuropsychiatry, Second University of Naples, Via Pansini 5, 80131 Naples, Italy*
[b] *Ospedale Bambino Gesù, Rome, Italy*
[c] *Department of Child Neuropsychiatry, 'Fondazione Istituto Neurologico C. Mondino', IRCCS, Pavia, Italy*
[d] *Human Nutrition Research Center, University of Pavia, Pavia, Italy*

Methods: We performed a prospective add-on study in 56 refractory epilepsy young patients (age 1–23 years, mean 10.4 years), all with both symptomatic and cryptogenic, generalized or partial epilepsies

Results: Patients have been treated for 1–18 months (mean 5 months). A 50% reduction in seizure frequency was gained in 37.5 and 26.8% of patients after 3 and 6 months, respectively, at 12 months, this number fell by 8.9%.

Conclusion: This initial experience with the ketogenic diet was effective in difficult-to-treat patients with partial and generalized epilepsies, though its efficacy dropped significantly by 9–12 months.

Original article

Effects of the ketogenic diet on nutritional status, resting energy expenditure, and substrate oxidation in patients with medically refractory epilepsy: A 6-month prospective observational study

Anna Tagliabue [a,*], Simona Bertoli [b], Claudia Trentani [a], Paola Borrelli [c], Pierangelo Veggiotti [d]

18 soggetti
8 maschi; 10 femmine
età media 12 anni

Table 2
Nutritional status, resting energy expenditure, and substrate oxidation at baseline and after 6 months of KD.

	Baseline		6 months		*p* value
	Mean	Standard deviation	Mean	Standard deviation	
Body height *z*-score	−0.72	1.70	−0.76	1.73	ns
Body weight *z*-score	−0.81	2.42	−0.86	2.47	ns
BMI *z*-score	−1.33	2.17	−1.10	2.11	ns
REE (predicted, kcal)	1277	258	1233	224	ns
REE (measured, kcal)	1107	277	1081	237	ns
REE (%, measured versus predicted)	−16.4	12.1	−15.7	12.6	ns
REE/body weight (kcal/kg)	33.3	14.3	32.4	11.1	ns
REE/fat free mass (kcal/kg)	48.5	21.3	43.5	16.2	ns
Respiratory quotient	0.80	0.06	0.72	0.05	< 0.001
Fat oxidation (mg/min)	50.9	25.2	97.5	25.7	< 0.001
Carbohydrate oxidation (mg/min)	72.5	54.1	21.5	48.2	< 0.001

Clinical Nutrition 2012

Nutrition

Available online 30 March 2015

In Press, Accepted Manuscript — Note to users

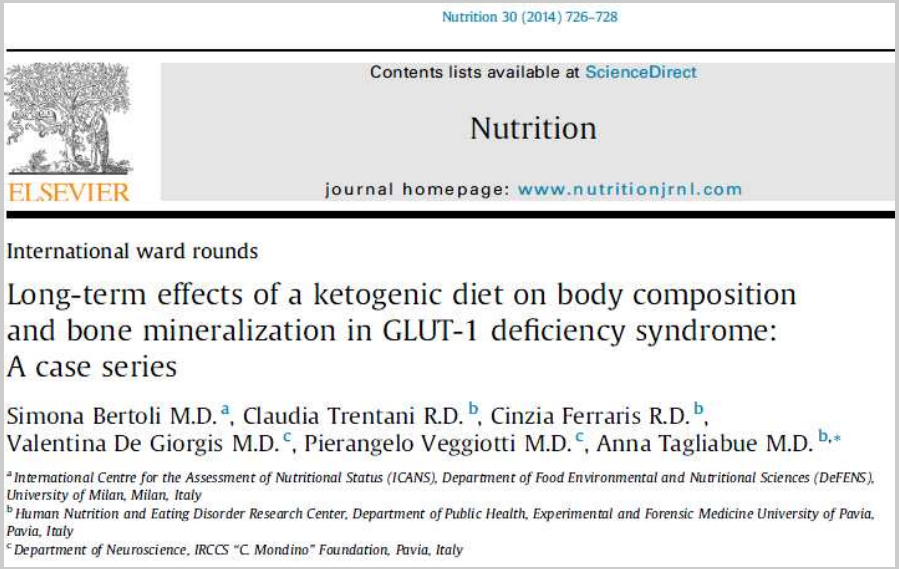
Short-term effect of ketogenic diet on anthropometric parameters, body fat distribution and inflammatory cytokines production in GLUT 1 Deficiency Syndrome

S. Bertoli[1], I. Giulini Neri[1], C. Trentani[2], C. Ferraris[2], R.S. De Amicis[1], A. Battezzati[1], Veggiotti[3, 4], V. De Giorgis[4], A. Tagliabue[2]

Table 3. Anthropometric measurements and biochemical parameters in 10 children undergoing a 3-months KD

	Preintervention		Postintervention		*P value*
	Mean	SD	Mean	SD	
Nutritional Status Parameters					
Body weight, kg	31,9	19,5	31,9	17,3	0,972
BMI, kg/m2	16,9	5,7	16,8	4,7	0,751
BMI z-score	-0,88	1,60	-0,63	1,51	0,421
Waist, cm	61,6	15,5	60,9	14,4	0,570
Waist z-score	0,02	0,72	-0,10	0,92	0,164
Bicipital skinfold, mm	6,4	2,9	7,0	3,5	0,492
Tricipital skinfold, mm	10,0	4,0	11,4	4,8	0,141
Subscapular skinfold, mm	7,6	4,5	7,1	2,7	0,647
Suprailiac skinfold, mm	11,3	7,6	11,7	6,0	0,679
% Body fat	18,2	5,9	20,4	5,1	0,290
SAT, mm	1,1	1,5	0,5	0,4	0,358
VAT, mm	2,8	1,3	3,2	0,8	0,257
SAT/VAT	0,3	0,3	0,2	0,1	0,565
Metabolic Parameters					
Blood glucose, mg/dl	80,9	12,5	77,6	7,2	0,245
Insulin, µU/ml	6,0	3,2	3,0	2,0	**0,001**
HOMA index	1,2	0,6	0,6	0,4	**0,002**
QUICKI index	0,38	0,03	0,44	0,05	**0,002**
Triglycerides, mg/dl	63,7	20,2	85,8	53,2	0,306
Total cholesterol, mg/dl	182,8	26,0	209,9	60,0	0,246
LDL cholesterol, mg/dl	110,6	19,0	132,8	52,6	0,269
HDL cholesterol, mg/dl	57,9	13,1	58,1	12,7	0,794
Total cholesterol/HDL cholestero	3,3	0,7	3,8	1,5	0,461
LDL cholesterol/HDL cholesterol	2,0	0,5	2,4	1,2	0,380
Uric Acid, mg/dl	4,1	1,4	5,8	2,1	**0,048**
Creatinine, mg/dl	0,4	0,1	0,4	0,2	**0,015**

All data are expressed as means ± SD. BMI, body mass index; SAT, Subcutaneous Adipose Tissue; VAT, Visceral Adipose Tissue, mm; HOMA, insulin resistance index; QUICKI, insulin sensitivity index; HDL, high-density lipoprotein; LDL, low density lipoprotein.



Nutrition 30 (2014) 726–728

Contents lists available at ScienceDirect

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International ward rounds

Long-term effects of a ketogenic diet on body composition and bone mineralization in GLUT-1 deficiency syndrome: A case series

Simona Bertoli M.D. [a], Claudia Trentani R.D. [b], Cinzia Ferraris R.D. [b], Valentina De Giorgis M.D. [c], Pierangelo Veggiotti M.D. [c], Anna Tagliabue M.D. [b,*]

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[b] Human Nutrition and Eating Disorder Research Center, Department of Public Health, Experimental and Forensic Medicine University of Pavia, Pavia, Italy
[c] Department of Neuroscience, IRCCS "C. Mondino" Foundation, Pavia, Italy

- Our data suggest that **maintaining a KD for more than 5 y does not pose any major negative effects on body composition, bone mineral content, and bone mineral density in adults with GLUT-1 DS,** a finding that is at variance with previous reports focusing on children with intractable epilepsy.
- The discrepant findings might be explained by the fact that our patients were adults and had a normal bone mineralization at baseline. The observed increase in muscle strength following the beginning of a KD and the use of multivitamin and mineral supplements also might have been contributing factors that helped bone health in our patients
- Further studies with larger sizes are needed to confirm and expand our findings.

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Clinical Nutrition ESPEN

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Original article

Short-term impact of a classical ketogenic diet on gut microbiota in GLUT1 Deficiency Syndrome: A 3-month prospective observational study

Anna Tagliabue [a, *], Cinzia Ferraris [a], Francesca Uggeri [b], Claudia Trentani [a], Simona Bertoli [c], Valentina de Giorgis [d], Pierangelo Veggiotti [d], Marina Elli [b]

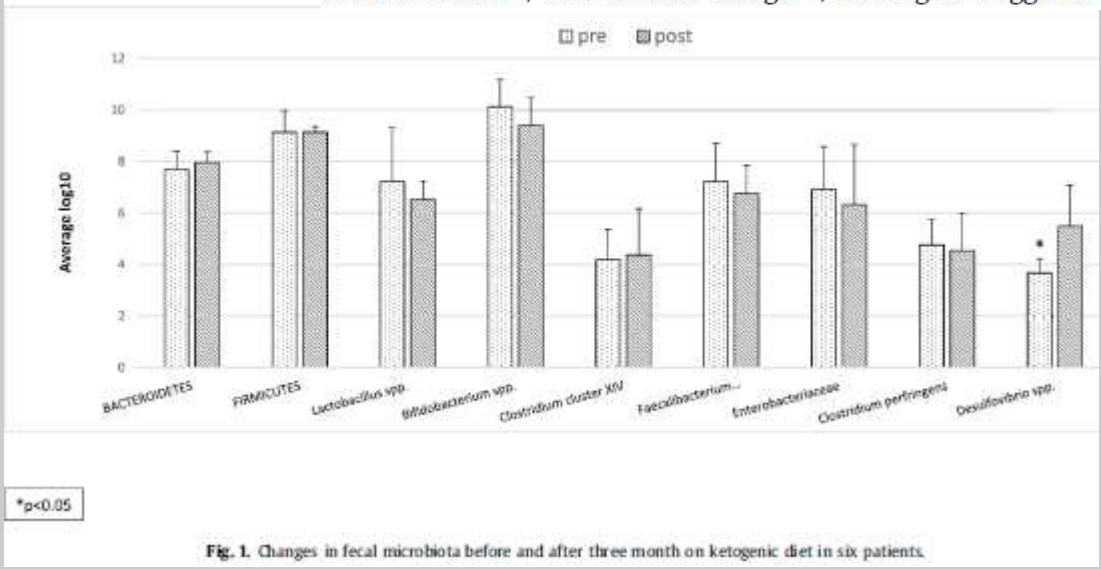


Fig. 1. Changes in fecal microbiota before and after three month on ketogenic diet in six patients.

Results: Compared with baseline, there were no statistically significant differences at 3 months in Firmicutes and Bacteroidetes. However fecal microbial profiles revealed a statistically significant increase in *Desulfovibrio* spp. ($p = 0.025$), a bacterial group supposed to be involved in the exacerbation of the inflammatory condition of the gut mucosa associated to the consumption of fats of animal origin.

Conclusions: A future prospective study on the changes in gut microbiota of all children with epilepsy started on a KD is warranted. In patients with dysbiosis demonstrated by fecal samples, it my be reasonable to consider an empiric trial of pre or probiotics to potentially restore the «ecological balance» of intestinal microbiota.

Ketogenic dietary therapies in adults with epilepsy: a practical guide

Natasha E Schoeler,[1] J Helen Cross[1,2,3]

Key points

- Ketogenic dietary therapies can be an effective treatment option for adults with drug-resistant epilepsy, although controlled studies are needed.
- Adverse effects appear similar to those reported in children, and are usually non-critical and/or transient; short-term use of these diets does not detrimentally affect lipid profiles.
- Patients need a variety of biochemical tests before starting these diets; clinicians should discuss the risks and benefits of the diet and identify potential barriers to adherence.
- Regular medical and dietetic monitoring is essential throughout dietary treatment, although there are many available resources to help patients become more independent and adventurous with their diet as their confidence increases.

Schoeler NE, Cross JH. Pract Neurol 2016;16:208–214

In sintesi

- La dieta chetogenica è utilizzato in tutto il mondo nell'epilessia refrattaria in età pediatrica a partire dalle prima sperimentazioni sull'effetto sedativo del digiuno
- La *dieta chetogenica classica* formulata in base al rapporto in grammi tra nutrienti grassi e non grassi è il regime dietetico più studiato ed induce livelli levato di chetosi
- La terapia dietetica ha effetti collaterali e deve essere applicata da un equipe interdisciplinare esperta secondo le linee guida esistenti a livello internazionale
- Nell'epilessia dell'adulto vi sono meno studi ma quelli esistenti forniscono risultati sovrapponibile a quelli in età infantile

And special thanks to

Monica Guglielmetti

Samantha Citrini

Claudia Trentani

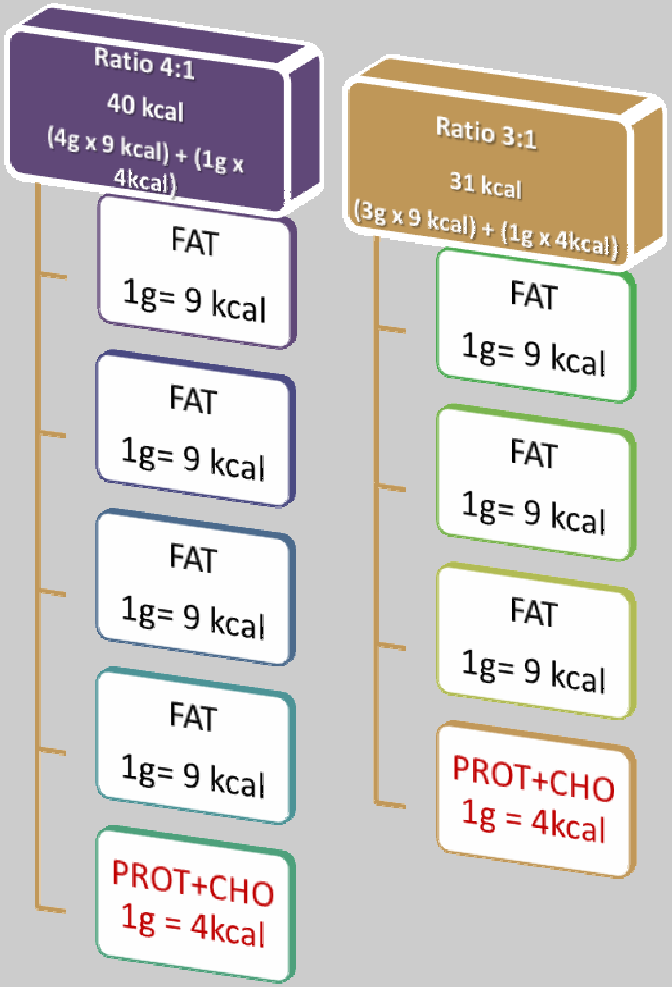
Cinzia Ferraris

Marilde Viale

Sara Bellodi

Save the date: Pavia 14 – 16 giugno 2017
«Applicazione clinica dieta chetogenica»
terza edizione

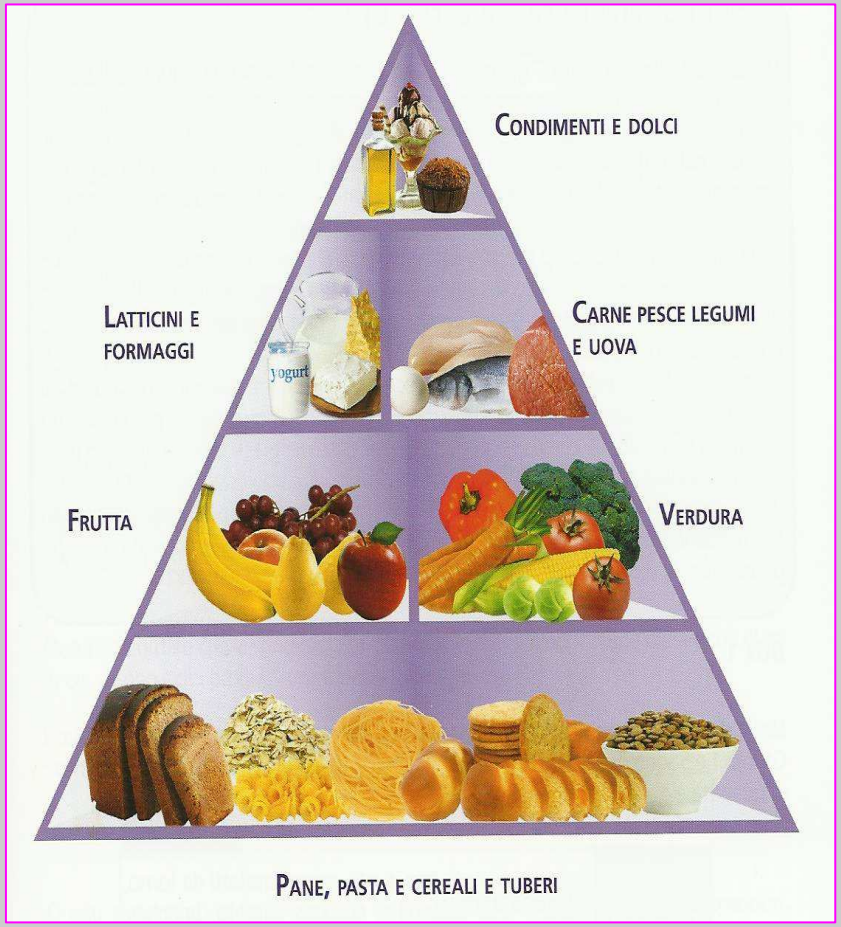
Dieta chetogenica classica



- La KD è costruita in blocchi
- Gli elementi costitutivi della KD sono le unità caloriche

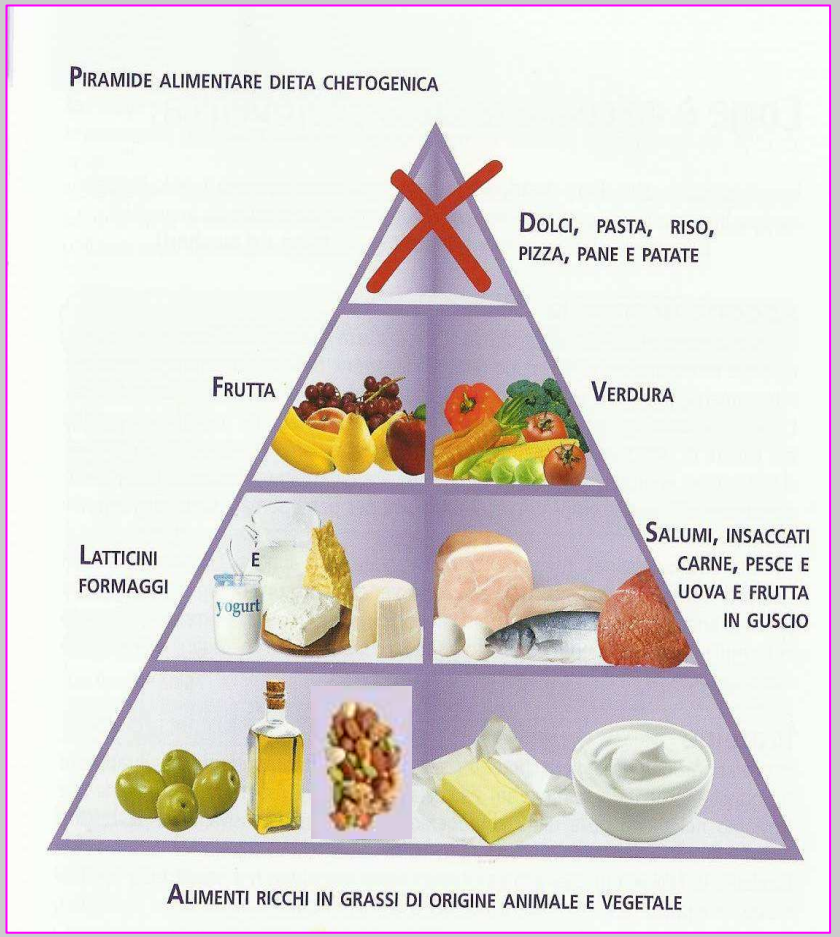
Es 1000 kcal con R=4:1
1000:40=25 unità caloriche
L = 25x4 = g 100 (grassi)
P+CHO = 25x1 = 25 g (non grassi)
Stabilisco il fabbisogno proteico
Calcolo la quota di CHO
Suddivido in pasti

Balanced diet



R = 0.1 - 0.2

Classic Ketogenic diet



R = 3 - 4

Problematiche nutrizionali

- Mantenere apporto energetico per la crescita
- Basso apporto carboidrati
- Eccesso lipidico
- Apporto proteico condizionato dal rapporto chetogenico
- Carenze vitaminiche e minerali e di acqua
- Necessità integrazioni
- Aderenza prescrizione dietetica

In pazienti spesso con stato nutrizione basale compromesso