Latest Nutritional Management strategies in treating Crohns Disease

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Acknowledgments

- Dr Bhuvaneshwari Shankar
- Ms Lekha
- Ms Divya Lakshmi
- Dr S Srinivas
- No Conflicts of Interest

My Story so far……

- Graduated from GMKMCH, Salem
- Post graduate training in the U.K from 2000
- Initially trained as a General Paediatrician & Neonatologist
- MRCPCH-2005
- Higher specialist training,paediatric gastroenterology – CCT and FRCPCH
- Alder Hey Childrens Hospital,Liverpool
- Paediatric Endoscopy fellowship at Sheffield
- Honorary Lecturer-University of Liverpool
- Joined Apollo Family in November 2011.

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My Alma Mater


Royal Liverpool Children's NHS
Welcome to
Alder Hey Hospital
← Eaton Road entrance
← Accident and emergency

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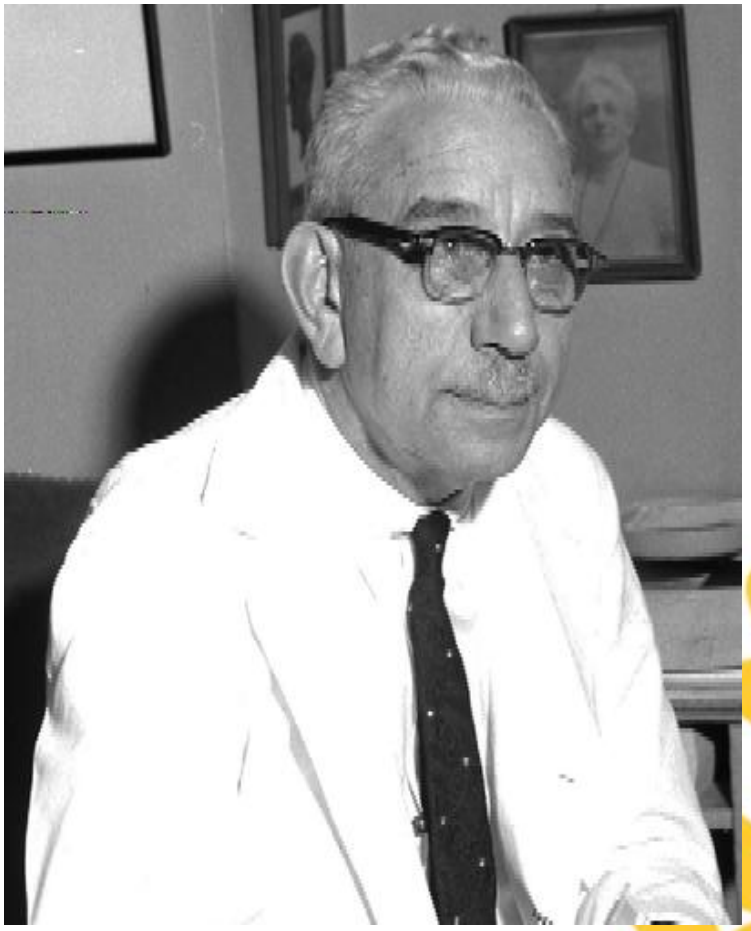
1904&1932



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History of Crohns

- Decsribed by two Doctors
- 1904-Antoni Lesniowski
- 1932-Burrill Bernard Crohn
- A series of terminal ileitis which was later described as what we now call as Crohns Disease

	CD	UC	IC	IBD Total	Data collection
Scotland[8]	0.7–2.3*	1.5–1.9*	–	–	R
Norway[68]	2.5	4.3	0	6.8	P
France[9]	2.1	0.5	0.6	–	P
Sweden[10]	2.6	1.9	0.7	5.3	P
Wales[11]	2.2	0.7	–	–	R
Denmark[12]	0.2	2.0	0	2.2	R
Sweden[14]	1.2	1.4–3.2†	2.2	4.6–7.0†	P
Wales[15]	1.4	0.8	0.5	2.6	P
UK and Ireland[17]	3.0	1.5	0.6	5.2	P
Scotland[3]	2.5	1.3	–	–	R
Denmark[4]	2.3	1.8	0.2	4.3	R
Norway[19]	2.1	2.0	–	–	P
Australia[6]	0.1–2.0‡	–	–	–	R
USA[23]	4.6	2.1	0.3	7.0	P
Czech Republic[7]	4.8	2.7	1.8	0.3	R
The Netherlands[21]	2.1	1.6	3.6	5.2	P
Sweden[5]	1.7–8.4§	3.3–1.8§	0.2	5.2–10.5§	P

IBD, inflammatory bowel disease; CD, Crohn disease; UC, ulcerative colitis; IC, indeterminate colitis; R, retrospective data collection; P, prospective data collection.

* Incidence numbers for the years 1968 and 1983; † incidence numbers for the years 1984 to 1986 and 1993 to 1995; ‡ incidence numbers rising from 1971 to 2001; § incidence numbers for the years 1990–1992 and 1999–2001.

Adapted from van der Zaag et al.[21] with permission.

IBD-Growing incidence!!

Disease	1973	2003
CROHNS	0.1	4.6
UC	0.5	3.2

Incidence in the UK

- 5.2 per 100,000
- Boys>Girls
- CD>IC>UC
- Asian>Ethnic
- Mean 11.9 years
- 5% Under 15
- 15% over 60
- Certainly increasing 25% in 20 years
- UC>CD

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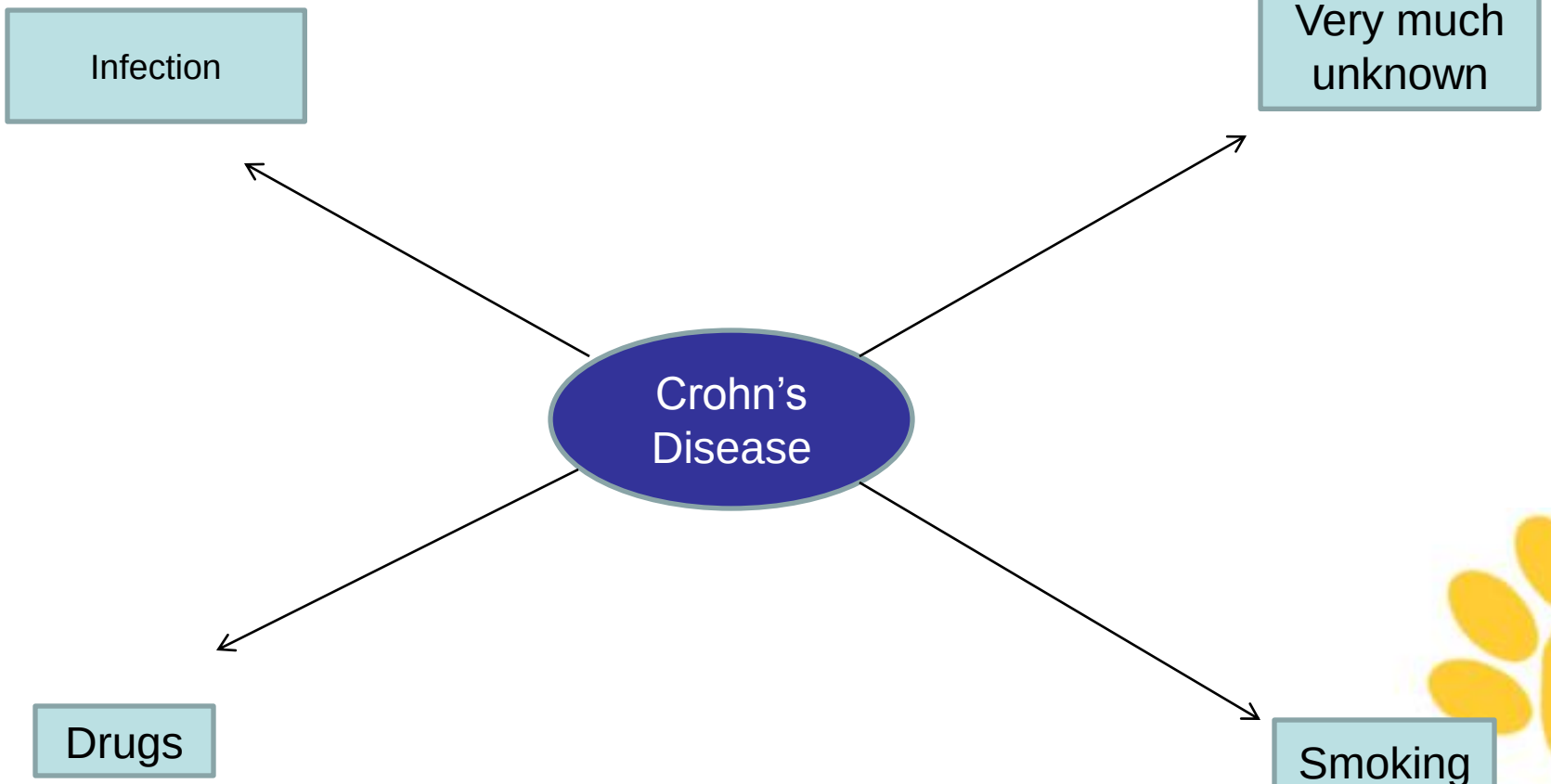
Etiology of Crohns



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Explored or being explored areas

- Epidemiological
- Gut/environmental interface
- Inflammatory process
- Genetics/Mutations
- Chromosome 16(CARD 15/NORD 2)

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Genetics

- Long known that Crohn's / UC is commoner in families / twins
- Not simple inheritance
- Sibling with CD/UC means 15-30x the risk
- 1 in 7 patients have a relative with the illness

Genetics (2)

THE HUMAN GENOME PROJECT

- 1996: Oxford group
- Showed Crohn's and UC share some susceptibilty genes
- Chromosomes 3, 7 and 12

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SMOKING !

- **Increased risk of:**
  - Getting it in the first place
  - Aggressive disease
  - Relapse
  - Hospital admissions
  - Surgery
  - Cancer

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An Infective Cause for Crohn's?

- M. Paratuberculosis
- E. Coli
- Viruses eg: measles
- Post-infective bacteria
- Clostridium
- Bacteroides
- Toothpaste
- Cornflakes
- Hygiene
- "Allergy"
- Refined sugars
- Trauma
- Pollutants

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Description

Aetiology

Pathophysiology

Predisposing factors

Symptoms

Signs

Investigations

Complications

Alternatives

Management

Prognosis

Symptoms
-depend on site of disease

- **Abdominal pain**
- **Weight loss**
- **Diarrhoea +/- blood**
- **Obstructive symptoms**
- **Complications of fistulae**
- **Complications of malabsorption**
  - B12, Ca/Vit D, Zn, etc

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What do children present with?

- *''Classical Triad''*
- *Abdominal pain,diarrhoea,weight loss*
- *Toronto-1980-89-80% presented*
- *UK-98-99-25%*
- *44%-NO DIARRHOEA BUT ABDO PAIN IN 72%*
- *Extra-intestinal-10% Erythema nodosum*

Many children with CD present with vague complaints such as lethargy, anorexia and abdominal discomfort or with isolated growth failure. A significant minority have markedly impaired final adult height [17, 18]. Neglect to record growth parameters, particularly for those not presenting to a paediatrician, has been identified [7, 17, 20]. Other symptoms may include fever, nausea, vomiting, delayed puberty, psychiatric disturbance and erythema nodosum [7]. The clinical course of CD is characterised by exacerbations and remission. CD tends to cause greater disability than UC.

Table 1

Presenting symptoms and signs of children in UK with CD; data from the national study [7]

Patients	CD (n = 379)	IC (n = 72)	UC (n = 172)
Common symptoms			
Abdominal pain	274 (72%)	54 (75%)	106 (62%)
Diarrhoea	214 (56%)	56 (78%)	127 (74%)
Bleeding	84 (22%)	49 (68%)	145 (84%)
Weight loss	220 (58%)	25 (35%)	53 (31%)
Lethargy	103 (27%)	10 (14%)	20 (12%)
Anorexia	94 (25%)	9 (13%)	11 (6%)
Other symptoms			
Arthropathy	28	3	11
Nausea/vomiting	22	1	1
Constipation/soiling	4		
Psychiatric symptoms	3		
Secondary amenorrhoea	1		1
Signs			
Anal fistula	17		
Growth failure/delayed puberty	14	1	
Anal abscess, ulcer	8		
Erythema nodosum/rash	6		1
Liver disease	3	2	5
Appendicectomy	2		
Toxic megacolon			1

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PORTO CRITERIA

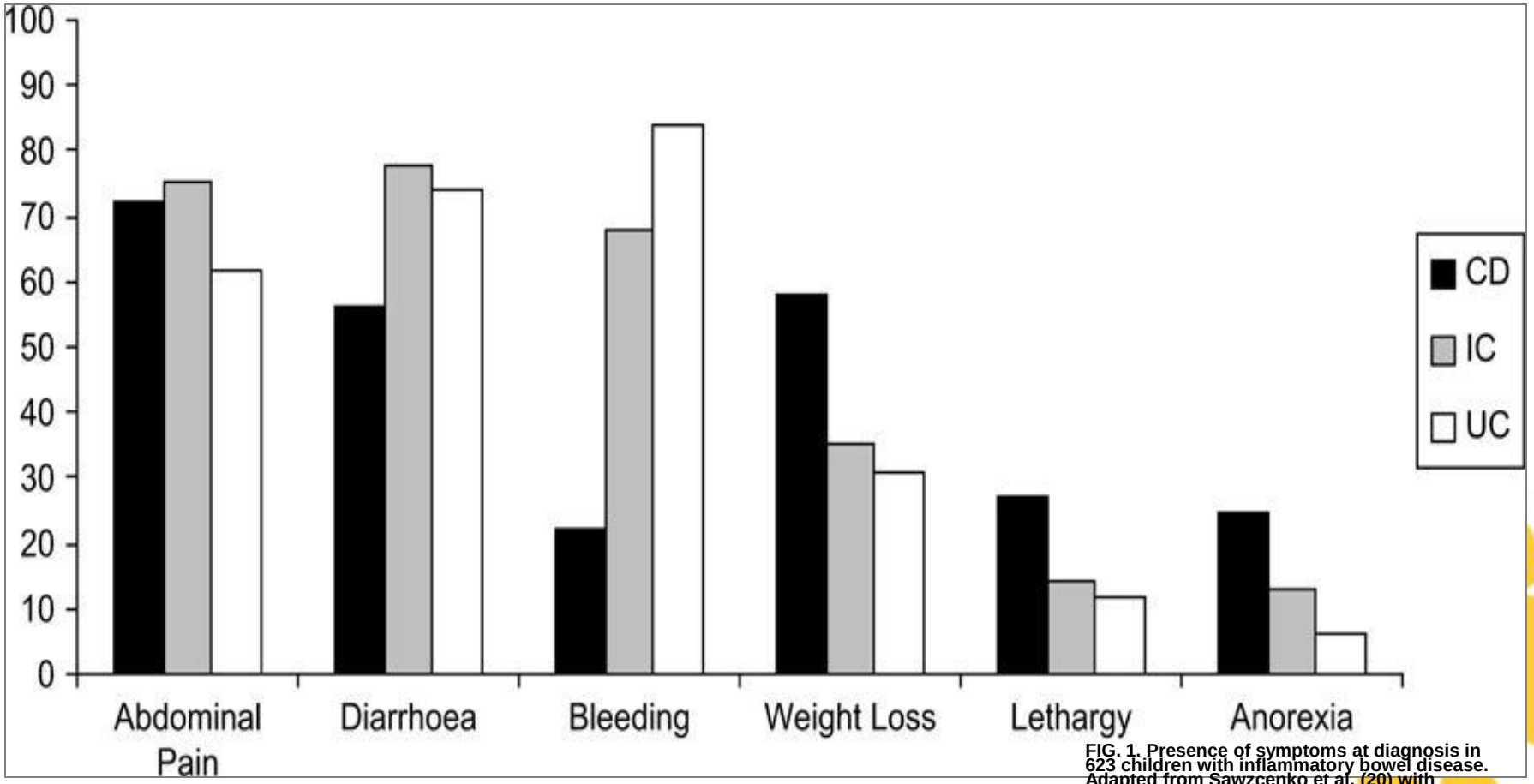

FIG. 1. Presence of symptoms at diagnosis in 623 children with inflammatory bowel disease. Adapted from Sawzcenko et al. (20) with permission.

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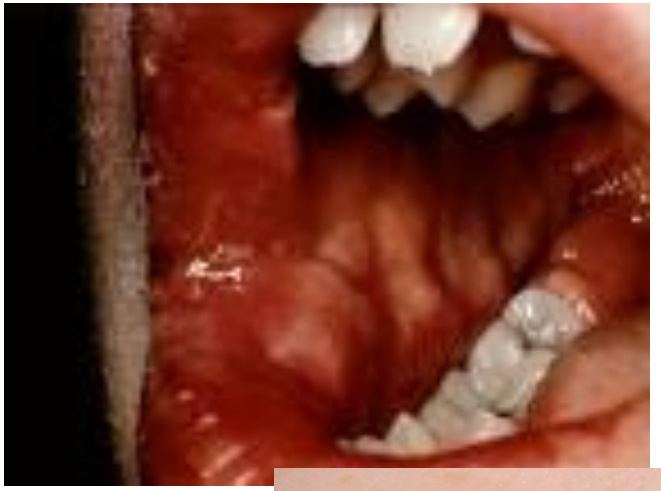
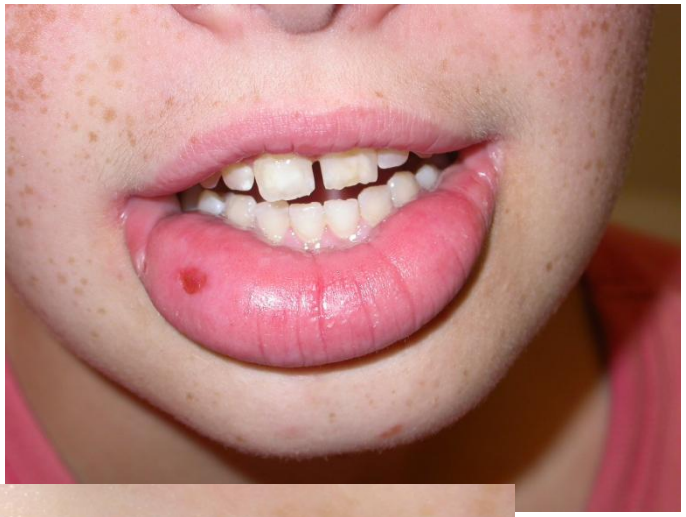
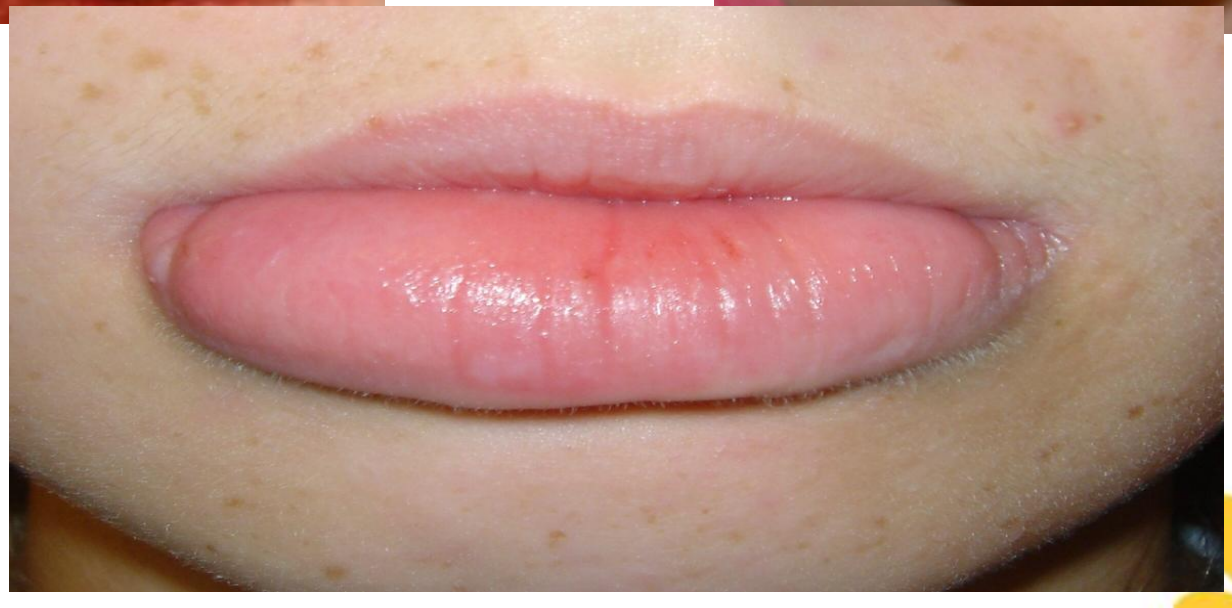
Oral apthous ulcers-OFG







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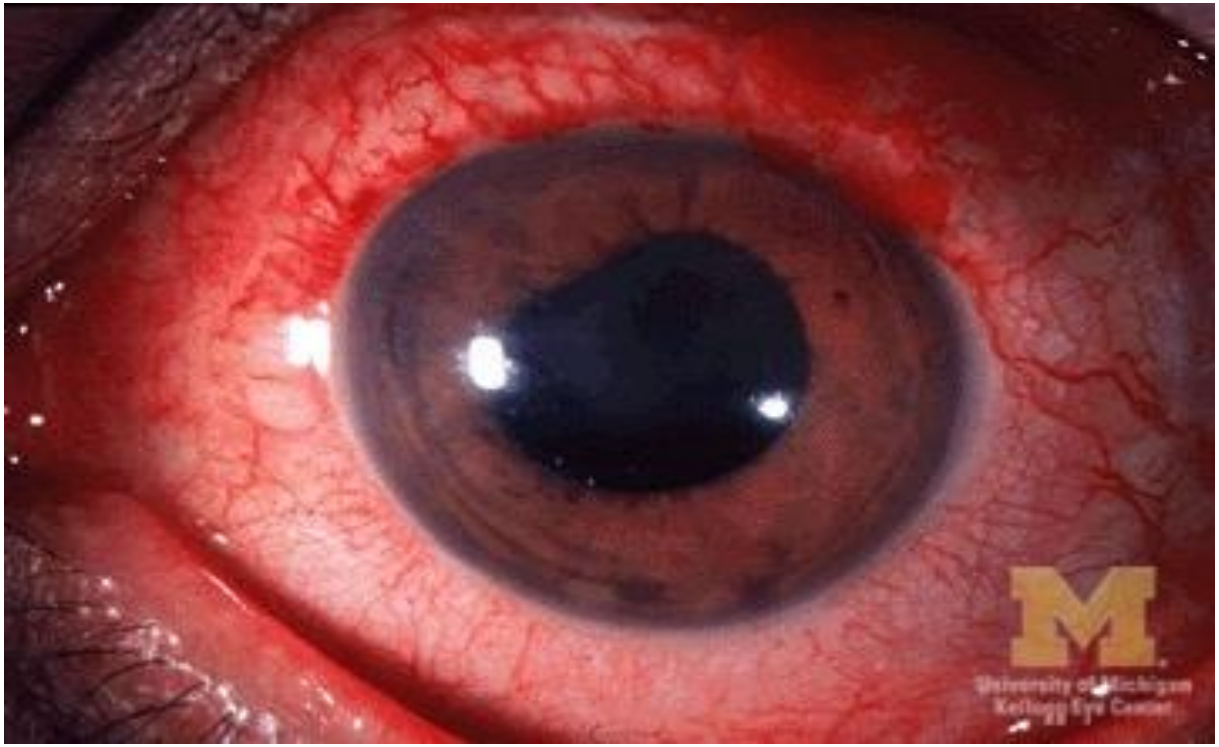
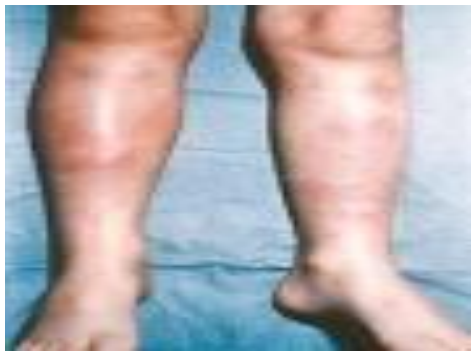
Uveitis



- Recurrent red Eye
- Red eye
- Associated with GI Symptoms



Erythema Nodosum

- **IBD**
- **TB/ Sarcoid**
- **OCP, sulphonamides**
- **Streptococcal infections**
- **Yersinia, psitticosis**
- **Lymphogranuloma venereum**
- **Connective tissue disorders**
- **Tuleraemia**

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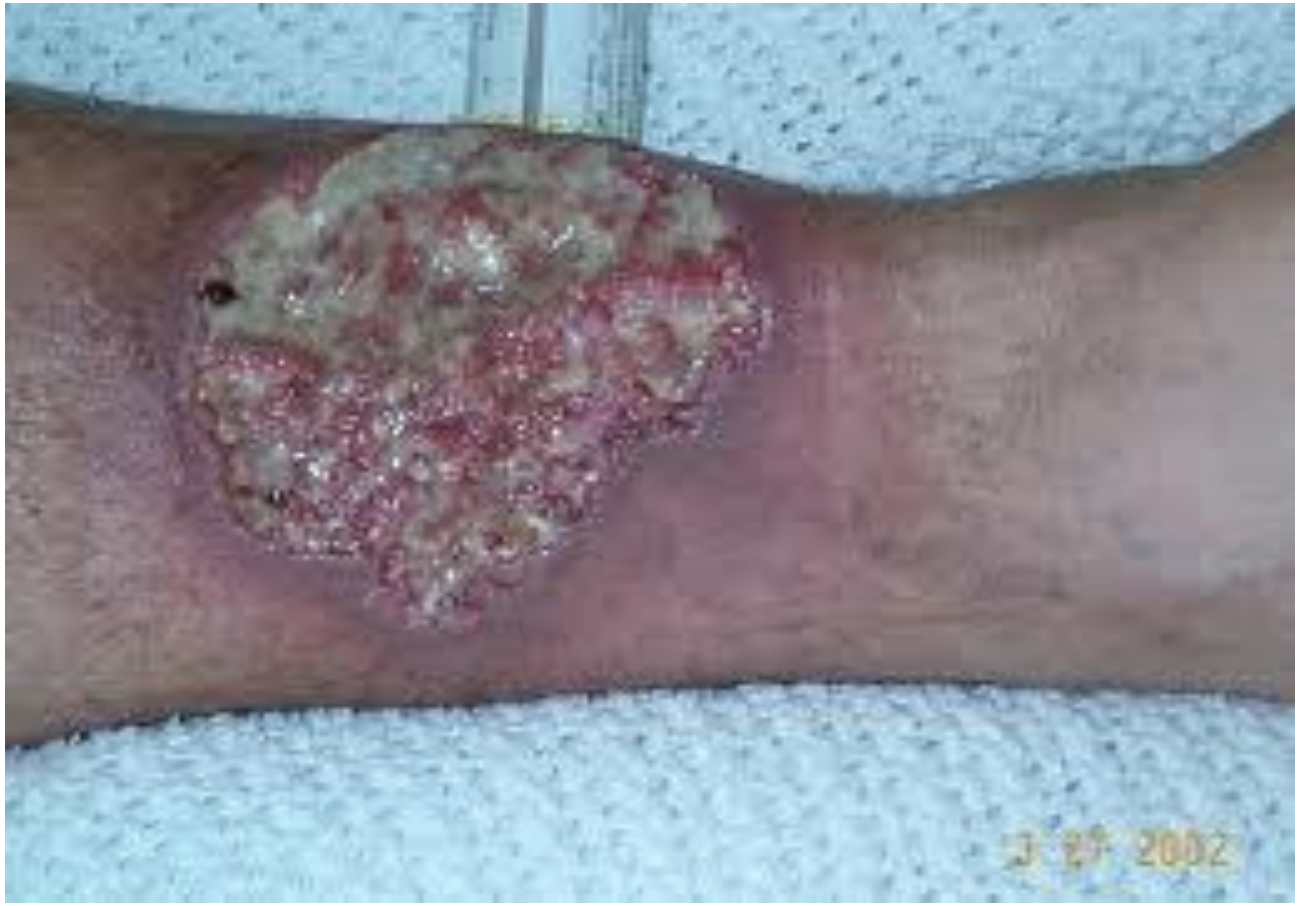
Pyoderma Gangrenosum



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Other manifestations

- Arthropathy with effusion
- Sacro-ileitis
- Failure to thrive
- Weight loss
- Nocturnal stooling
- Recurrent Diarrhoea
- List is endless.....

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How do you diagnose?

- Clinical-History,History,History
- Biochemical
- Endoscopic
- Radiological
- Histological
- +/- nuclear medicine

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What Bloods –are they useful?

- FBC
- ESR
- LFT-esp albumin
- CRP
- Stool
- TB and C difficile

Blood test	Sensitivity	Specificity
Haemoglobin & Platelets	90.8%	80%
ESR(Known already)	82	78
CRP	60%(Poor sensitivity)	
2 out of 3	85.7%	89.8%
1 out of 2(PLT+Hb)	90.8%	80%
Albumin	Poor correlation	
Beattie et al 1995 39 (26 cd/13 uc) 37 c Platelets	88% (CD)	70%(UC)
CD at least one abnormal	UC-8% All normal	
Albumin was reduced	Not significant	

ESR inessential predictor in combination with platelets and Hb.Only 3 patients has elevated ESR.

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DO NOT GET DISUADED BY NORMAL BLOOD RESULTS-THINK IBD!

Results

ESR inessential predictor in combination with platelets and Hb.Only 3 patients has elevated ESR.

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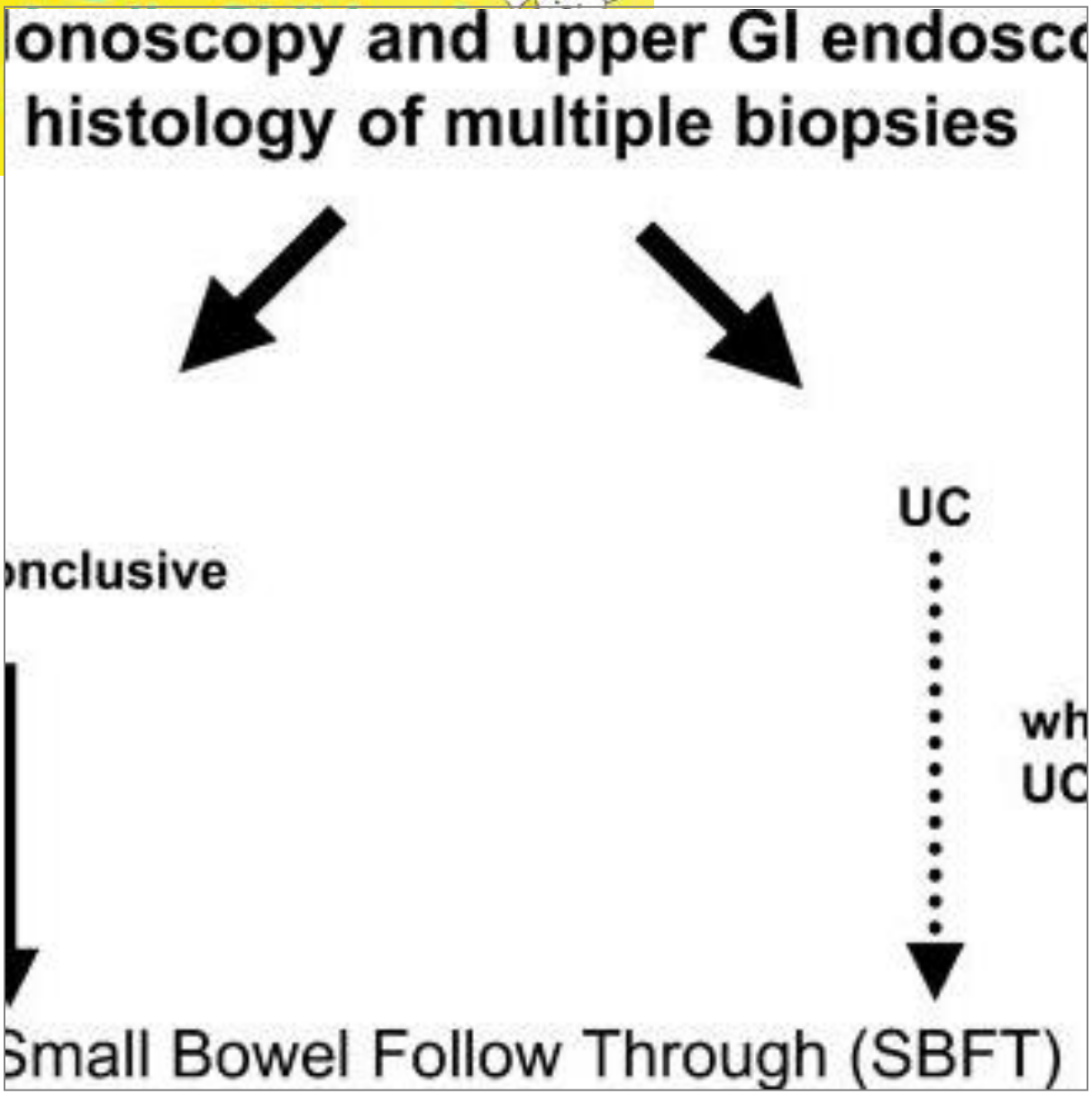
Degree	UC	CD
Mild (all 4 normal)	21%	54%
Moderate/Severe(all 4)	3.8%	4.3%
ESR	26% Normal	18% Moderate/Severe
Haemoglobin	32% Normal	
platelets	50%	
Albumin	60%	

	Crohn disease	Ulcerative colitis
Endoscopy (and visualization of oral and/or perianal regions)	Ulcers (aphthous, linear, or stellate) Cobblestoning Skip lesions Strictures Fistula Abnormalities in oral and/or perianal regions Segmental distribution	Ulcers Erythema Loss of vascular pattern granularity Friability Spontaneous bleeding Pseudopolyps Continuous with variable proximal extension from rectum
Histology	Submucosal (biopsy with sufficient submucosal tissue) or transmural involvement (surgical specimen)	Mucosal involvement
	Ulcers, crypt distortion Crypt abscess	Crypt distortion Crypt abscess Goblet cell depletion Mucin granulomas (rare)
	Granulomas (non-caseating, nonmucin) Focal changes (within biopsy) Patchy distribution (biopsies)	Continuous distribution

Histology for both Crohn disease and ulcerative colitis included acute and chronic inflammation with architectural changes, loss of glands, and branching of crypts. Crohn disease abnormalities in oral region included lip swelling, gingival hyperplasia, aphthous ulcers; Crohn disease abnormalities in perianal region included tags, fissures, fistulae, and abscess.

Fig. 2



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HOSPITAL
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BSPGHAN
working for children with digestive and liver disorders
British Society of Paediatric Gastroenterology Hepatology and Nutrition

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CICRA - Crohn's in Childhood Research Association and

NACC - National Association for Colitis & Crohn's Disease

CICRA
registered charity
number 278212

Colitis and Crohn's NACC
registered charity
number 1117148

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Treatment-Considerations

- **No available Surgical or pharmacological cure!**
- **Be open and honest**

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Considerations

- **Induction of remission and treating relapse**
- **Growth-Measure,treat suppression**
- **Nutrition +/- gastrostomy or NGT**

Enteral nutrition

- **Liquid formula: Elemental (single amino acids), semi-elemental (small peptides of 4/5 amino acids), polymeric (whole protein)**
- **Calorie density of most feeds is between 0.7 and 1.5 kcal/mL**
- **Oral, NG, gastrostomy tube**

Exclusive EN	Partial EN
Sole dietary source	+ plus normal diet
Induce remission	Maintain remission Nutrional support
Duration of 6-12 weeks followed by introduction of new food over 2-4 weeks	No defined duration, usually prolonged

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History of EN in Crohn's disease

- Efficacy suspected when patients awaiting surgery (nil orally and TPN) showed improvement
- ? possible role of luminal antigens in triggering acute attack and avoiding further damage by 'total bowel rest'
- Initial studies: elemental diets- amino acids (reduced antigenicity) and low fat (MCT-require little luminal lipolysis and micellar solubilization before absorption) to provide 'bowel rest'
- Elemental diets as effective as corticosteroids ìn remission
- Later, due to better nitrogen absorption and reduced osmotic load of peptide or whole protein diets than amino acid diet, polymeric enteral diets tried and found equally effective.

BMJ 1984;288:1859-62/ Arch Surg 1973;107:329-33

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Mechanism of action?

- Restoration of altered **intestinal permeability**
- **Decreased antigenic effects** of food proteins
- Avoidance of pro-inflammatory trigger factors such as food additives
- **Improvement of nutritional status** and repletion of nutrient, trace element or vitamin deficiency implicated in tissue repair mechanisms or in immune defense
- Effect on the **composition of the intestinal microflora** and modulation of the intestinal mucosal immune response

- **Clinical response to EN is associated with –**

✓ **Correction of the imbalance between proinflammatory and anti-inflammatory cytokines (reduced IL6, increased TGFβ)**

✓ **Reduction in lymphokine-secreting cells in the intestinal mucosa**

Gut 1987; 28:1073–1076/ Aliment Pharmacol Ther 2000; 14:281–289/2008;27:293-307/ Inflamm Bowel Dis 2005; 11:580–588/ JPGN 2004;38:270-5/ JPEN 2005;29:S173-5/ Cochrane Database Syst Rev 2007; CD000542

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EEN and Crohn's disease

- Disease remission (70-80%) in new CD cases
- Improved quality of life

- Improvement of weight and height parameters (in 10 weeks to 6 months)
- Improved PCDAI scores

- Improvement in inflammatory markers
- Mucosal healing at endoscopy (74% vs 33% with steroids at 10weeks , $p<0.05$)

APT 2004;20:167-72/ 2009;30:501-7/ Pediatr Research 2007;61:356-60
J Gastroenterol Hepatol 2006;21:1609-14, Clin Gastroenterol Hepatol 2006;4:744-53

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EEN and Crohn's disease

Factors determining EEN use

- Physician belief (62% European vs 4% American Ped gastroenterologist)
- Patient and parent consent and compliance
- Cost, palatability and invasiveness of NG use
- Growth and nutritional status
- Situations precluding use of steroids

JPGN 2003;36:464-

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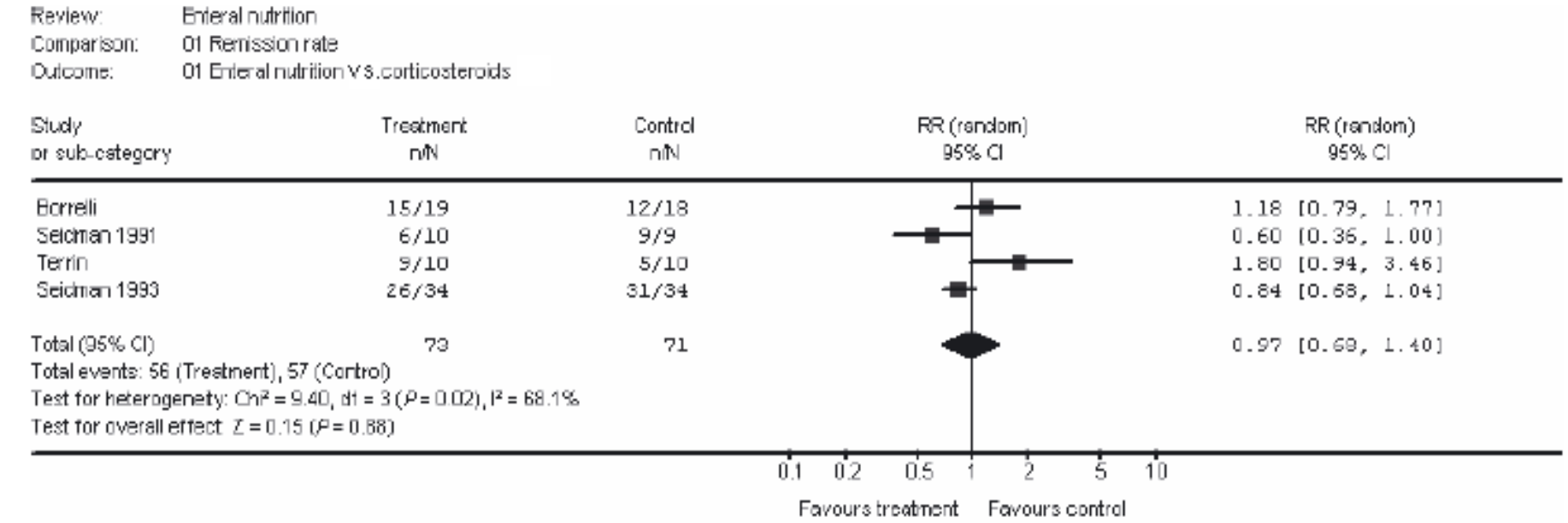

Meta-analysis (children)

n-147, 5 trials, pooled RR 0.95 (95% CI 0.67-1.34)

N- 144, 4 trials, pooled RR 0.97 (0.7-1.4)*

Limited data, good studies required

Equally effective as steroids in inducing remission

Aliment Pharmacol Ther 2007; 26, 795–806*, JPGN 2000;31:

EEN and Crohn's disease

Children

- **EEN equally effective as steroids**
- **Growth issues are vital**
- **Growth failure ~50% Underweight ~ 90%**
- **Better compliance to EEN- parental control, support by dieticians and physicians, evident benefit on weight and height growth**

Adults

- **Less effective than steroids (6 trials, pooled OR of 0.33 favoring steroids 95% CI 0.21 to 0.53)**
- **Growth not important**
- **Poor compliance ~21% in meta-analysis ***

Arch Dis Child 2007; 92: 767–70. Gastroenterol 1995; 108: 1055–67/
Cochrane Datbase syst rev 2007 24;(1):CD000542.

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EEN vs steroids

EEN
-Improves nutrition
-No side effects
-Mucosal healing better
-Motivated, compliant patient
-Cost, palatability
-Polymeric preferred (better acceptance and taste
lower cost, no NG feeds)

Steroids
-Easy to administer
-Cheap
-No extra counselling
-Side effects: growth, bone density
-Poorer mucosal healing

Arch Dis Child 2007;92:767-7

EEN and remission

- **Duration of EEN variable 3-12 weeks, majority 6-8 weeks**
- **Mean time for obtaining remission 11-18 days***
- **Recommendation: 3-4 week trial for observation for efficacy and total duration of min 8 wks, may be increased to 12 weeks**
- **No difference in the efficacy of elemental versus non-elemental formulas (10 trials, n-334, OR 1.10; 95% CI 0.69 to 1.75).**
- **No difference in efficacy based on fat content (7 trials, n- 209,low fat vs high fat < 20 g vs > 20 g/1000 kCal ,OR 1.13; 95% CI 0.63 to 2.01).**

J Dig Dis 2012;13:107-12/ *APT 2007;26:795-806/ JPGN 2012;54:298
Cochrane Datbase syst rev 2007:CD000542

EEN and remission

EEN and site of disease

- **Initial SB> colon (remission rate, isolated colonic 50%, ileocolonic 82%, ileal 97.1%)***
- **Equal in isolated colon vs isolated SB (15/19 vs 10/13)**
- **Cochrane review- insufficient data to favour one disease site over another, use in all**

Mode of administration

Both oral EEN and continuous NG feeding for 8 weeks are equally effective to induce remission [oral (75%) vs (85%) NG]^

Aliment Pharmacol Ther ^2011; 33: 1332–1339// * 2009;30:501-7
Dig Dis Sci 2005;50:1471-5/ Coch rev 2007;1:CD 000542

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Enteral nutrition for maintenance of remission

- **Advantage: minimizing use of steroids/ immunosuppressive drugs and maintaining good nutrition**
- **Supplemental EN (any type, along with normal food, duration of EN - 1 year or more)**
- **Significantly higher rate of clinical remission in those on EN vs without EN**
- **Higher amounts of enteral formula associated with higher remission rates:**

  ≥30 vs. <30 kcal/kg ideal body weight/day or half the requirement as EN
- **Problems:**
  - ✓ Patient selection (better compliance given EN)
  - ✓ Several patients on concomitant medications (5-ASA or azathioprine)
  - ✓ Available evidence is inadequate, large RCT are necessary
- **Enteral nutritional supplementation could be considered as an alternative or as an adjunct to maintenance drug therapy in Crohn's disease**

Eur J Gastroenterology & Hepatology 2010, 22:1–8
CochraneDatabase of Syst Rev2007, Issue 3. CD005984

EEN and remission

Lack of response (~20-30% of patients)

- **Partial EN (significantly poorer response 42% vs 15%)***
- **Poor compliance (meta-analysis- 21% of adults * vs 9-15% children, parental supervision)**
- **Inadequate energy intake**
- **Intolerance of the feed**
- **Resistant disease- severe disease, stricture**

Arch Dis Child 2007; 92: 767–70. Gastroenterol 1995; 108: 1055–67 Gut 2006;55:3

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Role of diet as an etiological agent

- No particular diets seem to have any particular triggers or help in remission of crohns disease.
- Any dietary intervention will have to be done under supervision.
- Linear growth and puberty will have to the main focus.
- "Listen to your belly"

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Diet in IBD

- Lack of evidence
- Most of advice is anecdotal
- Various diets have been advised to be avoided
- High fiber diet
- Caffeine, alcohol, sorbitol, carbonated drinks
- Fat containing diet
- hot & spicy food
- No routine use of TPN

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Lactose elimination in Crohns Disease

- There are inflammatory bowel disease (IBD) patients avoid lacteal products without evidence of lactose malabsorption, probably because of incorrect patient perceptions and arbitrary advice from physicians and diet books
- Spanish Study 2004
- 7/24 in IBD (CD&UC) and 5/25 (control)
- No difference
- 2002-von tirpitz et al,Germany in their study mention that milk intolerance is a problem in relapse due to decrease lactase levels but not predominant cause in CD.
- The key points are-Lactase enzyme activity , SIBO, Small intestine transit time.

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Fish Oil-Omega-3 in Crohns disease

- Cochrane review in 2009
- Randomized controlled trials with placebo
- 6 studies
- 3 reported a significant reduction in 1 year follow up
- But two large studies did not find any differences.

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Probiotics in EEN

- **Lactobacilli GG, Escherichia coli strain Nissle 1917, VSL#3, Saccharomyces boulardii**
- **All trials had small numbers**
- **No statistical difference was seen**
- **no evidence to suggest that probiotics are beneficial for the maintenance of remission in CD.**

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"*Fermentable, Oligo-, Di-, Mono-saccharides And Polyols*".

- **No evidence it is of benefit in IBD**

Cochrane review on EEN-2007&2009

- **Paediatric trials and meta analysis**
- **Showed feeds to be equally effective as corticosteroids.**
- **Intolerance to formula and inadequate volume are the main pitfalls in all studies.**
- **Remission rates are three times more with EEN when compared to PEN**

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Enteral nutrition :Inducing remission and maintaining remission---Is it elemental, semi elemental ,polymeric?

- Liquid formula: Elemental (single amino acids), semi-elemental (small peptides of 4/5 amino acids), polymeric (whole protein)
- Calorie density of most feeds is between 0.7 and 1.5 kcal/mL
- Oral, NG, gastrostomy tube

Cincinnati Children's

Pediatric Crohn's Disease Activity Index Calculator

Pediatric Crohn's Disease Activity Index, Hyams et al., Development and validation of a pediatric Crohn's disease activity index. J Pediatr Gastroenterol Nutr 1991;12:439-447. [PubMed link]

History (Recall; 1 week)

Abdominal pain:

- (•) None
- ( ) Mild-- Brief, does not interfere with activities
- ( ) Mod/severe - daily, longer lasting affects activities, nocturnal

Stools (per day):

- (•) Formed stools or up to 1 liquid stool, no blood
- ( ) Up to 2 semi-formed with small blood, or 2-5 liquid with or without small blood
- ( ) Any gross bleeding, or ≥ 6 liquid, or nocturnal diarrhea

Patient Functioning -- General Well-Being

- (•) No Limitation of activities, well
- ( ) Occasional difficulty in maintaining appropriate activities, below par
- ( ) Frequent limitation of activity, very poor

Laboratory (values obtained within the past week)

Sex: Male | Age(whole years): 4 | Hematocrit %: 36 | ESR (mm/hr): 0 | Albumin (g/dl): 4.5

Examination

Weight

Apollo Children's HOSPITALS
Touching little lives.

Success of EEN

- No side effects.
- Compliant patients took it all orally-No NGT or PEG Feeds or hospital admissions.
- Team work.
- Support for parents.
- Co-operation of child and compliance.
- Increasing number of patients opting for EEN.
- From start of EEN none of them have had steroid therapy.

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Touching little lives.

Limitations of EEN

- **Lack of availability or alternatives other than peptide feeds in India.**
- **Cost in non-affordable patients-total cost is around 20k for 8 weeks.**
- **Co-operation of child and family is paramount.**
- **Review after completion of feeds only through telemedicine.**

Apollo Children's HOSPITALS
Touching little lives.

Conclusion

- EEN equally effective as steroids in inducing remission (70-80%) in CD children, less effective in adults
- Polymeric formula preferred over elemental (oral or NG) due to lower cost, better taste and equal efficacy
- Minimum 8 weeks duration recommended
- No definite effect of site of disease, fat composition or added glutamine to formula
- Requires commitment of physician, dietician, patient and family
- Better designed studies are required