

Nutrition in Pediatric Crohn's disease

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Institut national
de la santé et de la recherche médicale



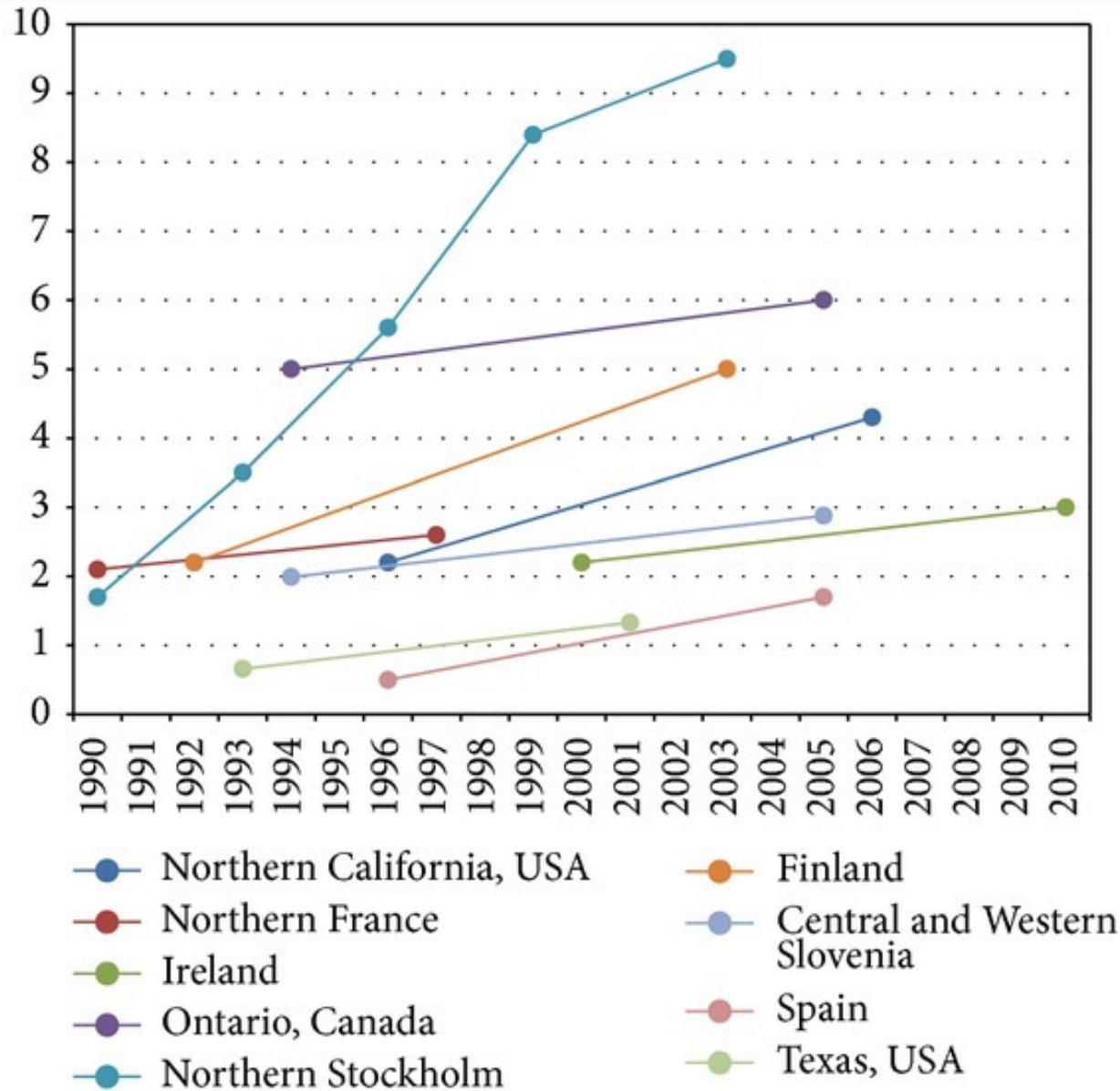
Nutrition in Pediatric Crohn's disease

- **Impaired growth in pediatric CD**
 - *Observation*
 - *Mechanisms*

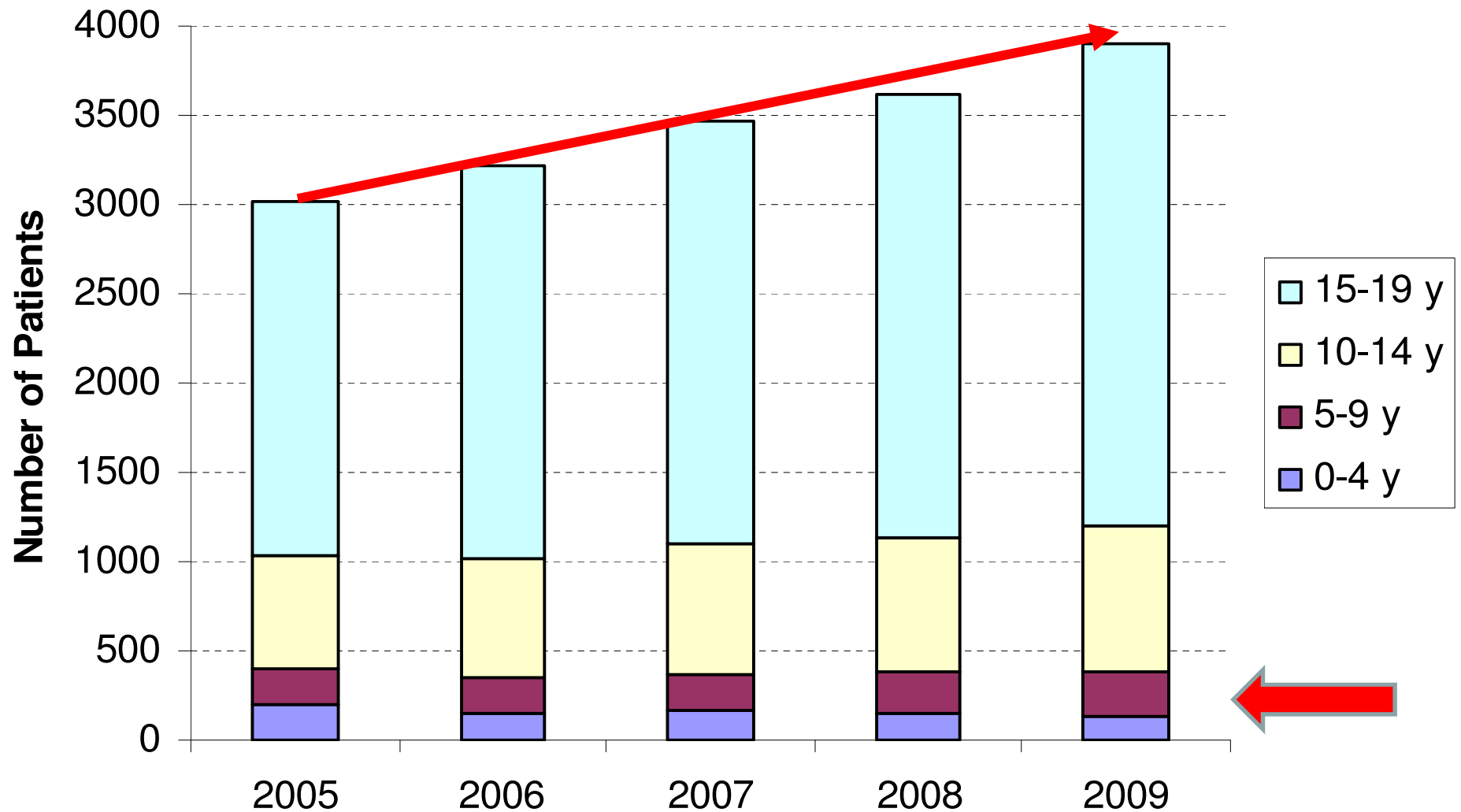
- **Treatment options in pediatric CD**
 - *Enteral feeding ?*
 - *How does it work ?*



Increasing incidence of Crohn's disease



Hospital Prevalence of Pediatric Inflammatory Bowel Diseases In France : *a 5-Year National Survey 2005-2009*

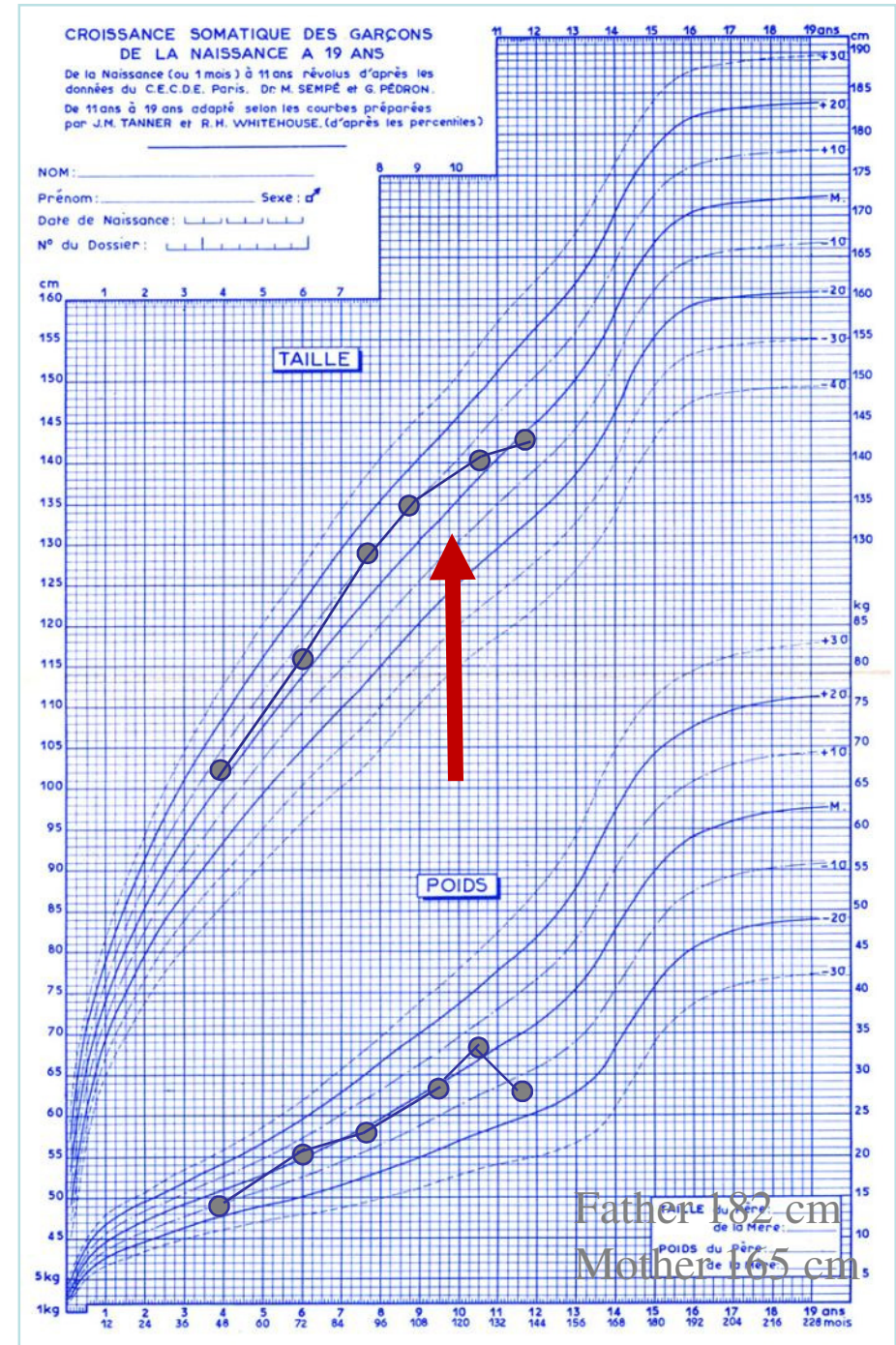


Goulet et al 2012

Weight loss

- Diarrhoea
- Abdominal pain
- Asthenia, anorexia
- Biological inflammation

Crohn's disease

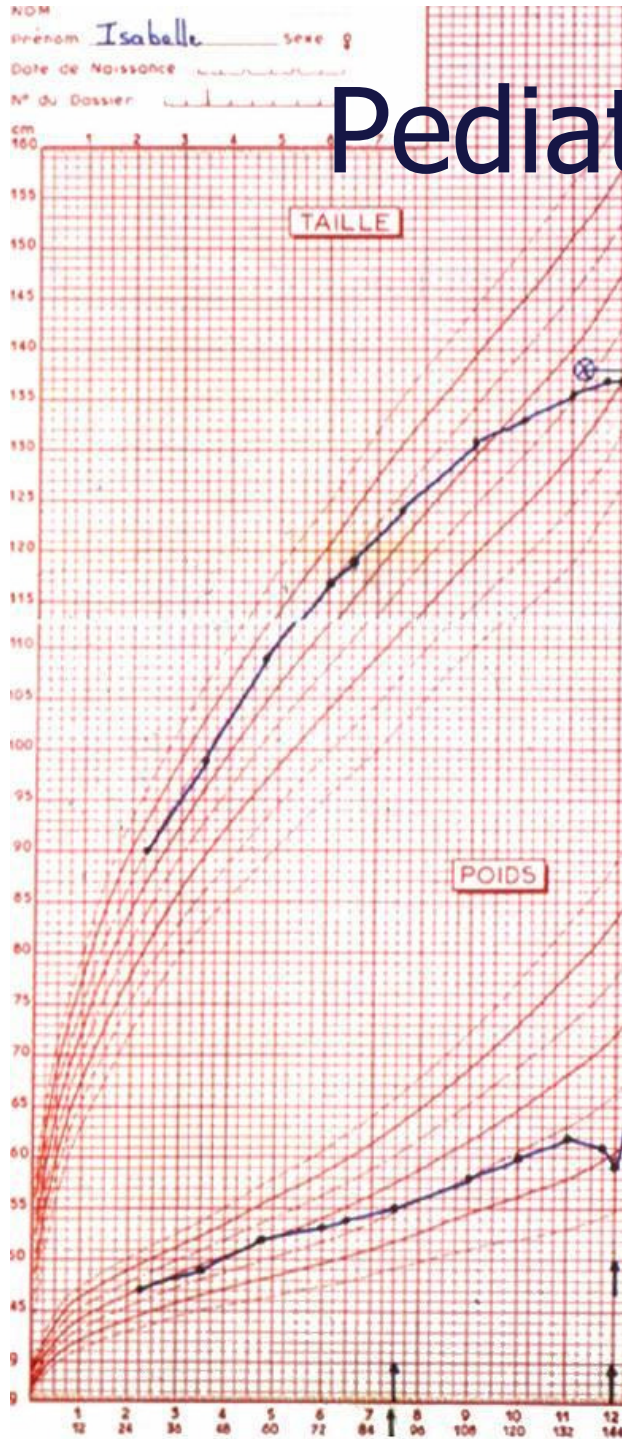


Pediatric Crohn's disease

Growth failure in 30 to 70% of cases

- MOTIL KJ et al - Gastroenterology 1993 ;105:681-91
- HILDEBRAND H. et al - JPGN 1994 ; 18: 165-73
- MARKOWITZ J. et al - JPGN 1993 ; 16: 376-80
- KIRSCHNER BS. et al - JPGN 1993 ; 16: 368-69
- GRIFFITHS AM. et al - GUT 1993 ; 34: 939-43
- FERGUSON A. et al - BMJ 1994 ; 308: 1259-63

Pediatric Crohn's disease

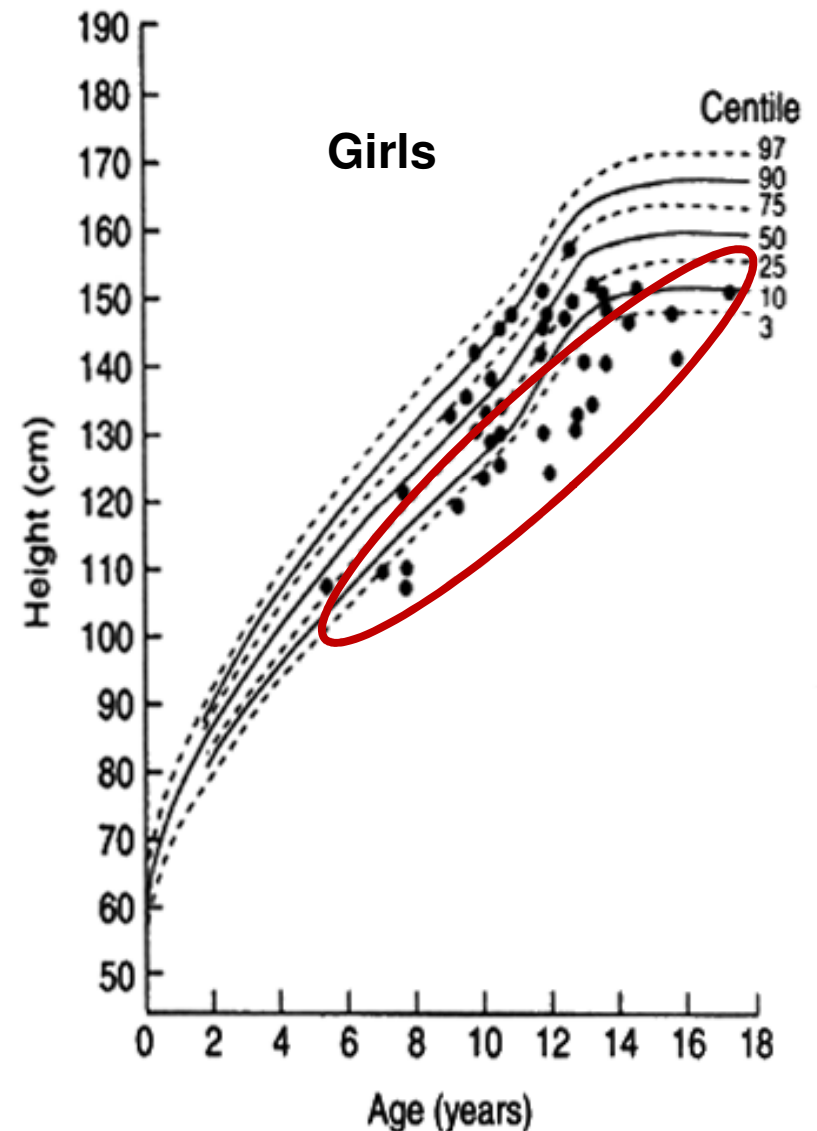
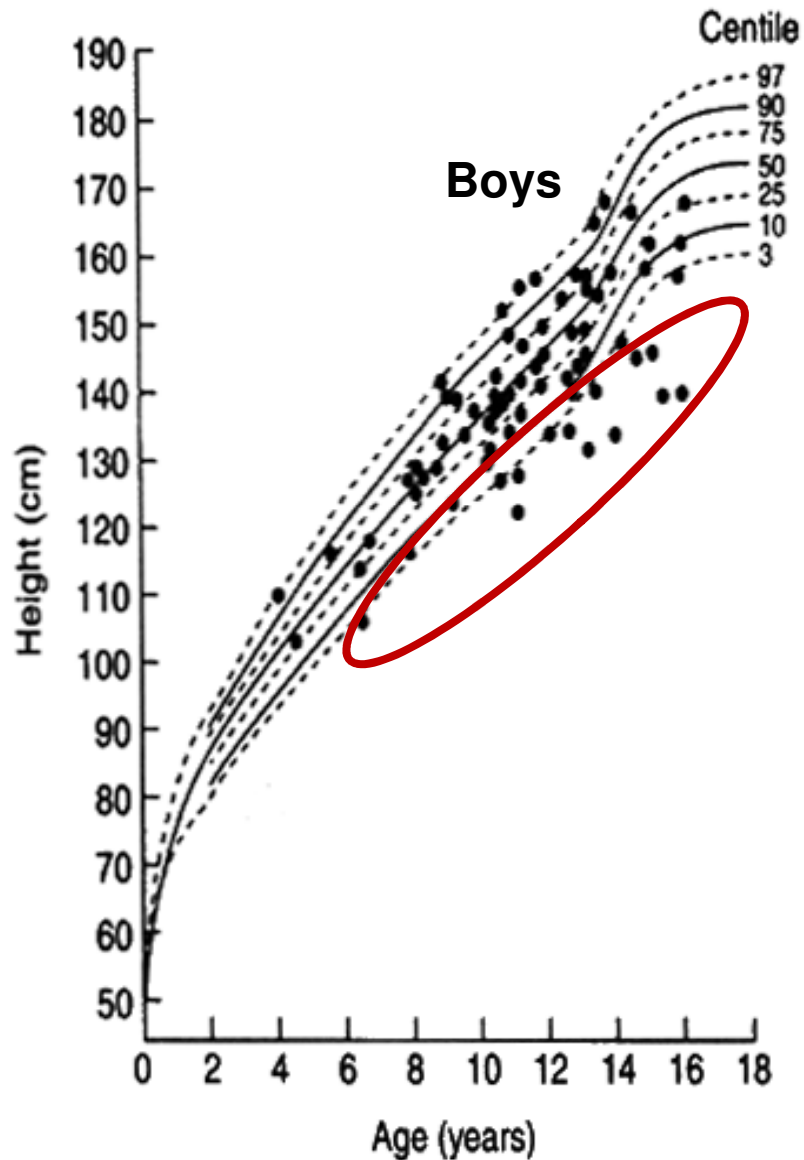


Height / age : 90%

Weight / age: 65%

Weight / height : 75%

Linear growth in pediatric Crohn's disease



Savage et al. Act Paediatr, 1999

The « rendez-vous » of growth

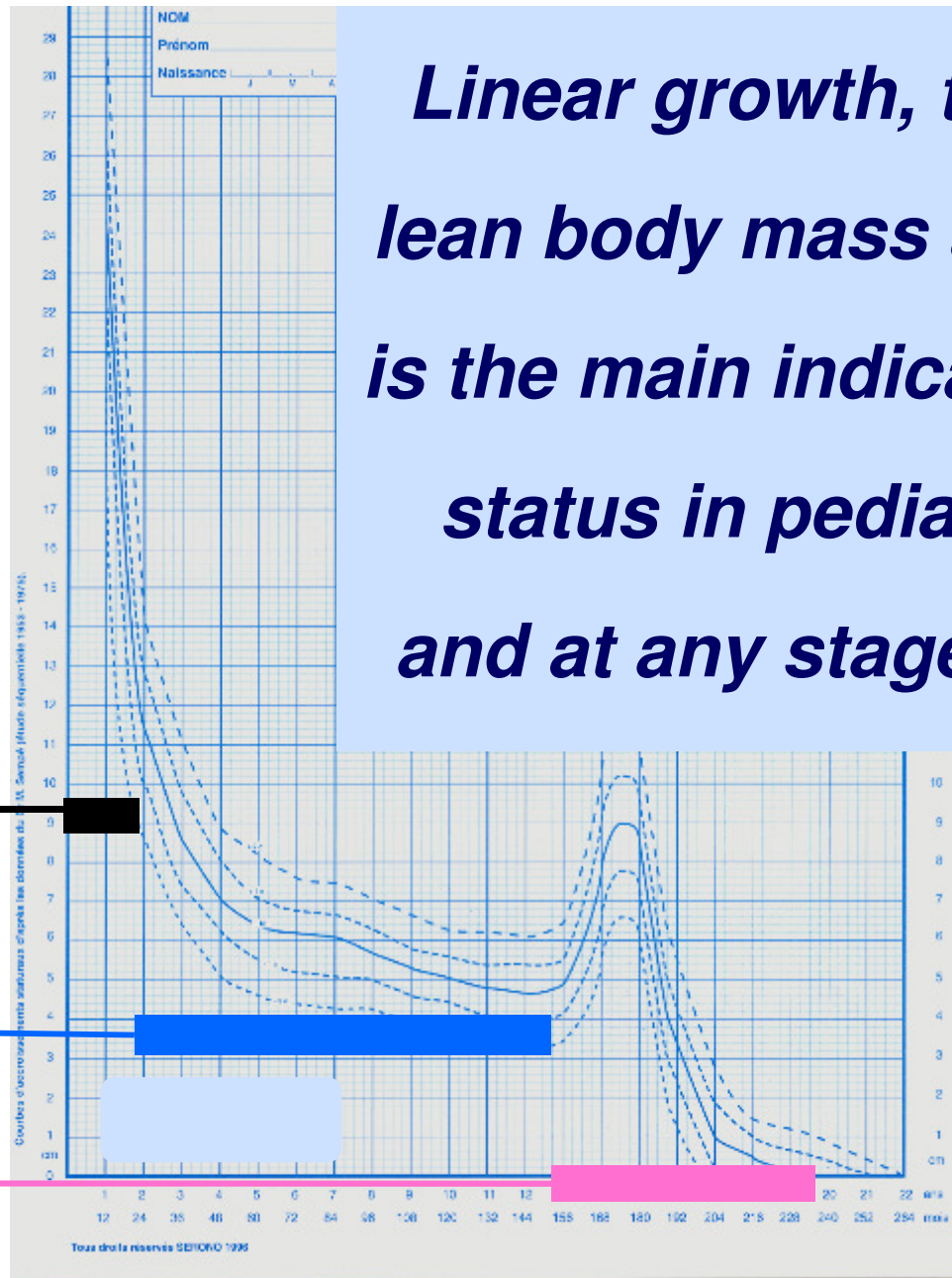
Growth velocity

Linear growth, that is reflecting lean body mass and protein gain, is the main indicator of nutritional status in pediatrics at any age and at any stage of development

Infant

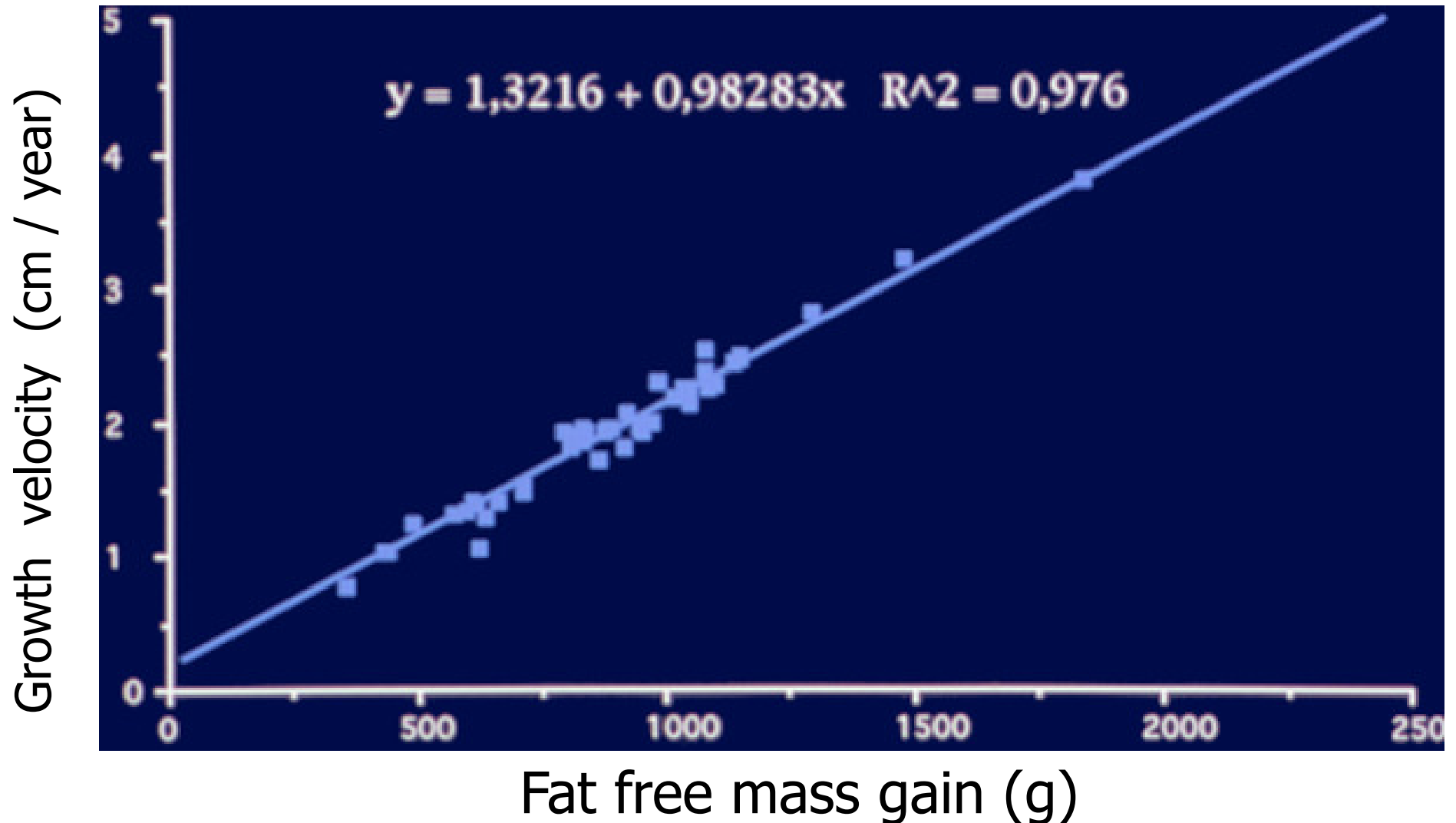
Child

Adolescent



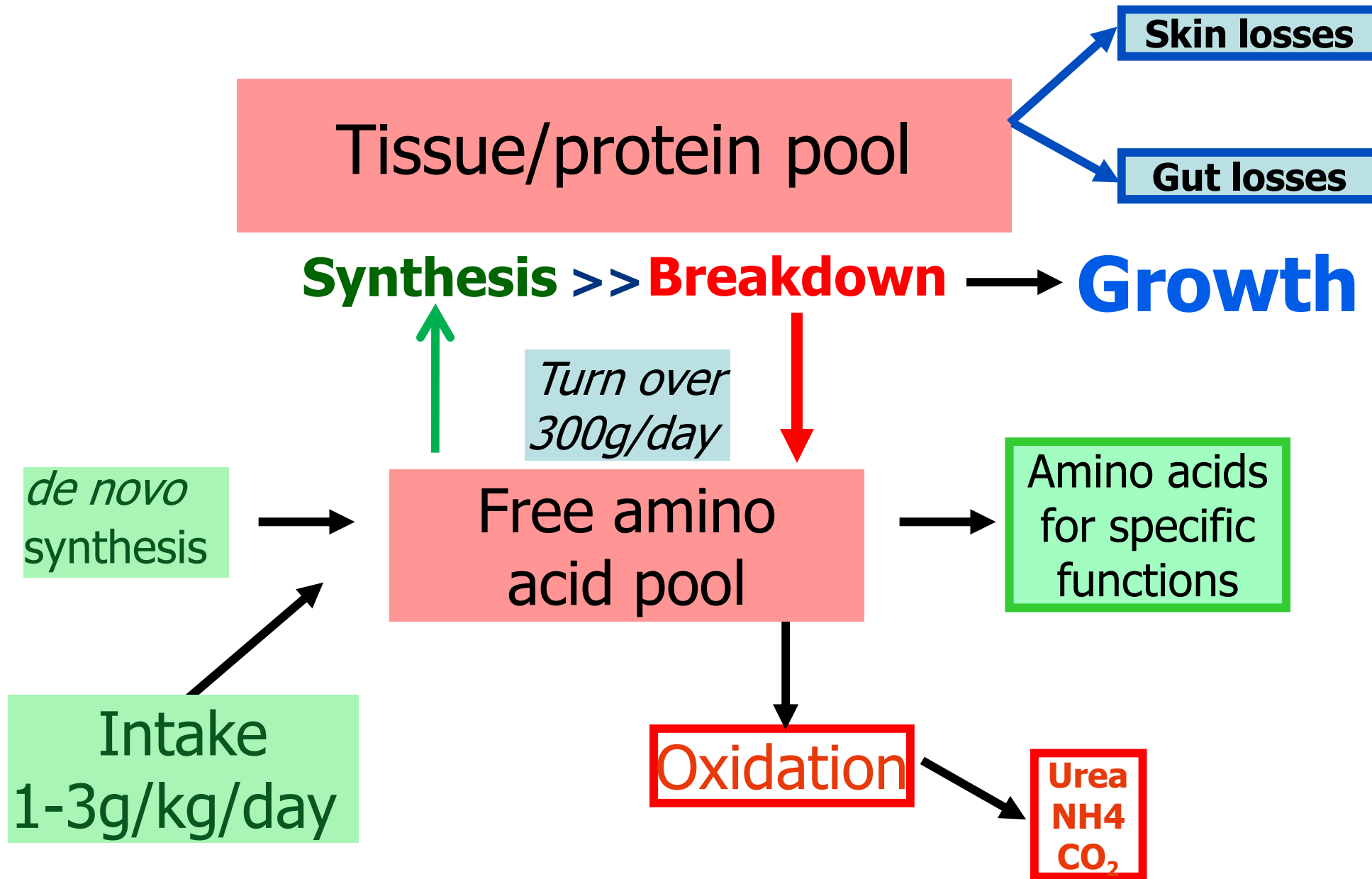
Nutritional changes during childhood

Linear relation between fat free mass gain and growth velocity

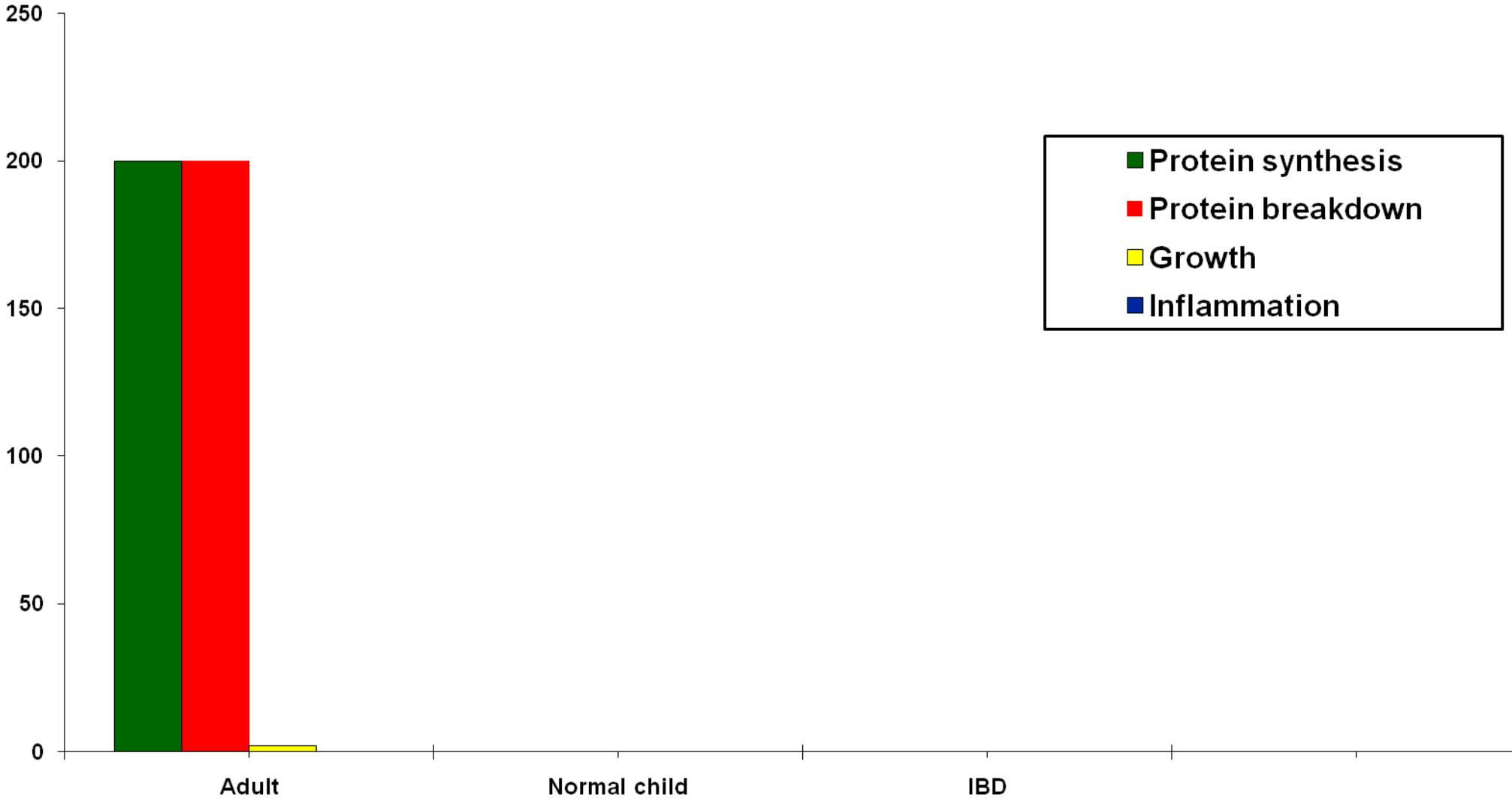


Personnal datas Goulet et al 1989

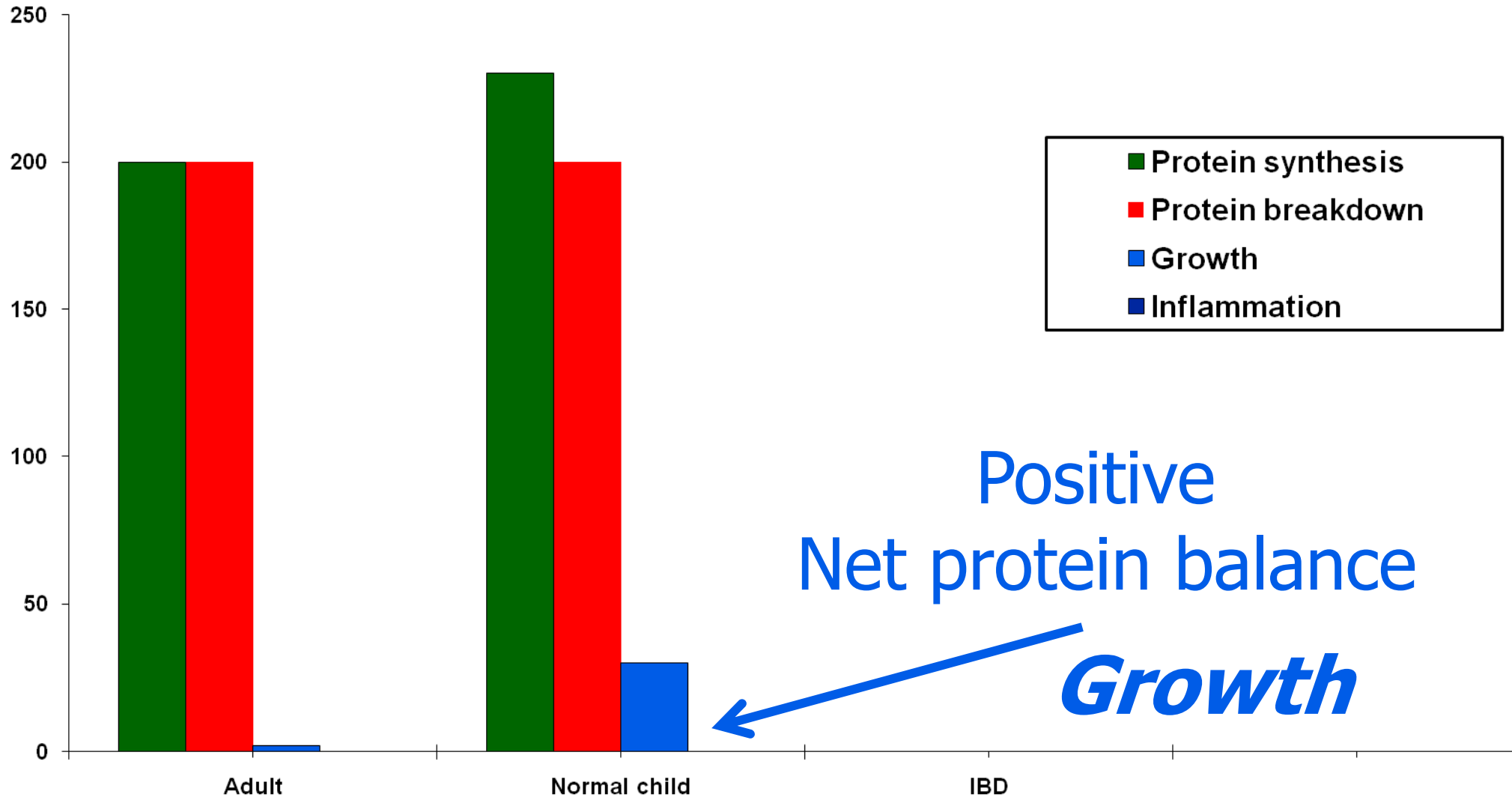
Protein metabolism and protein intake



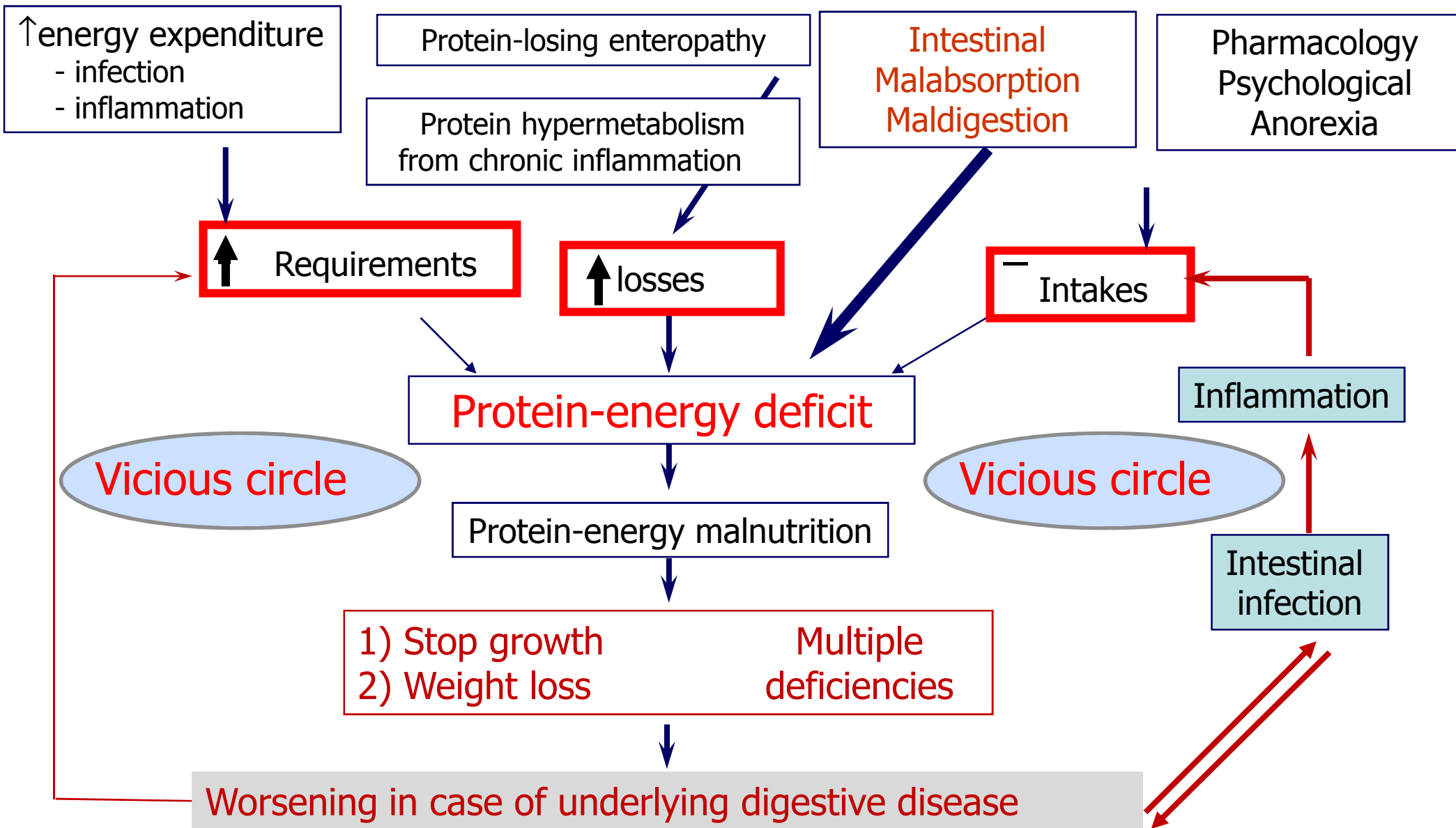
Protein metabolism and growth



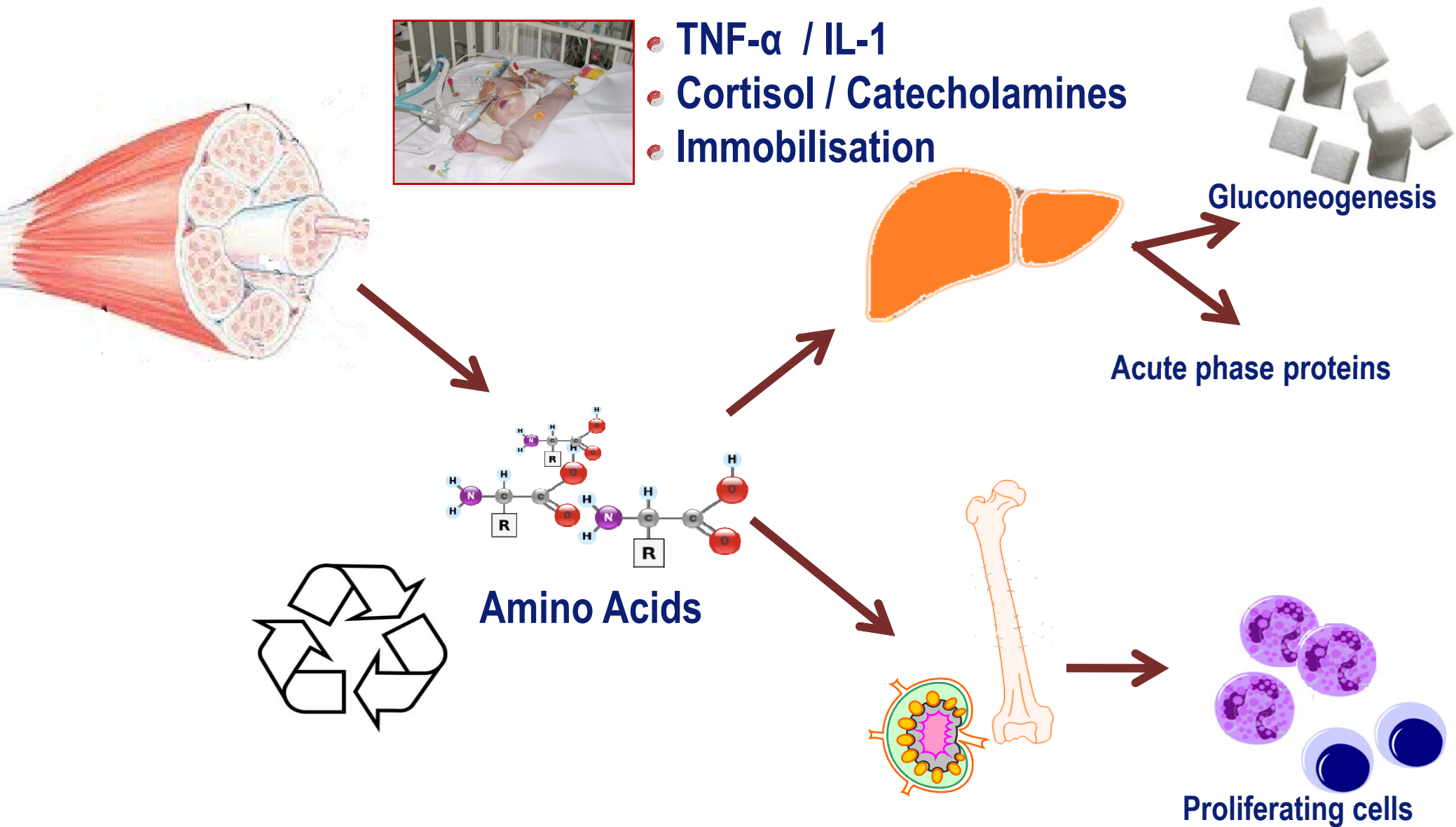
Protein metabolism and growth



Causes and mechanisms of PEM in Pediatrics

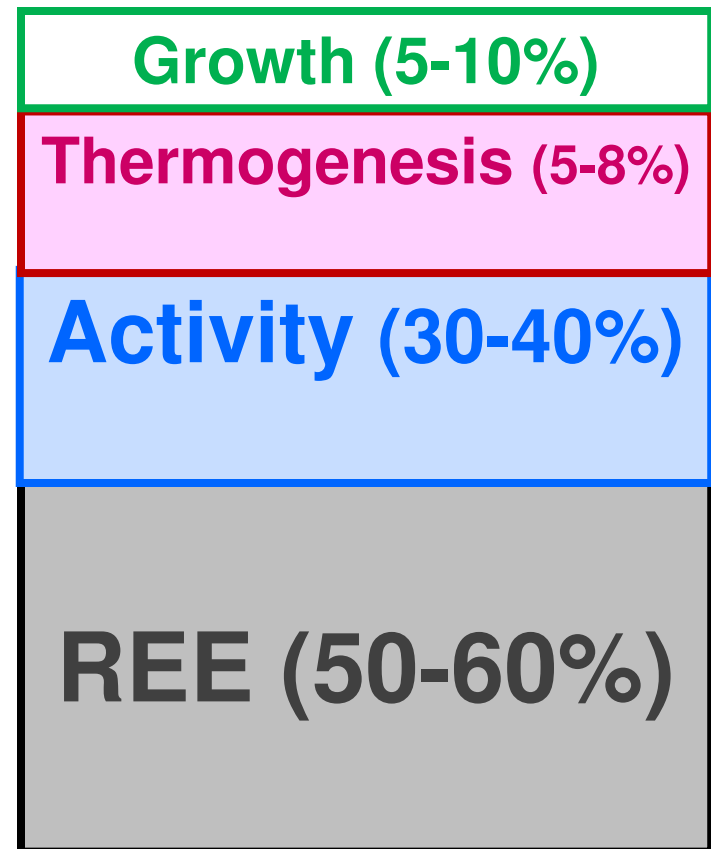


Acute Phase: protein turnover and breakdown



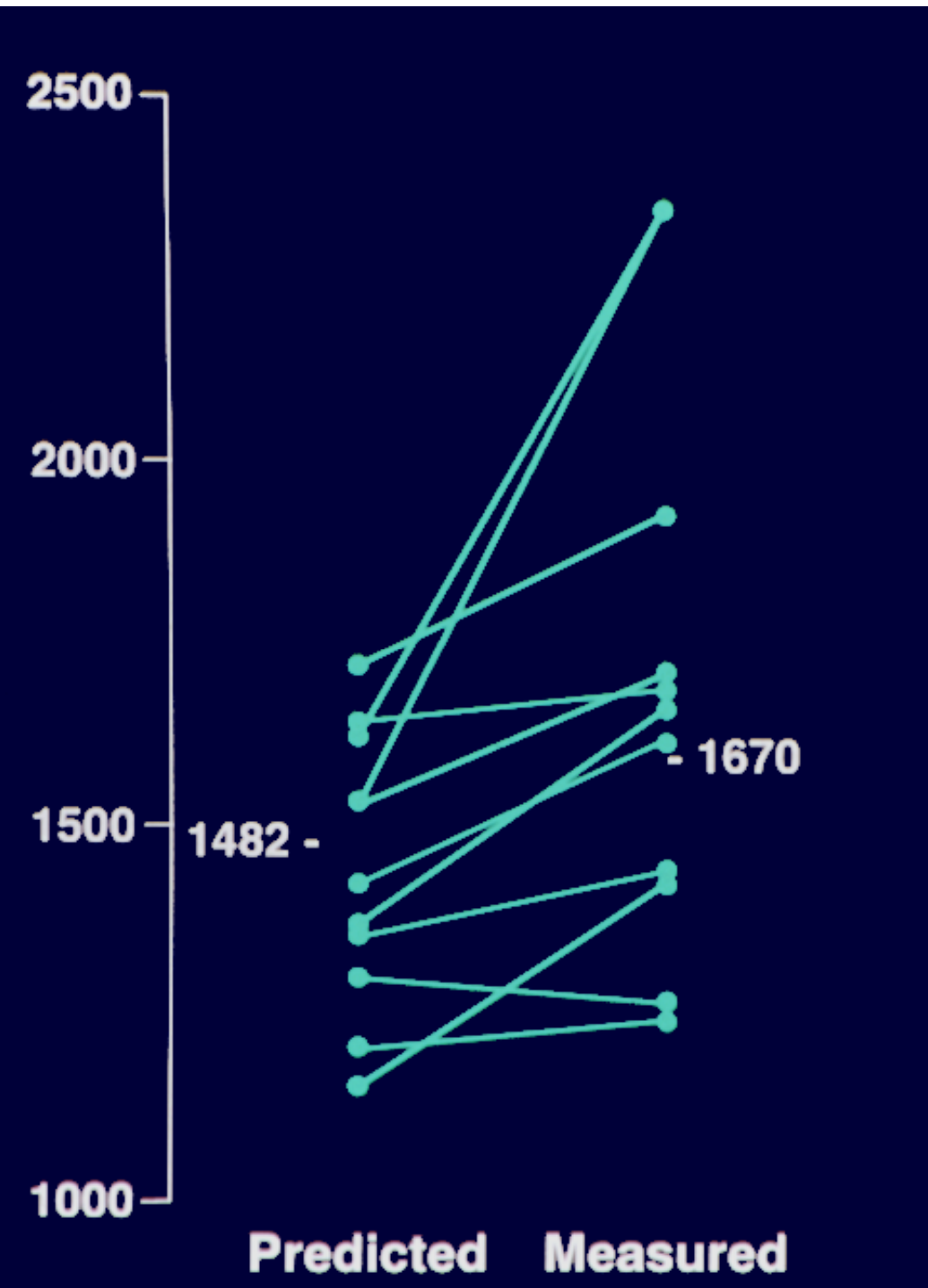
Energy metabolism and growth

↗ requirements
↘ provisions



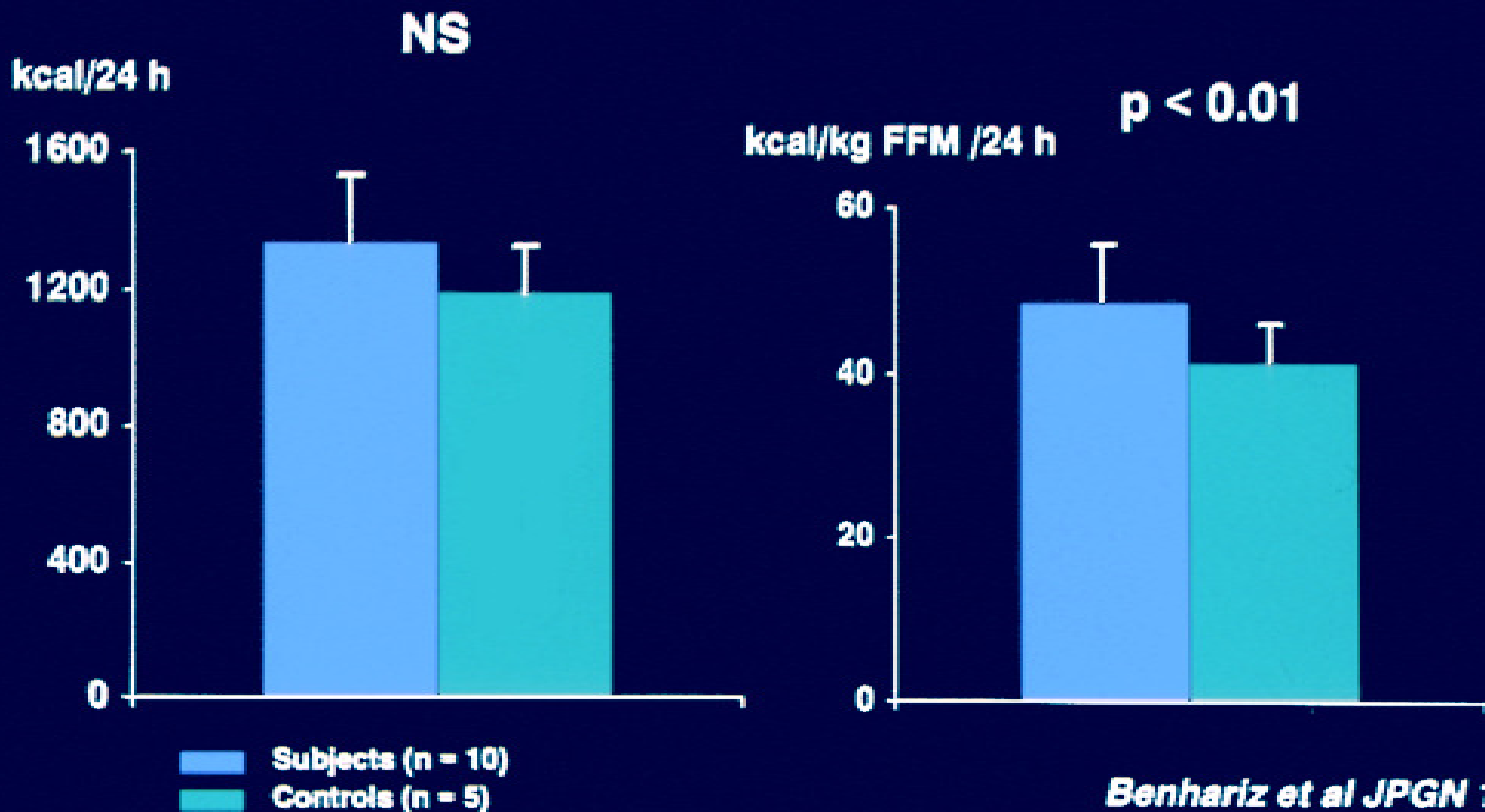
Pediatric Crohn's disease

Energy expenditure in adolescent with Crohn's disease

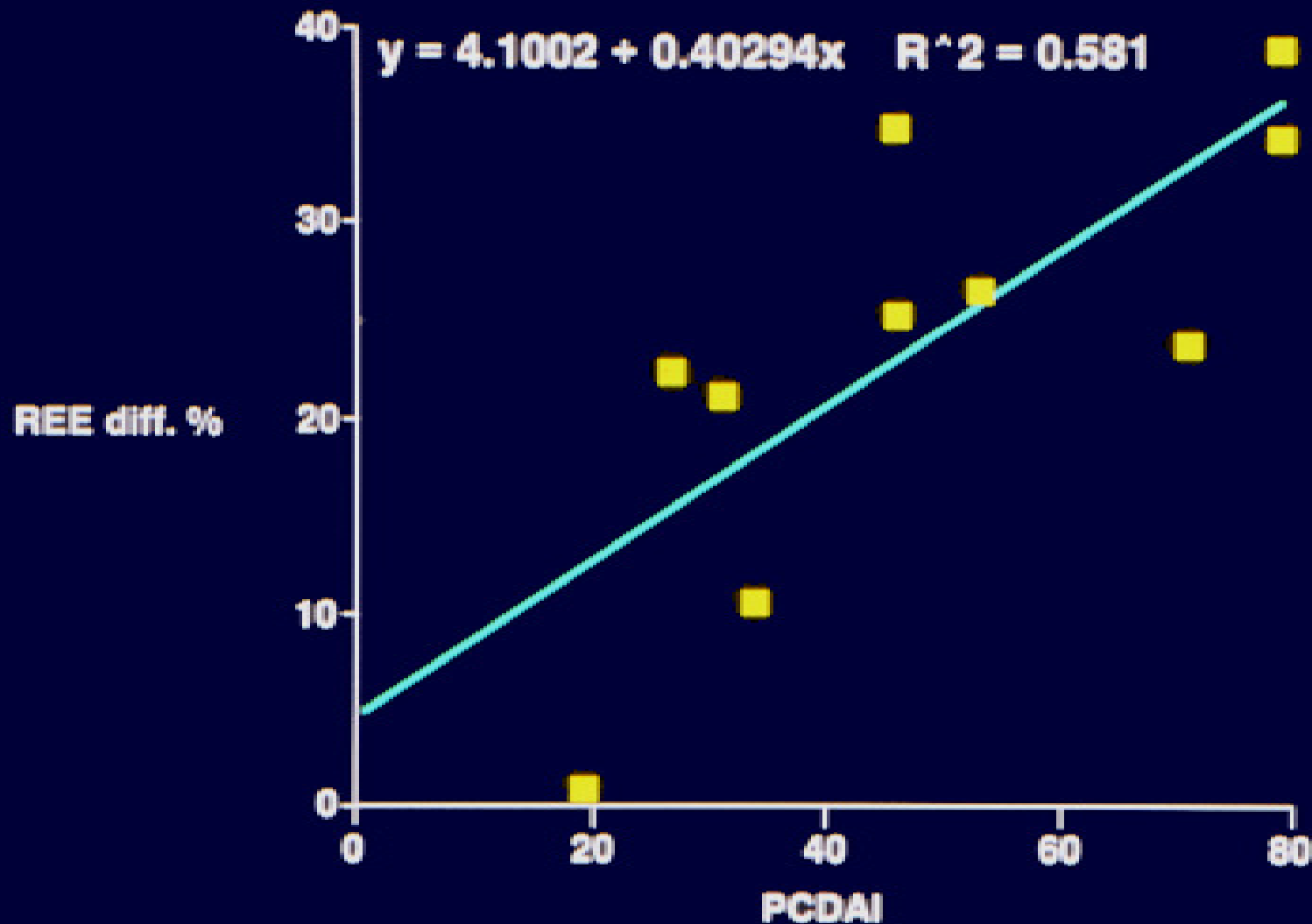


Benhariz....Goulet 1995

Energy expenditure in preadolescents with Crohn's disease

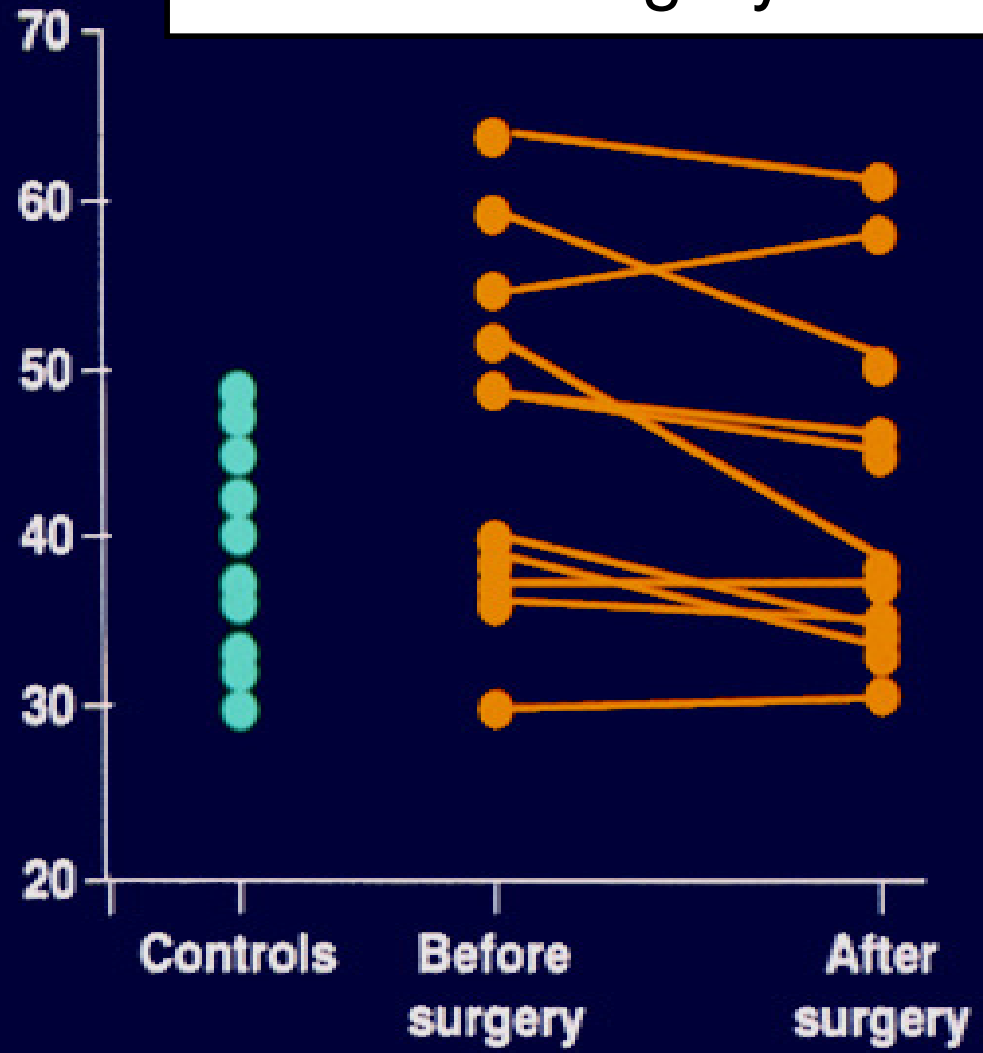


Linear regression analysis between increased REE and PCDAI





Decreased REE
after surgery



Pediatric Crohn's disease

Body mass regulation

- Control of hunger and satiety
- TNF- α or IL-1 might induce leptine
- Model of AIDS associated anorexia

Sarraf et al 1997 and Zumbach et al 1997

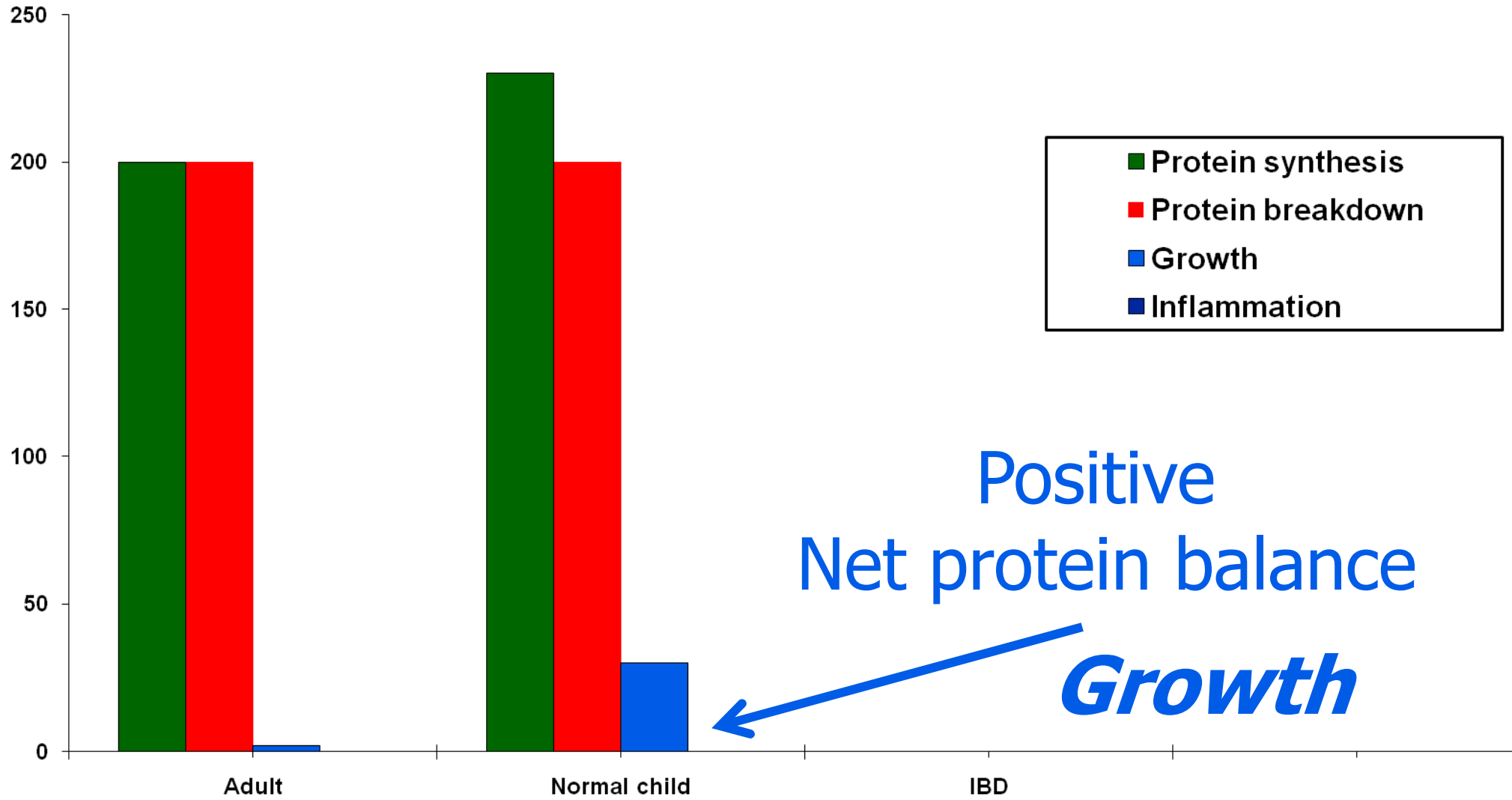
Pediatric Crohn's disease

Impaired protein metabolism

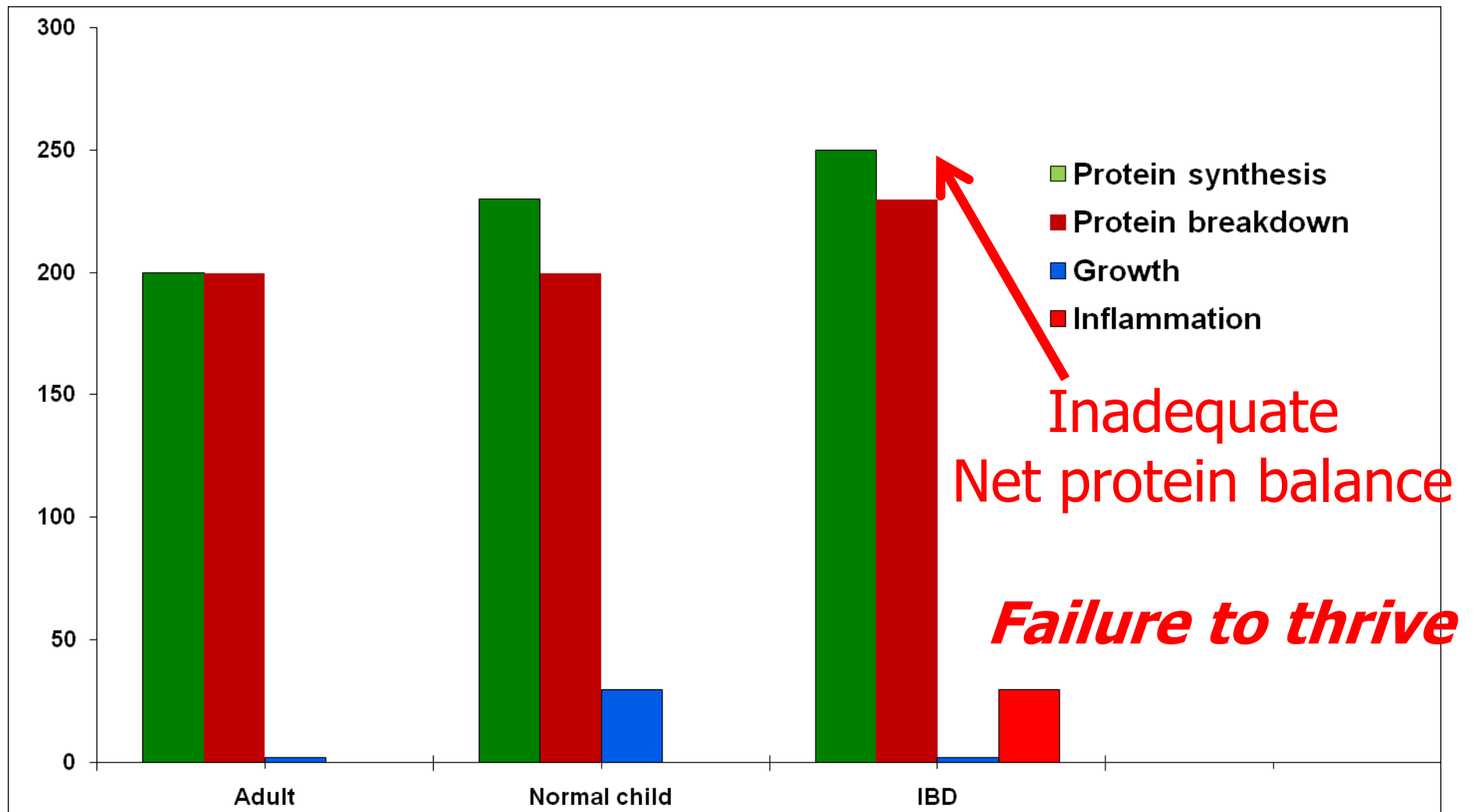
- Motil et al Gastroenterology 1982
- Thomas et al Gut 1992; 33: 675-7

Increased turn over

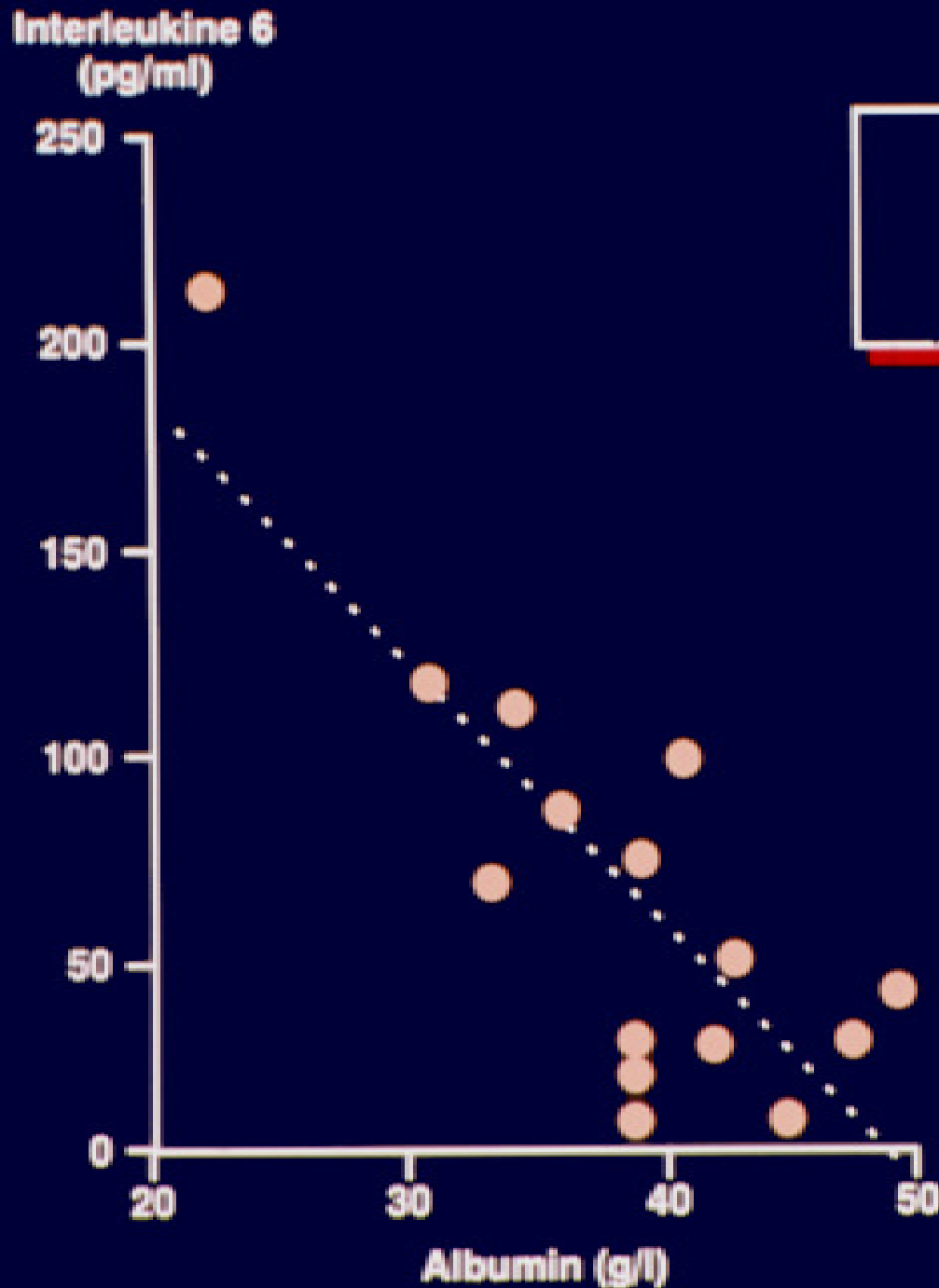
Protein metabolism and growth



Protein metabolism and impaired growth in children with inflammation

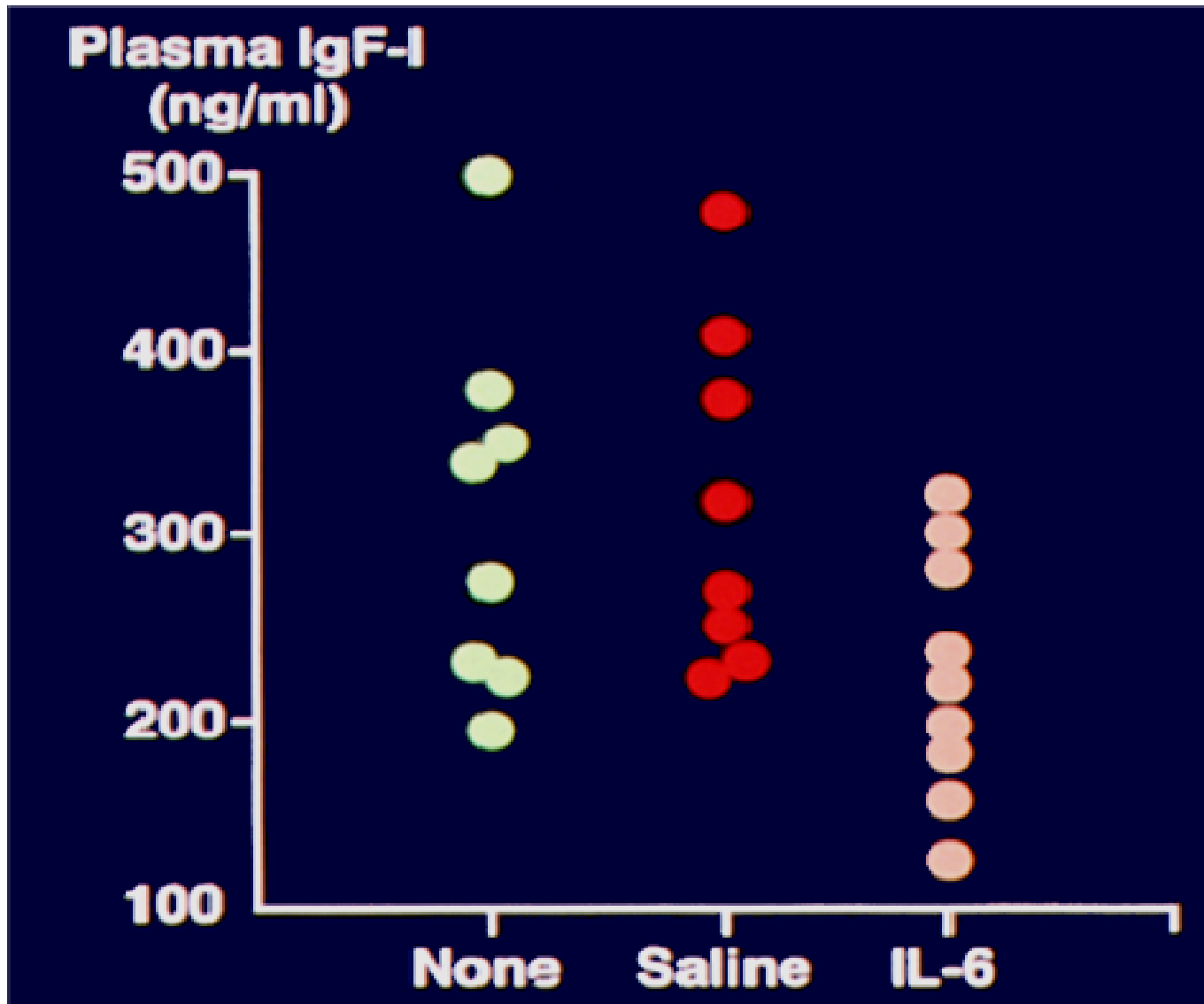


IL-6 and albumin in Crohn's disease



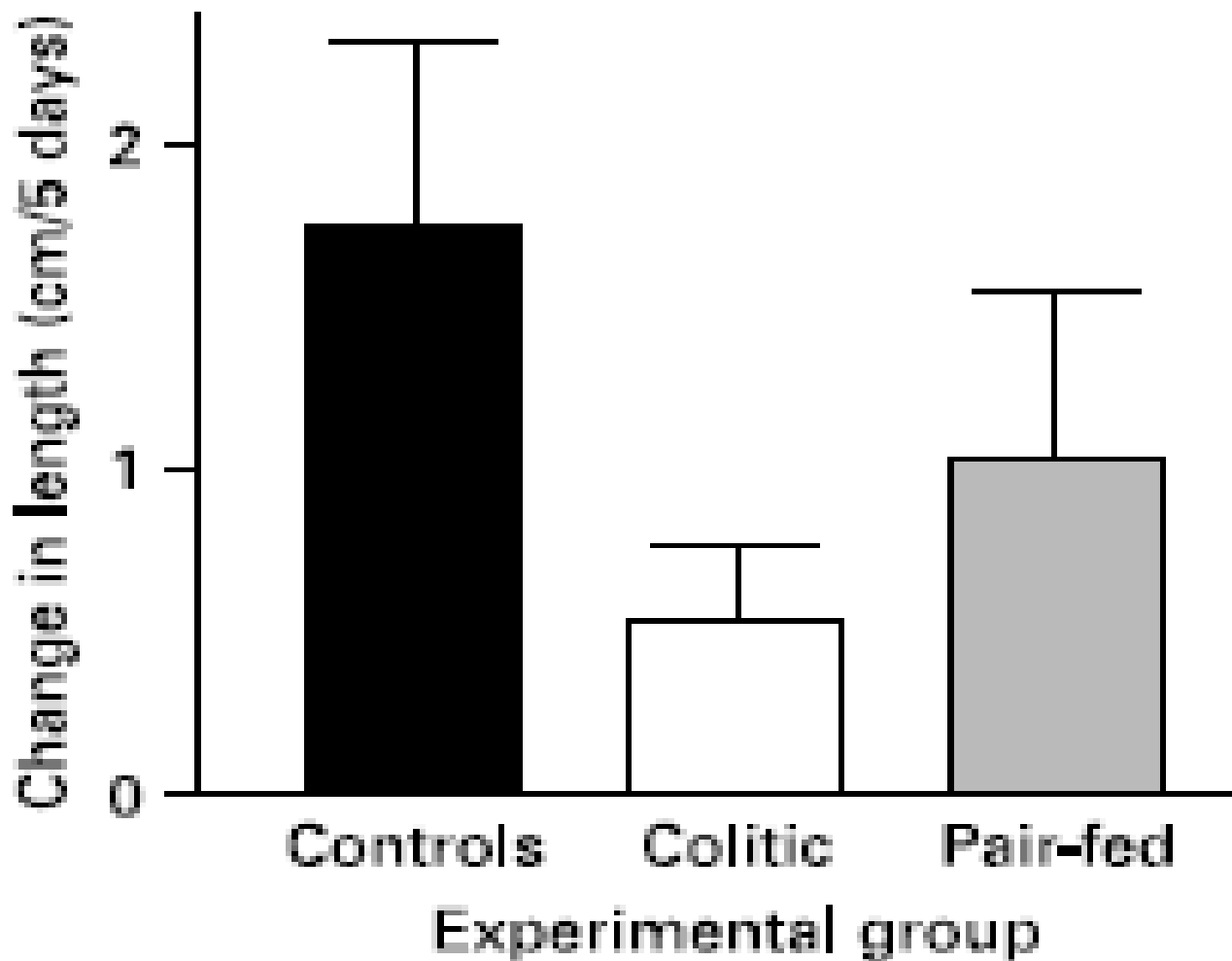
Mahida et al, Gut 1991

Effect of IL-6 on plasma IGF-1 in transgenic mice



De Benedetti JCI, 1997

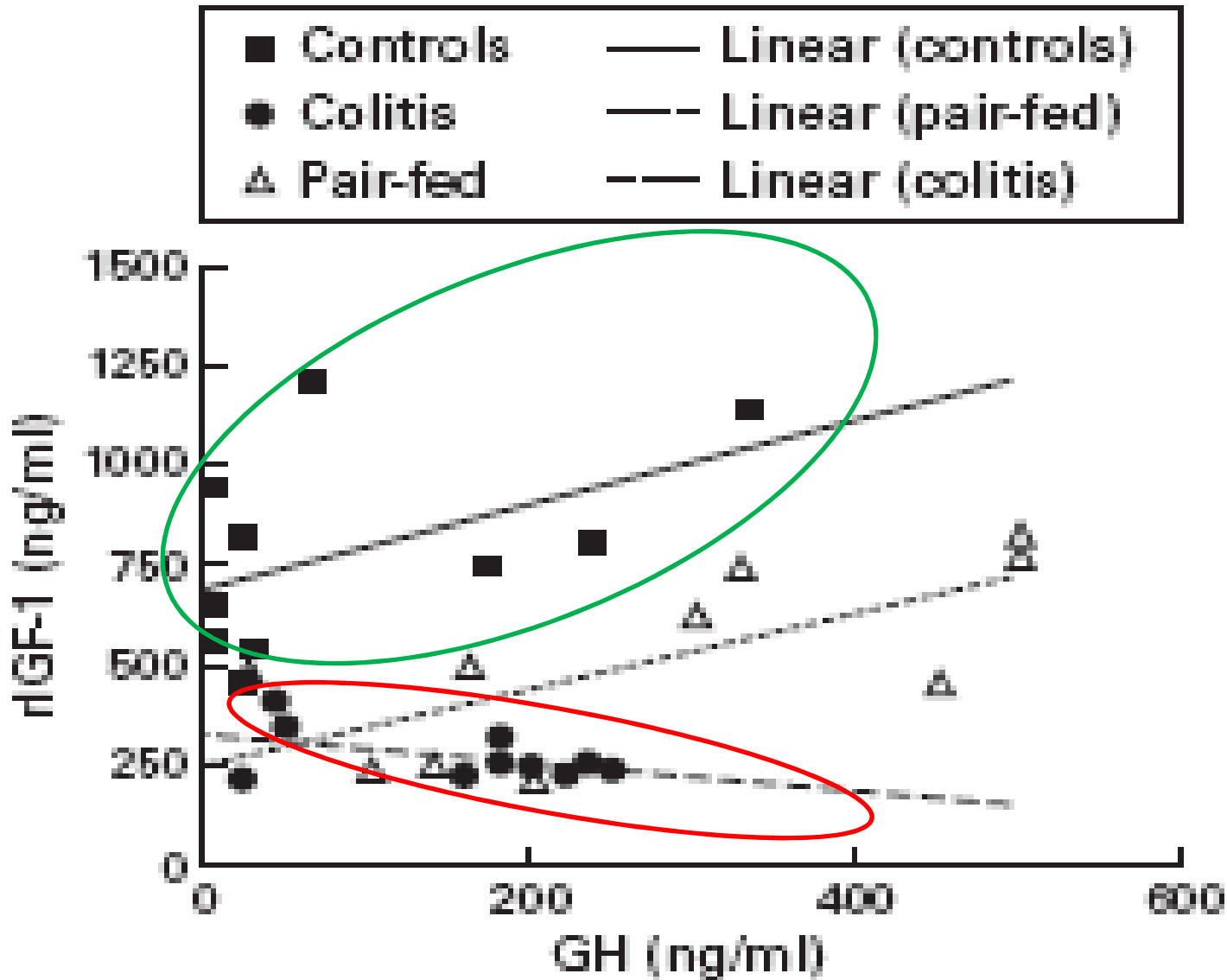
Impaired growth and inflammation



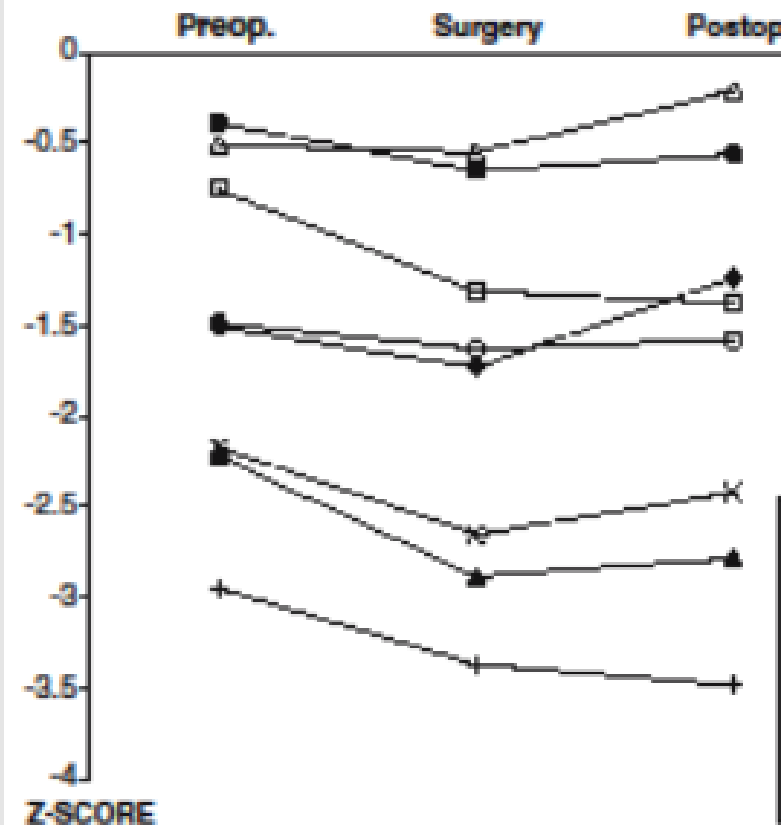
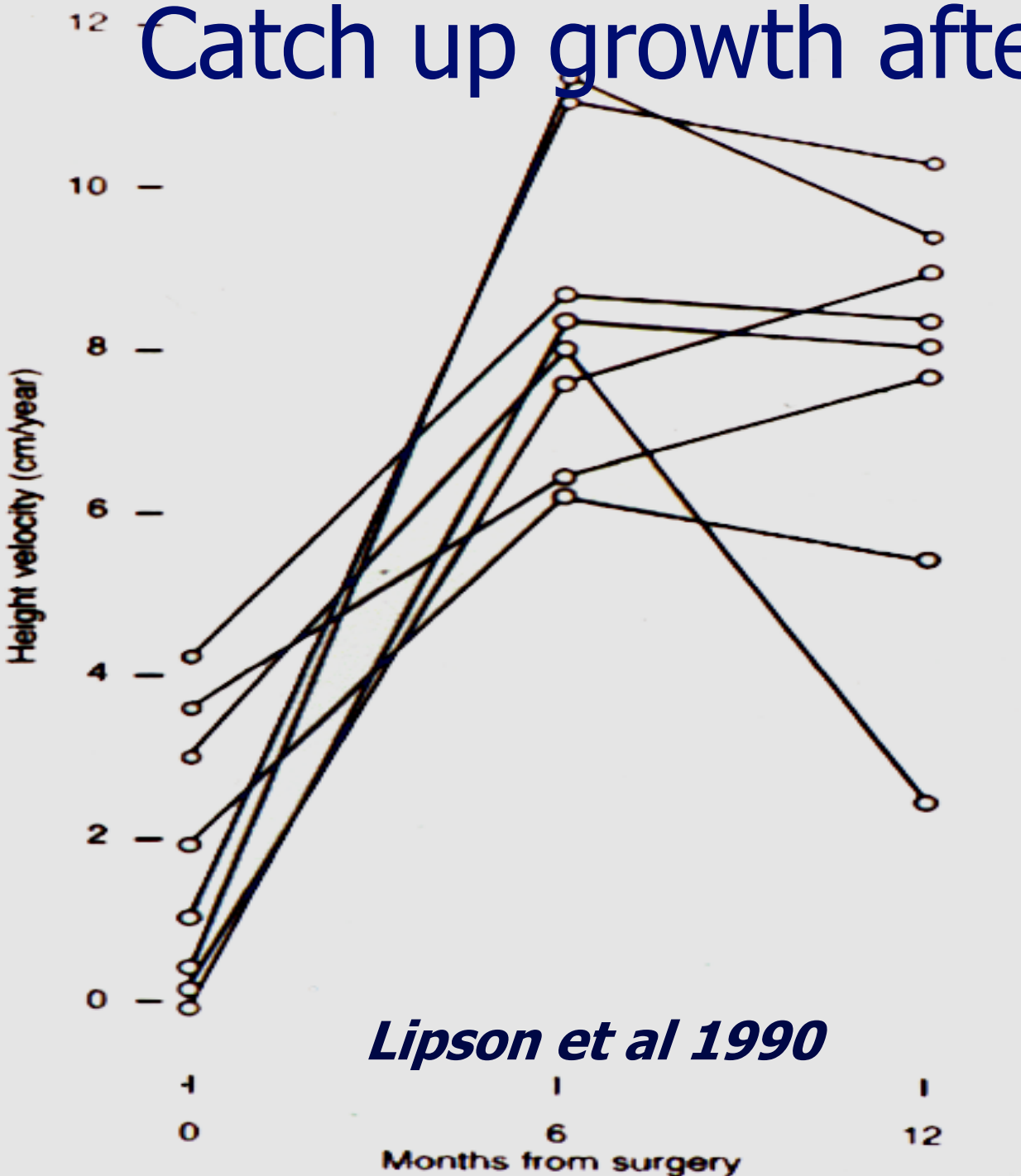
***Specific impact of inflammation
Since « pair-fed » animals grow better than colitis group***

Ballinger , Gut 2000

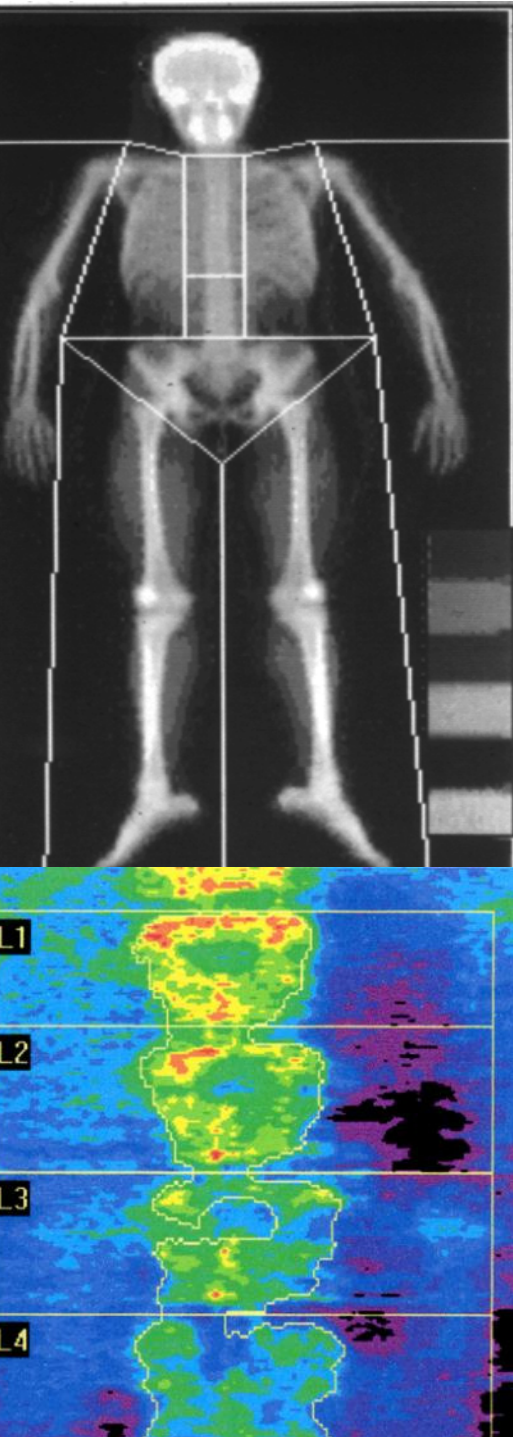
Relationship between plasma concentrations of GH and IGF-1 *Ballinger, Gut 2000*



Catch up growth after surgery



Singh Ranger G, et al. *Pediatr Surg Int.* 2006;22:347-52.



Pediatric Crohn's disease

Defective bone mass accretion

- Negative energy balance
- Pro-inflammatory cytokines
- Steroids
- Impaired Ca & Vit D metabolism
- Decreased physical activity
- Ballinger et al Horm Res 2002; suppl 1: 7-10
- Mushtaq et al Arch Dis Child 2002; 87 : 93-6
- Ahmed et al JPGN 2004; 38: 276-281
- Semeao et al J Pediatr 1999 ; 135 : 593-600.
- Issenman et al Inflamm Bowel Dis 1999 ; 5 : 192-9
- Ahmed et al JPGN 2004; 38: 276-281

Nutrition in Pediatric Crohn's disease

- Impaired growth in pediatric CD
 - *Observation*
 - *Mechanisms*
- **Treatment options in pediatric CD**
 - ***Enteral feeding ?***
 - ***How does it work ?***



Therapeutic options in pediatric crohn's disease

Refractory

Surgery
Biologics

Severe

AZA/6MP-MTX

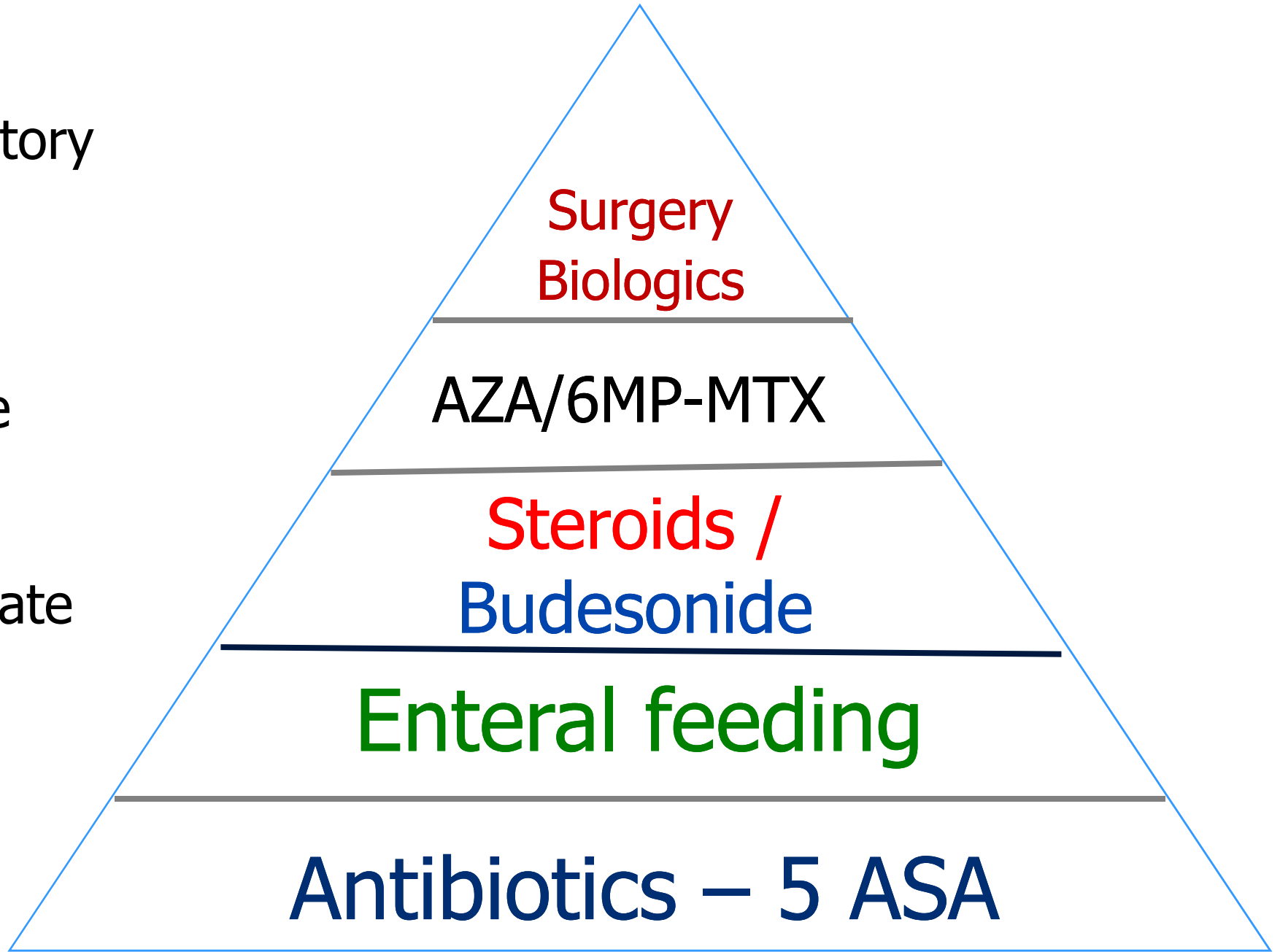
Moderate

Steroids /
Budesonide

Enteral feeding

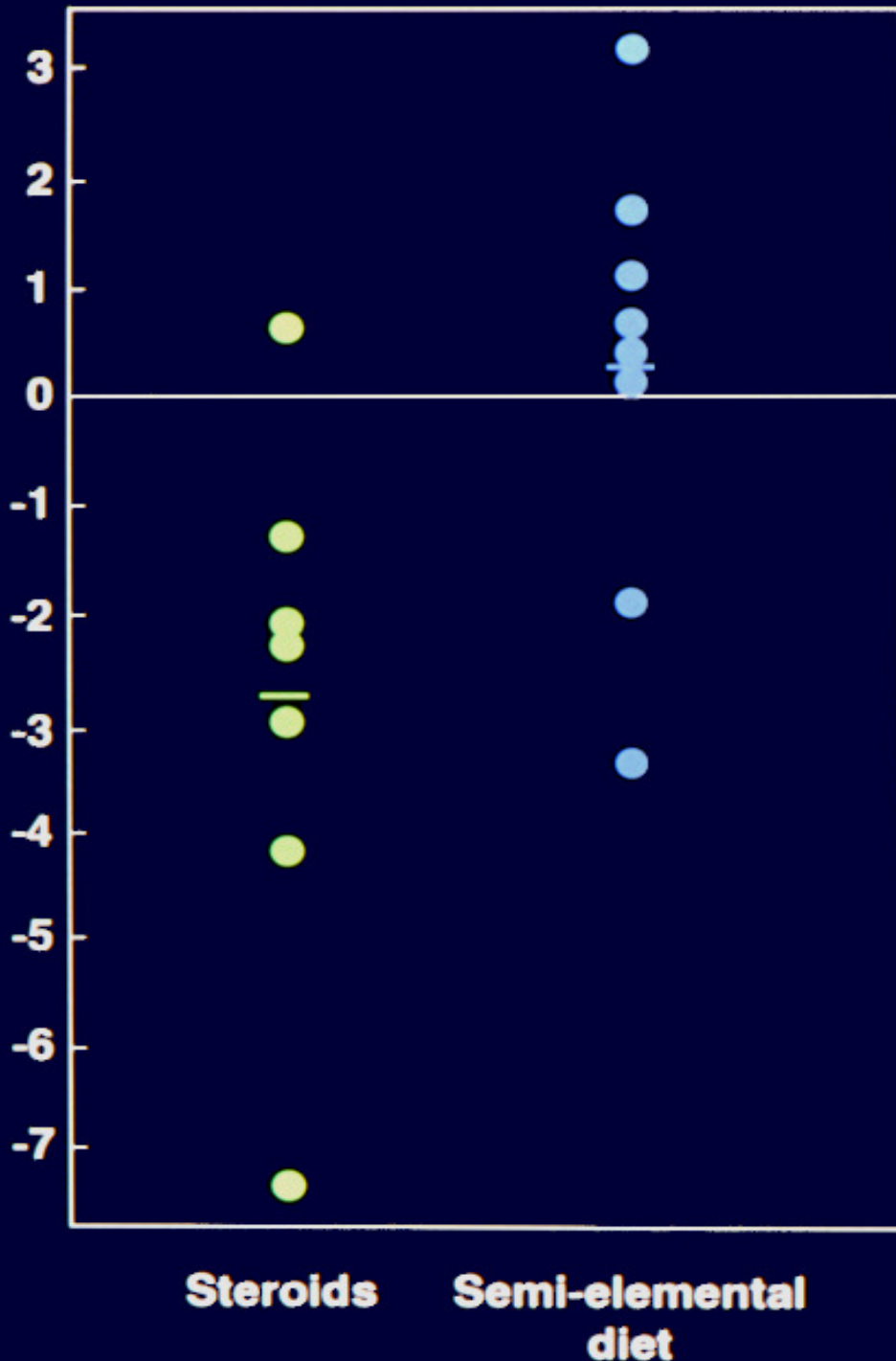
Mild

Antibiotics – 5 ASA



Pediatric Crohn's disease

Weight
velocity
standard
deviation
score

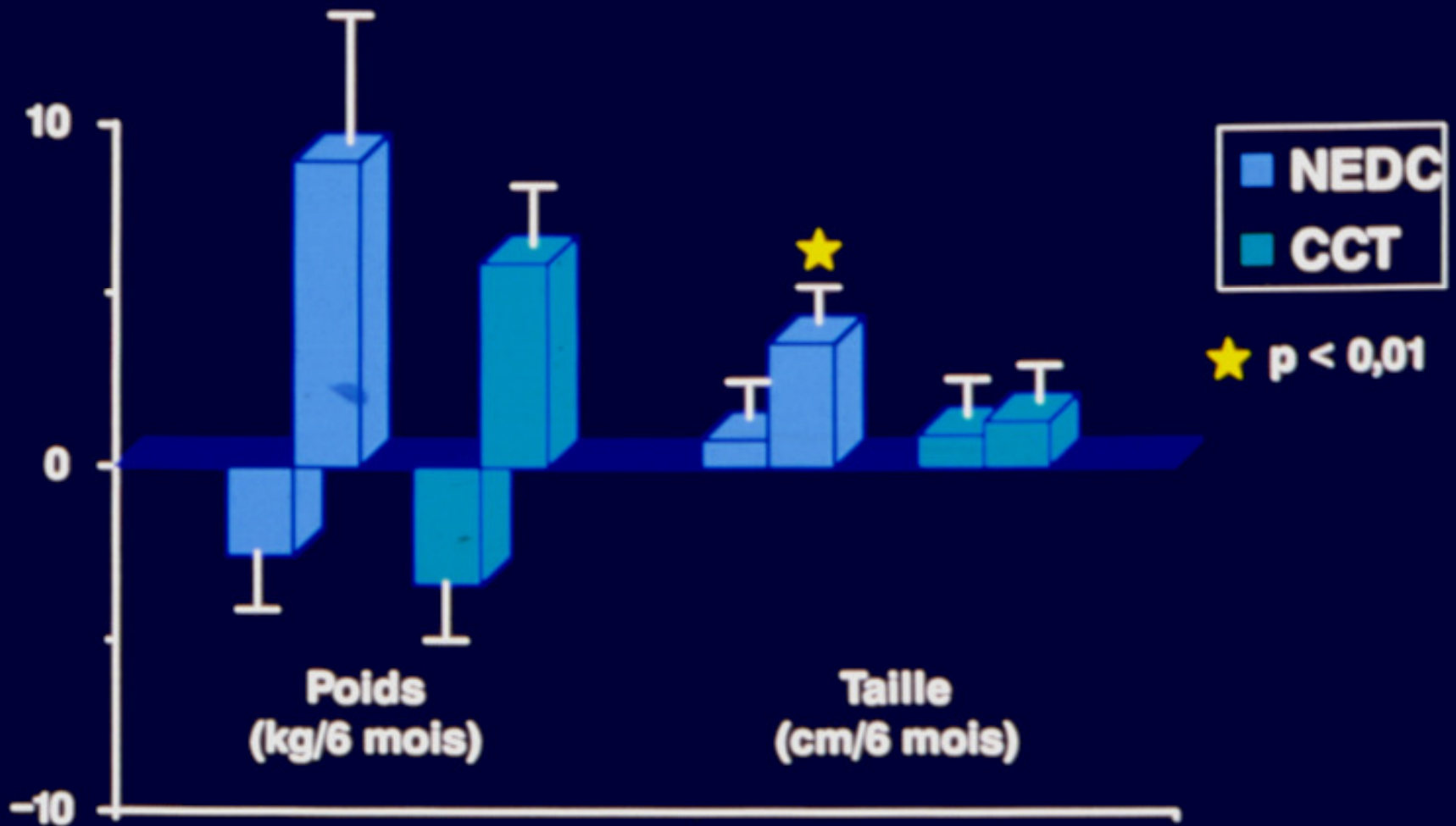


Both ETF and steroids achieve disease remission while only ETF restore growth

Sanderson et al 1987

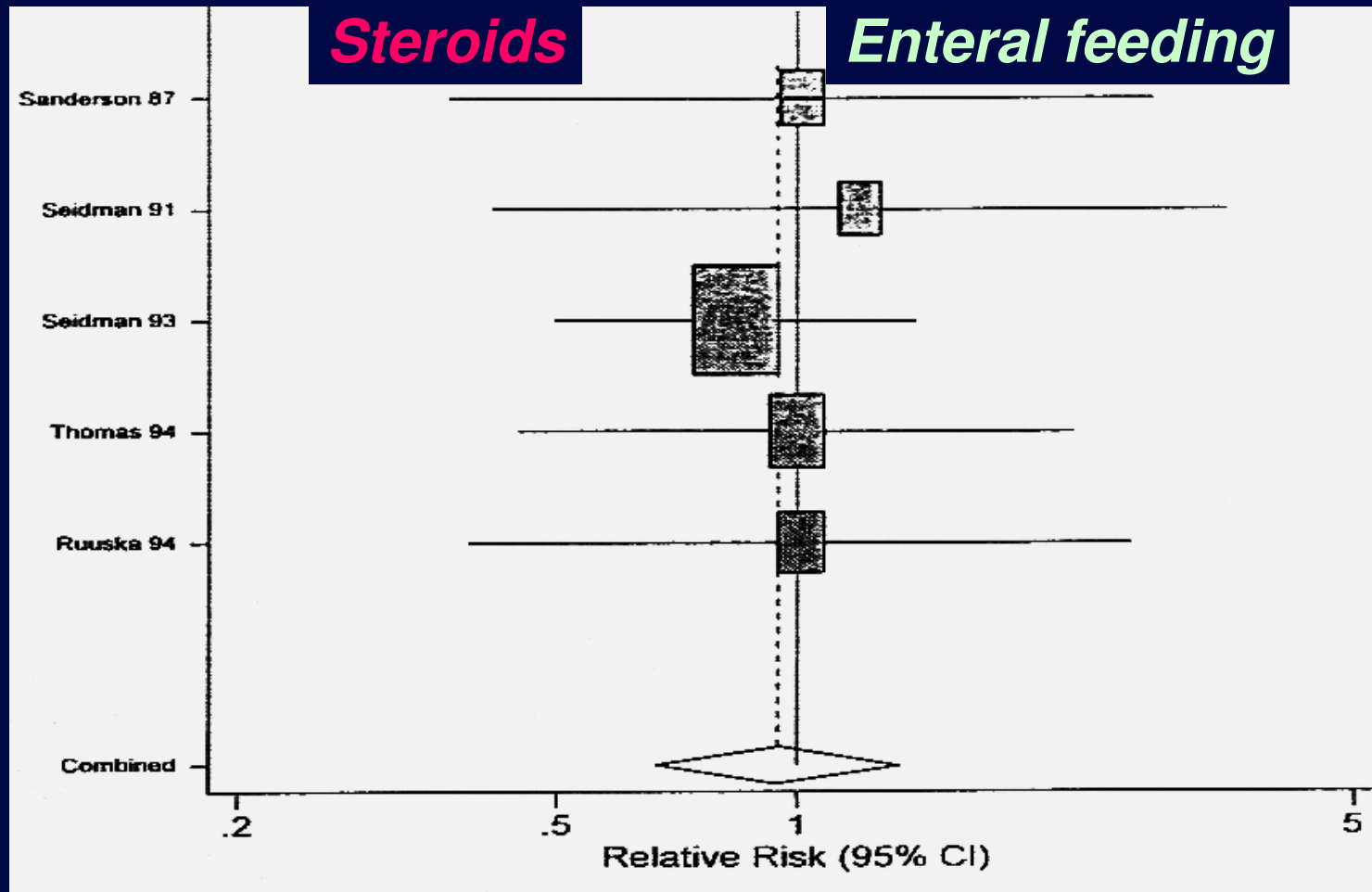
Growth during treatment

Enteral feeding versus steroids



Pediatric Crohn's disease

Randomized controlled trials

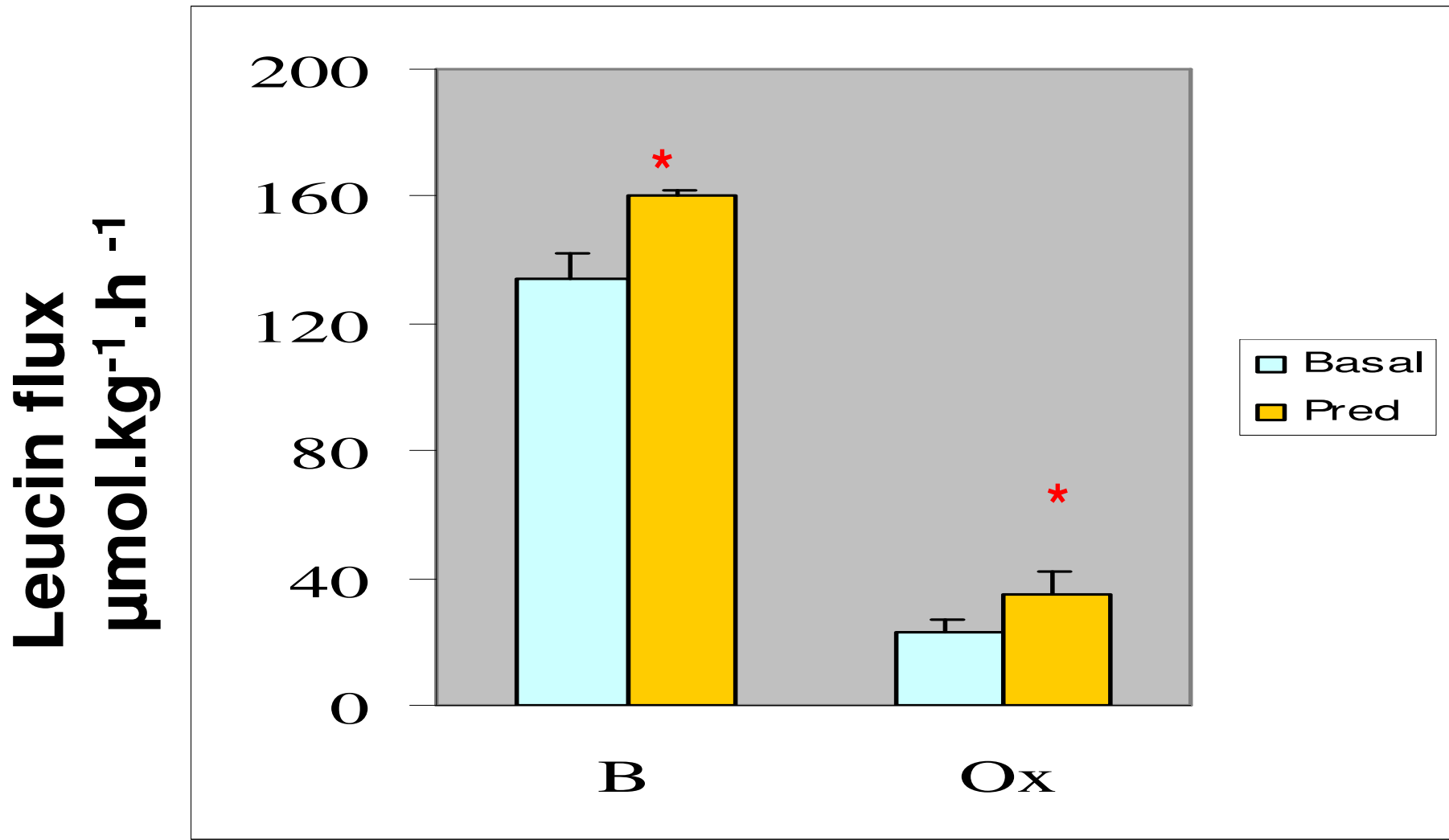


Heuschkel et al., J Pediatr Gastroenterol Nutr. 2000

Deleterious effects of steroids in addition to growth impairment



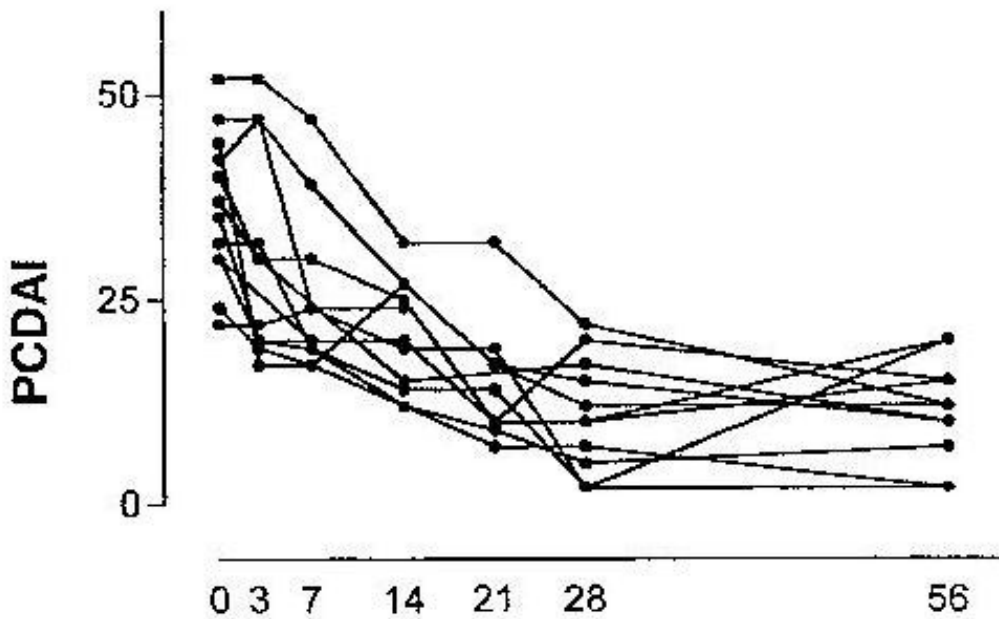
Prednisone and leucin metabolism



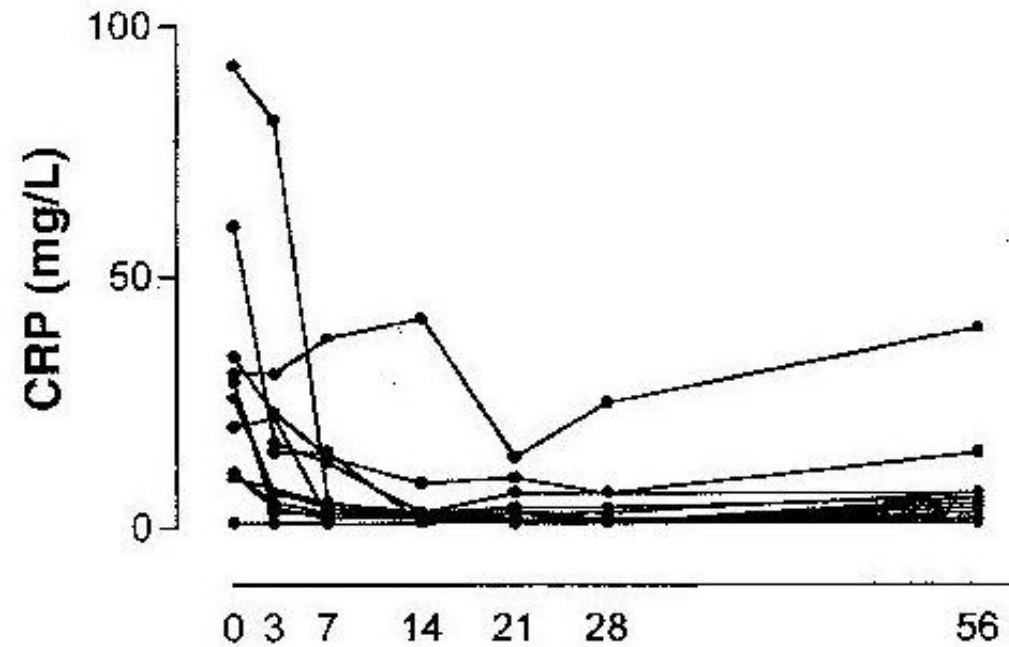
Darmaun et al, 1999

Enteral feeding and et Crohn's disease

PCDAI

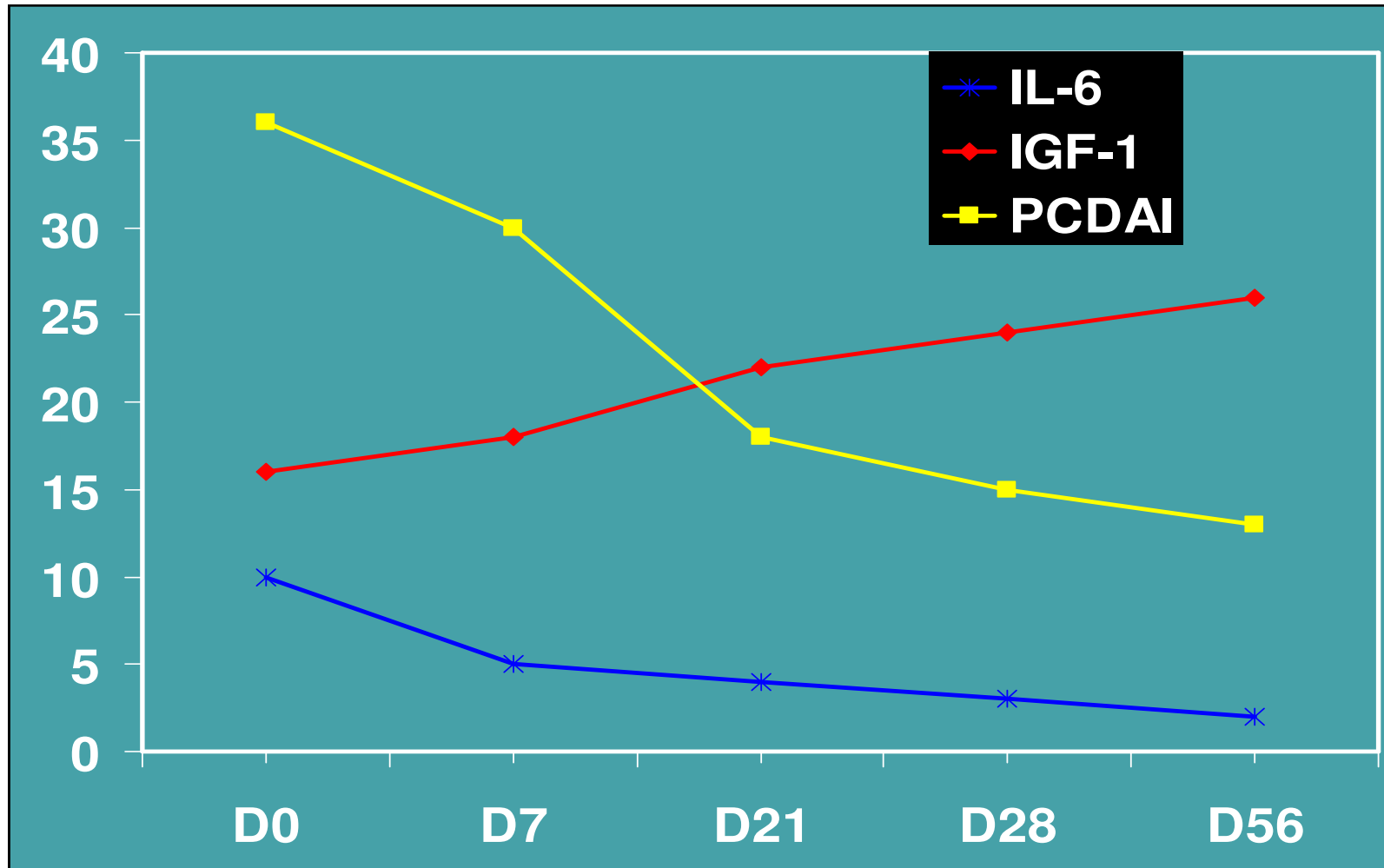


CRP



Bannerjee et al JPGN 2004; 38: 270-75

Enteral feeding and et Crohn's disease



Bannerjee et al JPGN 2004; 38: 270-75

Enteral feeding and et Crohn's disease

Intestinal mucosa healing

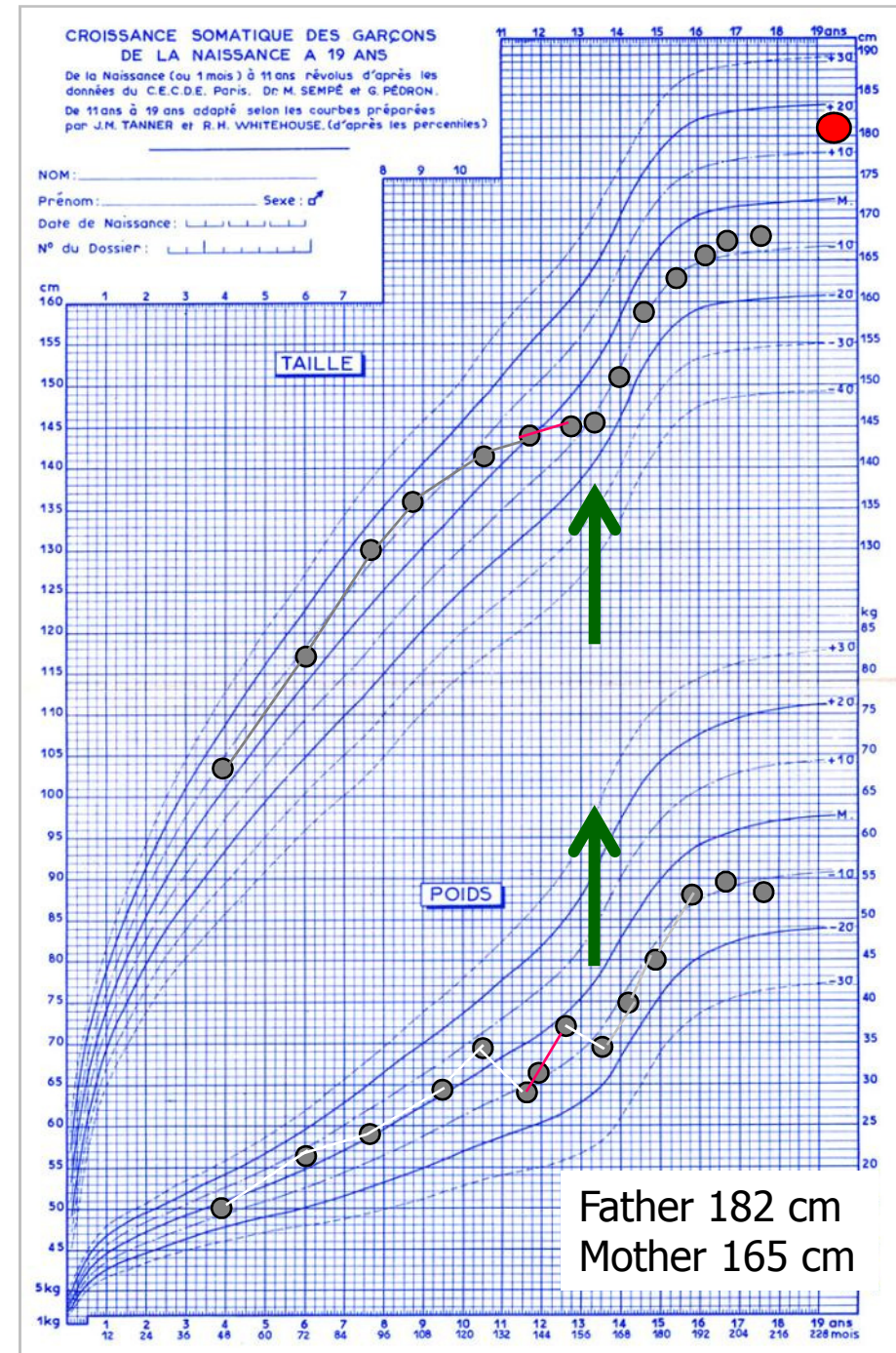
- Improved histological score
- Decreased PCDAI: 42.1 to 3.7
- Decreased Stromelysin-1 m RNA

Heuschkel et al J Pediatr Gastroenterol Nutr 1999

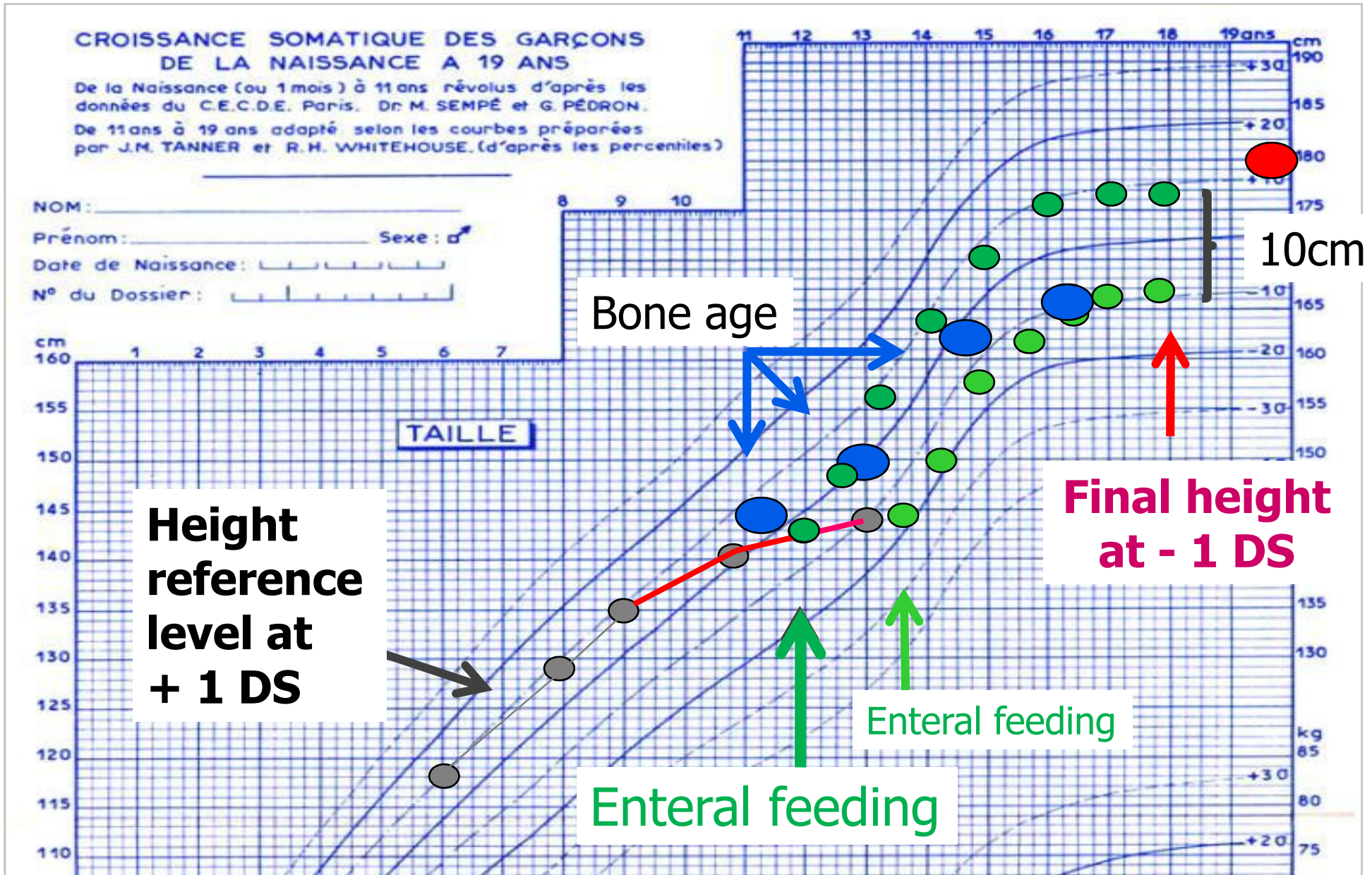
Enteral feeding in Crohn disease

- 2500 kcal/day
- Continuous 12/24 h
- Polymeric diet

Improved growth



Avoiding a life long penalty



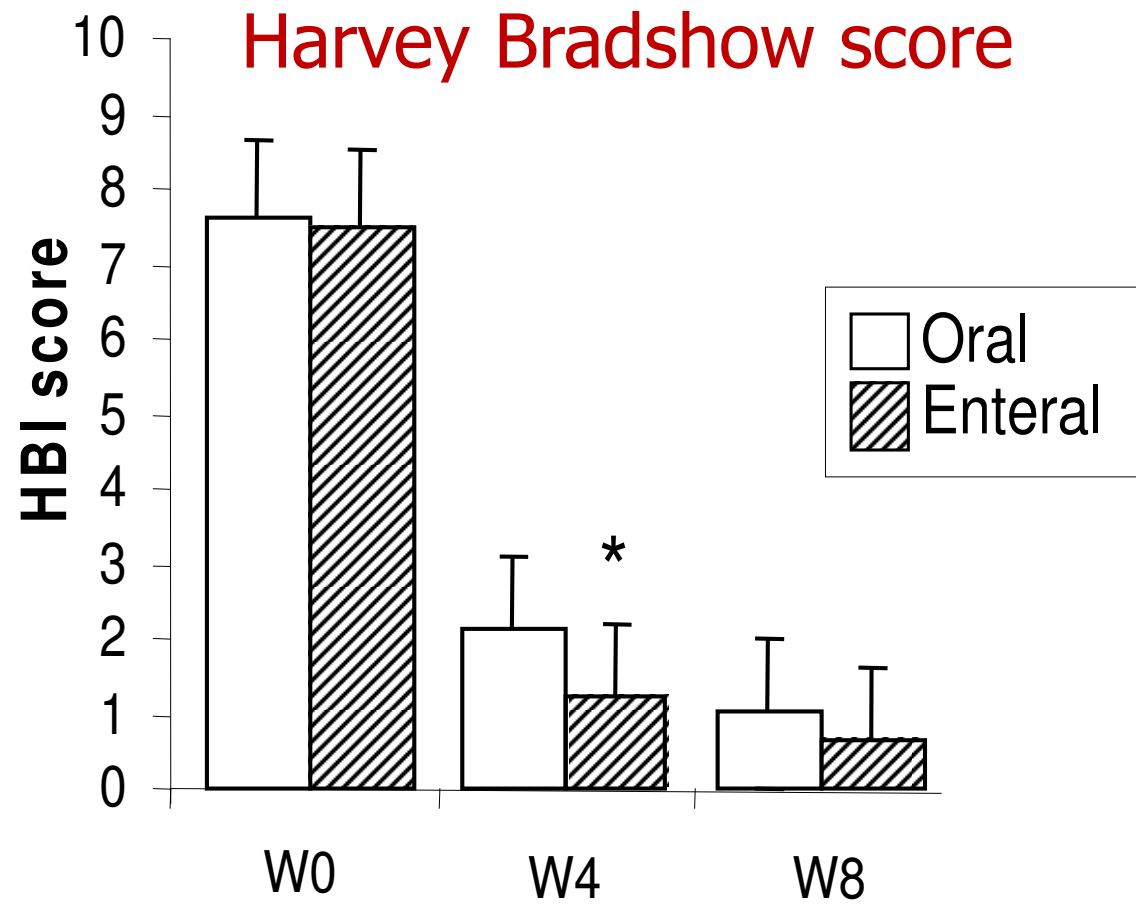
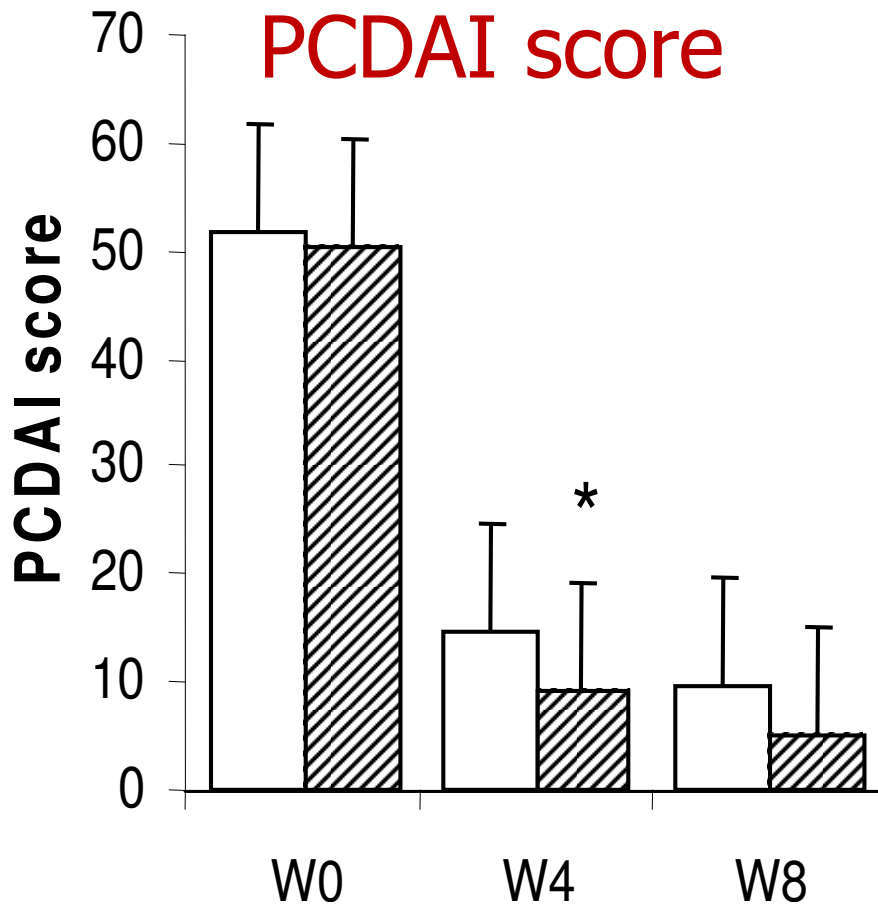
EFFICACY OF FRACTIONATED ORAL VERSUS CONTINUOUS ENTERAL NUTRITIONAL THERAPY IN PEDIATRIC CROHN'S DISEASE

Amandine Rubio, Cécile Talbotec, Hélène Garnier, Jacques Schmitz, Johan Svahn,
Olivier Goulet , Frank Ruemmele

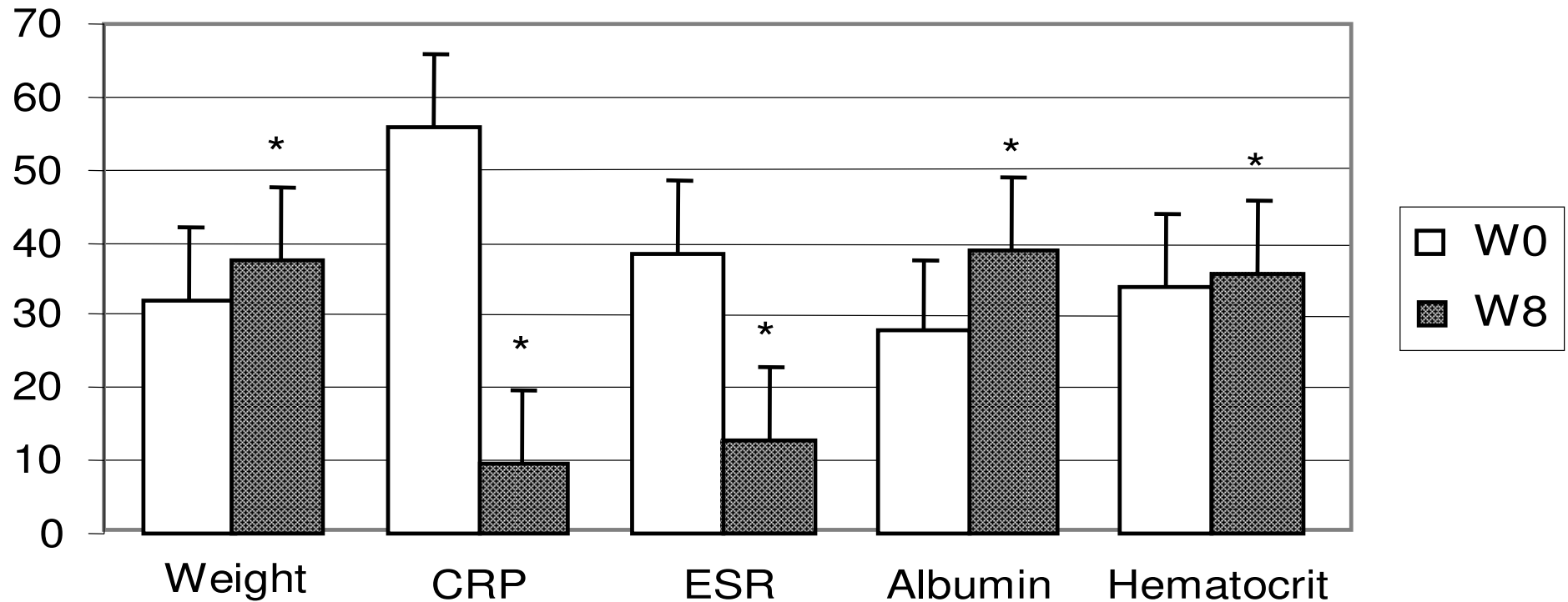
**Retrospective review of the medical records of 85 patients
with active severe Crohn's disease
treated by exclusive nutritional therapy (Modulen IBD®)
by oral or continuous enteral route via a naso-gastric tube.**

J Pediatr Gastroenterol Nutr 2009

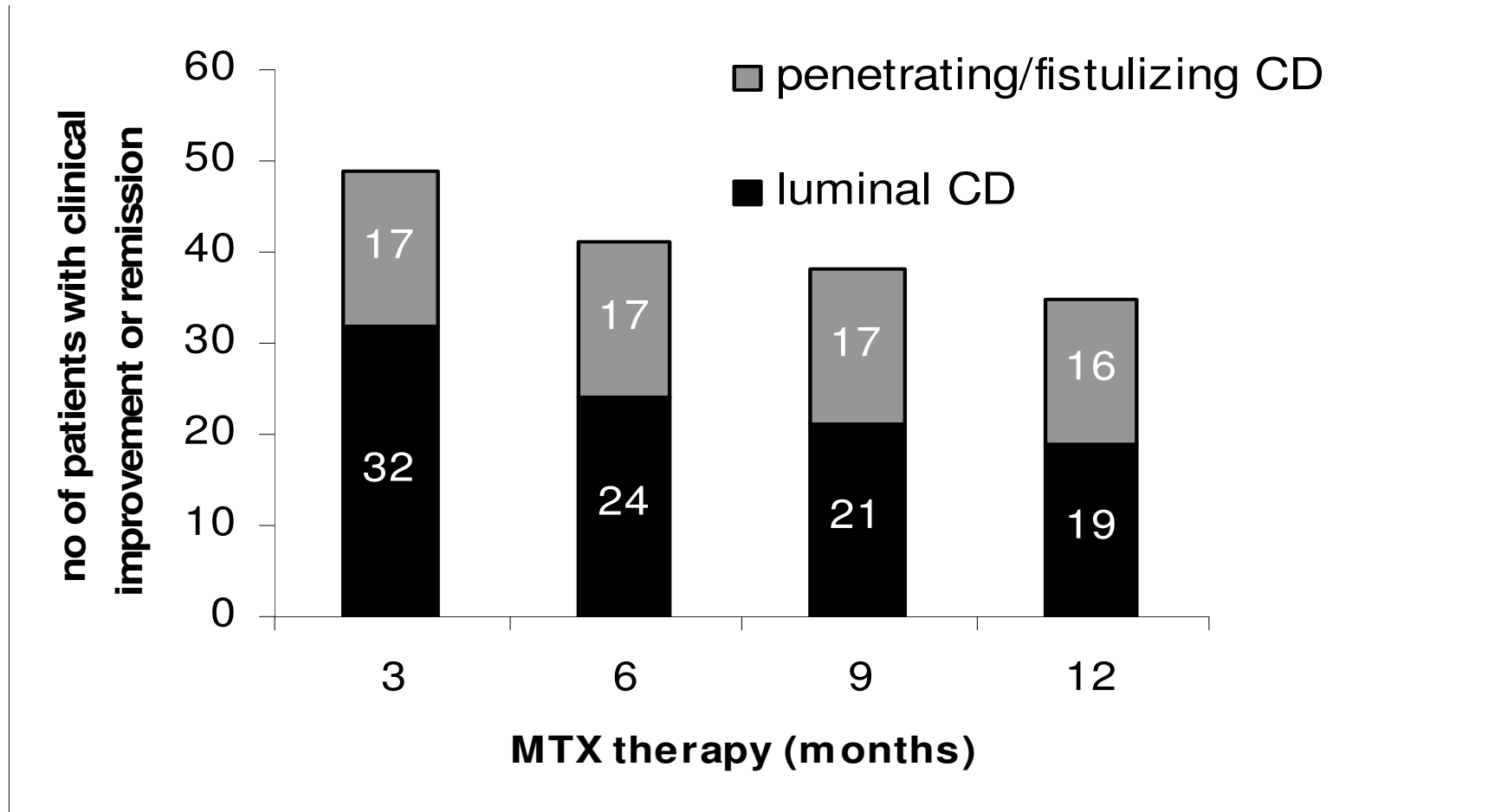
Efficacy of fractionated oral versus continuous enteral tube feeding in pediatric CD



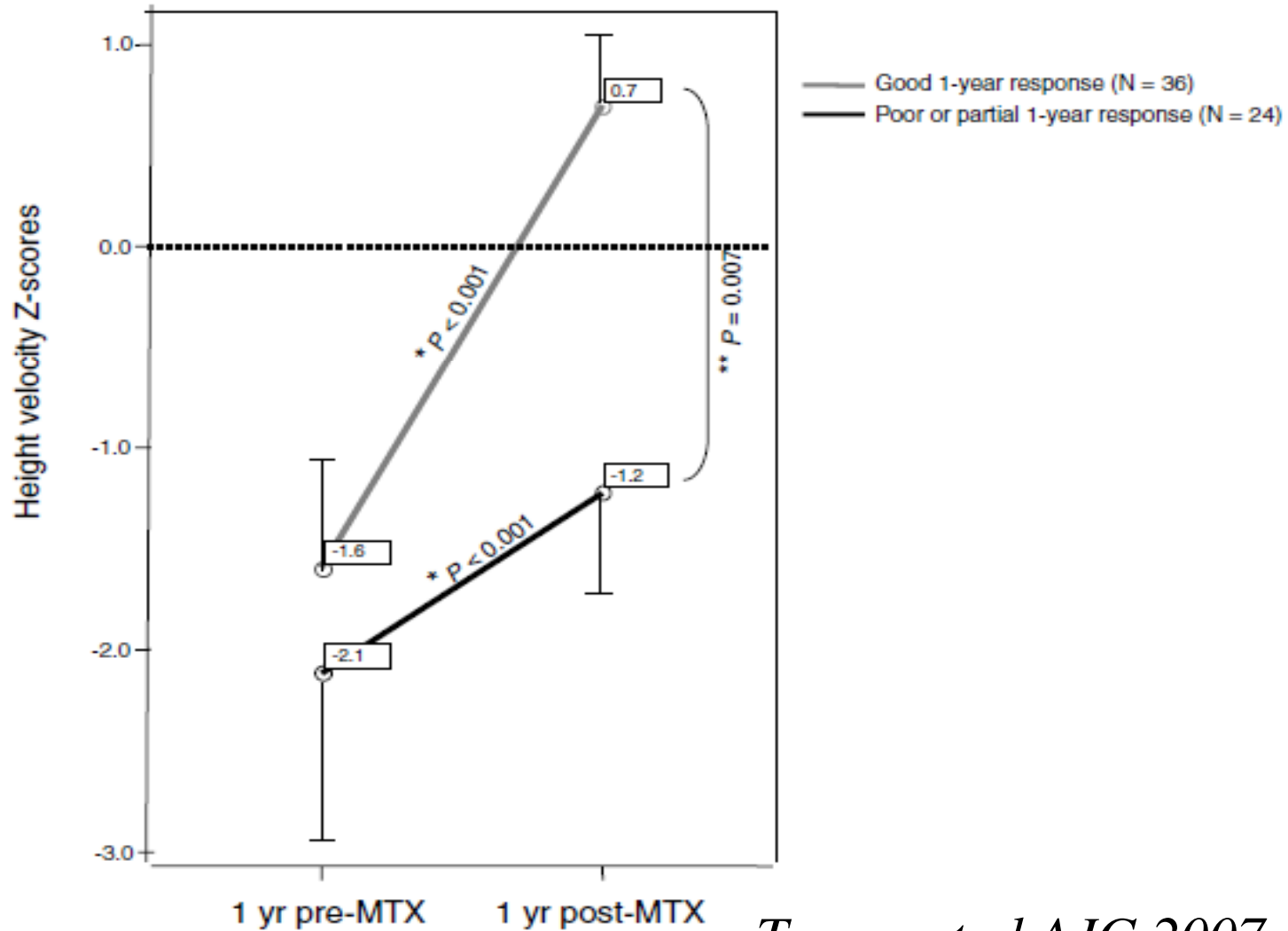
Efficacy of fractionated oral versus continuous enteral tube feeding in pediatric CD



French MTX study



French MTX study



Turner et al AJG 2007

Infliximab heals intestinal inflammatory lesions and restores growth in children with Crohn's disease

O. Borrelli^a, C. Bascietto^a, F. Viola^a, M. Bueno de Mesquita^a,
M. Barbato^a, V. Mancini^a, S. Bosco^b, S. Cucchiara^{a,*}

Infliximab: **retreatment** *versus* **baseline treatment**

	Retreated ^a		P	Non-retreated ^b		P
	Baseline ^c	6 months after beginning therapy		Baseline	6 months after beginning therapy	
Weight Z score	-0.67 ± 0.43	-0.29 ± 0.49	<0.01	-0.21 ± 0.44	-0.19 ± 0.42	NS
Height Z score	-1.15 ± 0.81	-0.62 ± 0.99	<0.01	-0.86 ± 0.42	-0.83 ± 0.40	NS

Values as mean ± S.D.

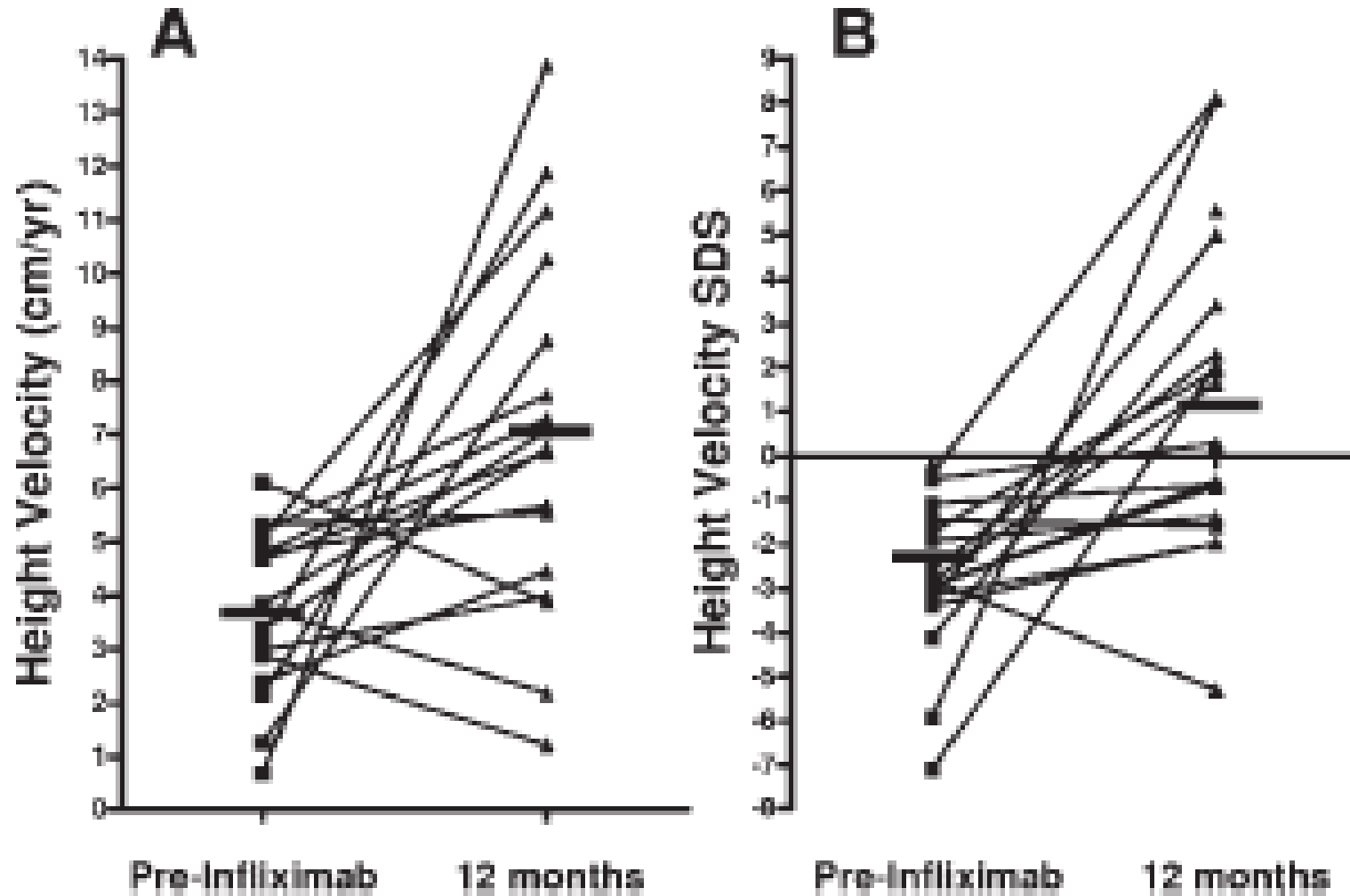
^a Children undergoing retreatment infusion.

^b Children receiving only a baseline therapeutic programme.

^c Before starting the baseline infusion programme.

Borelli et al Digestive and liver diseases 2004

Anti TNF: Infliximab and growth



Nutrition in Pediatric Crohn's disease

- Impaired growth in pediatric CD
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- Treatment options in pediatric CD
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 - ***How does it work ?***



Enteral feeding in Pediatric Crohn's disease

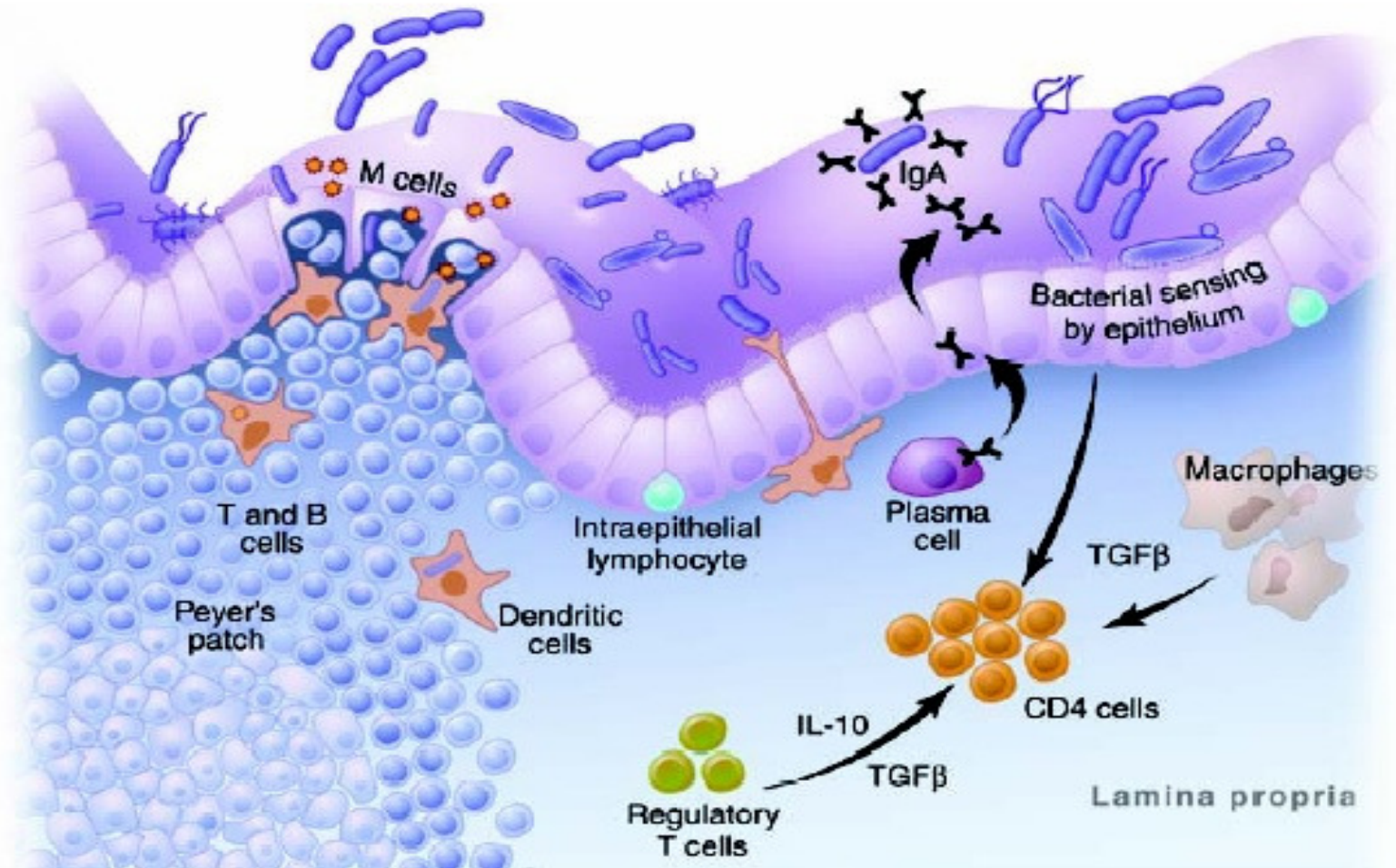
How does it work ?

- Decreased hormonal secretion/bowel rest
- Reduced antigen load from diet
- Changes in intestinal permeability
- Improved nutritional status (Gln, n-3...)
- Anti-inflammatory action of diet (*TGF* β 2)
- **Changes of intestinal bacterial flora**

Murch and Walker Smith 1998

Microbiota-Mucosal Immune System Cross-talk

Mucosal sensing of commensal bacteria is an integral part of local immune physiology.

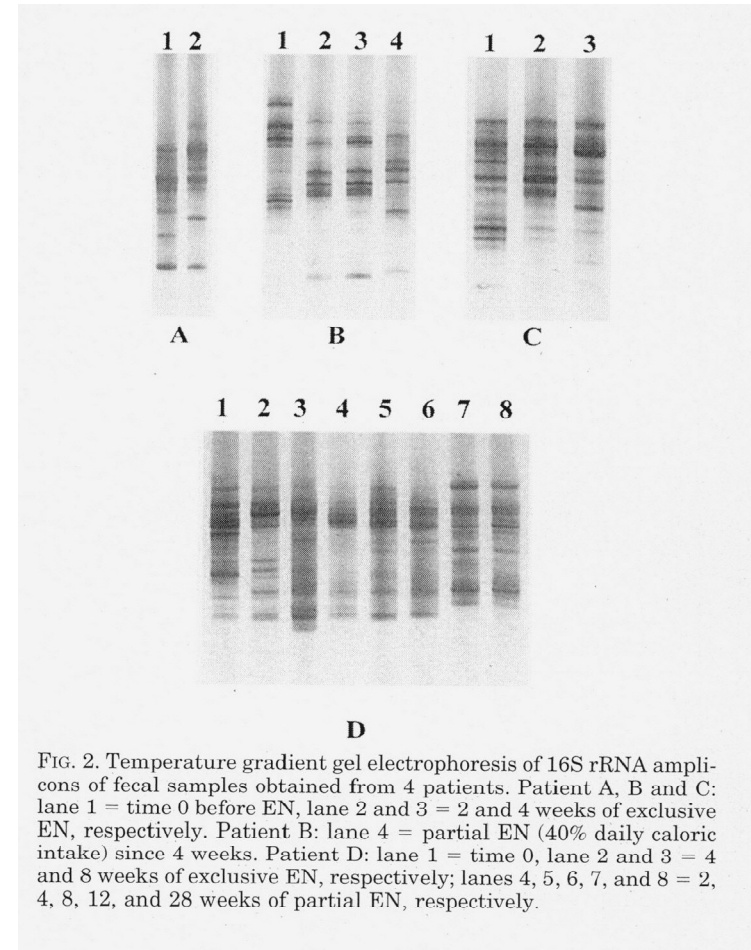


Impact of intestinal microbiota in IBD

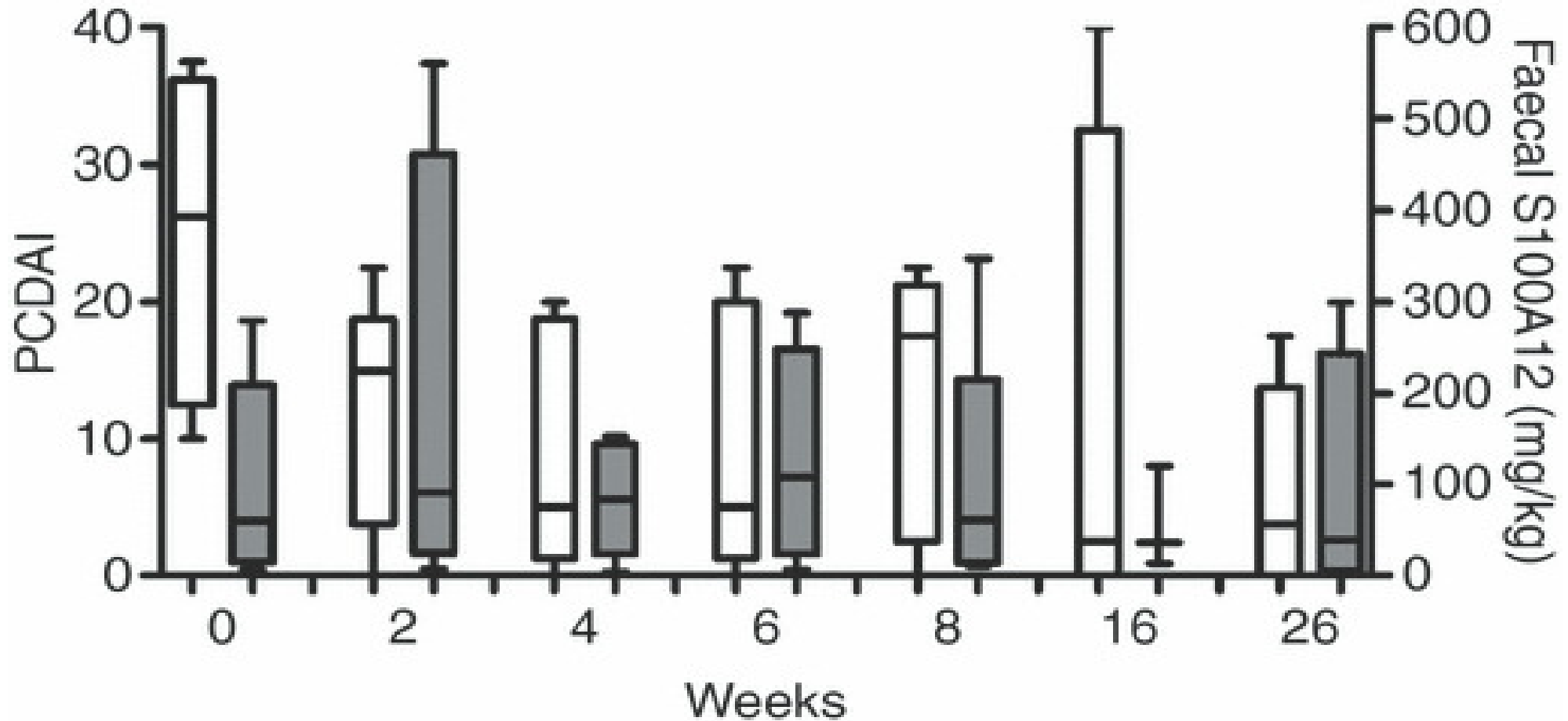
- Microbiota modifications related to inflammation
 - Lupp C et al. Cell Host Microbe 2007;2:119-129
- Increased number of mucosa bacteria in IBD
 - Frank DN et al. Proc Natl Acad Sci USA 2007;104:13780-13785
- Role of bacteria in disease severity
 - Sokol H et al; Proc Natl Acad Sci USA 2008;105:16731-16736
 - Baumgart M et al. ISME J 2007;1:403-418
 - Frank DN et al. Proc Natl Acad Sci USA 2007;104:13780-13785
- Effects of bacterial metabolites on gut mucosa

Effects of enteral nutrition on gut microbiota in Pediatric Crohn's disease

- **Observational study**
- **Changes in Biodiversity of Microflora using TGGE**
- **Patients maintained on supplements**
- **Possibly related to the low residue or prebiotic properties of polymeric feeds**

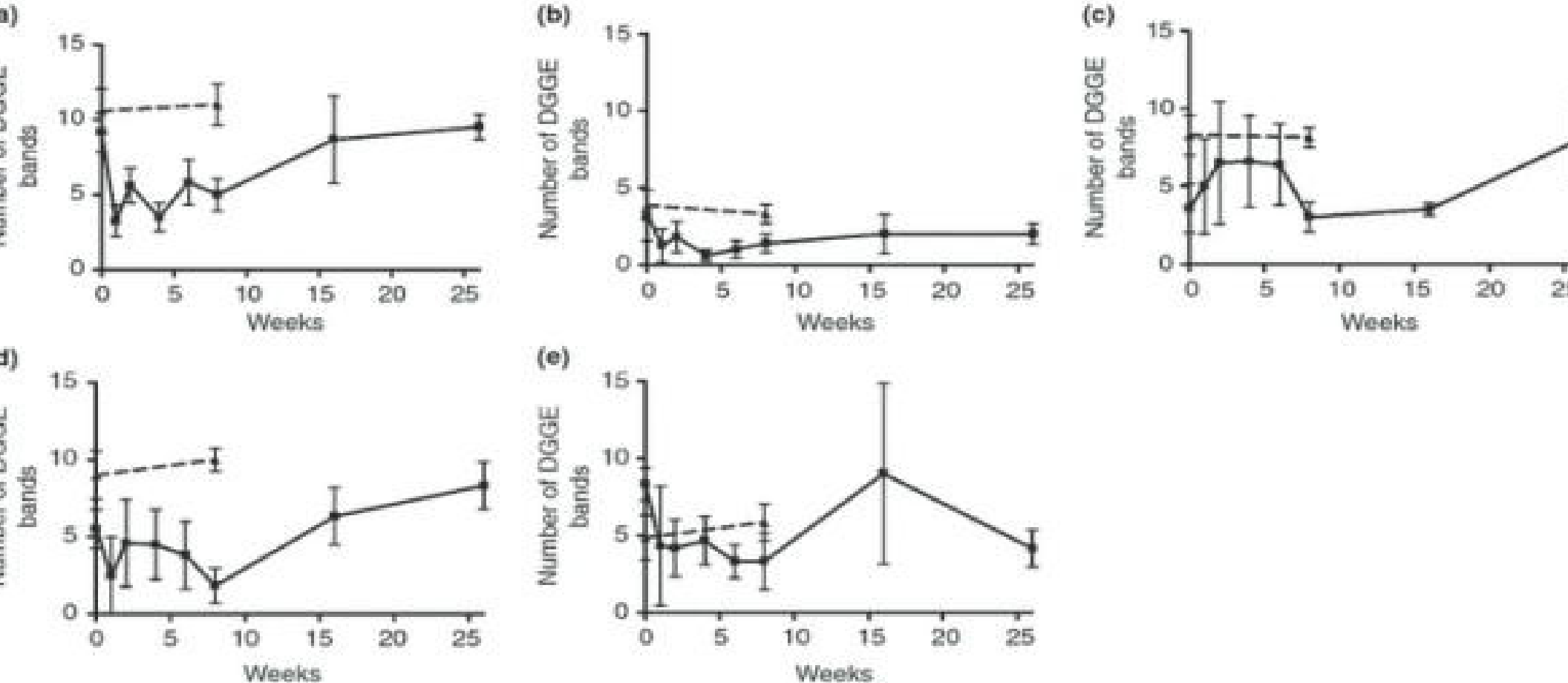


Effects of enteral nutrition on gut microbiota in Pediatric Crohn's disease



- Significant correlation between S100A12 and PCDAI ($R= 0.5299$, $p=0.0018$)

Effects of enteral nutrition on gut microbiota in Pediatric Crohn's disease



Band count was significantly different at weeks 0 and 8

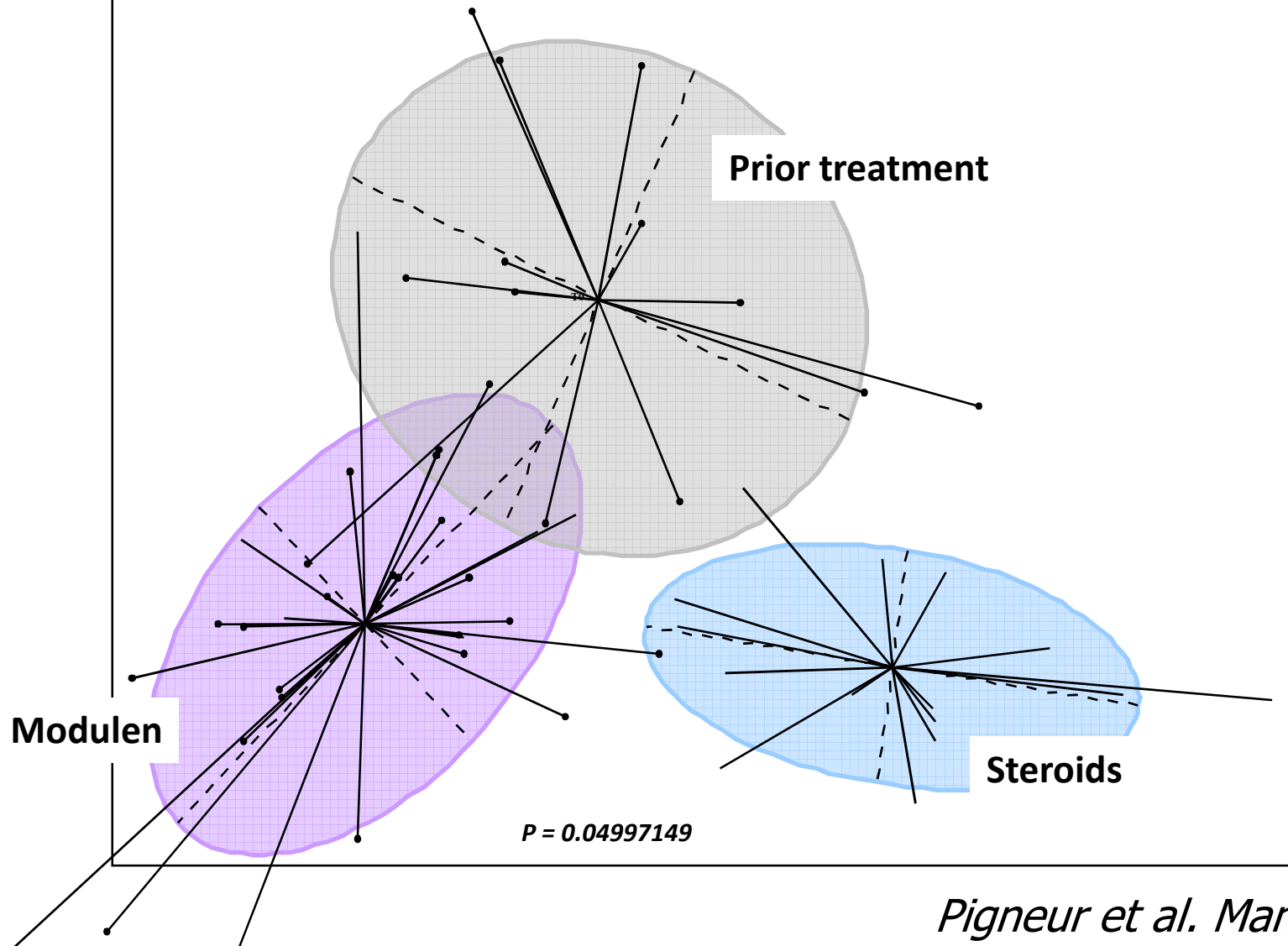
Eubacteria

Bacteroides-Prevotella

Clostridium leptum

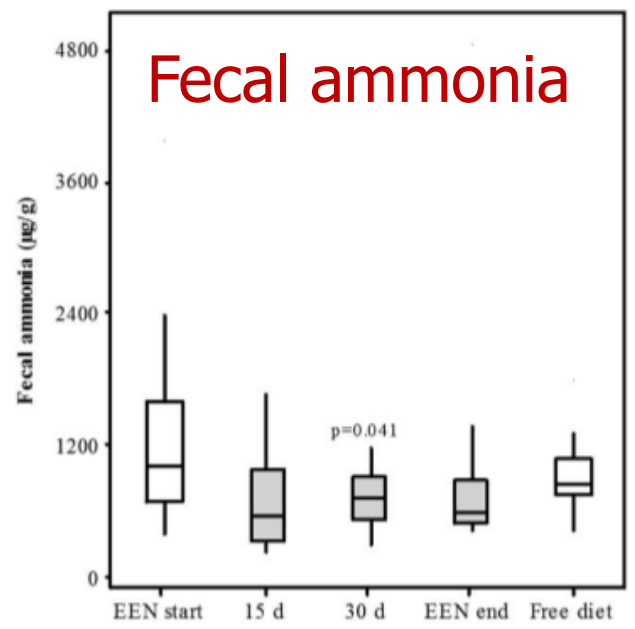
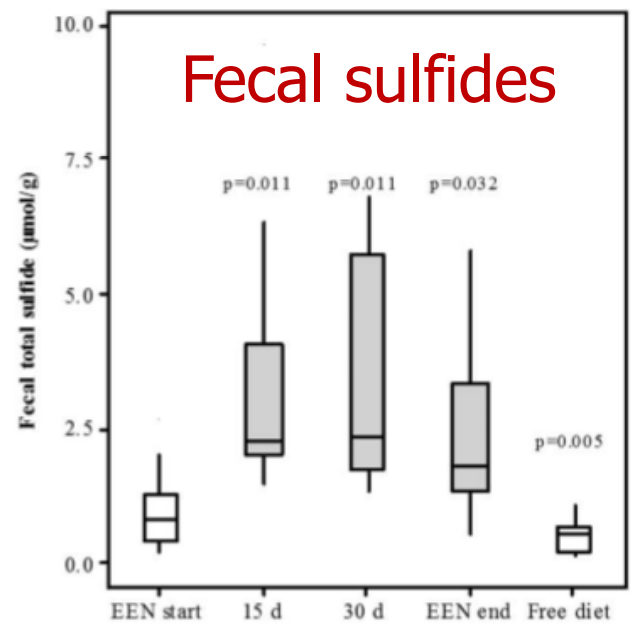
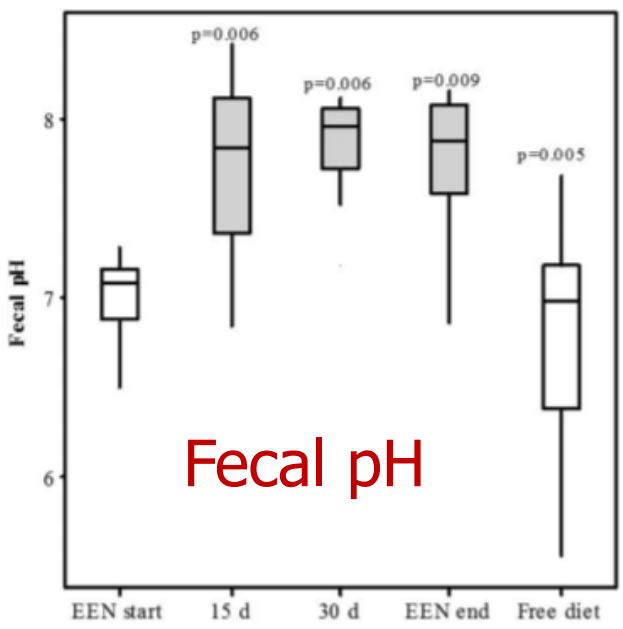
Leach ST, Mitchell HM, Eng WR et al. *Alimentary Pharmacology & Therapeutics*. 2008; 28(6):724-33

Effects of enteral nutrition on gut microbiota in Pediatric Crohn's disease



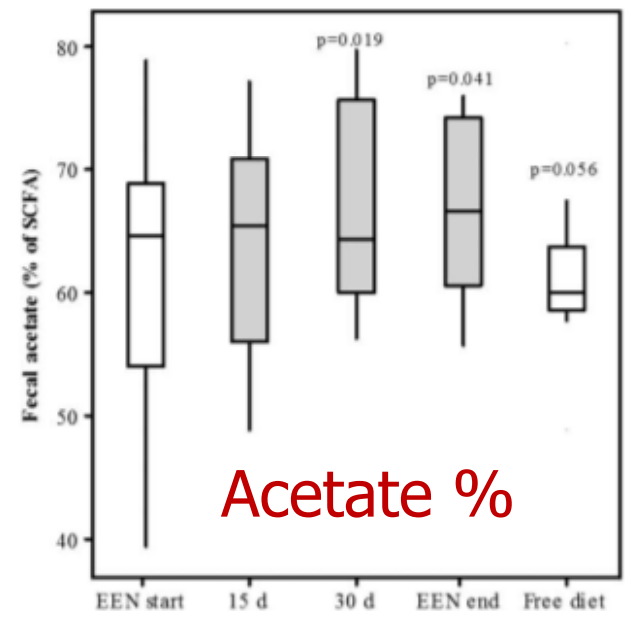
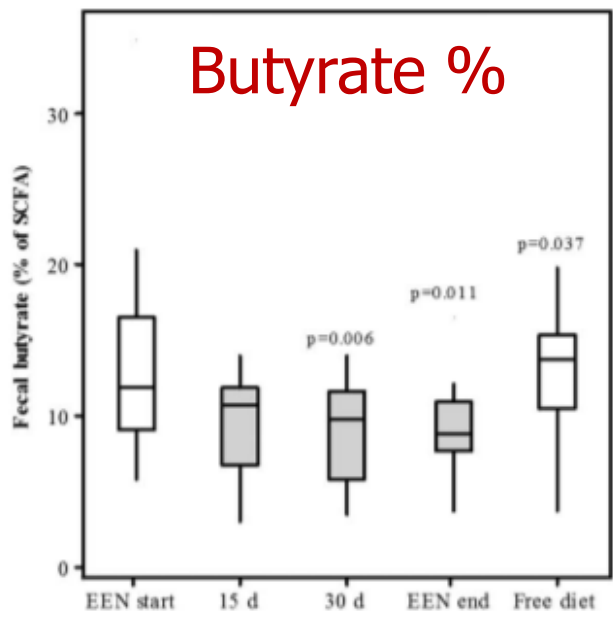
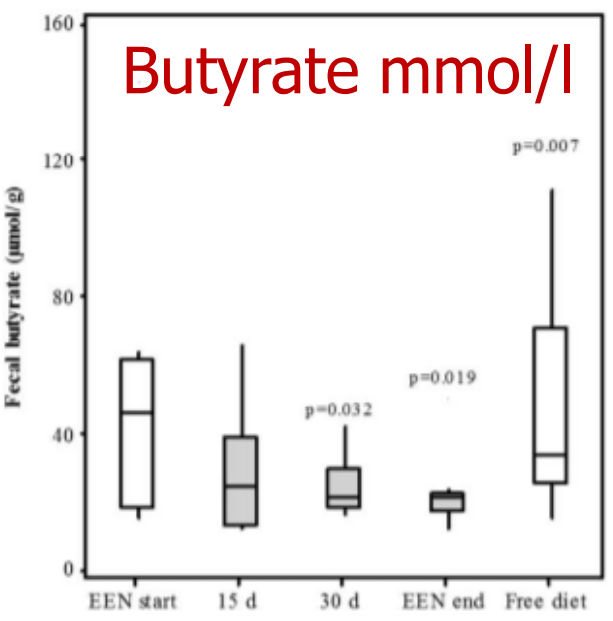
Decline in Presumptively Protective Gut Bacterial Species and Metabolites Are Paradoxically Associated with Disease Improvement in Pediatric Crohn's Disease During Enteral Nutrition

Effects of enteral nutrition on gut microbiota



Decline in Presumptively Protective Gut Bacterial Species and Metabolites Are Paradoxically Associated with Disease Improvement in Pediatric Crohn's Disease During Enteral Nutrition

Effects of enteral nutrition on gut microbiota



Decline in Presumptively Protective Gut Bacterial Species and Metabolites Are Paradoxically Associated with Disease Improvement in Pediatric Crohn's Disease During Enteral Nutrition

Effects of enteral nutrition on gut microbiota

TABLE 3. Concentration (\log_{10} 16S Ribosomal RNA Gene Copy Number/g Dry Feces) of Dominant Bacterial Species in Children with CD at Treatment Initiation (Start of EEN) and Pairwise Changes (Δ) During the Course of EEN in Children with Active CD

Median (IQR) \log_{10} 16S Ribosomal RNA Gene Copy Number/g Dry Feces	Start of EEN	Δ 15-Day Start	<i>P</i> *	Δ 30-Day Start	<i>P</i> *	Δ End Start	<i>P</i> *	Δ Free Diet End	<i>P</i> *
Total bacteria	11.4 (0.5)	-0.0 (0.8)	0.834	0.2 (0.6)	0.442	0.2 (0.8)	0.290	0.1 (1.0)	0.576
<i>Bacteroides/Prevotella</i>	9.4 (1.5)	0.3 (1.7)	0.727	-0.1 (1.2)	0.485	-0.3 (1.5)	0.556	0.1 (2.4)	0.834
<i>Clostridium leptum</i>	10.2 (1.1)	-0.5 (1.0)	0.197	-0.2 (1.5)	0.230	-0.1 (2.1)	0.965	0.5 (1.4)	0.147
<i>Faecalibacterium prausnitzii</i>	9.4 (1.6)	-0.3 (1.3)	0.170	-0.8 (1.5)	0.023	-0.7 (2.1)	0.197	1.0 (1.5)	0.023
<i>Clostridium coccooides</i>	10.2 (1.1)	-0.1 (0.4)	0.450	0.2 (1.4)	0.563	0.2 (1.5)	0.838	0.0 (1.0)	1.000
<i>Bifidobacteria</i>	9.8 (2.1)	-0.3 (1.2)	0.230	-0.1 (1.4)	0.108	-0.1 (1.6)	0.120	0.7 (1.7)	0.031
<i>Lactobacilli</i>	7.1 (2.3)	-0.9 (1.7)	0.838	-0.0 (1.3)	1.000	0.3 (1.7)	0.205	-0.2 (1.7)	0.760
<i>Escherichia coli</i>	9.5 (2.7)	-0.4 (1.5)	0.364	-0.4 (3.1)	0.442	-0.5 (1.9)	0.505	-0.4 (2.7)	0.576

**P* value of pairwise changes (Δ) presented in the preceding column; with bold fonts are displayed statistically significant differences ($P \leq 0.05$).

Nutrition in Pediatric Crohn's disease

Take home messages

- Growth failure is very frequent at diagnosis; it is related to abnormal protein metabolism
- Growth velocity should be carefully assessed during the course of the disease
- Enteral feeding and/or immunomodulation using dietetic may control the disease activity (remission)
- The beneficial effects of enteral feeding are probably related to changes in the intestinal microbiota
- Puberty and target size may be achieved without any use of steroids but early association of azathioprine

Merci de votre attention



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