

Program Director: Robert N. Baldassano, MD
Colman Professor of Pediatrics, Children's Hospital of Philadelphia

Present State of the Art on Dietary Management in Crohn's Disease

Dr. Eytan Wine, University of Alberta, Canada

The New Kid on the Block: The Crohn's Disease Exclusion Diet for Induction of Remission Rotem Sigall-Boneh, RD, Wolfson Medical Center, Israel

> NASPGHAN October 18, 2019





Financial Support for this presentation was provided by Nestlé Health Science. The views expressed herein are those of the presenters and do not necessarily represent Nestlé's views. The material herein is accurate as of the date it was presented, and is for educational purposes only and is not intended as a substitute for medical advice.

Reproduction or distribution of these materials is prohibited.

© 2019 Nestlé. All rights reserved.



Present State of the Art on Dietary Management in Crohns Disease

Eytan Wine, MD, PhD, FRCPC

Associate Professor of Pediatrics and Physiology Division of Pediatric Gastroenterology and Nutrition Department of Pediatrics, University of Alberta Edmonton, Alberta, Canada

Nestlé Nutrition Institute Satellite Symposium NASPGHAN, Chicago, IL, USA October 18, 2019

Conflicts of Interest

- I declare the following conflicts of interest:
- I have received honoraria from:
 - Nestlé Health Sciences (advisory board; speaker fee)
 - AbbVie (advisory board; speaker fee)
 - Janssen (conference travel support)
- My laboratory is funded by:
 - Crohn's and Colitis Foundation of America (CCFA)
 - Canadian Institutes of Health Research (CIHR)
 - Weston Foundation
 - IMAGINE SPOR Network

Presentation Overview

- Why diet in IBD?
- Exclusive enteral nutrition (EEN) works!
- However... not the perfect treatment
- Looking into mechanisms
- Is there anything better out there?

Presentation Overview

- Why diet in IBD?
- Exclusive enteral nutrition (EEN) works!
- However... not the perfect treatment
- Looking into mechanisms
- Is there anything better out there?

Diet and Crohns Disease: What's out there?

#1 question
I get

#3 research priority

The Recent Buzz: Diet and IBD



Dietary interventions for induction and maintenance of remission in inflammatory bowel disease (Review)

Limketkai BN, Iheozor-Ejiofor Z, Gjuladin-Hellon T, Parian A, Matarese LE, Bracewell K, MacDonald JK, Gordon M, Mullin GE

Authors' conclusions

The effects of dietary interventions on CD and UC are uncertain. Thus no firm conclusions regarding the benefits and harms of dietary interventions in CD and UC can be drawn. There is need for consensus on the composition of dietary interventions in IBD and more RCTs are required to evaluate these interventions. Currently, there are at least five ongoing studies (estimated enrollment of 498 participants). This review will be updated when the results of these studies are available.

Presentation Overview

- Why diet in IBD?
- Exclusive enteral nutrition (EEN) works!
- However... not the perfect treatment
- Looking into mechanisms
- Is there anything better out there?

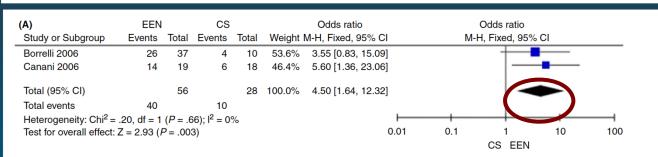
Meta-analysis: EEN vs. Steroids

Induction of remission: equivalent; OR 1.26 (0.77, 2.05) favouring EEN

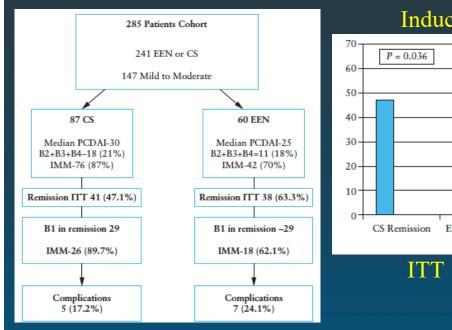
SWAMINATH ET AL. · AP&T Alimentary Pharmacology & Therapeutics — WII FY EEN CS Odds ratio Odds ratio Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI M-H. Fixed, 95% CI Borrelli 2006 15 19 12 18 9.1% 1.88 [0.43, 8.20] Canani 2006 32 10 6.7% 0.71 [0.07, 6.89] Hojsak 2014 57 17 0.15 [0.01, 2.64] 48 17 15.4% Kierkas 2013 11 16.7% 1.27 [0.38, 4.22] Lambert 2013 0.68 [0.15, 3.16] 23 26 14.2% Levine 2014 1.43 [0.61, 3.35] 31 109 32.8% Luo 2015 9 10 18 2.3% 9.00 [0.94, 86.52] Sanderson 1987 2.8% 1.17 [0.06, 22.94] Total (95% CI) 226 225 100.0% 1.26 [0.77, 2.05] Total events 179 161 Heterogeneity: $Chi^2 = 6.27$, df = 7 (P = 0.51); $I^2 = 0\%$ 0.01 Test for overall effect: Z = 0.91 (P = 0.37) Favours CS Favours EEN

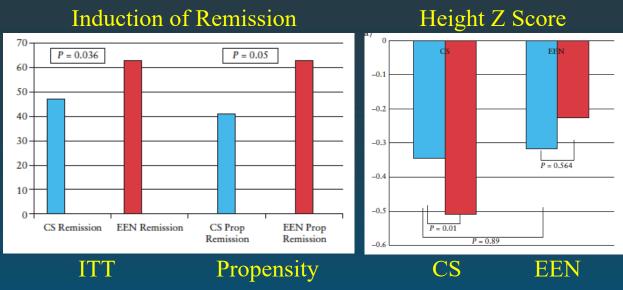
FIGURE 2 Comparison of remission induction for EEN vs CS

Mucosal Healing: EEN is superior: OR 4.5 (1.46, 12.23)



Differences in Outcomes Over Time With Exclusive **Enteral Nutrition Compared With Steroids in** Children With Mild to Moderate Crohn's Disease: Results From the *GROWTH CD* Study





Mucosal Healing and Bacterial Composition in Response to Enteral Nutrition Vs Steroid-based Induction Therapy—A Randomised Prospective Clinical Trial in Children With Crohn's Disease

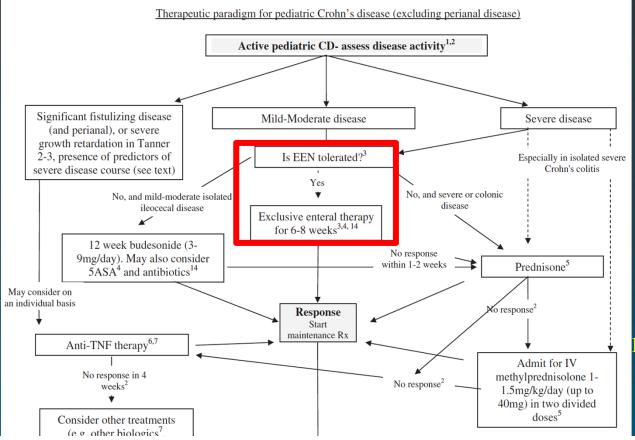
Bénédicte Pigneur, a,b,o Patricia Lepage, Stanislas Mondot, Jacques Schmitz, Olivier Goulet, Joël Doré, d,* Frank M. Ruemmelea,b,*

		EEN group	CS group	p-Value	
		[n = 13]	[n = 6]		
z-score BMI		-0.05 ± 0.9	0.35± 1.0	NS	
Harvey-Bradshaw Index <5		13 [100%]	5 [83%]	< 0.05	
Haemoglobin [g/dL]		11.0 ± 1.1	11.9 ± 0.9	NS	
	Median	10.7 [8.7-12.1]	12.2 [10-12.6]		
CRP [mg/L]		12.3± 19.3	42.8 ± 74.8	NS	
	Median	6 [1-75]	14 [6-195]		
ESR [mm]		16.5± 24.5	21.2 ± 23.7	NS	
	Median	8 [4-94]	12 [7-69]		
Alb					
	EEN (13)	Steroids (6)			
Plat			\	.0.05	
Median CDEIS	1 (0-21)	7 (3	-14)	p<0.05	

Pigneur *et al.*, JCC 2019;13:846-55.

CONSENSUS/GUIDELINES

Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease



Ruemmele *et al.*, JCC 2014;8:1179-207.

Presentation Overview

- Why diet in IBD?
- Exclusive enteral nutrition (EEN) works!
- However... not the perfect treatment
- Looking into mechanisms
- Is there anything better out there?

Exclusive Enteral Nutrition: 6-8 weeks

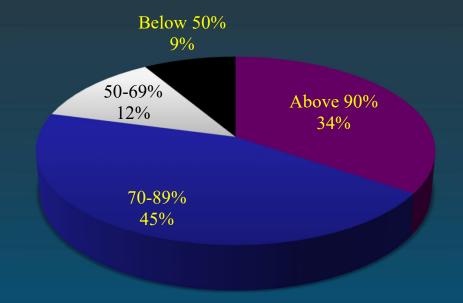


- + At least as effective as steroids
- + Improves nutritional status
- + Improves Bone
- + Associated Mucosal Healing
- + No Side Effects

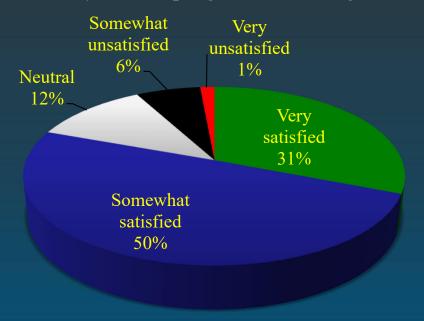
- Difficult for patients
- Difficult for Parents
- Difficult for Physician
- Demands Resources & Dedication
- Limited long-term benefit

EEN Program Assessment and Challenges

What percentage of your patients actually fully follow your guidance on EN?



How satisfied are you with the way your EN program is running?



Global Variation in Use of Enteral Nutrition for Pediatric Crohn Disease

Morgan Lawley, Jessica W Wu, Victor M Navas-López, Hien Q Huynh, Matthew W Carroll, Min Chen, Pavel Medvedev, Andrew S Day, Séamus Hussey, Rotem Sigall-Boneh, Arie Levine, Eytan Wine

Major Barriers	Overall	CAN	US	UK	SPN	E-O
Don't think it's as effective	3%	0%	11%	0%	5%	3%
Poor adherence due to palatability	42%	29%	63%	18%	30%	62%
Poor adherence due to monotony	58%	57%	84%	18%	55%	62%
Too much effort/easier to write a prescription	11%	14%	5%	0%	10%	16%
Lack of dietitian/nurse support	21%	29%	11%	0%	33%	14%
Too costly to my practice	1%	0%	5%	0%	0%	3%
Too costly to my patients***	19%	48%	58%	0%	0%	14%
Other	8%	24%	5%	27%	3%	5%
No barriers*	18%	5%	5%	55%	23%	14%

If we could figure out how diet affects IBD we could come up with better solutions!

Lawley et al. JPGN 2018;67(2):e22-e29.

Presentation Overview

- Why diet in IBD?
- Exclusive enteral nutrition (EEN) works!
- However... not the perfect treatment
- Looking into mechanisms

Thank you Prof. Levine!

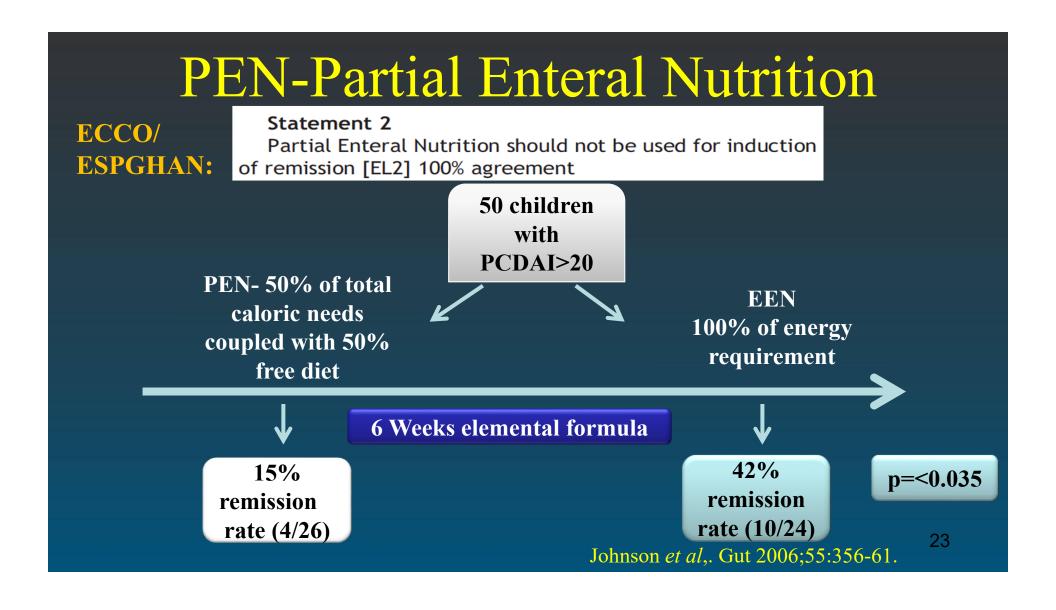
• Is there anything better out there?

Presentation Overview

- Why diet in IBD?
- Exclusive enteral nutrition (EEN) works!
- However... not the perfect treatment
- Looking into mechanisms
- Is there anything better out there?

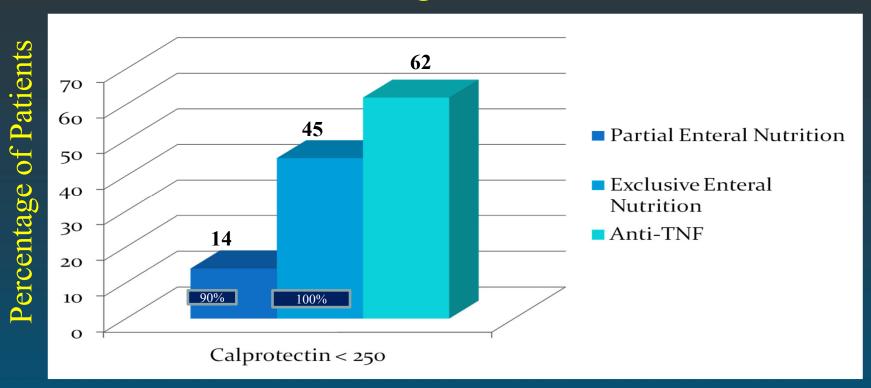
Alternatives to EEN

- PEN
- Trigger-based diet
- Specific carbohydrate diet
- CD-TREAT
- Personalized diets (microbe driven?)
- Crohn disease exclusion diet (CDED)



PLEASE Study:

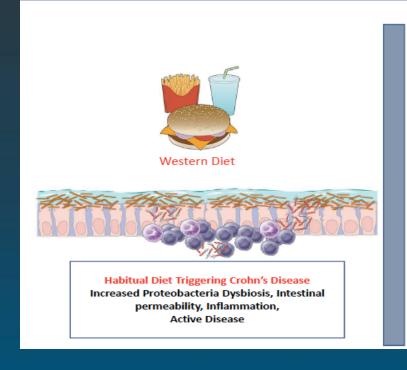
Greater Mucosal Healing with More Restrictive Diet

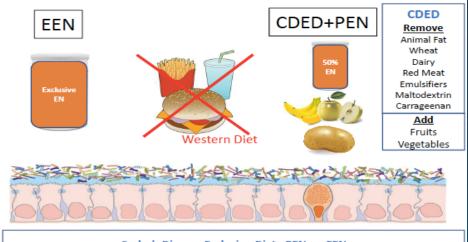


Lee et al,. Inflamm Bowel Dis 2015;21:1786-93. 24

Crohn's Disease Exclusion Diet is Equally Effective but Better Tolerated than Exclusive Enteral Nutrition for Induction of Remission in Mild to Moderate Active Paediatric Crohn's Disease: A Prospective Randomized Controlled Trial

Dietary Therapy: Crohn's Disease Exclusion Diet + Partial Enteral Nutrition vs. Exclusive Enteral Nutrition





Crohn's Disease Exclusion Diet+ PEN vs. EEN

Primary endpoint: CDED+PEN is better tolerated than EEN Secondary endpoints:

Both CDED+PEN and EEN are effective to achieve remission at week 6 CDED+PEN is superior to sustain remission and reduce inflammation at week 12 CDED+PEN: associated with reduction in Proteobacteria and Intestinal Permeability

The New Kid on the Block: The Crohn's Disease Exclusion Diet for Induction of Remission

Rotem Sigall Boneh, RD
Clinical and research dietitian
Wolfson Medical Center, Holon, Israel

October 18, 2019 Chicago, IL

Disclosures

- Speaker for Nestlé Health Science and Takeda
- Consulting for Nestlé Health Science

Why use the CDED?

Includes whole food, easier to perform and maintain compared to EEN, with better tolerance

Offers effective treatment for short and long term-induction and maintenance of remission

Includes fiber and substrates required to produce SCFA

Is designed to be nutritionally balanced

The Crohn's Disease Exclusion Diet (CDED)

- Previously demonstrated in case series
 - ✓ CDED+PEN induced remission, decreased inflammation in children and adults and was associated with mucosal healing
 - ✓ CDED+PEN induced remission and decreased inflammation in children and adults who LOR to anti-TNFα

Journal of Crohn's and Colitis, 2017, 1205–1212 doi:10.1093/ecco-jcc/jjx071 Advance Access publication May 19, 2017 Original Article

Partial Enteral Nutrition with a Crohn's Disease Exclusion Diet Is Effective for Induction of Remission in Children and Young Adults with Crohn's Disease

Rotem Sigall-Boneh, RD,* Tamar Pfeffer-Gik, RD,* Idit Segal, MD,* Tsili Zangen, MD,* Mona Boaz, RD, PhD,^{†,‡} and Arie Levine, MD*[‡]

Original Article

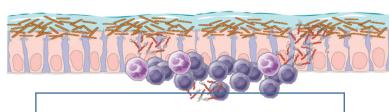
Dietary Therapy With the Crohn's Disease Exclusion Diet is a Successful Strategy for Induction of Remission in Children and Adults Failing Biological Therapy

Rotem Sigall Boneh,^a Chen Sarbagili Shabat,^a Henit Yanai,^{b,c} Irit Chermesh,^d Siyan Ben Ayraham,^a Mona Boaz,^{e,f} Arie Levine^{a,c}

Sigall Boneh et al. Inflamm Bowel Dis 2014;00:1-8

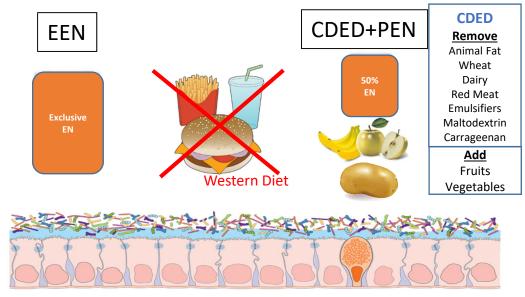
<u>Crohn's Disease Exclusion Diet + PEN</u> vs. Exclusive Enteral Nutrition **Gastroenterology 2019**





Habitual Diet Triggering Crohn's Disease

Increased Proteobacteria Dysbiosis, Intestinal permeability, Inflammation, **Active Disease**



Crohn's Disease Exclusion Diet+PEN vs. EEN

Primary endpoint: CDED+PEN is better tolerated than EEN Secondary endpoints:

Both CDED+PEN and EEN are effective to achieve remission at week 6 CDED+PEN is superior to sustain remission and reduce inflammation at week 12 CDED+PEN: associated with reduction in Proteobacteria and Intestinal Permeability

Levine A et al. Gastroenterology 2019;157:440-450

CDED Trial - RCT Comparing CDED+PEN to EEN Followed by PEN

78 patients mild to moderate CD, mean age 14.2±2.7 years

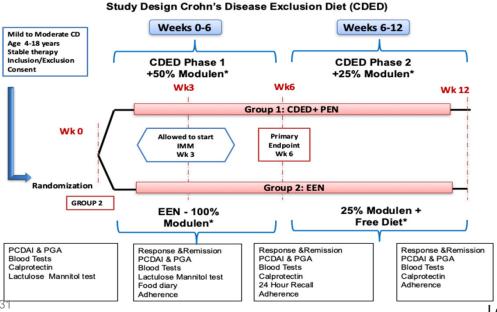


Table 1. Baseline Participant Demographics

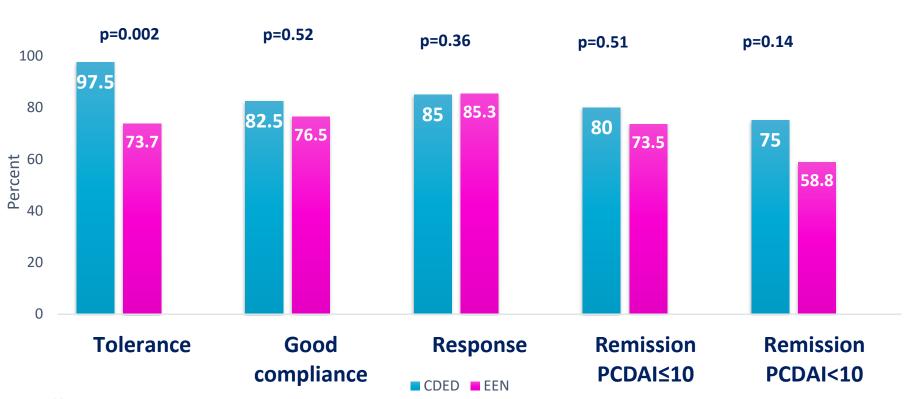
Variable	CDED n = 40	EEN n = 34	P
Mean age, yr ± SD	13.8 ± 2.8	14.5 ± 2.6	.247
Gender (males %)	26 (65)	20 (59)	.58
Disease duration, mo ± SD	2.4 ± 6	2 ± 4.8	.88
Median PCDAI (interquartile range)	25 (20–35)	27.5 (18.75–32.5)	.89
Median CRP (g/L)	23.6 (9-55)	24 (9.7-53)	.85
Range 1.1-146 g/L			
Immunomodulators, n (%)	3 (7.5)	4 (11.5)	.69
Disease location Paris			.5
Classification, n (%)			
L1	18 (45)	14 (41)	.94
L2	2 (5)	1 (2.9)	
L3	19 (47.5)	15 (34)	
L4a	14 (35)	13 (38.2)	
L4b	2 (5)	3 (8.8)	

*Modulen will be given ORALLY

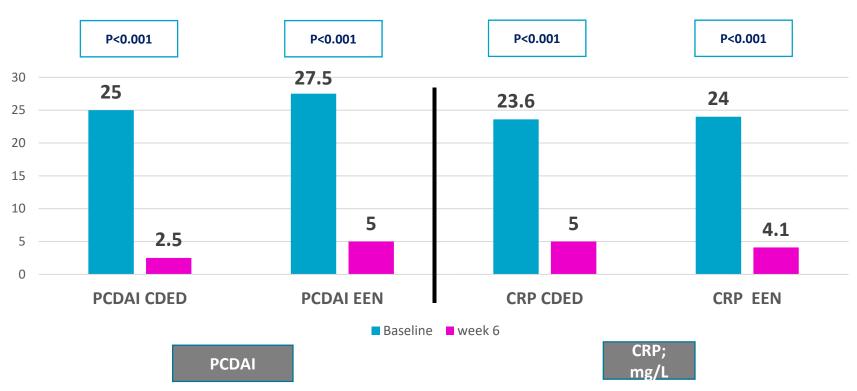
Levine A et al. Gastroenterology 2019;157:440-450

Primary and Secondary Endpoints

Similar Response and Remission Week 6



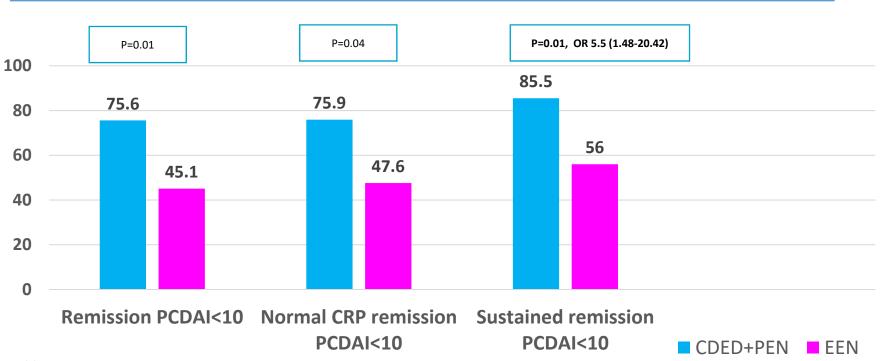
Change in Median PCDAI and CRP Baseline & Week 6



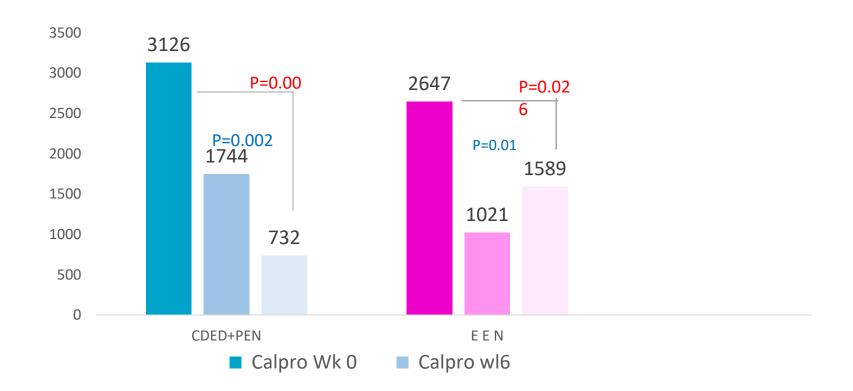
What happens by week 12?

Sustained remission week 12

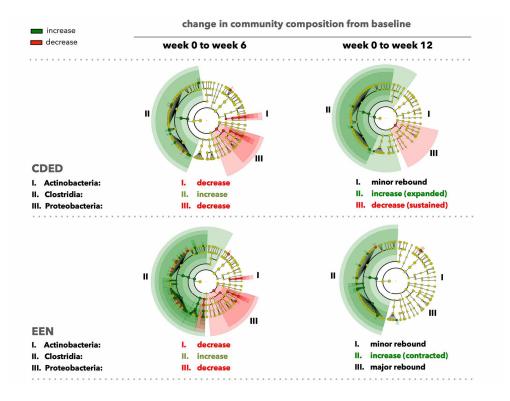
IMM Week 6-12 CDED 37.5% vs. EEN 45%; P=0.6

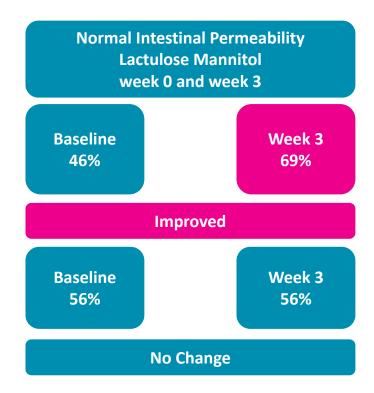


Median Calprotectin changes over 12 weeks



Microbiome & Intestinal Permeability







Crohn's Disease Exclusion Diet

Developed by Prof. Arie Levine

The CDED

Sustainable

Multi-seasonal
Progressive Exposure

No regional limitation

Balanced, allows growth

Palatable

Foods added for correction of dysbiosis and to improve nutritional status

Increased:

- Fruits and Vegetables and Resistant Starch
- High quality of lean protein sources

Contains:

- Complex carbohydrate
- Healthy oils

Reduction in exposure to dietary components is the main mechanism of action

Reduced:

- Animal and saturated Fat
- Taurine
- Wheat
- Heme/iron
- Emulsifiers
- Maltodextrins
- Carrageenan's
- Sulphites
- Dairy products

KEEP IT BALANCED

CDED – Mandatory and Allowed Foods

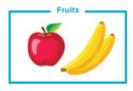
Mandatory foods



Fresh chicken breast minimum of 150-200g/day (unlimited)

Carbohydrate-rich foods

2 fresh potatoes/day peeled, cooked and cooled before consumption



2 bananas/da

1 apple/day peeled

2 eggs/day

Allowed foods

Protein-rich foods

One portion once a week of fresh lean fish replacing the



White rice (unlimited)

Rice noodles without preserva-

tives - one portion per day

Unlimited intake of rice flour for balong



1 avocado/day not more than 1/2 avocado per meal

5 ripe strawberries/day

1 slice of melon/day



2 tomatoes/day (or 6 cherry tomatoes). Additional tomatoes may be used to prepare home made tomato sauce

2 cucumbers/day peeled

1 carrot/day

Fresh spinach (1 cup uncooked leaves/day)

3 lettuce leaves once daily



Oil; olive oil, canola oil

Spices (pure): salt, pepper, paprika crinamon, cumin, curcumin

Fresh herbs: mint, oregano, coriander, rosemary, sage, basil, thyme, dill, parsiav Other seasonings: onlons (all types), garlic, ginger, fresh lemon juice

Sweeteners: honey (3 tbsp/day), table suga (4 tsp/day)

CDED – Disallowed Food

Disallowed foods



Processed meat and fish,

Seafood

Red meat, pork, turkey, other parts of the chicken

Soy products

Dairy products

Ice-cream

Non-dairy milk beverages



Wheat products breeklast

Gluten free products not

Soy products

Legumes (lentils, peas,

Corn

Frozen potatoes

All other flours



Dried fruits

All other fruits



Frozen vegetables

Kale

Leeks

Aspargus

Artichoke

All other vegetables not mentioned as allowed

Margarine Sauces

Salad dressings

Syrups (maple syrup, com

Jam of any kind

Artificial sweeteners

Mixed spices

Other oils (soy oil, sunflower oil, corn oil, etc.) and oil sprays



All soft drinks

Fruit juice

Other sweetened beverages

Alcoholic beverages

Coffee



Canned products

Packaged snacks (poteto

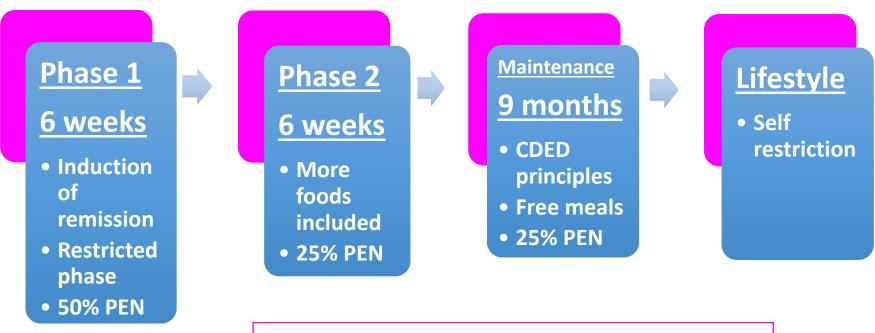
Candy, chocolate, cakes, cookies

Chewing gum

All types of nuts

Visit www.modulifexpert.com and register.

CDED- Program for life

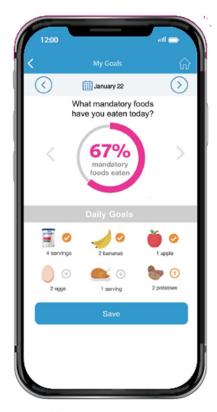


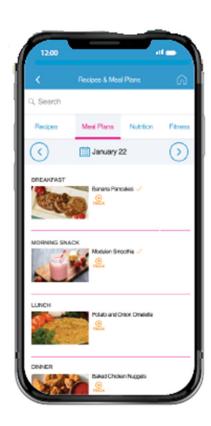
The first 12 weeks are "All or None"

It will only work if patients adhere to it properly



Patient Support Platform- by HCP only





Track food intake, diet adherence and well being



Watch videos with helpful tips for each phase of CDED diet



Access a robust database of CDEDfriendly recipes and meal plans



Message nutrition experts about the CDED diet, anywhere, anytime



CDED History and Near Future

Journal of Crohn's and Colitis, 2017, 1205–1212 doi:10.1083/ecco-jcc/jpx071 Advance Access publication May 19, 2017 Original Article

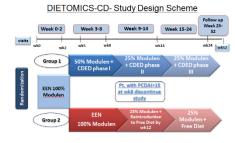
Original Article

Dietary Therapy With the Crohn's Disease Exclusion Diet is a Successful Strategy for Induction of Remission in Children and Adults Failing Biological Therapy

Rotem Sigall Boneh,^a Chen Sarbagili Shabat,^a Henit Yanai,^{b,c} Irit Chermesh,^d Sivan Ben Avraham,^a Mona Boaz,^{e,f} Arie Levine^{a,c}

IBD, 2014

First CDED RCT; 2019



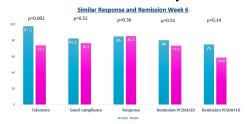
CDED-ADULTS; 2021

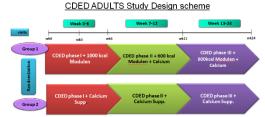
JCC,2017

Partial Enteral Nutrition with a Crohn's Disease Exclusion Diet Is Effective for Induction of Remission in Children and Young Adults with Crohn's Disease

Rotem Sigall-Boneh, RD,* Tamar Pfeffer-Gik, RD,* Idit Segal, MD,* Tsili Zangen, MD,* Mona Boaz, RD, PhD,^{†,‡} and Arie Levine, MD*[‡]







Conclusions

- CDED+PEN is an effective treatment for induction of clinical and biochemical remission after 6 weeks as shown in RCT
- Re-exposure to free diet after EEN increased inflammation and reduced sustained remission
- CDED+PEN allows patients an easier treatment approach with the same efficacy as EEN
- CDED is a nutritional balanced, sustainable, palatable, multi-seasonal dietary program with an established support system; including recipes, mobile app and HCP training sessions
- The CDED+PEN program should be used as instructed, especially during the first 12 weeks
- More studies are warranted

THANK YOU FOR LISTENING!

Visit

www.modulifexpert.com

and register.

Nutrition-related resources and tools are available from Nestlé Nutrition Institute: www.nestlenutrition-institute.org

Visit MyCEeducation.com
Offering CE to dietitians and nurses