CASE STUDY: SEVERE INFLAMMATORY BOWEL DISEASE

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Topics of Review:

- Previous Admission
- Clinical Course: Case Study Admission
- Inflammatory Bowel Disease Overview
- Nutrition Care Process:
 - MNT for hospital admission
 - FMHx
 - PMH
 - Social Hx
 - Dietary Hx
- Discussion Topics:
 - Isotretinoin (Accutane®)
 - Low FODMAP Diet

Medical Presentation: Case Study Adm

- M.A.: 28 year old male
- Presented to Emergency Department at Thornton Hospital with severe ulcerative colitis (UC) flare
 - recurrent bloody stools (4-5BM/day), severe abd pain, bloating
- Clostridium difficile (C. diff) positive (likely from previous adm)
- Admitted January 3, 2013 through April 2, 2013
- Length of Hospital Stay: 89 days

Previous Adm: Dec 13-21, 2013

- Presentation: UC flare
 - severe bloody stools (12-15BM/day)
 - abdominal pain
 - bloating
 - Additional Dx: Cronh's Disease (CD)
- Treatment
 - Prednisone taper
 - Glucosteroid- monitor blood glucose
 - Remicade
 - Tumor necrosis factor alpha (TNF-α) blocker used to treat severe, unresponsive UC
 - Discharge
 - Clinical Improvement
 - Noted rising CRP (Table 1)

Anthropometrics/Weight Loss Hx

- UBW: 155-160lb
- December Adm Weight: 156lb
 - 74" (6ft 2in.)
 - BMI 20, IBW 190lb, 82%IBW
- Case Study Adm Weight: 132lb
 - BMI 17, 69%IBW
- Lowest Weight during Case Study Adm: 102lb
 - BMI 13, 54%IBW
- Discharge Weight: 114lb
 - BMI 14.6, 60%IBW

Table 3: Weight History

Date	Weight (lbs)	Date	Weight (lbs)
12/13/12	156	3/9	105
1/3/13	132	3/10	108
1/4/	131	3/11	106
1/25	129	3/14	114
1/28	132	3/15	111
1/31	123	3/16	108
2/23	102	3/22	106
2/25	106	3/24	108
2/26	106	3/25	110
2/27	104	3/26	111
3/4	112	3/29	114

CASE STUDY ADMISSION: CLINICAL INTERVENTIONS

Initial Procedures

- C. Diff+: Surgery postponed to January 9, 2013
- Initial Surgical Intervention:
 - Laparoscopic-assisted total abdominal colectomy
 - End ileostomy
 - Mucous fistula
 - discharge mucous or gasses from the non-functioning portion of the colon and rectum
 - Laparascopic assisted splenic flexure mobilization:
 - COMPLICATIONS: stool spillage into abdomen d/t torn bowel during surgery
 - Abd irrigated, drained

Clinical Course: Numerous Complications

- 1/3 Detection of C. Diff
- 1/9 OR: Laparocopic-assisted total abdominal colectomy with end ileostomy and mucous fistula and laparascopic assisted splenic flexure mobilization: stool spillage into abdomen d/t torn bowel
- 1/16 Ileus pattern on KUB
- 1/17: IR unable to drain intraabdominal abscess
- 1/20 Blair MD: CT abdomen and pelvis: "slightly interval worsening of the multiple dilated loops of small bowel with several areas of narrowing compared to prior CT abdomen and pelvis imaging; persistent fluid collection within the right posterior pelvis and under the right rectus abdominal muscle"
- 1/25 EGD: 450cc bilious fluid detected, removed via suction
- 1/30 Febrile, bandemia
- 2/1 Continued fever (101.6F max), emesis, >5L ileostomy OP. Sigmoidocopy: mild patchy erythema and loss of vascularity throughout the terminal ileum, severe ulcerated and denuded rectal stump not consistent with diversion colitis. A larger ulcer (8mm) was also seen 25cm from the stoma
- 2/4 OR: Complete protectomy, repair of small bowel enterotomy, and abdominal abscess washout. Intubated
- 2/6: Extubated
- 2/7 Re-intubated d/t increasing respiratory effort
- 2/9 OR: Soft tissue infection 2/2 enterocutaneous fistula: exploratory laparotomy, takedown enterocutaneous fistula, small bowel section, abdominal washout
- · 2/10 OR: abdominal washout, abthera wound vac placement, intra-operative ileoscopy
- 2/11 OR: abdominal washout, end ileostomy, abthera wound vac placement
- 2/13 OR: abdominal washout, retention sutures for partial abdominal wound closure, abthera wound vac placement
- 2/15 OR: abdominal washout with abdominal closure, wound vac placement
- 2/18: Extubated, ~2L bloody stool output
- Post 2/18 complications: wound vacuum malfunction due to obstructions, high fistula output with leakage, and continued high ileostomy output/leakage

Summary of Complications

- Non-draining, intraabdominal absess \rightarrow N/V
- EGD: 450cc bilious fluid
- Fever, bandemia, emesis, high ileostomy/fistula output
- Further surgical interventions:
 - Protectomy (removal of anus)
 - numerous fistula closures
 - 5 abdominal washouts
- Post Surgeries: Sepsis \rightarrow progression to SIRS
- Further Complications:
 - wound vac malfuction d/t obstructions
 - high fistula and ileostomy output (max 6.4L) and leakage

Output Hx: Table 2

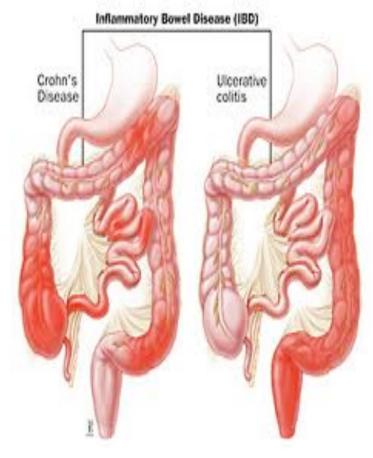
Table 2: Ileostomy, Stoma, and Measurable Output History

Date	Right Lower Quadrant	Left Lower Quadrant	Measurable	Total Output (ml)
	Ileostomy Output (ml)	Stoma/Fistula Output	Output (ml)	
		(ml)		
2/11	0	825		825
2/12	0	2025		2025
2/13	0	1085		1085
2/14	0	1025		1025
2/15	25	675		700
2/16	25	1575		1600
2/17	10	1255		1265
2/18	10	2155		2165
2/19	0	300		300
2/20	0	750		750
2/21	300	1825		2125
2/22	0	2850		2850
2/23	0	4750		4750
2/24	0	6040		6040
2/25	0	2100		2100
2/26	250	2510		2760
2/27	0	1925		1925
2/28	316	2575	100	2991
3/1	100	4500	350	4950
3/2	0	5500	500	6000
3/3	40	5900	100	6040
3/4	200	6200		6400
3/5	75	6100		6175
3/6	0	3725		3725
3/7	55	4400		4455
3/8	35	2300		2335
3/9	0	4500		4500
3/10	40	4175		4175
3/11	20	2150		2170
3/12	0	1130		1130
3/13	150	1650		1800
3/14	310	3020		3300
3/15	175	700		875
3/16	70	400		470
3/17	50	650		700
3/18	220	500		720
3/19	40	395		435
3/20	0	575		575
3/21	0	700		700
3/22	0	450		1350
3/23	5	250		255
3/24	0	95		95
3/25	0	150		150
3/26	0	355	70	405
3/27	0	460		460
3/28	0	700		700
3/28	0	1100		1100
3/30				550
	35	550		
3/31		545		580
4/1	0	300	165	765

INFLAMMATORY BOWEL DISEASES: CRONH'S DISEASE, ULCERATIVE COLITIS

Crohn's Disease vs Ulcerative Colitis

- Cronh's Disease (CD)
 - transmural inflammation of the digestive tract
 - affects any portion of GI tract from the mouth to the most distal bowel in a discontinuous fashion
- Ulcerative Colitis (UC)
 - Inflammation generally restricted to mucosa
 - contiguous disease that usually begins in the rectum and progresses up the colon at varying lengths



Pathophysiology: CD and UC

- Etiology unknown: likely involves complex interactions between the GI immunologic system, gut microflora, genetics, and environmental factors
- Both conditions: Inappropriate T-cell activation → release of inflammatory cytokines
- GI Dysbiosis:
 - Increases in Enterobacteriaceae, Bacteroidetes, Enterococci, Clostridium difficile, E. coli, Shigella flexneri, and Listeria spp
 - Decreases in Firmicutes, Eubacterium rectale, Bacteroides fragilis, B. vulgatus, Ruminococcus albus, R. callidus, R. bromii, and F. prausnitzii

Medications, FDIs, Surgical Management

- Corticosteroids
 - Monitor BG
 - Ca-Vit D suppl recommended with long term use.
- Anti-inflammatory agents (aminosalicylates)
- Immunosuppressive agents (cyclosporine, azathioprine, mercaptopurine)
 - Monitor renal & hepatic function
- Antibiotics (metronidazole)
 - Diarrhea: losses of Na/K, Zn, Mg
- Monoclonal antitumor necrosis factor (anti-TNF) (Remicade)
- CD: 50-70% will require surgery: resections of the intestine
- UC: 20% of will require a colectomy and ileostomy

Complications, Symptoms, Prognosis

- CD complications
 - abscesses, deep-ulcers, fistulas, fibrosis, submucosal thickening, localized strictures, narrowed segments of bowel, obstructions
- UC complications
 - less common
 - bleeding from deep ulcerations, bowel rupture, severe abdominal bloating
- Symptoms:
 - diarrhea, abdominal pain and bloating, fever, weight loss, anemia, food intolerances, malnutrition, and growth failure in children
 - bloody stools more common in UC
- Px
 - Mortality ratio: 1.4 to 5 times the general population
 - Increased risk of small bowel malignancy

NUTRITION CARE PROCESS

Medical Nutrition Therapy (MNT): Hospitalization

- Initial Nutrition Presentation:
 - Weight Loss Trigger: 24lb in <1month (severe weight loss)
 - BMI 17, 69%IBW
 - Low Prealbumin 8 (12/15), CRP 22.2 (12/15)
 - Low ionized Ca (1.11)
 - Low Na/Cl (130/95) \rightarrow likely related to loose stools
 - Low Cr (0.57)
- Nutrition Diagnosis:
 - Inadequate protein-energy intake r/t medical condition, suboptimal appetite prior to admit AEB 24lb weight loss, depleted prealbumin.
- Estimated Needs:
 - Mifflin: 1621 x 1.3-1.5
 - 2100-2400kcal (35-40kcal/kg), 90-120g protein (1.5-2g/kg)
 - Maintenance Fluids: 2100-2400kcal (1ml/kcal)

Diet Order History: Table 4

Date	Diet Order	Enteral Nutrition	Parenteral Nutrition
1/3/2013	Clear Liquid		
1/4	Low residue		
1/8	NPO		
1/9	Clear liquid		
1/10			TPN 40ml/hr x 24 +IL 20ml/hr x 12
1/11	Low residue		TPN 40ml/hr x 24 +IL 20ml/hr x 12
1/12	Low residue		discontinued
1/13	Low residue		TPN: Rx unknown
1/15	NPO		discontinued
1/17	Clear liquid		
1/18	low residue		
1/19	NPO		
1/20	CLEAR LIQUID		
1/21	low residue		
1/21	full liquid		
1/22	NPO		TPN 40ml/hr x 24 +IL
1,22			20ml/hr x 12
1/22	sip water/ice		TPN 40ml/hr x 24 +IL
-,			20ml/hr x 12
1/23	clear liquid		TPN 40ml/hr x 24 +IL
1/25	cical inquite		20ml/hr x 12
1/23	full liquid		TPN 40ml/hr x 24 +IL
			20ml/hr x 12
1/25	NPO		TPN 90ml/hr x 24 +IL
-,			20ml/hr x 12
1/25	clear liquid		TPN 90ml/hr x 24 +IL
-,			20ml/hr x 12
1/27	full liquid		TPN 90ml/hr x 24 +IL
-,			20ml/hr x 12
1/28	low residue		TPN 90ml/hr x 24 +IL
-,			20ml/hr x 12
1/31	NPO		TPN 90ml/hr x 24 +IL
-,			20ml/hr x 12
2/1	low residue		TPN 90ml/hr x 24 +IL
			20ml/hr x 12
2/2	NPO		TPN 90ml/hr x 24 +IL
			20ml/hr x 12
2/2	sip water/ice		TPN 90ml/hr x 24 +IL
			20ml/hr x 12
2/3	clear liquid		TPN 90ml/hr x 24 +IL
-, -			20ml/hr x 12
2/4	NPO		TPN 90ml/hr x 24 +IL
-, -			20ml/hr x 12
2/6	sip water/ice		TPN 90ml/hr x 24 +IL

		I	
			20ml/hr x 12
2/9	NPO		TPN 90ml/hr x 24 +IL
			20ml/hr x 12
2/11			TPN 90ml/hr x 24 +IL
			20ml/hr x 12
2/14	NPO	Peptamen AF 10ml/hr	TPN 90ml/hr x 24 +IL
		x 24hrs	20ml/hr x 12
2/17	NPO	Peptamen 60ml/hr	TPN 90ml/hr x 24 +IL
			240ml twice weekly
2/18	Clear liquid	Peptamen 60ml/hr	TPN 90ml/hr x 24 +IL
	-		240ml twice weekly
2/18 2/19	Peptamen 50mlhr	Peptamen 60ml/hr	not received
2/19	NPO, Clear Liquid,	Peptamen 60ml/hr	TPN 480ml total + IL
	Carb limited,		320ml total
	Peptamen AF 60ml/hr		
	x 24 hrs		
2/20	CHO limited, full	Nocturnal Peptamen	TPN 640ml total +IL
-/	liquid, nocturnal TF	60ml/hr	80ml
	peptamen 60ml/hr	,	
2/21	Regular diet + 2 cans	Nocturnal Peptamen	discontinued
-,	Peptamen Prebio TID	60ml/hr	
2/24	General		
3/7	clear liquid		
3/7 3/8	General		
3/14	NPO		
3/15	NPO		TPN 320ml total + IL
			160ml total
3/16	NPO		TPN 357ml total +IL
			200ml total
3/17	NPO		TPN 908ml total +IL
			60ml total
3/18	NPO		TPN 1387ml total + IL
			160ml total
3/19	NPO		TPN 1900ml total+ IL
-,			266ml total
3/20	NPO		TPN 100ml/hr x
-,			24hrs + IL 20ml/hr x
			12hrs
4/2	NPO		Discharge: nocturnal
-,-			cyclic TPN 2400ml +
			IL 20ml/hr x 12 hrs
			12 2011/11 A 12 113

TPN Hx

- Post initial surgery: Supplement to oral diet
 - Continuous D15%, AA5% @40ml/hr + 20%IL 20ml/hr x 12hrs via PICC
- Post proctecomy 2/9/13:
 - Intubated: Penn State Equation
 - Continuous TPN @90ml/hr + IL
 - TG increased from 61 to 282: d/c IL
 - Extubated: resumed oral diet, placed on cyclic TPN
 - POCT-BS: 45-474
 - d/c cyclic, restarted on continuous
 - Continued high fistula and ileostomy output (max 6.4L/day)
 - Made NPO, restarted on TPN @40ml/hr per MD (38% lower end needs)
 - Energy needs NOT met via TPN until 5 days after NPO
 - Weight decreased from 114lb to 106lb

Tube Feeding: Appropriate?

- Post Proctecomy
 - Trickle TF Peptamen AF via NG @ 10ml/hr → advanced to 60ml/hr, then d/c 9 days after initiation
 - Why were TF indicated now, but not after the first surgery? Need for weight gain?
 - Contraindications: Need for bowel rest, high output fistula (>1L) indicating malabsorption
 - *To confirm malabsorption: look at ileostomy output, compare to TF

Regular vs Low Residue Diet

- Advanced to Regular diet February 21
 - Indication: need for weight gain
 - Sample diet: pizza, French fries, hot dogs, cookies and ½ lb cheeseburger
 - High Fat
 - Increased output: >2L, Max 6.4L/day
 - Fat malabsorption likely d/t CD, UC, and increased gastrointestinal inflammation 2/2 to multiple surgeries and recent SIRS
 - At urgent request from family to control output, M.A. was made NPO March 14 and re-started on TPN @100ml/hr + 20ml/hr x 12 hrs
 - Discharged on cyclic (?) TPN 2400ml +IL 20ml/hr x 12 hrs nightly

Low FODMAP Diet

- FODMAP: fermentable, oligosaccharides (fructans and galactans), disaccharide (lactose), monosacchride (fructose), and polyols
- FODMAPs: poorly absorbed in the small intestine, osmotically active, and rapidly fermented by bacteria → functional symptoms secondary to luminal distention
- Breath Hydrogen Testing
 - Hydrogen>Methane = poor absorption
- Sustained reduction in symptoms of abdominal bloating and cramping in 74% of 62 patients with functional gastrointestinal disorders
- Pilot study: 10 ileostomates- frequency of pouch emptying reduced. Increasing FODMAPs was associated with a 22% effluent volume increase.

FODMAP	Excess fructose	Lactose	Oligosaccharides (fructans and/or galactans)	Polyols
Problem high FODMAP food source	Fruits: apples, pears, nashi pears, clingstone peaches, mango, sugar snap peas, watermelon, tinned fruit in natural juice	Milk: cow, goat and sheep (regular & low-fat), Ice cream Yoghurt (regular & low-fat)	Vegetables: artichokes, asparagus, beetroot, Brussels sprout, broccoli, cabbage, fennel, garlic, leeks, okra, onions, peas, shallots.	Fruits: apples, apricots, cherries, longon, lychee, nashi pears, nectarine, pears, peaches, plums, prunes, watermelon Vegetables: avocado,
	Honey Sweeteners: fructose, high	Cheeses: soft & fresh (e.g. ricotta, cottage)	Cereals: wheat & rye when eaten in large amounts (e.g. bread, pasta, couscous, crackers,	cauliflower, mushrooms, snow peas Sweeteners: sorbitol(420),
	fructose corn syrup Large total fructose dose: concentrated fruit sources; large serves of		biscuits) Legumes: chickpeas, lentils, red kidney beans, baked beans	mannitol(421), xylitol(967), maltitol (965), isomalt (953) & others ending in '-ol'
	fruit, dried fruit, fruit juice		Fruits: watermelon, custard apple, white peaches, rambutan, persimmon	
low-FODMAP food source	Fruit: banana, blueberry, carambola, durian, grapefruit, grape, honeydew melon, kiwifruit, lemon, lime, mandarin, orange, passionfruit, paw paw, raspberry, rockmelon, strawberry, tangelo.	Milk: lactose-free, rice milk Cheese: 'hard' cheeses including brie, camembert Yoghurt: lactose-free Ice cream substitutes:	Vegetables: bamboo shoots, bok choy, carrot, celery, capsicum, choko, choy sum, corn, eggplant, green beans, lettuce, chives, parsnip, pumpkin, silverbeet, spring onion (green only), tomato	Fruits: banana, blueberry, carambola, durian, grapefruit, grape, honeydew melon, kiwifruit, lemon, lime, mandarin, orange, passionfruit, paw paw, raspberry, rockmelon Sweeteners: sugar
	Honey substitutes: maple syrup, golden syrup Sweeteners: any except polyols	gelati, sorbet Butter	<i>Onion/garlic substitutes:</i> garlic-infused oil <i>Cereals:</i> gluten-free & spelt bread/cereal products	(sucrose), glucose, other artificial sweeteners not ending in 'ol'

Table 1 Food sources of FODMAPs (where FODMAPs are problematic based on standard serving size) and suitab	uitable alternatives
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Past Medical Hx, Family Medical Hx

- PMH:
 - UC Dx: 2008 (age 23). Sx of severe abd cramping/pain started after eating Carl's Junior burger.
 - ER 2010 \rightarrow remission until Thanksgiving 2012
 - Thanksgiving 2012: beginning of UC flare
 - Severe soy allergy as baby: 3 hospitalizations
 - "One in 20 million" allergy
 - No longer has allergy
- FMHx
 - Paternal Uncle: colon cancer survivor
 - Paternal first cousin: Celiac Disease
 - Mother: Diverticulosis

Social Hx

- Attended small Catholic private school K-8th grade
 - 30 classmates: 15 boys, 15 girls
 - 3 boys (including M.A.) dx with severe IBD, all required J-pouchs and semi/total colectomies
 - 10% of class with IBD vs 0.396% worldwide prevalence
- Education: BA and MA in English Literature
 - FODMAP Diet compliance associated with time availability, higher education status, and use of specific cookbooks
- Support system:
 - Married mother and father, 2 brothers
 - Tight group of friends
 - Does not attend support groups

Potential triggers of UC Flare Thanksgiving 2012

- Stress
 - Sharing room with younger brother in parents house
 - Trying to find job in struggling economy
 - Hired for office job at County: increased stress
- Dietary Intake
 - Typical Western diet
 - High fat, high animal protein, high omega 6:omega 3, low to moderate fruits and vegetables
 - Increased alcohol consumption
 - From rare EtOH intake to nightly glass of wine

Sample Diet: Table 5

Table 5: Typical Meal Items Prior to Hospitalization, Preferences and Aversions

Meal	Items (portions)
Breakfast	High fiber cereal, banana, Lactaid milk
Lunch	Turkey Sandwich (whole wheat bread, lettuce, tomatoes, pickles,
	teaspoon mayonnaise), Salad (lettuce, cherry tomatoes, olives, light
	range or light Italian dressing
Dinner	Main Dishes: Chicken breast, spaghetti with meal balls, fettuccini
	Alfredo, steak, ribs, vegetable meatball soup, clam chowder
	Side Dishes: white rice, Spanish rice
Snacks	Cheeze-its, yogurt, quesadilla (flour tortilla, mozzarella cheese),
	Hebrew National Hot dogs
Preferences	Hamburger, sausage, pastrami, deli sandwiches, pizza, donuts, ice
	cream
Aversions	nuts, seeds, vegetable and fruit skins, white enriched bread

Isotretinoin (Accutane®)

- M.A. reports undergoing "2 rounds" of Accutane for severe acne as a teenager
- Accutane:
 - Maker: Roche Pharmaceuticals
 - Vitamin A analog approved by FDA for severe nodulocystic acne in 1982
 - Pulled from the US market in 2009, citing "high costs from personal-injury lawsuits" (multi-million dollar settlements)
 - Generic forms still available

Isotretinoin (Accutane®) and IBD

- Several studies link IBD (particularly UC) to Accutane exposure
- Case-controlled analysis of claims data from 8,189 cases of IBD (4,428 UC, 3,664 cases CD)
 - Accutane exposure strongly associated with increased risk of UC (OR 4.36, 95%CI 1.97, 9.66), but not CD (Crockett)
 - Dose-responsive relationship: higher doses, dose escalation, and longer durations associated with the highest risk of UC.
- As of January 2012, there were 6,000 cases pending against Roche Pharmaceuticals

References

- Pronsky S, Zaneta P, Crowe J. Food Medication Interactions. 16th ed. Birchrunville: Food-Medication Interactions, 2010. Print.
- Kumar, Abbas, et al. Robbins Basic Pathology. 8th ed. New York: Elsevier, 2007. 123-127. Print.
- Inflammatory Bowel Disease. Centers for Disease Control and Prevention. 1 May 2012. Web. Accessed 15 Mar 2013. <u>http://www.cdc.gov/ibd/</u>
- Mahan, Kathleen, Escott-Stump S. Krause's Food & Nutrition Therapy. 12th. St. Louis : Elsevier, 2008. P 707-742.
- Gottschlich, MM. The ASPEN Nutrition Support Core Curriculum: A Case-Based Approach—The Adult Patient. American Society for Parenteral and Enteral Nutrition. 2009. P 508-540.
- Thoreson R, Cullen JJ. Pathophysiology of inflammatory bowel disease: an overview. Surg Clin North Am. 2007;87(3):575-85.
- Prakash S, Rodes L, Coussa-charley M, Tomaro-duchesneau C. Gut microbiota: next frontier in understanding human health and development of biotherapeutics. Biologics. 2011;5:71-86.
- Seibold F. Food-induced immune responses as origin of bowel disease? Digestion. 2005;71(4):251-60.
- Peppercorn MA, Odze RD. Colorectal cancer surveillance in inflammatory bowel disease. Up-To-Date. 4 Oct 2012. Web. Available at: <u>http://www.uptodate.com/contents/colorectal-cancer-surveillance-in-inflammatory-bowel-disease#H2</u>. Accessed March 2, 2013.
- Rowe WA. Inflammatory Bowel Disease. Medscape. 13 Sep 2012. Web. Accessed 22 Mar 2013. Available at: <u>http://emedicine.medscape.com/article/179037-overview#aw2aab6b2b5</u>
- Gibson PR, Shepherd SJ. Evidence-based dietary management of functional gastrointestinal symptoms: The FODMAP approach. J Gastroenterol Hepatol. 2010;25(2):252-8.
- Shepherd SJ, Gibson PR. Fructose malabsorption and symptoms of irritable bowel syndrome: guidelines for effective dietary management. J Am Diet Assoc. 2006;106(10):1631-9.
- Reddy D, Siegel CA, Sands BE, Kane S. Possible association between isotretinoin and inflammatory bowel disease. Am J Gastroenterol. 2006;101(7):1569-73.
- Crockett SD, Porter CQ, Martin CF, Sandler RS, Kappelman MD. Isotretinoin use and the risk of inflammatory bowel disease: a case-control study. Am J Gastroenterol. 2010;105(9):1986-93.
- Accutane Lawsuit: Recall Class Action Lawyer. Resource4thePeople. 6 Mar 2013. Web. Accessed 6 Mar 2013. Available at: http://www.resource4thepeople.com/defectivedrugs/accutane.html