

Lady with abdominal pain

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History

- **F/ 30**
- **Chinese**
- **Accountant**
- **Non smoker**
- **Non drinker**
- **Unremarkable past medical history**
- **No history of GI surgery**
- **No family hx of GI cancer/ inflammatory bowel disease**
- **No known history of psychiatric illness**

History

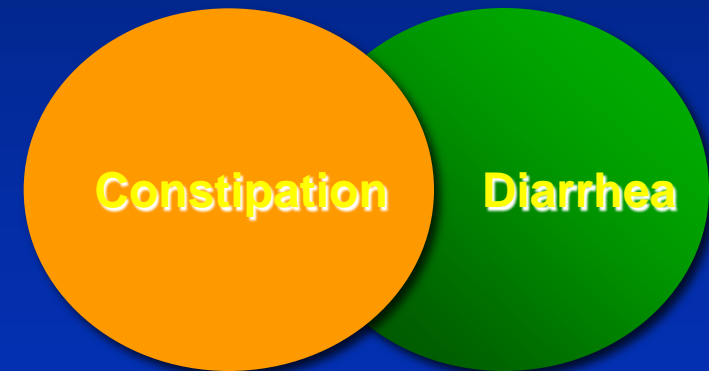
- Presented to private practitioner for
- Colicky central abd discomfort for 6 months
 - 1-2 times per week
 - occur at day time
 - Relieved by defecation
 - Bloating
- Constipation
 - BO 2-3 times per week with hard stool
 - No blood in stool but occ mucus passage
- No weight loss

Investigation

- WCC 4
- Hb 12
- Plt 300
- ESR 10
- CRP < 5
- TSH N
- Cr 80
- Na 140
- K 3.5
- ALT 30
- Alb 40
- FBS 6

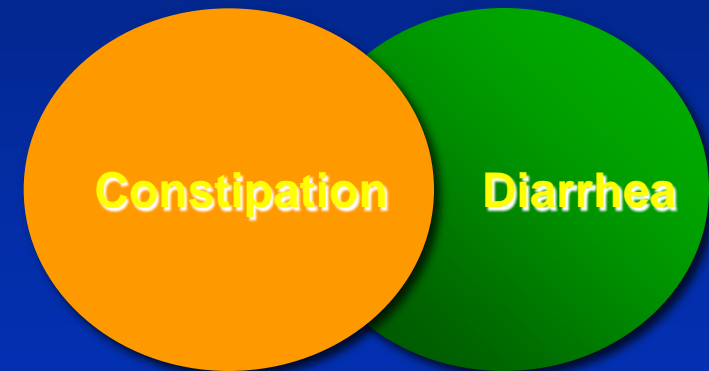
ROME III CRITERIA

- **Recurrent abdominal pain or discomfort**
 - with onset at least 6 months prior to diagnosis
 - at least 3 day/ months
 - in the last 3 months
 - associated with 2 or more of the following
 1. Relieved with Defecation
 2. Onset Associated with a Change in Frequency of Stool
 3. Onset Associated with a Change in Form (Appearance) of Stool



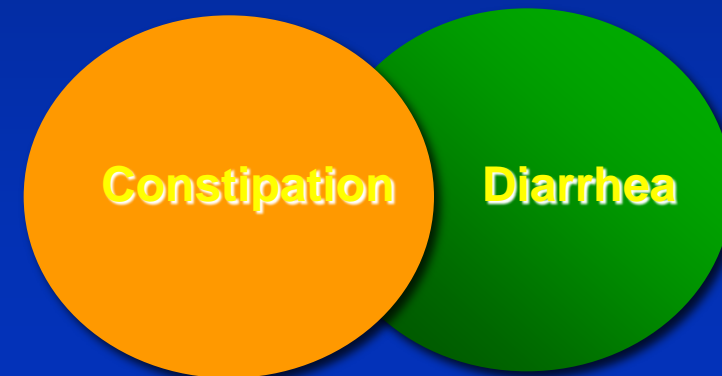
ROME III CRITERIA

- Symptoms that cumulative support the diagnosis:
 - **Abnormal stool frequency**
> 3 bowel movement per day or < 3 bowel movement per week
 - **Abnormal stool form**
lump/ hard or loose watery stool
 - **Abnormal stool passage**
straining, urgency or feeling of incomplete emptying
 - **Passage of mucus**
 - **Bloating or feeling of abdominal distension**



Subtype of IBS

- **IBS with constipation**
 - hard or lumpy stools >25% & loose or watery stools <25% of bowel movement
- **IBS with diarrhoea**
 - loose or watery stools >25% of bowel movement & hard or lumpy stools <25%
- **Mixed IBS**
 - loose or watery stools >25% of bowel movement & hard or lumpy stools >25%



“Red flags”

- Anemia
- Fever
- Persistent diarrhea
- Rectal bleeding
- Weight loss
- New onset of symptoms in patients 50+ years of age
- Nocturnal symptoms of pain and abnormal bowel function
- Family history of GI cancer, inflammatory bowel disease, or celiac disease

Progress

- OGD: normal
- Colonoscopy: haemorrhoid
- CT abd: normal
- Refer to HA hospital because of persistent symptoms
- What can we offer to her ?

Current management components of IBS

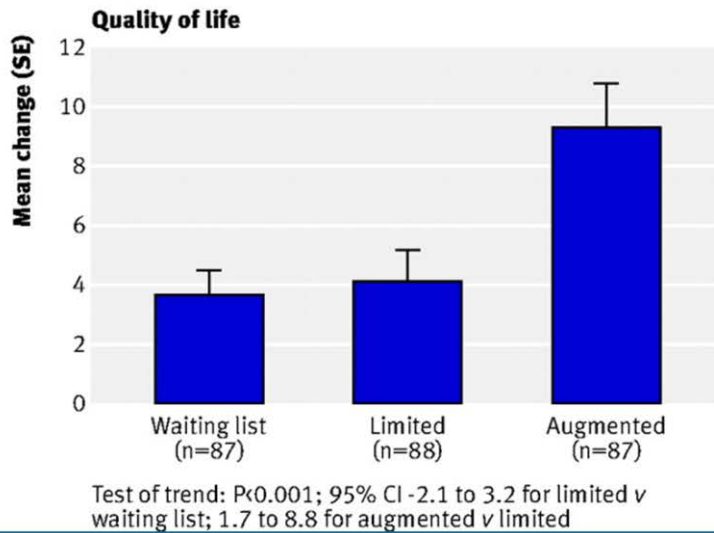
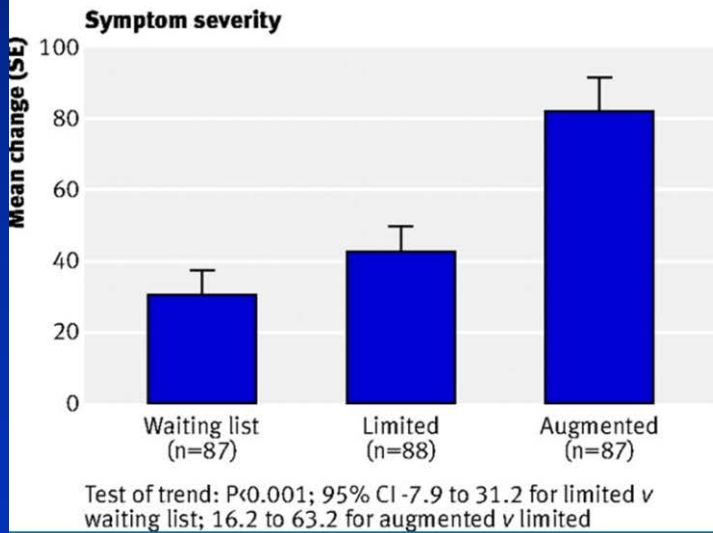
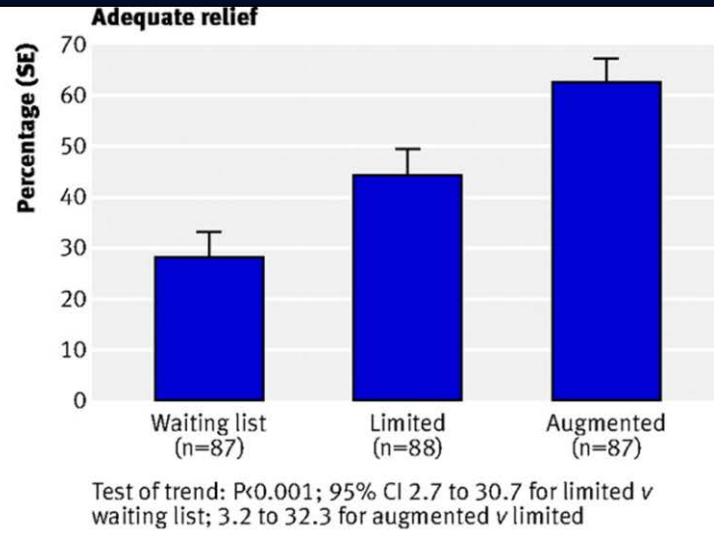
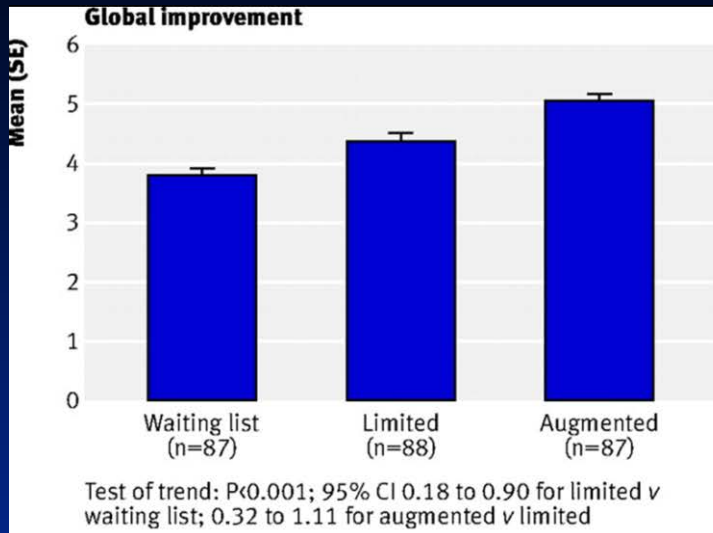
- Education
- Reassurance
- Lifestyle modification
- Fiber
- Pharmacological treatment
- Alternative treatment

Current management of IBS

- Establish a **positive** diagnosis
- Build up therapeutic physician-patient relationship
- Reassure patient that there is no serious organic disease or alarming symptoms

Therapeutic relationship

- Compare placebo effect and patient-health care provider interaction
- 262 patients
- Group 1: waitlist
- Group 2: sham acupuncture with little interaction with HCP
- Group 3: sham acupuncture with much more interaction with HCP



Physical exercise

- 20-60 minutes of moderate to vigorous activity 3-5days per week for 12 week
- Clinical improvement in severity of IBS symptoms and less likely of worsening of IBS symptoms

Dietary modification

- **FODMAPS** (Fermentable oligosaccharides, disaccharides, monosaccharides and polyols)

excess fructose	lactose	fructans	galactans	polyols
<p>fruit apple, mango, nashi, pear, tinned fruit in natural juice, watermelon</p> <p>sweetners fructose, high fructose corn syrup, concentrated fruit sources, large servings of fruit, dried fruit, fruit juice</p> <p>honey corn syrup, fruisana</p>	<p>milk milk from cows, goats or sheep, custard, ice cream, yogurt</p> <p>cheeses soft unripened cheeses, such as cottage cheese, cream, mascarpone, ricotta</p>	<p>vegetables asparagus, beetroot, broccoli, brussel sprouts, cabbage, eggplant, fennel, garlic, leek, okra, onion, shallots, spring onion</p> <p>cereals wheat and rye</p> <p>fruit custard apple, persimmon, watermelon</p> <p>misc. chicory, dandelion, inulin</p>	<p>legumes baked beans, chickpeas, kidney beans, lentils</p>	<p>fruit apple, apricot, avocado, blackberry, cherry, lychee, nashi, nectarine, peach, pear, plum, prune, watermelon</p> <p>vegetables cauliflower, bell pepper, mushroom, sweet corn</p> <p>sweetners sorbitol, mannitol, isomalt, maltitol, xylitol</p>

Dietary modification

- Study on IBS patients on high FODMAPs diet has ↑GIs such as abd pain, bloating, flatus ¹
- Trial of low FODMAPs diet can be conducted for 4-6 weeks, follow by rechallenge of any potentially more well absorbed carbohydrates e.g. fructose, lactose ²
- Exclusion diets however have not been definitely shown to be of benefit, their routine use outside of a clinical trial is not recommended³

1. Ong DK, *J Gastroenterol Hepatol* 2010;25:1366-73,

2. Jacqueline S Barrett *Ther Adv Gastroenterol* 2012;5:261-8
AJG 2009 Vol 104 Supp 1

Current management components of IBS

- Education
- Reassurance
- Lifestyle modification
- **Fiber**
- Pharmacological treatment
- Alternative treatment

Fiber

- **Insoluble Fiber**
 - **Wheat Bran, Corn fiber**
- **Insoluble fiber undergo minimal change in GI tract**
 - **form faecal mass & reduce colonic transit time**
 - **improve constipation but may worsen abd pain**



Fiber

- **Soluble Fiber**
 - **Psyllium, Calcium polycarbophil**
- **Soluble fiber dissolves in water and form gels**
 - fermented by colonic bacteria
 - short chain fatty acid
 - reduce colonic transit and intracolonic pressure
 - improved both constipation and possibly abd pain



Fiber

- **Recent data favor use of Soluble fiber over insoluble fiber for IBS patients with improvement of global IBS symptoms and constipation**
- **Adverse event rare**
- **In clinical practice, sudden increase fiber intake may cause bloating, abdominal distension and flatulence**
- **Trial of fiber is reasonable in IBS-C patients with dosage titration to symptoms**

Current management components of IBS

- Education
- Reassurance
- Lifestyle modification
- Fiber
- **Pharmacological treatment**
- Alternative treatment

Pharmacological therapy

- **Pharmacological agents are only adjunctive**
- **Chronic use of drugs should be minimized**
 - **life long nature of disorder**
 - **lack of convincing therapeutic benefit**
 - **heterogeneous population**
 - **lack of disease markers**
 - **high placebo response rates**

Antispasmodic agents

- Short term relieve abdominal pain, bloating, faecal urgency
- Intestinal smooth muscle relaxation e.g mebeverine, pinaverine
- Anticholinergic or antimuscarinic properties e.g. hyoscine
- Evidence of long term efficacy not available
- S/E: dry mouth, dizziness, blurring of vision

Antidepressant

- **Tricyclic antidepressant, Serotonin reuptake inhibitor**
- **Analgesic properties independent of mood effects**
 - **Facilitation of endogenous endorphin release**
 - **Blockade of norepinephrine reuptake**
 - **Enhancement of descending inhibitory pathways**
 - **Blockade of pain neuromodulator**
- **TCA potential slow intestinal transit and may benefit in IBS-diarrhoea patient**
- **SSRI has potential prokinetic effect and may work better in IBS-Constipation patient**

Antidepressant

- **Systematic review showed both TCA and SSRI has improvement global symptoms control in IBS patient and appear to reduce abdominal pain**
- **No head to head comparison on TCA vs SSRI on symptom control, but SSRI seems better tolerated**
- **Data on long term safety and tolerability limited in IBS patients**
- **Lower dose required than in treatment for depression**
- **Delayed onset of action, titrate after 3-4 wks interval**

Antidiarrheals

Loperamide

- Only antidiarrhoeal drugs studied in RCT for IBS-D
- Improve stool frequency and consistency
- But no effect on overall IBS symptoms
- Long term safety and tolerability lacking

Laxative

- Laxative has not been studied in RCT in IBS adults patient
- Small trial in IBS-C adolescent patient show PEG improve in stool frequency but not abdominal pain

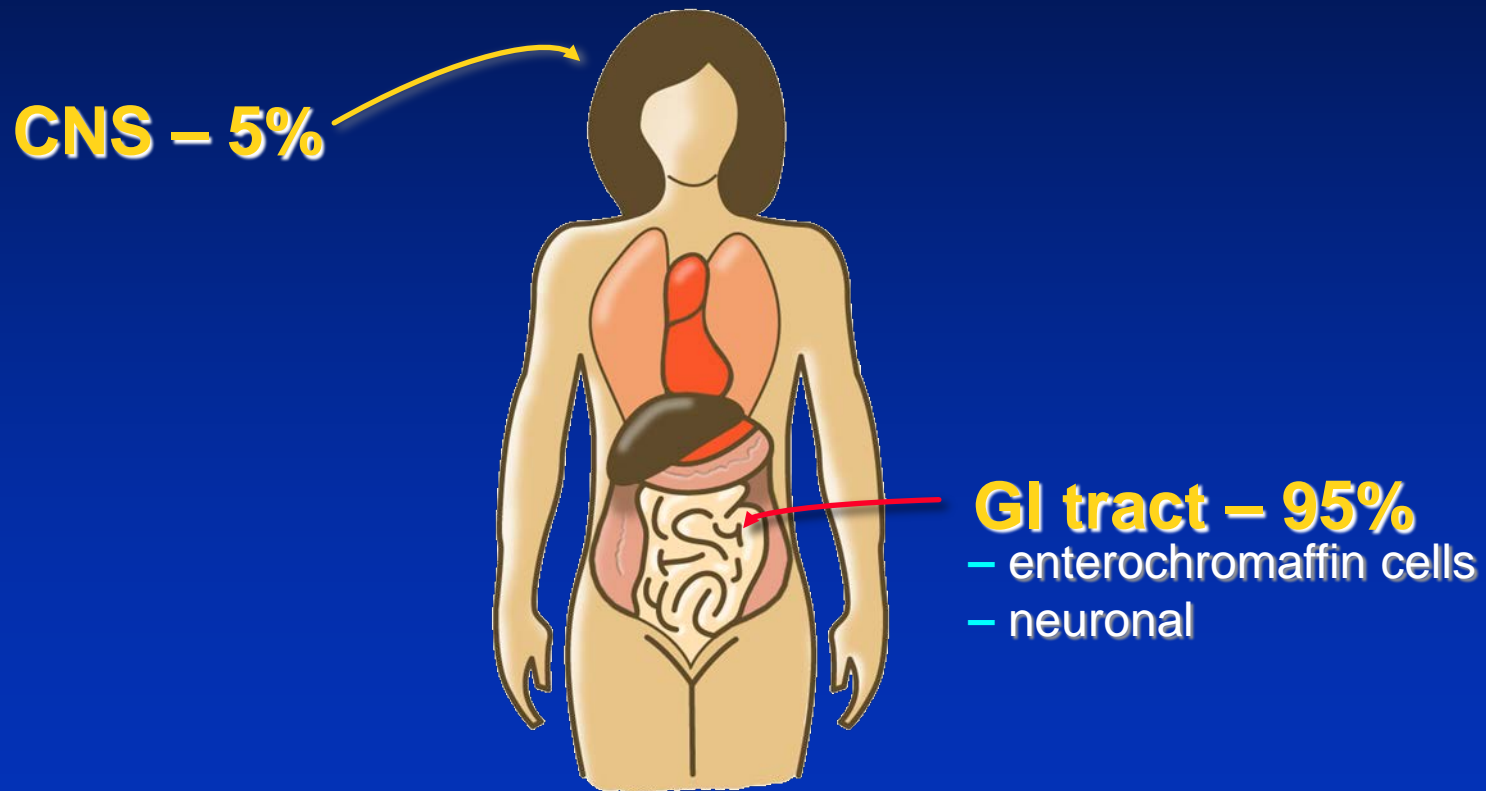
Summary of symptomatic treatment

	Lower abdominal pain	Bloating	Altered stool form	Altered stool passage	Urgency
Antispasmodic ¹	X	X			X
Tricyclic antidepressants and SSRIs ²	X				
Laxative ³			X	X	
Fiber ⁴			X	X	
Antidiarrheals ¹			X	X	X

1. American Gastroenterological Association. *Gastroenterology*. June 1997;4.112:2120-2137. 2. Drossman and Thompson. *Ann Intern Med*. 1992;116(pt 1):1009-1016. 3. *Drug Facts and Comparisons*[®]. 1999:316. C.J.Bijkerk. *Aliment Pharmacol Ther* 2004;19:241-51

Novel therapy

Physiological distribution of 5HT



Alosetron

- **5-HT₃ receptor antagonist**
- **Reduce colonic tone**
- **Blunt the gastrocolic reflex**
- **Decrease visceral sensation**
- **Improved global IBS symptoms in female and male IBS-D**
- **Approved by FDA in Feb 2000 for IBS-D female patients**



Alosetron

- **Adverse event :**
 - constipation *dose dependent*
 - ischaemic colitis *dose independent*
- **Withdrawal from market in November 2000**
- **Approve in June 2002 for chronic severe IBS-D patients who failed to respond to conventional therapy**

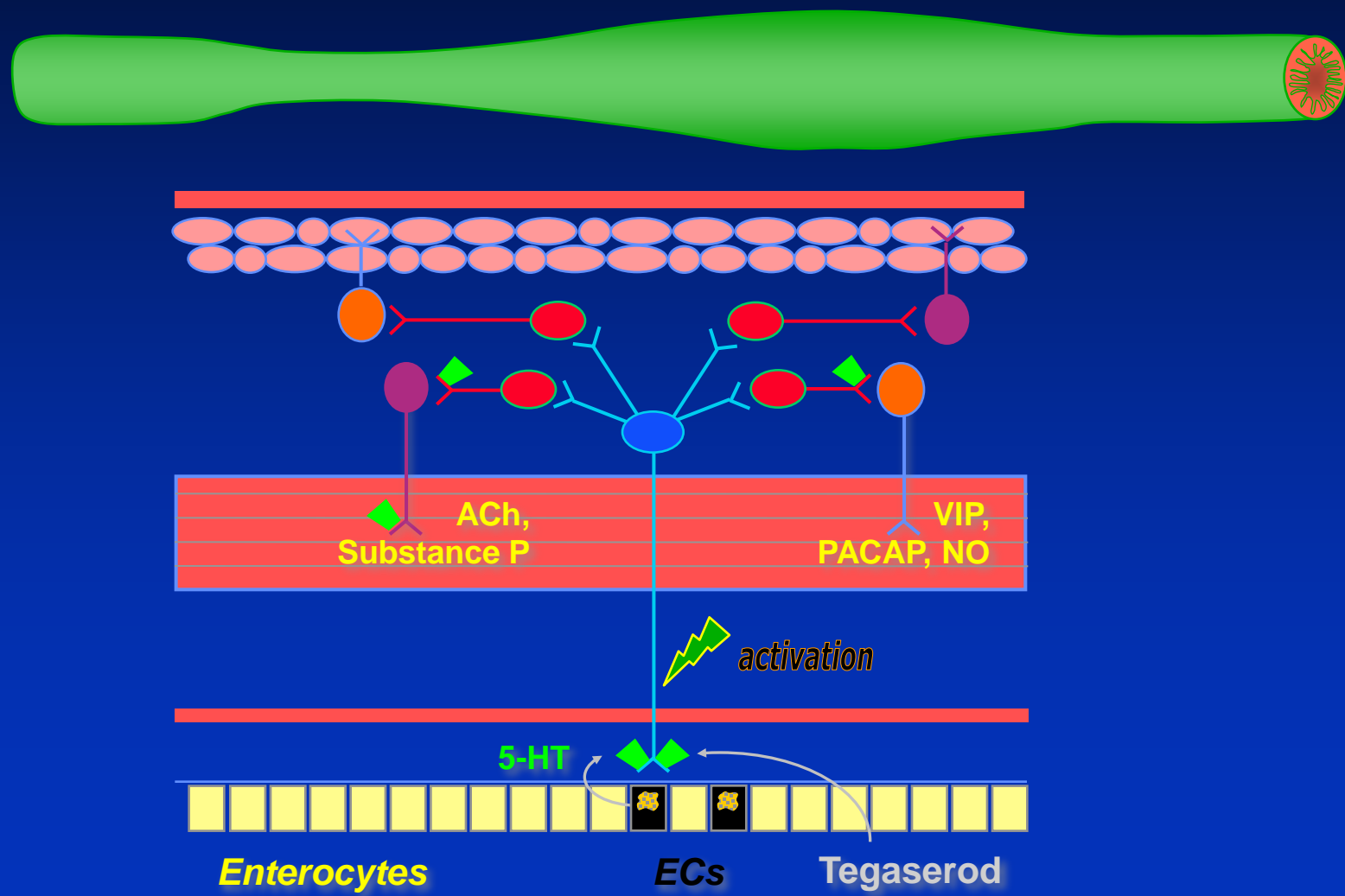
Alosetron

- **Recommended dose: 0.5mg bd**
- **Can increase to 1mg bd after 4 week if**
 - **drug well tolerated**
 - **symptoms not adequately controlled**
- **Discontinue if**
 - **s/s of severe constipation or ischaemic colitis**
 - **no clinical response after 1mg bd for 4 weeks**

Tegaserod

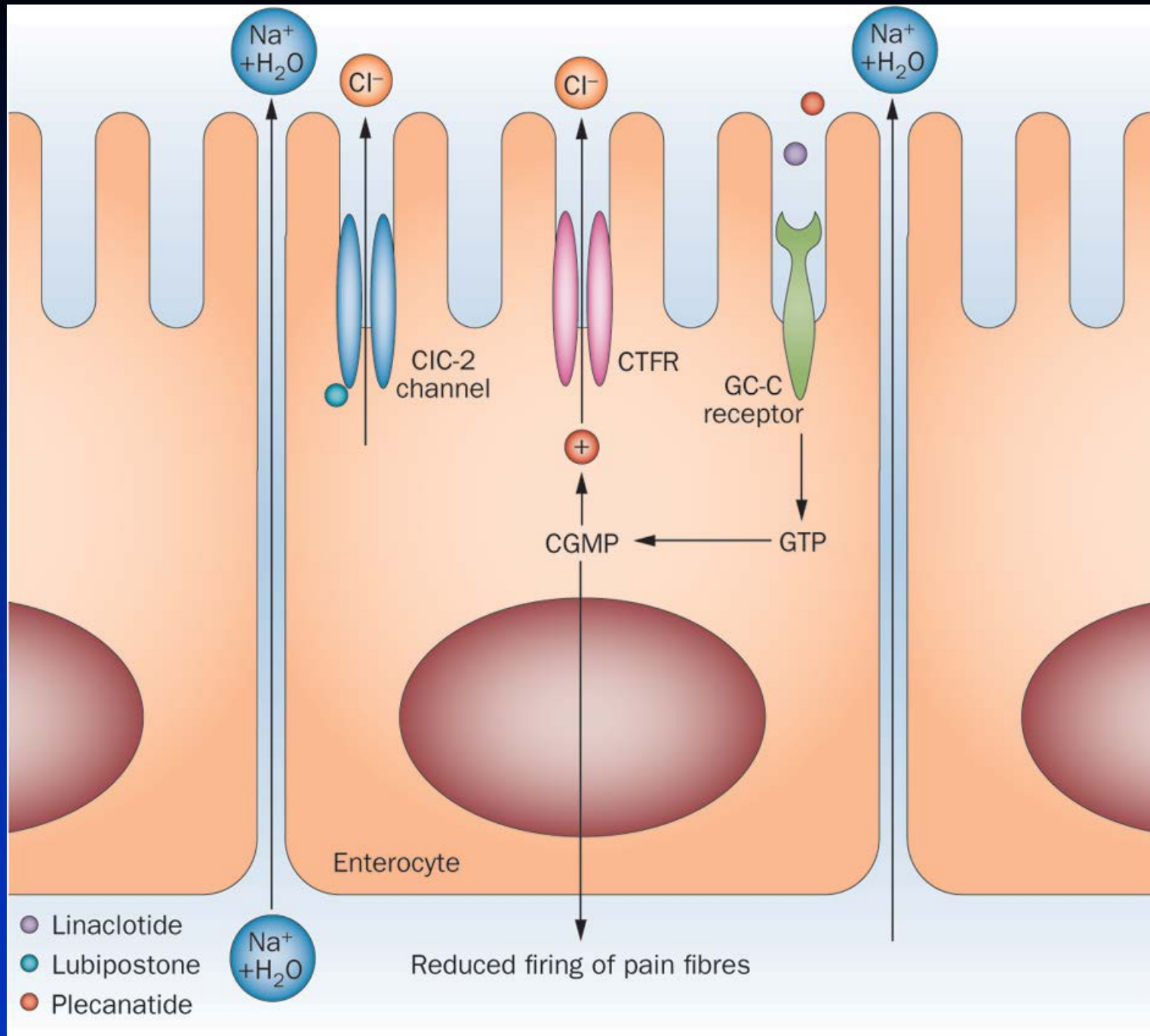
- Partial 5-HT₄ receptor agonist
- Stimulate release of neurotransmitter
- Increase colonic motility
- Improved global IBS symptoms in female IBS-C/IBS-M

Tegaserod



Tegaserod

- **Adverse event :**
 - diarrhoea
 - cardiovascular events e.g MI, unstable angina/ stroke
- **Withdrawal from market in March 2007**



Lubiprostone

- **Selective C-2 chloride channel activators**
- **C-2 chloride channel**
 - **lower capacity chloride channel**
 - **physiological regulation of paracellular permeability and intracellular volume**
- **Poorly absorbed in the systemic circulation and work topically in the small intestine**
- **Approved by FDA for chronic idiopathic constipation at dose of 24 µg BD**

Lubiprostone

- Phase 3 study for IBS-C with lubiprostone 8mcg bd vs placebo for 12 week

—○— placebo
—■— Lubiprostone 16 mcg

*Abdominal pain
bloating,
constipation

10 11 12

Lubiprostone

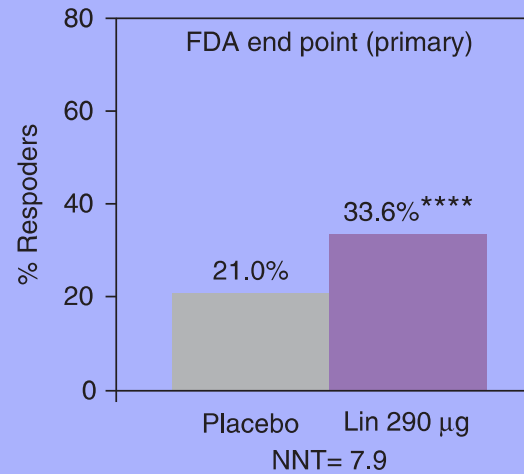
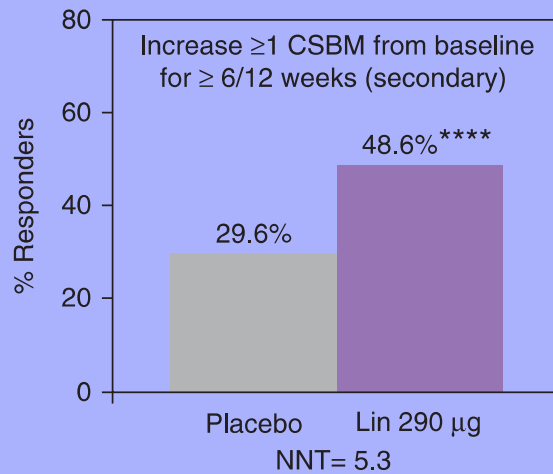
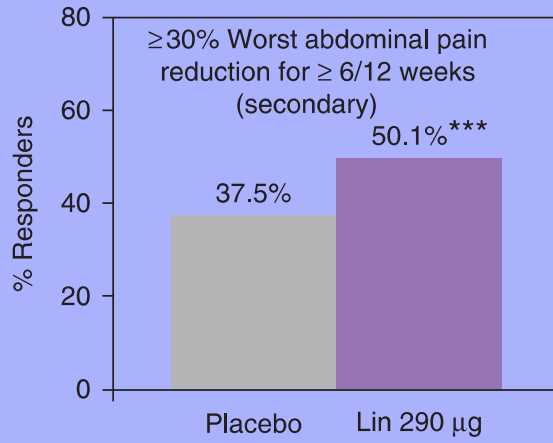
- **Approved IBS-C female patient**
- **Side effects: nausea, diarrhoea**
- **No long term safety data**
- **Reserved for IBS with severe constipation with unsuccessful treatment**

Linaclootide

- **Peptide agonist of Guanylate cyclase 2C**
- **Guanylate cyclase-2C**
 - **intestinal transmembrane receptor**
 - **responsible for chloride, bicarbonate and fluid secretion in intestinal lumen**

Linaclootide

- Phase 3 study for IBS-C with linaclootide 290mcg daily vs placebo for 12 week



Linaclotide

- **Approved by FDA for IBS with constipation**
- **Side effects: diarrhoea**
- **No long term safety data**
- **Reserved for IBS with severe constipation with unsuccessful treatment**

Miscellaneous

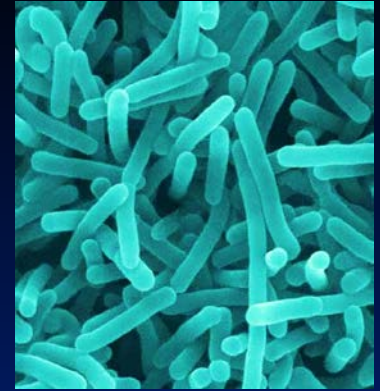
Rifaximin

- **Nonabsorbable antibiotic**
- **Approved by FDA for traveller's diarrhoea at dose of 200mg bd x 3days**
- **Higher dose use in trial for IBS-D patient at does 400mg tid x 10-14 days**
- **With improvement in bloating, abd pain, diarrhoea**
- **May be due to suppression of gas producing bacteria**

Rifaximin

- Short term course provide symptoms relieve for 10-12 weeks
- Symptoms may recur after 3-9 months
- No data to support the long term safety and efficacy

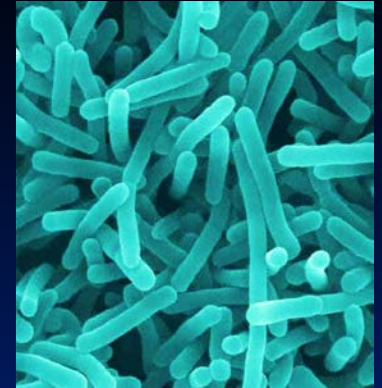
Probiotic



- **Microorganism that have beneficial properties to the host**
- **E.g Lactobacillus, Bifidobacterium**
- **Potential benefit**
 - **Suppression of growth/ epithelial binding by pathogenic bacteria**
 - **ferment carbohydrate without gas production**
 - **modulation of pain perception through induce expression of opioid or cannabinoid receptor**
- **Improved IBS symptoms particular bloating & flatulence**

Probiotic

- Short term heterogenous study
- Modest magnitude of benefit
- Lactobilli alone not effecitve
- Trends toward bifidobacteria and certain combination of probiotics



Peppermint oil



- **Antispasmodic properties**
- **Smooth muscle relaxation via calcium channel blockade**
- **Provide short term relieved in abdominal pain**
- **Efficacy based on few small studies**
- **Few adverse event report**

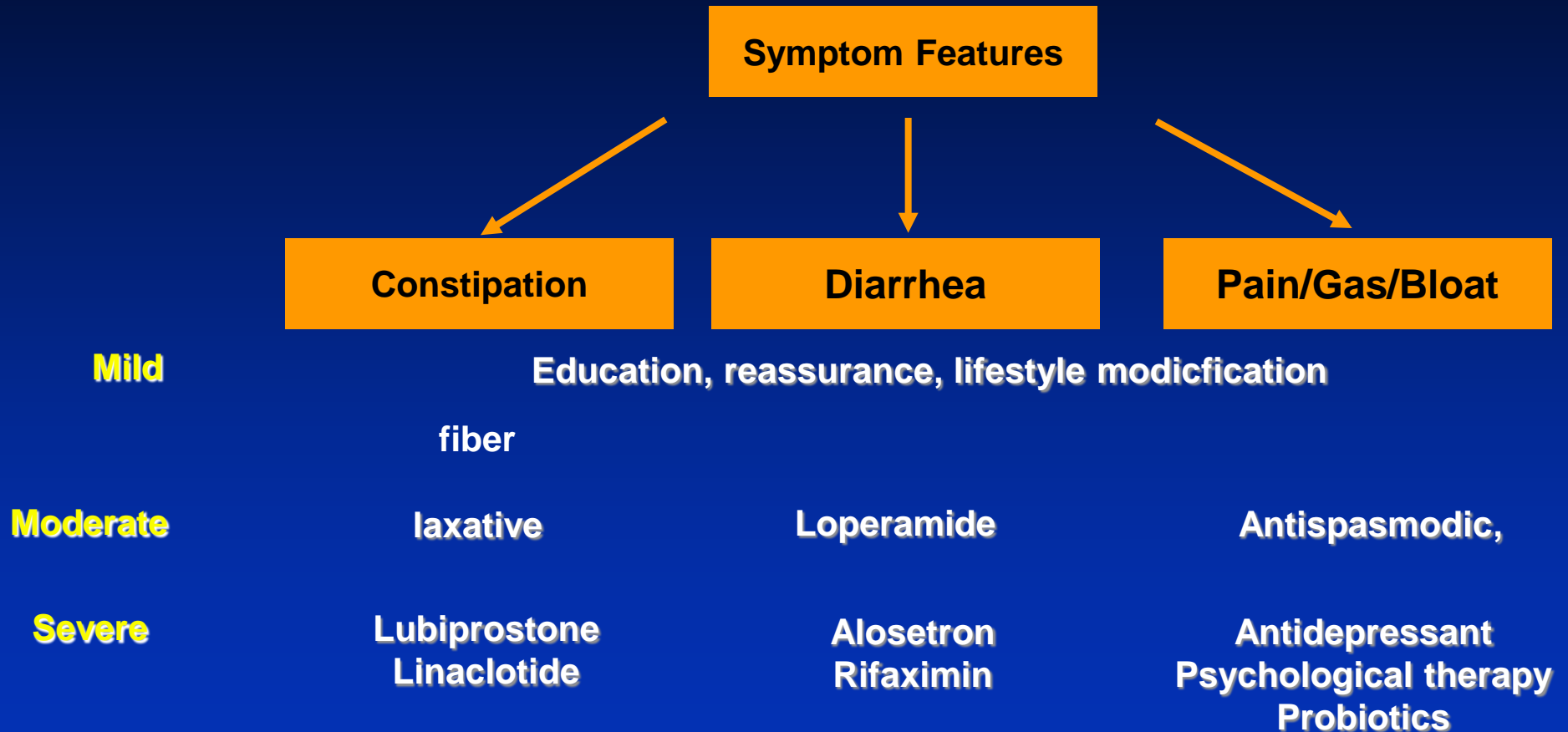
Herbal therapy

- Different herbal preparation has been shown to improve global IBS symptoms
 - STW 5 (Iberogast), fixed combination of hydroethanolic herbal extracts)
- Cannot combine to evaluate in meta-analysis due variable component, preparation, prurity
- Also concerns of potential hepatotoxicity
- Further work need before any recommendation made

Psychological therapy

- Different psychological therapies has been shown to improve global IBS symptoms
- Cognitive behavioral therapy, dynamic psychotherapy, hypnotherapy, Except relaxation therapy
- Unknown exact biological mechanism
- Most of study performed on patient refractory on standard treatment, so efficacy as first line treatment uncertain
- Best reserve for more refractory patient

MANAGEMENT OF IBS



Take Home Points

- IBS is a chronic medical condition characterized by abdominal pain, diarrhea or constipation, bloating, passage of mucus and feelings of incomplete evacuation
- Precise etiology of IBS is unknown and therefore treatment is focused on relieving symptoms rather than “curing disease”

Take Home Points

- **Cornerstone of treatment is a successful patient-physician therapeutic relationship, education and reassurance**
- **Specific pharmacological therapies are determined by individual patient symptoms**
- **Life-style and dietary modifications may relieve symptoms**
- **Psychological therapy may consider for refractory patients**

THANK YOU