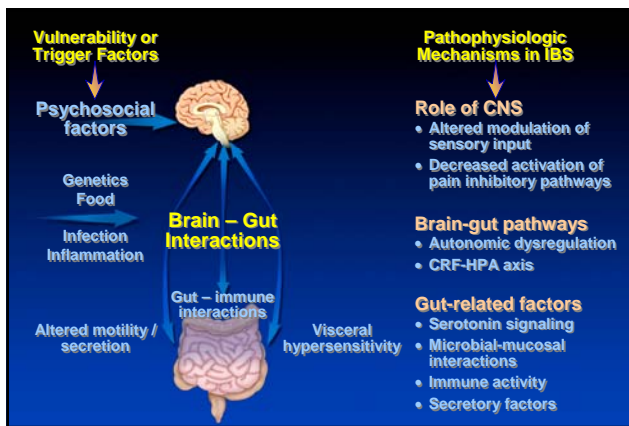
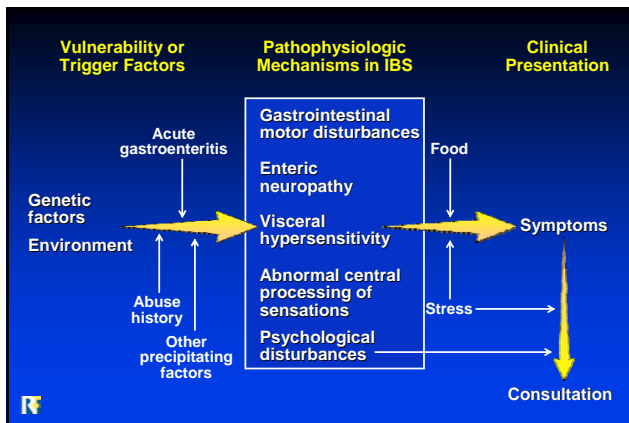


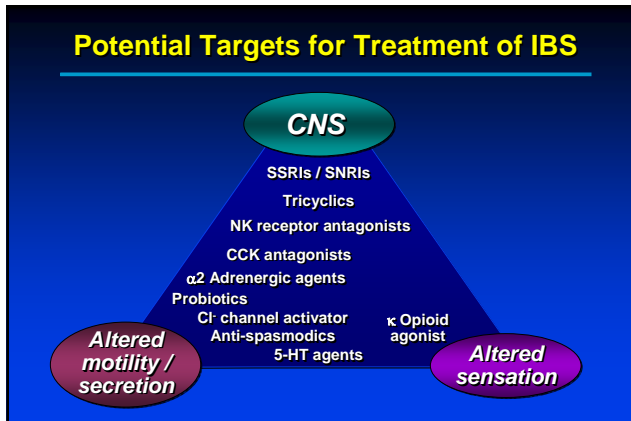
Has Our Understanding of IBS Pathophysiology Improved Its Treatment?

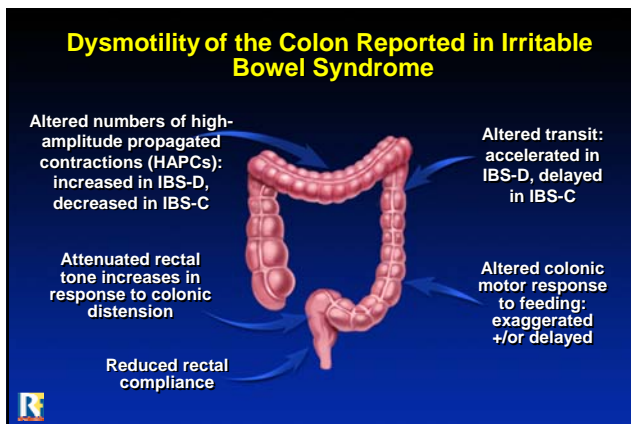
Lin Chang, M.D.
Center for Neurobiology of Stress
David Geffen School of Medicine at UCLA
VA Greater Los Angeles Healthcare System











Pharmacotherapy in IBS Directed Towards Improving Bowel Habits

Symptom	Drug	Dose
Diarrhea	Loperamide	2-16 mg
	Cholestyramine	4 g with meals
	Alosetron	0.5-1.0 mg bid (for women with severe IBS)
Constipation	Psyllium	3-4 g bid with meals, then adjust
	Methylcellulose	2 g bid with meals, then adjust
	Calcium polycarbophil	1g qd to qid
	Lactulose	10-20 g bid
	Sorbitol	15 ml bid
	Polyethylene glycol	17 g in .236 liters water qd
	Magnesium hydroxide	20-40 ml qd
	Tegaserod	6 mg bid (restricted use)
	Lubiprostone	8 mcg bid (for women with IBS-C)

Loperamide for IBS-D

- Only antidiarrheal studied in IBS
- Three RCTs of low-intermediate quality
- Loperamide is not more effective than placebo at reducing pain, bloating, or global symptoms of IBS, but it is effective for the treatment of diarrhea, reducing stool frequency, and improving stool consistency (Grade 2C)

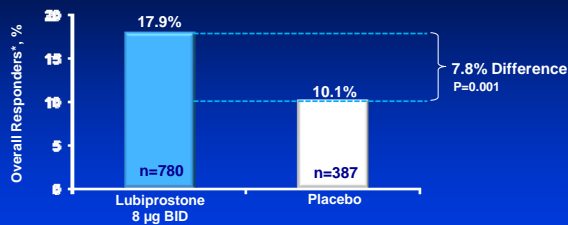
ACG IBS Task Force, *Am J Gastro* 2009; 104 (S1): S1-S35

5HT₃ Antagonists: Alosetron for IBS-D

- Central and peripheral effects
 - Slow GI transit
 - Increase colonic compliance
 - Decreases visceral perception
- Clinical trial results¹
 - 8 studies, 4987 patients
 - RR symptom remain = 0.79 (95% CI 0.69 to 0.90)
 - NNT = 8 (95% CI = 5 to 17)

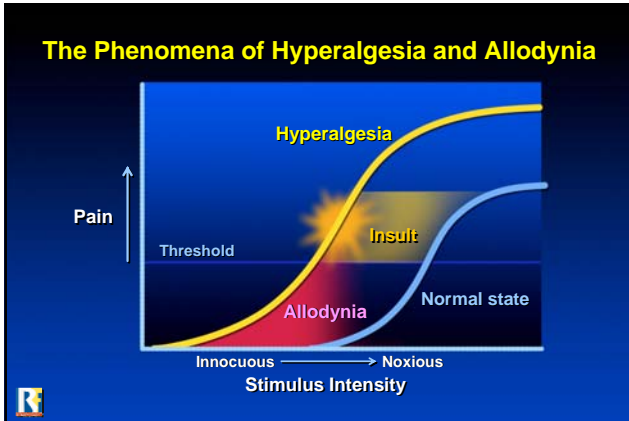
¹Ford AC et al. *Am J Gastroenterol* 2009;104(7):1831-43

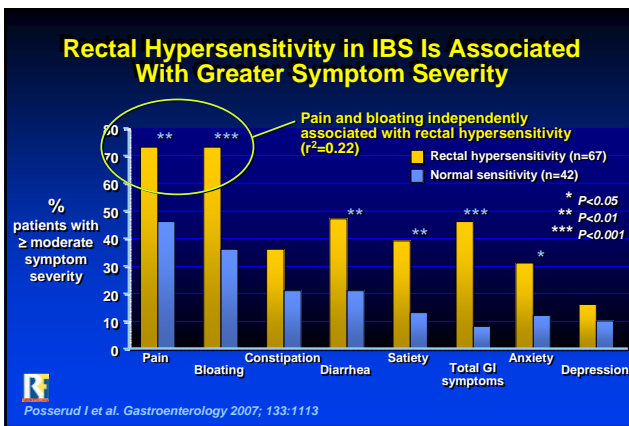
Efficacy of the Selective CIC-2 Chloride Channel Activator Lubiprostone for IBS-C

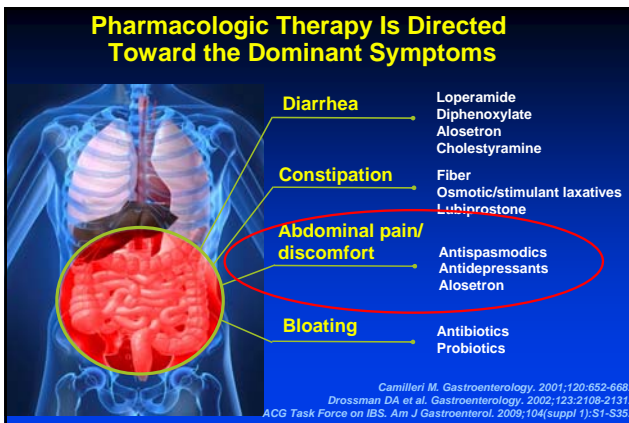


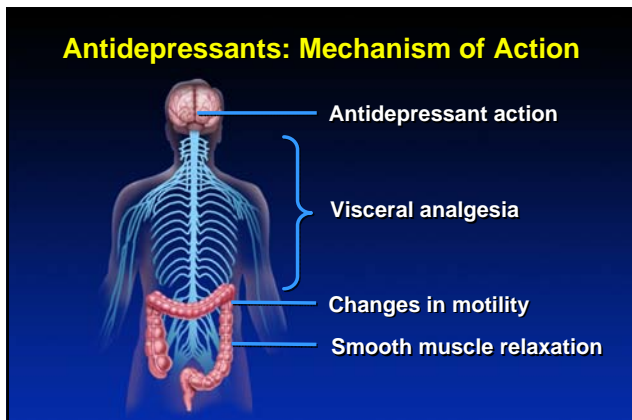
Combined analysis in Rome II IBS-C patients using intent to treat, last-observation-carried-forward analysis

¹Data combined from 2 studies, monthly responder for at least 2 of the 3 months during treatment. Drossman DA et al. *Aliment Pharmacol Ther*. 2009;29:329-341.









Antidepressants

Subgroup analysis according to class of drug

- **Tricyclic antidepressants**
 - 9 studies, 575 patients
 - RR symptom remain = 0.68 (95% CI 0.56 to 0.83)
 - NNT = 4 (95% CI = 3 to 8)
- **SSRIs**
 - 5 studies, 230 patients
 - RR symptoms remain = 0.62 (95% CI 0.45 to 0.87)
 - NNT = 3.5 (95% CI = 2 to 14)

Ford AC et al. Gut, 2008;58:367-378

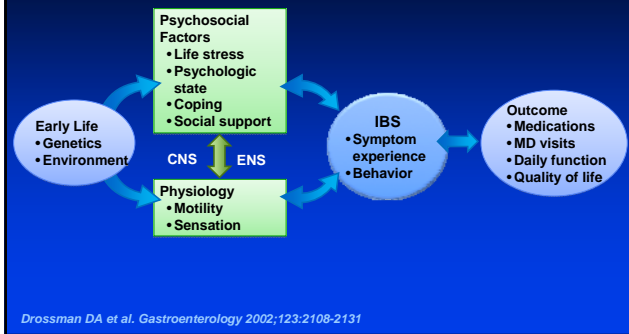
Tricyclic Antidepressant Treatment: Receptor Action Sites, Dose and Patient Indications

TCA	Dose (mg/d)	Anticholinergic effect	5-HT reuptake	Antihistamine effect	Patient Indications
Desipramine	10-150	+	+++	+	Most empiric evidence for efficacy. Less sedation and constipation
Nortriptyline	10-150	++	+	++	Least sedating
Amitriptyline	10-150	++++	+++	++++	Very sedating
Doxepin	10-150	++	+++	++++	Very sedating

SSRI Treatment: Receptor Action Sites, Dose and Patient Indications

SSRI	Dose (mg/d)	Anticholinergic effect	5-HT reuptake	Antihistamine effect	Patient Indications
Citalopram	10-20	nil	++++	nil	Less side effects and drug interactions
Escitalopram	10-20	nil	++++	nil	Less side effects and drug interactions
Fluoxetine	20	nil	++++	nil	Long $t_{1/2}$ life; less withdrawal effects
Sertraline	25-150	nil	++++	nil	Requires dose ranging
Paroxetine	20	+	++++	nil	Short $t_{1/2}$ life; more likely withdrawal effects. Greater anticholinergic effect; use in IBS-D

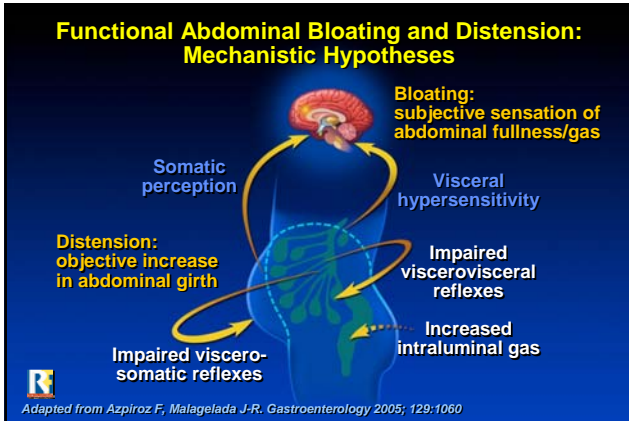
IBS Conceptual Model

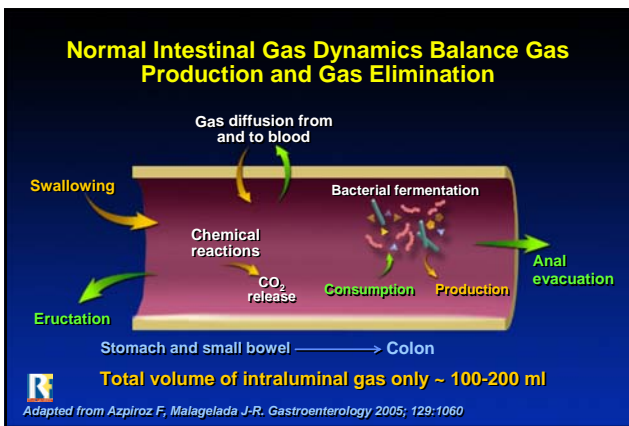


Psychosocial Therapies Are More Effective Than Usual Care at Relieving Global IBS Symptoms

Treatment Modality	Studies (n)	N		RR (95% CI)
		Patients	Controls	
Cognitive behavioral therapy (CBT)	7	279	212	0.60 (0.42-0.87)
Hypnotherapy	2	20	20	0.48 (0.26-0.87)
Multicomponent psychological therapy	4	106	105	0.69 (0.56-0.86)
Dynamic psychotherapy	2	138	135	0.60 (0.39-0.93)
Stress management	1	18	17	0.34 (0.16-0.73)

Ford AC et al. Gut. 2009;58:367-378.





Alterations in Intestinal Microflora May Occur in IBS

- Abnormal colonic fermentation in IBS, e.g., increased hydrogen production (King, 1998)
- Quantitative alterations in GI microbiota (Balsari, 1982; Si, 2004), and related to predominant bowel habit, e.g.,
 - ↓ *Lactobacillus* species in IBS - diarrhea
 - ↑ *Veillonella* species in IBS - constipation (Malinen, 2005)
- Significant differences between microbiota in IBS and in health have been confirmed using more sophisticated molecular characterization (Kassinen, 2007)
- Further studies are required in large, community-based IBS patient samples

