

# Alternative treatments

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# Dietary options

- Ketogenic diet (KD)

- LCT

- MCT

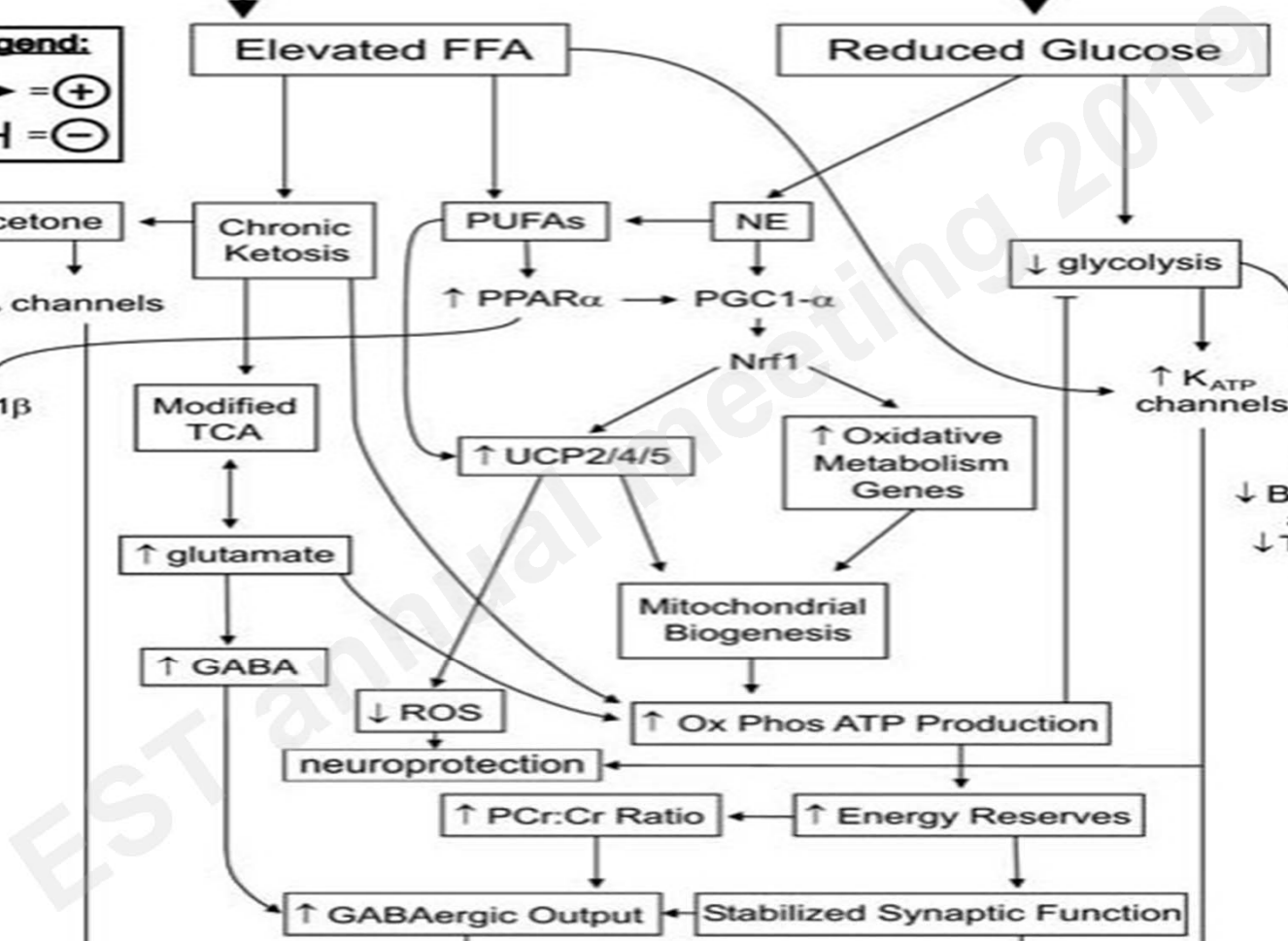
- Modified Atkins

- low GI diet \*

\* satisfactory preliminary result

# Ketogenic diet (KD)\*

- High fat
  - Low carbohydrate
  - Calorie control
  - Adequate protein
- 
- Therapeutic diet for epilepsy
  - As effective as an AED or VNS



Bough K., et al., *Anticonvulsant Mechanisms of the Ketogenic Diet*.Epilepsia, Vol. 48, No. 1, 2007



# Efficacy

- RCT (145 children) published in 2008
- Diet group
  - 38% = 50% Sz reduction
  - 7 % = 90% Sz reduction
  - 1.5%= Sz-free

Mean Sz frequency dropped by 1/3

No difference between Classical VS MCT

Neal, E.G., et al., *The ketogenic diet for the treatment of childhood epilepsy: a randomised controlled trial*. Lancet Neurol, 2008. 7(6): p. 500-6

# International guideline

*Epilepsia*, 50(2):304–317, 2009  
doi: 10.1111/j.1528-1167.2008.01765.x

## SPECIAL REPORT

### Optimal clinical management of children receiving the ketogenic diet: Recommendations of the International Ketogenic Diet Study Group

\*Eric H. Kossoff, †Beth A. Zupec-Kania, ‡Per E. Amark, §Karen R. Ballaban-Gil, ¶A. G. Christina Bergqvist, #Robyn Blackford, \*\*Jeffrey R. Buchhalter, ††Roberto H. Caraballo, †‡J. Helen Cross, †Maria G. Dahlin, §§Elizabeth J. Donner, ¶¶Joerg Klepper, §Rana S. Jehle, ##Heung Dong Kim, §§Y. M. Christiana Liu, \*\*\*Judy Nation, #Douglas R. Nordli, Jr., †††Heidi H. Pfeifer, †‡‡Jong M. Rho, §§§Carl E. Stafstrom, †††Elizabeth A. Thiele, \*Zahava Turner, ¶¶¶Elaine C. Wirrell, ###James W. Wheless, \*\*\*\*Pierangelo Veggiotti, \*Eileen P. G. Vining and The Charlie Foundation, and the Practice Committee of the Child Neurology Society

- International Ketogenic Diet Study Group
- 26 ped epileptologists & dietitian (9 countries)
- standardized protocol

# Indications

- Intractable epilepsy (any age, Sz type)

## Specific for

- Glucose transporter 1 (GLUT1) deficiency
- Pyruvate dehydrogenase deficiency
  - Essential energy for brain
  - Treat
    - seizures
    - non-epileptic symptoms



# GLUT1 deficiency

- GLUT1 protein
- transfers glucose from blood to CSF
- Low CSF glucose, normal plasma glucose
- No other cause (CNS infection/ SAH)
- Intractable Sz, MR, movement disorder
- Ketone → main energy source

# PDHD deficiency

- Mitochondrial dysfunction
- Lactic acidosis
- “Pyruvate-to-Acetyl CoA” defect
- Intractable Sz
- Ketone → bypass to TCA cycle



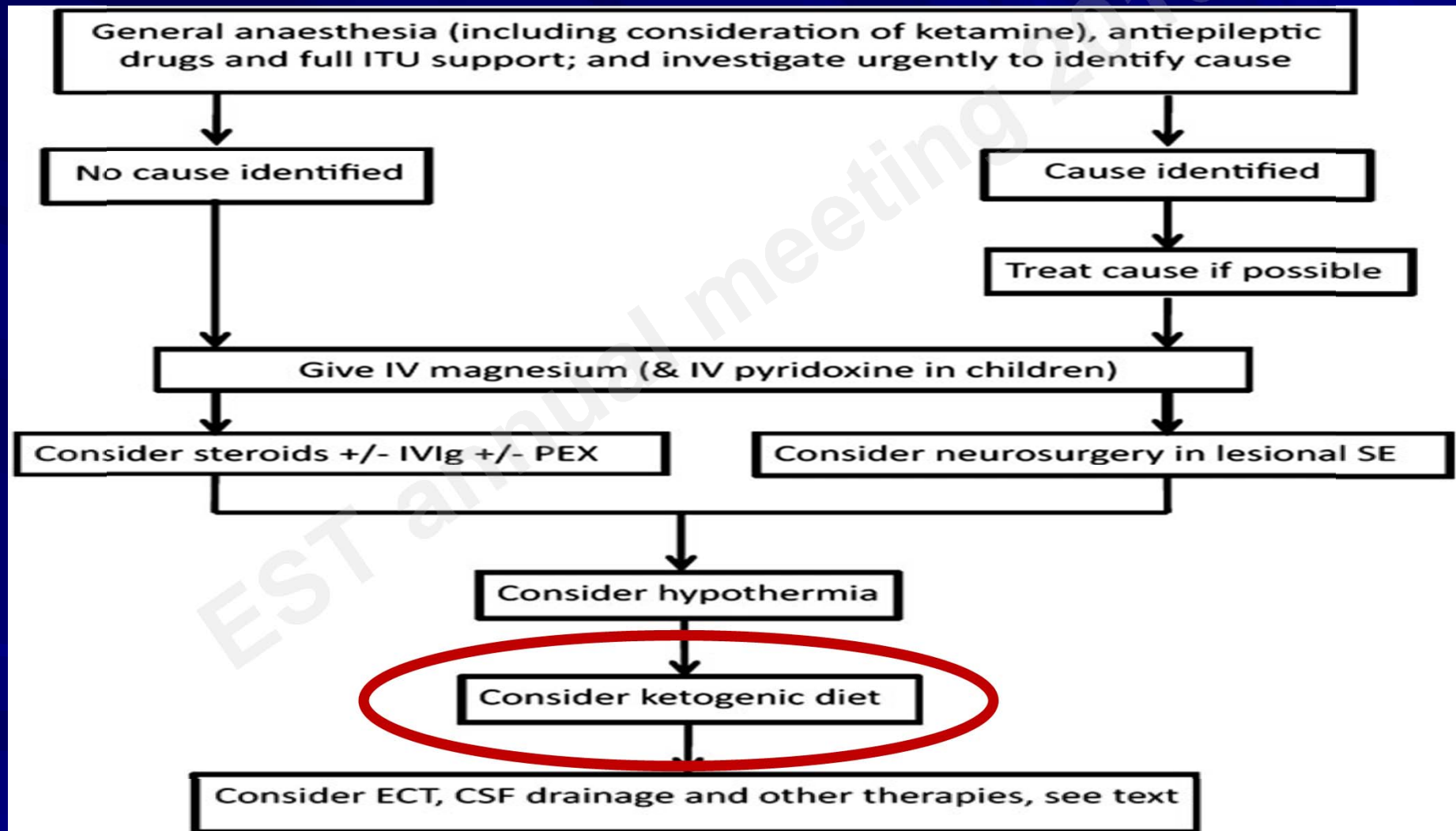
# Particular benefit in\*

- Tuberous sclerosis complex
- Myoclonic-astatic epilepsy
- Rett syndrome
- Dravet syndrome
- Infantile spasms
- infants or enterally fed patients

# Recent indication

- Super refractory status epilepticus
  - status epilepticus
  - continues or recurs
  - despite general anesthesia Rx for 24 h
- 20 cases report (no RCT yet)

# Super refractory SE



S. Shorvon and M. Ferlisi, The treatment of super-refractory status epilepticus: a critical review of available therapies and a clinical treatment protocol. Brain 2011: p1-17

# Absolute Contraindication

- Primary carnitine def
- Carnitine palmitoyl transferase (CPT) def
- Carnitine translocase def
- $\beta$ -oxidation defects
- MCAD/ LCAD/ SCAD
- Long-chain 3-hydroxyacyl-CoA def
- Medium-chain 3-hydroxyacyl-CoA def
- Pyruvate carboxylase def
- Porphyria

**Fatty acid transport  
& oxidation defect**



# Pre-KD evaluation\*

- Counseling
- Sz assessment
- Nutritional evaluation
- Lab evaluation



# Available formulas\*

- Classical formula (LCT)
- MCT formula
- Modified Atkins
- Low glycemic index (LGI)

## Diet route

- Bottle feed / normal food / tube feed
- Ketogenic parenteral nutrition

# Classical KD

- Widely used
- 4: 1 ratio of fat: protein - carbohydrate
- Main fat source = LCT
- Adequate protein  $> 1$  g/kg
- Low carb - just to prevent hypoglycemia
- Calorie control = 75 - 100% requirement
- Fluid restriction - not necessary

# MCT KD

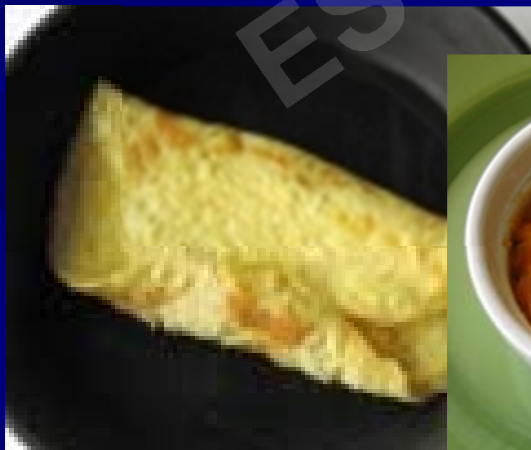
- Increasingly used → better ketosis
- 30%-60% fat: total energy
- More carbohydrate allowance
- Less restrictive, bigger meal
- Similar efficacy to LCT
- MCT can't be cooked → not palatable



# Examples LCT

- 6-year old girl, BW 20 kg
  - 1400 kcal/day, 24 gm protein (1.2 g/kg/day)
  - Classic 3:1 = 135 gm fat: 46 gm prot+carb

→ 22 gm carb /day !!



# Examples MCT

- 6-year old girl, BW 20 kg
  - 1400 kcal/day, 24 gm protein (1.2 g/kg/day)
  - MCT 50% total calories = 84 g/day
  - Protein ~ 7%, Carb ~ 15% = 53 g/day
  - LCT ~ 28% = 44 g/day
  - K:AK 1.66:1



# Ketosis induction

## ■ Rapid induction

- fasting (12 h - whenever ketosis)
- admission required
- risk of dehydration, glucose, acidosis
- diet titrating up to the target ratio
- caregiver training during admission

# Ketosis induction

## ■ Gradual initiation

- without fasting
- admission = optional
- slower but comparable Sz control at 3 m
- lower initial side effect

Bergqvist, A.G., et al., *Fasting versus gradual initiation of the ketogenic diet: a prospective, randomized clinical trial of efficacy*. Epilepsia, 2005. **46**(11): p. 1810-9.

# Maintenance phase

- Efficacy evaluation after 3 month
- Neuro
  - seizure control
  - cognitive improvement
- urine ketone - compliance
- serum ketone - Sz control



# Maintenance\*

- GI & nutritional assessment
- Blood tests
- Supplements
- Oral citrate
- Adverse effects
- Sick rules



# Sick rules

## ข้อแนะนำเมื่อมีอาการป่วย

1. แจ้งแพทย์ และแสดงบันทึกนี้ทุกครั้ง
2. งดการให้น้ำเชื่อมทุกชนิด
3. หลีกเลี่ยงยาเม็ดและยาฉีดที่มีส่วนผสมของน้ำตาล แอลกอฮอล์ และ แป้ง ในจำนวนสูง
4. หลีกเลี่ยงการให้น้ำเกลือ ถ้าจำเป็นต้องให้ ห้ามให้น้ำเกลือชนิดที่มีน้ำตาลผสมอยู่
5. จำกัดปริมาณน้ำตามที่กำหนดไว้ในแต่ละวัน
6. ถ้ามีการเสียน้ำ เช่น อาเจียน ท้องเสีย เพิ่มปริมาณน้ำได้ชั่วคราวตามเหมาะสม
7. ถ้าป่วยหนัก จำเป็นต้องนอนโรงพยาบาล ควรตรวจน้ำตาลในเลือดตามเหมาะสม

\* ถ้ามีข้อสงสัย ติดต่อ pediatric neurology  
fellow รพ. จุฬาลงกรณ์ 022564996 ต่อ 130

## บันทึกการซัก

ผู้ป่วย ketogenic diet

ภาควิชากุมาร รพ. จุฬาลงกรณ์

ชื่อ .....

HN .....

สูตรอาหาร .....

วันที่เริ่ม .....

Diagnosis .....

.....

.....

.....



# side effects

## Early

- Dehydration
- N/V, diarrhea
- Hyperlipidaemia
- Hyperuricaemia
- HypoCa, HypoMg
- Metabolic acidosis

## Late

- Osteopenia
- Renal stones
- Low carnitine
- Fe def anemia
- Cardiomyopathy(rare)

**\* GI & metabolic effect**

**\* Mostly transient**

# Discontinuation

- Diet maintenance - 2 years if effective
- longer as necessary for GLUT-1, PDHD
- Sudden glucose intake / diet cessation → Sz
- Slow weaning over 2-3 months
- overall recurrence risk - 20%
- Higher in TSC, abnormal EEG, MRI

Martinez, C.C., P.L. Pyzik, and E.H. Kossoff, *Discontinuing the ketogenic diet in seizure-free children: recurrence and risk factors*. Epilepsia, 2007. 48(1): p. 187-90.

# Draw back\*

- Family - Difficult recipe
- Patient - Limited meal

## Options

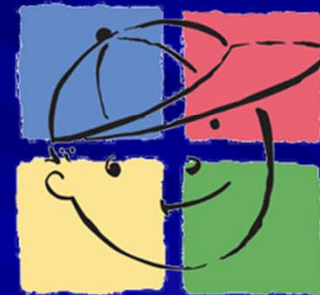
- MAD
- LGIT



# Support group

- Ketocalculator/Ketopaq.....+ support to help in menu planning

**THE CHARLIE FOUNDATION**  
TO HELP CURE PEDIATRIC EPILEPSY





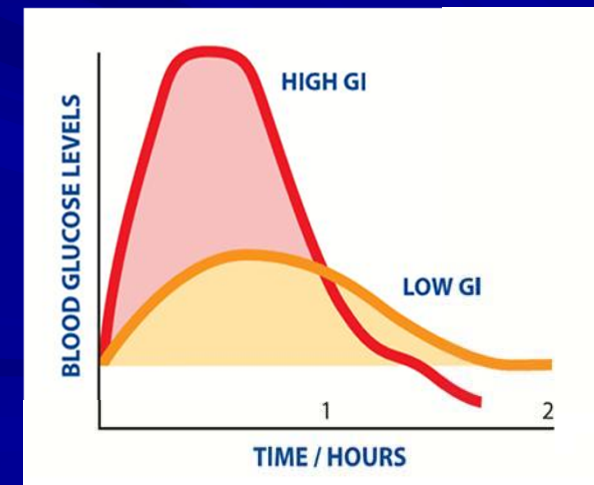
# Modified Atkins

- Similar composition to classical KD
- 1: 1 ketogenic ratio
- Restrict carbohydrate (10-20 g/d)
- No limit on protein, fluids, and calories
- Easier meal planning
- Preliminary effective

*Kossoff et al. Epilepsy Behav 2007:432–436.*

# Low GI

- Less fat than KD
  - More carbohydrate 40–60 g/day
  - CHO type → low glycemic index <50
  - e.g. lentils, grapefruit, whole grain bread
- 
- Less ketone level than KD
  - Still preliminary effective



*Pfeifer and Thiele. Neurology 2005;65:1810–1812.*

# Conclusion

## ■ KD

- proven option, good efficacy
- need good compliance

## ■ Mod Atkins

- easy, palatable