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Management of Irritable Bowel Syndrome in Primary Care

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This is to certify that I have examined this
Masters of Nursing Scholarly Project
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Abstract

Irritable Bowel Syndrome (IBS) is one of the most common diagnoses made in primary care accounting for approximately12% of all visits; further estimates report upwards of 20% of American have IBS. Patients present initially with abdominal pain and alteration in bowel movements that are dominant in constipation, diarrhea, or alternating between the two. These symptoms cause changes in health-related quality of life. Although several theories exist the cause of IBS is unknown; therefore, there is no cure, only management of symptoms. Currently, symptom management based on IBS subtype with multiple pharmacologic agents is the norm. Although antispasmodics have been reported as effective, the choice of pharmacotherapy remains largely subjective based on patient response and ultimately the provider patient relationship influences the choices offered. Probiotics (live bacteria) are an emerging therapy option with no serious adverse reactions. Their ability to improve quality of life for the patient by way of reducing symptoms of abdominal pain and bloating, passing of flatus, and incomplete evacuation/straining is significant. Bifidobacterium infantis has the potential to significantly reduce IBS related healthcare costs and provide a resource for the primary care provider other than sending the patient to Gastroenterology for evaluation. Probiotic use in primary care is a safe option for treatment of IBS.

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Introduction to Irritable Bowel Syndrome

The American College of Gastroenterology Task Force, 2009, has estimated that 7-10% of the population in the United States (US) has Irritable Bowel Syndrome (IBS) making it more common than asthma or diabetes. Further estimates report upwards of 20% leaving one in five Americans with this disorder (Wald and Rakel, 2008). Approximately 5-7% of individuals with IBS are aware of their diagnosis while the remainder of the population remains undiagnosed yet symptomatic (Hungin, Whorwell, Tack, & Mearin, 2003). IBS is a compilation of altered bowel habits over a period of time and includes abdominal pain and discomfort. The effects of IBS are widespread. It is known that IBS is one of the most common diagnoses made in primary care accounting for approximately12% of all visits. In addition, a survey conducted by Russo, Gaynes, and Drossman (1999) found IBS to be the most common functional GI diagnosis comprising 35% of all outpatient referrals to gastroenterologists. This makes IBS the most common diagnosis for gastroenterologists as well. This trend continues with IBS accounting for 20%-50% of visits to gastroenterologists (Wald & Rakel, 2008). The current shortage of gastroenterologists has led to the need to diagnose and manage IBS in the primary care setting.

IBS sufferers present initially to primary care with abdominal pain and alteration in bowel movements that are dominant in: constipation (IBS-C), diarrhea (IBS-D) or mixed (IBS-M). They report straining, urgency or sensation of incomplete evacuation. These symptoms result in missed school and work days, decreased productivity, and missed social interactions. There is altered food intake, diminished desire to eat and changes related to food choices. IBS patients undergo more abdominal surgeries than the general population including: appendectomies, cholecystectomies, and hysterectomies. They also confront challenges from the

syndrome's complications resulting in a decreased health-related quality of life comparable to other major diseases including diabetes and kidney disease (El-Serag, Olden, & Bjorkman, 2002). Therefore, the most troublesome complication of IBS is the impact on health-related quality of life for those suffering with this diagnosis. Although IBS does not cause mortality in its sufferers its impact on quality of life has been linked to suicidal behaviors (Spiegel, Schoenfeld, and Naliboff, 2007).

Even after a diagnosis is made management of the disease and its resulting alterations in quality of life remain troublesome for patients and providers. There are many treatment options to consider. The majority of these remain focused on symptom management; however, further options include the use of antidepressants, antibiotics and emerging evidence on the efficacy of probiotic use on digestive microflora restoration.

Definition

Bockus, Bank, and Wilkinson (1928) were the first to describe IBS by defining its pathogenesis with the term neurogenic mucous colitis. Since its discovery IBS has been referred to by many different names including nervous colitis, spastic colon, spastic bowel and functional bowel disease (American Gastroenterology Association, 2010). Colitis however, is an inflammation of the colon which is not evident in IBS. It is clearly documented that IBS does not cause permanent damage to the intestines and does not lead to other serious organic diseases.

Diagnosing IBS is complicated as it is considered a syndrome rather than a definitive organic disease with a specific course and medical management. Sufferers exhibit chronic/recurrent motility disorders of the small and large intestines without organic pathology or anatomical abnormalities. Historically, IBS becomes the diagnosis when all other more severe diseases have been ruled out. It is associated with severe discomfort and presents with

abdominal pain and distention in association with alterations in defecation. Individuals with IBS have increased intestinal sensitivity which may exacerbate symptoms. Heredity, psychosocial factors, nutrition, and inflammation or infection have been proposed to contribute to IBS (Drossman, 2006).The American College of Gastroenterology Task Force (2009) has proposed that the best way to define IBS is by defining what it is not. IBS is not an anatomical or structural problem, an identifiable physical or chemical disorder, a malignancy, nor will it cause cancer, a precursor of other gastrointestinal diseases, and something you have to" just live with". Conversely a definition of what IBS constitutes is based on Rome Criteria. The Rome Foundation, beginning in 1989, is an international effort via a nonprofit organization that meets in Rome to establish evidenced-based data criteria for the diagnosis and management of functional gastrointestinal disorders including IBS. IBS includes a recurrence of abdominal pain or an uncomfortable sensation in the abdomen. To be classified as IBS, the abdominal discomfort will have a defined onset of at least six months and duration of at least 3 months. It is associated with at least two of the following symptoms: improvement of abdominal discomfort with defecation, and a change in the frequency or form of stool.

Epidemiology

As a chronic disease the effects of IBS can span the lifetime. Approximately 50% of people with IBS report symptoms beginning before they were 35 years-old, and many date the symptoms back to childhood. Although IBS is prevalent among young adults under 50 years-old (American College of Gastroenterology Task Force, 2009) it is not seen as a primary diagnosis after age 50. IBS occurs 1.5 times more frequently in women than men (American College of Gastroenterology Task Force, 2009).It remains unclear if this s a true prevalence or if men simply seek medical care less often than women. IBS occurs more frequently in lower

socioeconomic groups and it has a graded decrease in prevalence with increasing income (Andrews et al., 2005). While American and European cultures demonstrate similar frequency of IBS across racial and ethnic lines, discrepancies in prevalence are seen in non-western countries in south Asia and the Middle East. This is possibly related to the tools utilized having a lack of cultural adaptation (Khoshkrood-Mansoori et al., 2009).

Regardless of ethnic background in the US, IBS patients have a higher utilization of physician visits, diagnostic tests, and medications (Everhart & Renault, 1991). Costs for IBS reach over $20 billion in both direct and indirect costs (American Gastroenterology Association, 2001). Patients with IBS have more missed worked days and lower work productivity than their healthy counterparts. These issues are expected to remain prevalent in the United States in future years. Current healthcare reform, potentially giving access to the underinsured and uninsured, will add further burden. Hence, diagnosis of IBS, management of its symptoms, and consequences of its complications will require an increasing amount of financial and healthcare resources. In an effort to reduce healthcare consumption research regarding IBS is focused on the effects of probiotics, dietary intake and stress management.

Pathophysiology

Probiotics, dietary intake and stress management are able to directly affect the large intestine based on the anatomy and physiology of the colon. The colon is approximately six feet long and two inches in diameter. It connects the small intestine with the anus. The colon wall consists of four layers: serosa, muscularis, submucosa and mucosa. Haustra occur through periodic uncoordinated tonic contractions which bunch up the mucosa and propel stool. The submucosa is made up of loose connective tissue and contains veins, arteries, lymphatic vessels,

nerve fibers and ganglion cells. The inner mucosa layer is a smooth absorptive surface lined with columnar epithelial cells and goblet cells.

The composition of the colon wall assists in the function of the colon which includes: storage, movement of contents, absorption of water, electrolytes and bile acids and a minor role in the excretion of mucus, potassium, and bicarbonate. Colon movement is controlled by nerves, hormones and electrical activity in the colon muscles. Stimulation of the parasympathetic nerves increases intestinal contraction and mucus secretion and inhibits the rectal sphincter. Stimulation of the sympathetic nerves inhibits colonic motility and secretions while stimulating the rectal sphincter.

While the exact cause of alteration in transit is unclear it is known to be classified as irritable due to consistent underlying abnormalities in motility and visceral sensitivity. Theories exist to identify the role in the development of IBS. These theories include: a) CNS influenced altered bowel motility affecting both secratory and immune functions; b) visceral hypersensitivity related to the autonomic nervous system; c) psychosocial factors; d) neurotransmitter imbalance affecting the sympathetic and parasympathetic pathways as well as their communication with the CNS; and e) post-infection and inflammation resulting in alteration in the microflora of the colon and immune hypersensitivity. None of the theories explains all of the symptoms of IBS.

IBS symptoms are subtyped into IBS-C, IBS-D or IBS-M. Research has been mainly focused on the motility of the gastrointestinal tract. Altered contractility of the longitudinal or circular muscles appears to be related to exaggerated patterns of intestinal motility, causing either diarrhea or constipation based on which muscles type spasms with the most force. IBS is thus classified as diarrhea- fast-colonic transits, constipation- slow colonic transit, or mixed

classifications. There is a wide range of normal findings, from daily bowel movements to only a couple a week, with no definitive colonic transit time is the set normal. Several factors are associated with altered motility including; physical or psychological stress, dietary intake of lactose or high fat meals or fasting. The study of large and small intestine transit time has been and remains subjective.

Objectively, physiologic stimuli in the gut elicit reflex responses to perform digestive function. The gastrocolonic reflex normally occurs 30-45 minutes after a medium sized meal. Normally this occurs unnoticed, but in IBS pain, discomfort and altered bowel function exist related to perception in the gastrointestinal (GI) tract. Patients feel pain disproportionately due to changes with afferent signals from the dorsal horn neurons through the ascending pathways suggesting a central pain processing defect. Pain is a major component of IBS. Researchers have used balloon inflation in the colon via computerized barostat and been able to detect increases in cerebral cortical activity (Truong, Naliboff, & Chang, 2008) Further studies have found that IBS patients are able to detect the inflating balloon at much lower levels of inflation than those without IBS. This increase is noted with rapid rather than gradual distention. Subjectively, IBS patients have also reported that they have more gas-like sensations; however, when this has been studied, IBS patients have the same amount as non-IBS controls (Hernando-Harder et al., 2010).

Further subjective findings are related to psychosocial factors. Increased sympathetic nervous system activity and decreased parasympathetic nervous activity have been noted in people with IBS. This supports that the autonomic nervous system can modulate visceral sensitivity and the central nervous system can influence the motility and secratory activity of the GI tract by way of autonomic pathways via the enteric nervous system (Bockus et al., 1928). Through the three divisions of the autonomic nervous system the sympathetic, parasympathetic,

and enteric systems, GI motility, secretion and immune function are adjusted and coordinated (Hansen, 2003). Although the production of secretions is scant in the colon it is important to remember that the alkaline mucus lubricates the intestinal walls promoting stool passage and protects the mucosa from acidic bacteria. Adaption of the autonomic nervous system, including increased sympathetic nervous system action and decreased parasympathetic nervous system action is an important part of the body's response to stress. Increased stress results in GI function producing IBS symptoms.

Neurotransmitter imbalance may also contribute to IBS symptoms. Serotonin is a key neurotransmitter influencing bowel contractility and visceral hypersensitivity. Serotonin may provide a link between the enteric and central nervous systems. It has been postulated that people with IBS process CNS input differently than those without IBS.

CNS stimulation in the form of psychopathological disorders such as hypervigilence regarding bowel function, stress, anxiety, somatization, panic disorders or depression may also contribute to alterations in CNS processing. Patients with psychological disturbances have been documented to have more debilitating illnesses and are often referred to as hypochondriacs. Pychopathological disorders may also be linked to environmental factors to the extent that children learn behaviors modeled by their parents (Drossman, 2006). Motility disturbances have been found to correspond to an increase in hypothalamic corticotropin-releasing factor (CRF) production in response to the stress response. The connection between IBS exacerbations and psychosocial occurrences remains poorly understood (Longstreth et al., 2006). Interestingly, Axis I disorders coexists with GI symptoms in up to three quarters of patients. Therefore, a shift in the treatment of IBS to include treatment of psychopathological disorders has proven effective for some people. Heitkemper, Cain, Burr, Jun, and Jarrett (2010) propose a link between

childhood neglect and sexual abuse and IBS, an important factor to consider. Although research suggests psychological disturbances may exacerbate GI distress; they do not definitively cause IBS.

IBS commonly follows an episode of infectious gastroenteritis. In a retrospective study by Chaudhary and Truelove (1962) a significant portion of the study participants whom reported onset of IBS symptoms following an episode of gastroenteritis. Thabane, Kottachchi, and Marshall (2007) conducted a systematic review and meta analysis and found to be a six-fold increase in the development IBS after gastroenteritis. Additionally, the risk for development of IBS remained elevated for 2-3 years after the infectious process has ended. This is related to persistent sub-clinical inflammation which injures the enteric nervous system causing alterations in small intestinal permeability and gut flora. An example is traveler's diarrhea and then resulting IBS-D. The injury can lead to chronic mucosal inflammation which culminates in dysmotility. Hence, a pathogen causing gastroenteritis is able to disrupt intestinal flora altering the barrier function it provides by increasing permeability, and causes neuromuscular dysfunction with alterations in motility while eliciting chronic inflammation (Thabane & Marshall, 2009). Alterations of the gut flora during and after an infectious process are thought to be synergistic to the inflammation altering the enteric nervous system and alterations in intestinal permeability. Current research focuses on how probiotics can assist in promoting intestinal health and preventing or diminishing the effects caused by gastroenteritis. The phenomena of post-infectious IBS exist; however, biopsies from IBS patients do not show alteration in mucosa. This leaves this hypothesis unlikely and in need of more research. Furthermore, these patients appear to have spontaneous albeit gradual resolution of their IBS symptoms verses the chronic symptoms of other IBS sufferers.

A final IBS theory is that recurrent exposure to otherwise benign substances may produce an autoimmune inflammation response which is thought to lead to an alteration in motility. In their study based on IgG food sensitivity Atkinson, Sheldon, Shaath, and Whorwell (2004) found that elimination of the offending food produced a clinical decrease in reported symptoms. O'Mahony et al., (2005) compared the response of symptoms and cytokine ratios in IBS patients after probiotic dosing and reported interleukin-10 and interleukin-12, a monitoring tool for an anti-inflammatory state, was initially elevated and was found to normalize to a pro-inflammatory state after intake of the probiotic. The alteration of colonic flora and the connection between the mind and the body has shown to be increasingly significant in the pathogenesis of IBS and important in the determination of diagnosis and treatment of the syndrome.

Presentation

Diagnosis and treatment are based on the presentation of IBS. Supportive symptoms that relate to the diagnosis of IBS include: stool frequency, abnormal stool formation, and stool consistency as determined by the Bristol Stool Form Scale (Lewis & Heaton, 1997). The Bristol Stool Form Scale is presented in Figure 1 located in Appendix B. This is an important tool in providing continuity in stool consistency definitions, as what a patient reports as diarrhea or constipation may not be classified as such according to the scale. There may also be a feeling of incomplete evacuation, passage of mucus, and bloating.

The presence of abdominal pain is also required for IBS diagnosis. Pain is somehow related to defecation and can be described as crampy/sharp, burning, diffuse/radiating, continuous achy, or sharp exacerbation. The location varies by patient, but remains consistent for the individual. Most people present with sigmoid discomfort and suprapubic pain with radiation towards the rectum. Some refer to "labor-like pains" and less commonly, pain that radiates

toward their legs. Some will refer to a belt-like pain radiating from the left lower quadrant to the midline. Timing of the pain is unpredictable aside from a correlation with increased stress. Although post prandial fullness is common, it is usually relieved with defecation. It is common for people to report no pain at night while asleep and then an increase in pain while awake.

Although the pain follows predictable patterns relating to sleep/wake cycles it raises concern for the sufferer. People with IBS appear to be hyper vigilant about their stool consistency and frequency with an emphasis on a fear of anatomic abnormalities like colon cancer. Normal defecation ranges from three bowel movements a day to three a week. Criteria for the diagnosis of IBS are abdominal pain or discomfort coupled with altered bowel function over a period of at least three months.

The Rome III Criteria, reported by Chang (2006) and Drossman (2006), is the most current method for IBS identification. The Rome III effort encompassed 14 committees made up of 87 participants. The committees were divided into issues of gender, society, patient, social issues, pharmacology and pharmacokinetics with all committee work culminating in the final meeting in Rome. Rome III criteria include: a) frequency for threshold of symptoms; b) duration of symptoms; and c) refining the subtyping of IBS.

Once diagnosed, Rome III Criteria also classifies IBS into a predominant subtype based on presenting symptoms (Table 1) and the frequency of the alteration of stool pattern. Stools may be compressed and pencil-like due to rectosigmoid spasm. An IBS-C person may have scybala a dehydrated pellet-like stool. Often IBS-D is considered when soft stool is passed with gas. Fecal incontinence, an extreme of IBS-D, occurs in 20% of patients. It is associated with reflex relaxations associated with repetitive spastic distal colonic contractions. An IBS-M patient would describe a presentation which alternates between IBS-C and IBS-D.

Table 1

Predominant Stool Pattern Subtyping of Irritable Bowel Syndrome

Subtype	Pattern Definition
IBS with constipation (IBS-C)	Hard or pellet stools ≥25% and loose or watery stools <25% of bowel movements.
IBS with diarrhea (IBS-D)	Loose or watery stools ≥25% and hard or pellet stools <25% of bowel movements.
Mixed IBS (IBS-M)	Hard or pellet stools ≥25% and loose or watery stools ≥25% of stools.

Note: Based on Rome Foundation Definition (2010)

A further classification, important in the clinical setting, is that of severity which includes more than just symptoms. Lembo, Ameen, and Drossman (2005, p. 717), due to lack of IBS severity consensus, proposed "components of IBS severity include symptom intensity, time of assessment, whether the patient or physician (provider) makes the severity determination, the type of scale used to measure severity, and the degree of disability or impairment". Lembo et al. further hypothesized that severity can be divided into "components including health-related quality of life, psychosocial factors, healthcare utilization behaviors, and burden of illness" (p.717). Although it is subjective to the population studied an indicator that IBS severity may be

greater than previously acknowledged is the finding that the prevalence of severe or very severe IBS range from 3%-69% (Lembo et al., 2005).

Bloating, belching and abdominal distention are common associated complaints and happen regardless of meal consumption. It has been shown that people with IBS do not have more gas than people without IBS they just have intolerance. Jiang, Locke III, Choung, Zinsmeister, Schleck, and Talley (2008), while researching risk factors for abdominal bloating and visible distention found that bloating was a subjective sensation and distention is objective; however, these two phenomena have similar risk factors including an increase during times of stress. Furthermore, Jiang et al. found that 19% of the population experience bloating and about half of those with bloating who also experience distention were predominantly from the IBS-C group. Bloating is referred to as hepatic flexure syndrome and splenic flexure syndrome as these are the highest areas of the colon when upright and the passage of flatus relieves this discomfort. Bloating and distention have both been found to arise from an alteration in microflora. Related complaints include heartburn, indigestion, epigastric pain and nausea.

Corsetti, Caenepeel, Fischler, Janseens, and Tack (2004) reported that 13-87% of patients with either the diagnosis of IBS or functional dyspepsia (FD) fulfill the criteria of the alternate diagnosis. There may be a distinct subgroup with the diagnosis of both IBS and FD (Wang et al., 2008). Currently, 13%-87% of people with either FD or IBS are able to fulfill the criteria for the alternate diagnosis (Corsetti et al., 2004). Other extra-intestinal symptoms include increased urination frequency, dyspareunia and decreased libido. Symptoms are often exacerbated during the premenstrual period. Fibromyalgia is the only current co-morbidity (Longstreth et al., 2006).

Symptoms of IBS are seen in several disease processes and many patients are diagnosed with IBS only after suffering with symptoms for several months to years. On physical

examination most people will appear to be normal, although often somewhat anxious, and may have a palpable sigmoid cord or tenderness in the abdomen. Therefore an elusive presentation can make for a challenging diagnosis.

Diagnosis

IBS should not be a diagnosis of exclusion and yet it often is. There is no "Gold Standard" test to identify the etiology of and manage IBS. Rome III Criteria of functional gastrointestinal disorders is used as a guide for the diagnosis of IBS (Drossman, 2006). Use of the Rome Criteria for diagnosing IBS by non-gastroenterologists including surgical specialists has been poor (Charapata & Mertz, 2006). Changes in education have been made and functional gastrointestinal disorders are now addressed in undergraduate and postgraduate training as well as in clinical settings (Drossman, 2006). In an effort to have more non-gastroenterologists feel confident diagnosing IBS there is increasing international recognition and educational offerings related to IBS (Drossman, 2006).

Although training and recognition are growing; tests are still utilized to rule-out other diseases as IBS cannot be diagnosed by physical, radiologic, or endoscopic examination, or by laboratory tests (Bellini et al., 2005) Unnecessary, expensive and invasive diagnostic tests are often performed. These tests may include blood draws, colonoscopies, and imaging such as CT's of the abdomen and pelvis. Longstreth and Yao (2004) found IBS patients were three times more likely to undergo unnecessary abdominal surgeries. The American College of Gastroenterology Task Force (2009) recommend diagnostics for patients presenting with IBS symptoms (Refer to Table 2 and Figure 2 located in Appendix C) including: a) Complete blood count (CBC) with differential to screen for anemia, inflammation, and infection; b) Blood chemistry (CHEM-10) to evaluate for metabolic disorders and to rule out dehydration/electrolyte abnormalities in patients

with diarrhea; c) Liver Function Test; d) erythrocyte sedimentation rate to check for inflammation; e) Thyroid Function studies; f) stool for ova and parasites; and g) Serologic Celiac Sprue testing. Imaging recommendations include screening colonoscopy in those which are symptomatic or over 50yo/ 45yo for African Americans. Hemoccult stool testing or fecal immunochemical testing (FIT) can be performed to rule out occult blood in those who do not meet criteria for or refuse colonoscopy. Most importantly however is to focus on a thorough history. This will identify timing and circumstances related to the visit in addition to stool characteristics. In contrast a sudden change from an established pattern would require further testing and consideration of other problems.

The current Rome III Criteria are helpful, yet practitioners report concern regarding differential diagnoses. Symptoms indicative of an alternate diagnosis include red flags such as pain or diarrhea that wakes the patient from sleep, blood in the stool, weight loss, family history of cancer, fever, or abnormal findings on the physical examination (Torii & Toda, 2004). Diagnosis of IBS is dependent on meeting the Rome III Criteria and excluding differential diagnoses.

Table 2

Invasive verses Non-invasive Tests

Non-Invasive Tests	Invasive Tests
Stool for Ova and Parasites	CBC with differential
Stool for Clostridium Difficile toxin	CHEM- 10
Hemoccult Stool	Liver Function Test
FIT Testing	Erythrocyte Sedimentation Rate

Abdominal Imaging- Small Bowel Barium Follow through or computed tomography of the abdomen or pelvis	Thyroid Function Studies
Gallbladder Ultrasonography	Serum Calcium (hyperparathyroidism)
Hydrogen Breathe Test	Serologic Celiac Sprue
Breath Testing- Screen for lactose/fructose intolerance	Esophogastroduonenoscopy
	Small bowel biopsies for celiac disease
	Flexible Sigmoidoscopy
	Colonoscopy
	Double Contrast Barium Enema
	Abdominal Surgery

Current Pharmacologic Options

Once differential diagnoses are ruled-out the provider is left with the presenting symptoms which are mainly subjective. There is no standardization of care for IBS only treatment of the symptoms. Some drugs have evidence of working on more than one symptom. In many instances the effect of the drug is also subjective therefore evidence can be found to support the use of several drug classes.

Antibiotic.

A controversial drug class is that of antibiotic. Although antibiotics are the culprit of a change of colonic microflora as in the Clostridium Difficile infectious process, research regarding the use of antibiotics and probiotics in the treatment of IBS has grown exponentially. Rifaximim, which is a non-absorbed, broad-spectrum, antibiotic specific for enteric pathogens, is often reported as able to improve symptoms of bloating, diarrhea, abdominal pain, and constipation. The cause of this benefit remains unclear but is attributed to the suppression of gas producing bacteria in the colon.

Bulking Agents.

Where antibiotics are thought to suppress gas production bulking agents are known for increasing gas pains and cramping sensations. In terms of IBS-D bulking agents like Psyllium, Methylcellulose or Polycarbophil

may be used (these can also be effective in IBS-C). If severe enough an antidiarrheal like Loperamide may be of assistance.

Antidepressants.

Antidepressant drugs are found to be beneficial in patients with neuropathic pain and have a side effect of slowing colonic transit time therefore Tricyclic antidepressants – amitrityline and nortriptyline, Selective Serotonin Reuptake Inhibitors (SSRI) including but not limited to Fluoxitine, Paroxitine, and Citalopram, and Selective Norepinephrine Reuptake Inhibitors (SNRI) including Duloxetine are proposed to assist in IBS-D and abdominal pain.

Laxatives.

The pain associated with IBS-C may be helped with Osmotic laxatives including: Lactulose, Milk of Magnesia, or Polyethelene Glycol, or Stimulant laxatives such as Cascara

Segrada or Senna. Tegaserod, a 5-hydroxytryptamine (serotonin) 4 receptor agonist (5-HT4), which stimulated the release of neurotransmitters causing an increase in colonic motility was removed from the market in March, 2007 related to cardiovascular side effects. However, it was reintroduced with restricted use for IBS-C only in 2007 and is being marketed for women < 55 years-old. It was followed with another prokinetic, Lubiprostone, which is approved for use in women > 18 years-old. Lubiprostone is a chloride channel activator that increases chloride ions in the gut causing an increase in sodium and water in the gut to maintain balance.

Antispasmodic Agents.

An opposite effect of laxatives is created with antispasmotics. IBS with abdominal pain (gas, bloating) is historically treated most often with Antispasmodic agents such as Hycosamine, or Dicyclomine; of which hycosamine is also known to decrease fecal urgency with associated pain. Its method of action is the blockade of acetylcholine at parasympathetic sites in smooth muscle, secreatory glands, and CNS eliciting an antispasmodic and antidiarrheal effect. Additionally 5-hydroxytryptamine (serotonin) 3 receptor antagonists (5-HT3) such as Alosertron predominantly or Ondansetron have been utilized due to their ability to affect visceral afferent activity in the gastrointestinal tract via the enteric nervous system. There method of action is to block 5-HT3 receptors, which if stimulated cause hypersensitivity and hyperactivity of the colon. These medications have been used after failure on other pharmacological regimes as they are only approved for severe cases of IBS-D, also of note this medication is not approved for usage in men.

Probiotic Management

Probiotics is emerging as a promising treatment option for management of IBS symptoms. Probiotic usage historically has been proven beneficial in the treatment of Inflammatory Bowel Disease including Crohn's Disease and pouchitis. Probiotics work on the digestive microflora which are the plants that can be seen microscopically and inhabit the colon to maintain an ecological balance and prevent overgrowth of any one plant type. Probiotics or "good bacteria" contain live microorganisms which are utilized by the human body to restore the balance of microflora in the digestive tract (Encarta Online Dictionary, 2010).

Probiotics work in the colon. The colon is sterile at birth and is colonized by swallowed bacteria within one week from birth. There are typically 10^{9}-10^{10} organisms per gram of stool. A mixture of bacteria is necessary in the colon as it breaks down cellulose and waste material, deconjugates bile salts, synthesizes vitamin K, and controls the overgrowth of any one bacterium. Conversely, bacteria are known to manufacture gas, produce toxins which can cause colitis or diarrhea, and make ammonia. The mechanisms of action for probiotics according to Sartor (2004) include: inhibiting pathogenic enteric bacteria, and improving epithelial and mucosal barrier function. Pathogenic enteric bacteria are inhibited through probiotics decreasing the luminal pH, causing the secretion of bactericidal proteins, eliciting colonization resistance, and the blockage of epithelial binding resulting in the inhibition of epithelial invasion. Epithelial and mucosal barrier functions are improved by probiotics through the production of short chain fatty acids, enhanced mucus production and increased barrier integrity. Probiotics are also used to reduce intestinal permeability and are being researched regarding their ability to reduce pro-inflammatory cytokines.

Normal gut flora may be altered in a variety of ways including: illness, stress, antibiotic treatment, physiologic alterations of the gastrointestinal system, or changes in diet. Quigley and Flourie (2007) propose that probiotics are also able to assist the immune response and reduce cytokine production, which could possibly hinder an autoimmune response. American College of Gastroenterology Task Force (2009) has taken the stance that "there is evidence suggestive that some probiotics may be effective in reducing overall IBS symptoms but more data are needed" (p. S1).

A basis for the data being gathered is that the microflora is known to be important for intestinal function and changes in GI microflora have been found in people with IBS (Malinen et al., 2005 and Kassinen et al., 2007). Shanahan (2007) proposes that it is an uncertainty if the changes seen in microflora of IBS patients are its cause or effect. The theory of infectious gastroenteritis precipitating IBS supports the idea of changes in microflora are a precipitating event.

Although there are a variety of theories of the initiation of IBS symptoms the most common complaint by persons affected is that of abdominal pain and bloating. The majority of treatments to date have focused on diarrhea and constipation symptoms leaving abdominal pain often untreated. The use of probiotics has flourished in an effort to control pain and bloating symptoms. Prior to the use of probiotics people with predominant abdominal pain were encouraged to eliminate gas producing foods, given anticholinergic anti-spasmodic drugs, or were given a tricyclic antidepressant (nortriptyline) to delay intestinal transit time and blunt visceral sensation.

The use of probiotics is not a new avenue of research as complementary and alternative medicine has embraced the role of intestinal microbes for years. Sartor (2004) after studying

probiotics clinically in relation to Inflammatory Bowel Disease, found that probiotics (live microbial supplements), prebiotics (dietary supplements that promote the growth of beneficial bacteria) and symbiotics (a combination of probiotics and probiotics) are able to restore beneficial Lactobacillus (L.) and Bifidobacterium (B.) to the colon. Further studies have found Lactobacillus not as effective (O'Mahony et al., 2005). Bifidobacterium is the most promising along with VSL#3 (VSL Pharmaceuticals, Fort Lauderdale, FL) which was developed based on findings that people with IBS have decreased Coliforms, Lactobacilli, and Bifidobacteria (Balsari, Ceccerelli, Dubini, Fesce, & Poli, 1982) . VSL#3 contains 450 billion viable lyophilized bacteria, including Bifidobacterium (B. longum, B. infantis, and B. breve) Lactobacillus (L.acidophilus, L. casei, L. delbrueckii subspecies bulgarius, and L. plantarum), and Streptococcus salvarius subspecies thermophilus (Wald & Rakel, 2008).

Several trials regarding the efficacy of probiotics are available for review; however, five of the most cited trials will be reviewed here (Table 3 located in Appendix A). They are from Ireland, (O'Mahony et al., 2005) Finland, (Kajander et al., 2008) United States of America, (Kim et al., 2003) United Kingdom, (Whorwell et al., 2006), and France (Guyonnet et al., 2007). Although studies consisted of men and women, the majority of the study participants were women, with one study that was women exclusively (Whorwell et al., 2006). All of the studies included only participants that met the Rome II Criteria for IBS. They also all further stratified the IBS participants in terms of IBS-C, IBS-D or IBS-M. The trials varied in terms of the type, strength, dose and number of probiotics utilized.

O'Mahoney et al (2005) conducted a small 80 subject randomized double blind study. After inclusion criteria 67 subjects completed the study. The study looked at the response of symptoms and cytokine ratios in IBS patients after they received therapy of either L. salvarius

UCC4331 or a B. infantis 35624. Of the participants, 64% were women and 36% were men. All were recruited via advertising from Gastroenterology clinics. For 8 weeks each group received $1x10^{10}$ colony-forming units (cfu) bacterial cells in a malted milk drink, or a plain malted milk drink with placebo. Using Likert scales and Visual analog scales (VAS) scores were recorded daily regarding abdominal pain/discomfort, bloating/distension, and bowel movement difficulty for the 8 weeks of the trial and the 4 weeks following. A quality of life assessment tool, microbiologic stool studies, and blood sampling to determine the release of the cytokine interleukin-10 and interleukin-12 were done at the beginning and end of the treatment portion of the study. This global assessment of symptoms found improvement in all areas except bowel movement difficulty for the participant's receiving B. infantis 35624. At baseline interleukin-10 and interleukin-12 a monitoring tool for an anti-inflammatory state was elevated and was found to normalize to a pro-inflammatory state after intake of B. infantis 35624. Four subjects reported adverse reactions as follows: one had a one-time epistaxsis which spontaneously resolved, one had chest pain attributed to anxiety, one was hospitalized with unstable angina, and one was hospitalized for IBS-C exacerbation. There were no clinically significant changes found in any of the subjects during the study length in terms of serum blood count, chemistry or immunoglobulin levels. The small size of this study and the short duration limited the ability to generalize results; however, the researchers were able to show superiority of B. infantis 35624 in the reduction of the cardinal IBS symptoms. It was hypothesized that the probiotic may have immune-modulating effects. The study results established that there may be an inflammatory component to IBS. Furthermore, since there was no change in stool patterns this probiotic may be utilized in all subtypes of IBS.

A study by Kajander, et al., (2008) looked at 86 participants with 93% of them being women were recruited from primary care by a certified endoscopist. The participants ages ranged from 20-65. This was a randomized double blind placebo-controlled, parallel-group 5-month study where participants received an 80% lactose free, milk-based drink of either placebo or a multispecies probiotic supplement which included: L. rhamnosus GG, L. rhamnosus Lc705, Propionibacterium freudenreichii ssp., shermanii JS and B. animalis ssp. Lactis Bb12. The total cfu in each probiotic drink was $1x10^{7}$. All participants were allowed to continue on their current IBS medications; however they were not allowed to take any other probiotics or eat foods with probiotics in them. Analysis was based on a quality of life diary, a Likert scale measuring intensity of symptoms, (abdominal pain, distension, flatulence, and rumbling) bowel habits, and fecal and blood samples including C-reactive protein and cytokines. There were 43 subjects in each group. Ten in the probiotic group and 15 in the placebo group reported adverse reactions the majority of which were gastrointestinal or respiratory symptoms (probiotic 62% and placebo 65%). Further findings in the probiotic group were an eye operation, carotid artery atherosclerosis, an inflamed mole, cystitis and tenosynovitis. All but four of the placebo gastrointestinal complaints were found to have no association with the study. Confidence intervals of 95% were used. The Likert symptom score showed a 37% reduction of symptoms in the probiotic group compared to a 9% reduction in the placebo group. In terms of bowel habits a lessening of distension (P=0.023) and abdominal pain (P=0.052) was found in the probiotic group. No change was found in the form of bowel movements in either group. The quality of life data addressed bowel symptoms, fatigue, activity limitations, and emotional function. The probiotic group had a median 0.62 point (95% CI: 0.37-0.86) beneficial effect on the bowel symptoms domain. Also, a stabilization of intestinal microbiota was found when a high

similarity index between two points in time was noted. The probiotic group rose and the placebo group decreased. The difference between the groups (-4.8; 95%CI: -6.59 to -2.54) was significant (P= 0.0015). In terms of the inflammatory markers no significant changes were noted in either group. As with the O'Mahony et al. (2005) study beneficial effects of probiotic supplementation included a stabilization of intestinal microbiota. Conversely, there is no change in inflammatory markers found in this study which is a limitation symptom severity. There is an increase in quality of life. Although this study found probiotics to be a safe alternative for the management of IBS symptoms and stabilization of microbiota it is again a small study and relatively short duration of time.

Kim, et al., (2003) used a parallel group, double-blind, placebo controlled randomized study of 48 participants with 94% of them being female between 18-75 years-old. They were recruited through both primary and secondary care center. Inclusion criteria were IBS-D and bloating symptoms. A total of 25 participants were then randomized with N=13 receiving placebo and N=12 receiving VSL#3 in a powder form for this ten week study. No other IBS medications were permitted. Participants recorded relief of symptoms and used the Bristol stool scale to monitor stools. Ease of passage was recorded on a Likert scale. There were no adverse reactions with VSL#3. Five participants took antibiotics during the study for other ailments. This study found that VSL#3 had no effect on colonic transit time; however, it was able to decrease bloating symptoms. Abdominal bloating was reduced (P1/4 0.046) in the VSL#3 group 13.7 with a CI 95%, 2.5-24.9, but not in the placebo group (P ¼ 0.54) with a 1.7 CI 95%, 7.1-10.4. Limitations of this study include the small sample size and lack of ability to generalize the results, but it statistically has shown a reduction in IBS bloating symptoms.

A comparatively large-scale, multi-center, randomized, double-blind, placebo-controlled, dose ranging study was conducted by (Whorwell, et al., 2006). This study had 362 participants ranging in age from 18-65 years-old. Participants were recruited from 20 primary care sites. Participants were randomized to receive one of four capsule treatments: B. infantis 35624 at either $1x10^{6}$ or $1x10^{8}$ or $1x10^{10}$ cfu concentration or placebo. The capsule was taken once daily for four weeks. They were then followed for two weeks after the study. Daily symptoms were recorded using voice prompting over the telephone. Rescue medication of bisacodyl 5mg for constipation and loperamide 2 mg for diarrhea were allowed and tracked. No significant treatment effect was found. At the end of each week a global assessment of symptom management was recorded. Participants completed an IBS specific quality of life questionnaire and the Hospital Anxiety and Depression Scale. Analysis of these showed no changes during the 4 week study. Seventeen participants withdrew from the study related to adverse events and there was no difference in the amount of adverse events between the placebo and medicated groups. Probiotics were not found to change stool form or frequency which render them useful to all subtypes of IBS. In particular the dose of B. infantis 35624 $1x10^{8}$ was found to provide the most benefit for a variety of symptoms including pain, bloating, gas, and had increased bowel habit satisfaction. The $1x10^{10}$ capsule showed results similar to placebo and at no time was placebo ever more effective than probiotic at any dose. These results are significant because they showed improvement in more than one area and typical IBS pharmaco-management is achieved with one drug for one symptom. In addition, positive results were obtained in the primary care setting. As with similar studies quality control of the probiotic is in question as no standards exist. The effect waned after discontinuation leaving the length of the study a further limitation.

Another multicenter study was conducted by Guyonnet, et al., (2007). It encompassed the primary care setting consisting of 35 centers. The study was a randomized, double-blind, controlled trial with 274 IBS-C participants followed over a six week period. The participants ranged from 18-65 years-old with 199 of the participants being women. No other probiotics or prebiotics were allowed during the study. The test product was B. animalis DN-173 010 (Activia) with 1.25×10^{10} cfu per container of yogurt together with the two classical yogurt starters S. thermophilus and L. bulgaricus (1.2×10^{9} cfu/container. The control was a heat treated yogurt which contained non-living bacteria. Both products were prepared by Danone Research Palaiseau, France. Participants completed a health-related quality of life questionnaire specific to IBS symptoms prior to the study and at three and six weeks. Symptoms of bloating, abdominal pain, and stool characteristics were evaluated using a Likert scale. There was improvement in bloating, abdominal pain, and global digestive symptoms ($P< 0.05$) at six weeks in the test group but not the control group. Bloating and abdominal pain improved ($P=0.03$) higher at week three in the test group. Further symptom improvement did not change between the groups. Over the six week period the participants who had <3 BM/week had an increase in stool frequency ($P<0.001$) up to a mean of six BM/week with results starting at week one. Ten subjects were in the control group, and 13 in the test group. A total of seven subjects withdrew reporting minor adverse events. The use of probiotic food was found to be statistically significant, in terms of the health-related quality of life. Health-related quality of life scores were relatively unchanged in other studies. The study also demonstrated the ability to increase the amount of stool per week in IBS-C patients. Limitations include a high placebo response rate which has been reported from 40-45% and is related to the subjective questions involved in the data collection, and the study was conducted by the manufacturer of Activia.

These and other studies show probiotics exhibit promise in effectively reducing global IBS symptoms. Unfortunately probiotics are not FDA approved because they are not a drug. Due to this they are not covered under insurance and do not have the quality control of medications. Of note Proctor & Gamble Company has provided the manufacturing conditions for B. infantis in studies. It is known that Lactobacilli does not appear to be effective, while B. infantis 35624 and some combinations do exhibit efficacy in symptom management. The lack of stool alteration, aside from the B. animalis combination used by Guyonnet (2007), renders probiotics efficious in all subtypes of IBS. Furthermore, the ability of probiotics to effect more than one symptom of IBS is superior to the one symptom one drug approach of typical pharmacotherapy. Probiotic foods have the potential to relieve multiple symptoms and improve quality of life as do those in pill/capsule/powder form. The American College of Gastroenterology Task Force (2009) has given probiotics a weak recommendation relating to the low quality of the evidence. Studies remain ongoing and no single species, strain, or preparation has been identified as the drug of choice. The confusion surrounding the efficacy of probiotics is further fueled by the varied duration of treatments and different follow-up regimes. Probiotics are all considered safe with no adverse reactions, making the choice one of desired outcomes and patient preference.

Probiotics are a viable option for IBS sufferers, based on their desired outcomes, whether they have failed on pharmacologic management or not. Although they have been embraced by the Alternative Medicine community for years they are gaining recognition in the arena of evidenced-based medicine. Attention should be given to the support and empowerment of the patient regarding probiotic usage through the provision of education and counseling.

Education and Counseling

Education and counseling emphasis should be based on relief of IBS symptoms and an increase in health-related quality of life. Although a menu of phamacotherapeutic options exists for the treatment of IBS; patients typically do not experience relief of abdominal bloating, gas and pain. They should be informed of the various options for treatment including: bulking agents, 5-HT4 agonists, osmotic laxatives, stimulant laxatives, prostone, antidiarrheals, 5-HT3 antagonist, antibiotic, antispasmodic, tricyclic antidepressant, SSRI, SNRI and probiotics. Providers should explain the benefits and side effects of all drugs and explain that research is ongoing regarding the use of probiotics. Probiotics, as with medications, requires that dose and timing be titrated based on individual experience.

Education on use of medications

There is no standard of care in terms of the phamacotherapy of IBS; treatment is based on symptom management and highly individualized. A review of typical medications has been conducted in this paper with a more extensive review of research focusing on the use of probiotics. Most importantly there are no serious adverse reactions with the use of probiotics and studies suggest that Bifidobacterium infantis 35624 provides improvement of symptoms in IBS. Due to the lack of prolonged studies regarding probiotics the use, dose and after effect of these agents remains largely anecdotal. Furthermore, probiotics are not considered a medication and do not fall into a federally regulated classification. Considering the plethora of information accessible on the internet; patients should be counseled on which strain of probiotic would be most useful prior to purchasing them over the counter. Currently, Align is a gastroenterologist recommended, patented, daily dietary supplement. It is sold over the counter and is a capsule that is taken once daily. It contains Bifidobacterium infantis 35624. It is not FDA approved for the

treatment of IBS at this time, but is the most accessible for providers wanting to recommend treatment with probiotics. Align can be found at retail and drug stores. The cost of Align varies, with an approximate cost of $30 for 28 capsules. Probiotics are an option, along with the variety of pharmacotherapeutic options, which the primary care provider can safely recommend.

Counseling

There is no known prevention of IBS and to date there remains only management of symptoms with adjunctive therapies include cognitive, behavioral or diet modalities. IBS is a chronic condition with periods of exacerbation often associated with periods of stress. Although it does not have significant morbidity or mortality it can be disabling. Its affects are felt physically, psychologically, socially and economically. Reassurance of absence of organic pathology and that it will not alter their life expectancy is essential for the patient.

The acceptance of reassurance is achieved through the provider-patient relationship. This relationship is paramount in the treatment of IBS. Time constraints, such as those imposed by managed care regulations, on visit length make the establishment of a trusting relationship difficult (Wald & Rakel, 2008). Frequent follow-up visits in the primary care setting where a working partnership is established allows the patient to share openly without fear of judgment and allows time for teaching during the office visit.

Van Tilberg et al. (2008) posit that although patients continue with the traditional western medicine approach approximately one-third of IBS patients are seeking alternative medicine. Current research on all forms of Complementary Alternative Medicine (CAM) is promising. A detriment to CAM use is the published placebo response rates. In their meta-analysis of placebo response in CAM trials of irritable bowel syndrome Dorn et al. (2007) postulate that due to the response rate being similar to that of conventional medicine trials it is not enhanced in CAM.

CAM is typically an out of pocket expense for the patient leaving those in the lower socioeconomic classes less access. Providers are often not recommending these treatments; however, they become part of the treatment plan through the patient's use of them and should be documented accordingly. The majority of CAM is focused on stress reduction or cortical influences and includes having a hobby, exercising, meditation, biofeedback, cognitive behavior therapy, acupuncture and chiropractor (Wald, 2003). Cognitive behavior therapy is based on the idea that the mind can be taught to control functions of the body and research is documenting its positive effect (Wald & Rakel, 2008). There are also herbal remedies including studies on the use of peppermint. Although the research in these areas is growing and the results are positive they remain subjective in nature.

Subjective assistance can also be found through dietary counseling and includes educating the patient regarding fiber and fluid consumption. Increasing the amount of fiber in the diet is helpful for some patients while it precipitates increased bloating and distension in others. The recommended dietary intake of fiber is 25 grams; however, fiber supplements can also be utilized. (Polycarbophil compounds like Citrsucel and FiberCon may produce less flatulence than psyllium compounds like Metamucil). Drinking an adequate amount of water daily, 64 ounces, will assist in preventing constipation, and the avoidance of caffeine will decrease dehydration and feelings of anxiety.

Literature has mixed results regarding dietary modifications beyond fiber and fluid consumption recommendations. The continuum ranges from the elimination diet to no change is useful. Atkinson, Sheldon, Shaath, and Whorwell (2004), found clinical symptom improvement in subjects that eliminated foods they were found to have IgG sensitivity to. Patients report relief from simple modifications such as reporting a reduction in bloating and distention after avoiding

gas-producing foods like beans, onions, broccoli and cabbage, as well as eliminating foods that are high in fat. An avoidance of the sugar substitute sorbitol which has known side effects of bloating and diarrhea is effective (Longstreth et al., 2006). Lactose intolerance is seen in 40% of people with IBS. Often these people have no symptoms of intolerance until after age 30. These people should avoid lactose to lessen gas and bloating. Dietary adaptations should be made slowly allowing the body time to adjust. Further recommendations include slowing the rate at which one consumes food (Longstreth et al., 2006) which will avoid overeating and avoiding gum or carbonated beverages to lessen the swallowing of air. Food diaries may be helpful in determining causative agents. Whether the patient changes their diet or uses other adjuncts including probiotics the focus should remain on increasing comfort and providing for optimal health-related quality of life.

Implications for Practice

IBS changes in health-related quality of life account for a significant amount of primary care and gastroenterology visits. The diagnosis and treatment of IBS is costly yet ongoing research into this syndrome and its management is promising. The cause of IBS is unknown; therefore, there is no cure, only management of symptoms. Recognition of the mind body connection is helpful for providers. The impact of discomfort and distress on the patient may wax and wane over the years and at times may be disabling. Some estimates include that it is second to the common cold for work/school days missed. As previously stated, it is known that not all people who fit the Rome Criteria for diagnosis seek medical attention, and women are more likely to seek care than men.

Several algorithms based on the Rome Criteria exist to assist the provider in determining the diagnosis of IBS. Initially patients present with an alteration in bowel habits and associated

abdominal pain. The first step is to determine if they meet the Rome criteria, otherwise it is merely a matter of appropriate symptom evaluation and management. If they do meet the Rome criteria the next step is to determine if they have any of the red flag warning signs including: rectal bleeding, anemia, weight loss, fever, family history of colon cancer, onset of first symptoms after 50 years-old, or a major change in symptoms. If they have positive warning signs further evaluation is needed to find the cause. This ongoing evaluation may include a colonoscopy or other symptom specific diagnostic testing. If all of this testing is negative a final diagnosis of IBS may be confirmed. Conversely, if there no warning signs a hemoccult stool sample or FIT test and serologic celiac sprue testing should be the next step. If either of these is positive a full evaluation should be completed recognizing that a diagnosis of IBS may still result. If, however, these are both negative no further evaluation is needed and the diagnosis of IBS is confirmed as seen in Figure 2 in Appendix C.

Obtaining a diagnosis of IBS is challenging even with the guidance of algorithms, yet treatment of this syndrome is even more challenging. Currently, symptom management based on IBS subtype sometimes with multiple agents is the norm. Although antispasmodics have been reported as effective, the choice of pharmacotherapy remains largely subjective based on patient response and ultimately the provider patient relationship influences the choices offered. Probiotics are an emerging therapy option with no serious adverse reactions. Probiotics should not be used in immune-compromised patients as they have not been studied in this group. Probiotics ability to improve quality of life for the patient by way of reducing abdominal pain and bloating, passing of flatus, and incomplete evacuation/straining symptoms is significant. Clearly more and larger clinical trials are necessary for the widespread acceptance of probiotics in the scientific community; however, existing research is providing the evidenced-based

groundwork for their acceptance. Further complications in probiotic dosing are that no single species, strain, preparation has been identified as the probiotic of choice and the varied duration of treatment and follow-up have contributed to the confusion of their efficacy.

Probiotics are an enigma in many ways, but based on studied patient responses they work and they do not harm or worsen the condition of the patient. The cost of treatment of IBS in the US excluding indirect expenses such as lost productivity, lost wages, over the counter medications, and co-payments reaches into the billions. Probiotics, in particular Bifidobacterium infantis, appear to be more than an added expense in the treatment of IBS. By providing an increase in the patient's health-related quality of life they have the potential to significantly reduce IBS related healthcare costs and provide a treatment resource for the primary care. Furthermore, the patient has an established relationship with their primary care provider and through therapeutic listening and communication the patient can have their symptoms validated, diagnosed and managed in the primary care setting. Ultimately more research is needed towards the standardized use of probiotics and the management of the IBS patient in primary care.

Recommended Internet Resources

Numerous websites are available to provide information on IBS and its management. The American Gastroenterology Association has a link on their homepage that takes one to IBS specific information (American Gastroenterology Association, 2009) for patients. This site includes information regarding the basics of IBS, symptoms, diagnosing, treatment, living with IBS and the relationship between diet, stress and IBS. There is also an option to order brochures and DVD's for your patients at the end of the information.

The American College Of Gastroenterology website (American College of Gastroenterology Task Force, 2008) is similar to the American Gastroenterology Association site

with a strong commitment to providing accurate unbiased and up-to-date health information. It is an organization with a membership of over 10,000 individuals from 80 countries. This site proposes a commitment to serving the clinically oriented digestive disease specialist with an emphasis on scholarly practice, teaching and research. It is organized by disease and is developed by the American College of Gastroenterology physicians.

The World Gastroenterology Organization is a federation of over 109 societies and has a useful website for practitioners as well (World Gastroenterology Organization, 2009). It provides a global perspective regarding IBS. There are monthly research reviews and success stories from over 40 countries. The IBS guidelines link is easily referenced and includes clinical cascades for treatment at every resource level. Furthermore, they have a test practitioners can utilize to diagnose IBS and a list of patient frequently asked questions. A similar international site focusing on education and research is the International Foundation for Functional Gastrointestinal Disorders (International Foundation for Functional Gastrointestinal Disorders, 2011). It is an excellent site to refer people diagnosed with IBS due to the Irritable Bowel Syndrome Self Help And Support Group (2011). It comprises information, blogs, and offers of support through self help or in a group.

Finally, The National Institute for Diabetes, Digestive and Kidney Disorders is a federal health agency that offers a booklet on IBS as well as other resources for patients on digestive health topics (National Digestive Diseases Information Clearinghouse, 2007). Also, they sponsor a telephone hotline 301-654-3810 through the National Digestive Disease Information Clearinghouse.

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Appendix A

Table 3

Comparison of Probiotic Trials

	Trial				
Reference	Design	Numbers	Interventions	Treatment	Outcomes
O'Mahoney (2005)	Irish RCT, DB, NC single center study	N=80 64% female, C26%, D28%, M 45%	Lactobacillus salivarius 1X10 UCC4331 vs Bifidobacterium infantis 35624 1X10 vs placebo for 8 weeks.	No other IBS treatment allowed	B. infantis 35624 able to reduce cardinal IBS symptoms. Decrease in inflammatory marker establishing possible inflammatory component.
Kajander (2008)	Finnish RCT, DB single center study	N=86 93% female, C 30%, D 45%, M 25%	Lactobacillus rhamnosus GG, Lactobacillus rhamnosus LC705, Propionibacterium freudenreichii ssp. Shermanii JS DSM 7067, Bifidobacterium animalis ssp. Lactis Bb12 DSM 15954 vs placebo for 20 weeks	IBS meds permitted	Beneficial effect on bowel symptoms. Stabilization of microbiota. No change in inflammatory markers.
Kim (2005)	US RCT,	N=25 94%female,	VSL #3 vs placebo for 4-8	No other IBS meds permitted	VSL#3 had no effect on

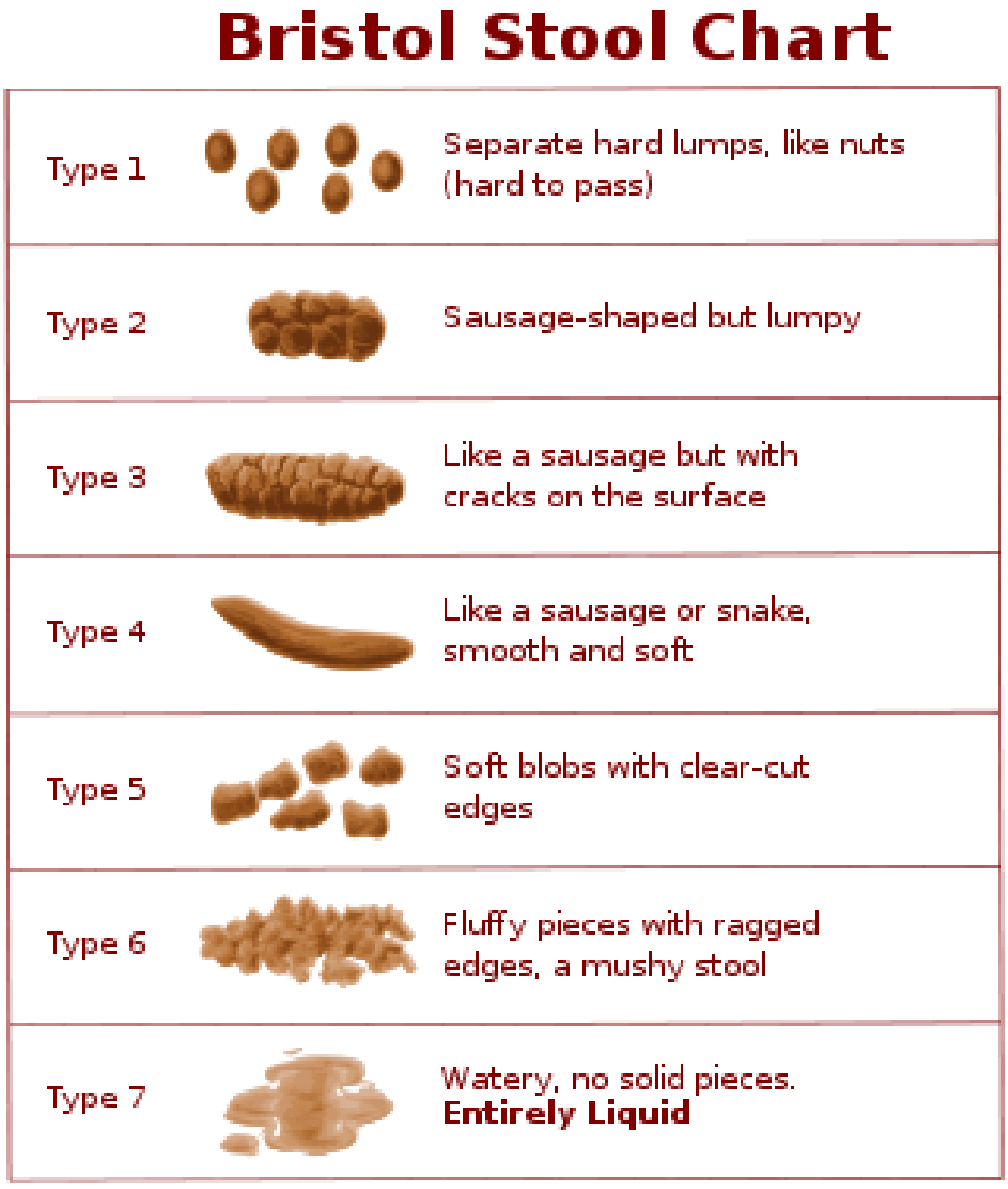
	DB single center study	C 33%, D 42%, M 25%. All had to have bloating score >24 on a 100mm VAS.	weeks.	apart from antidepressants.	colonic transit time Satisfactory relief of IBS symptoms (bloating) for 50% of weeks
Whorwell (2006)	UK RCT, DB 20 centers	N=362 100% female, C20.7%, D 55.5%, M 23.8%	Varied Bifidobacterium infantis 35642 vs placebo for 4 weeks.	Loperamide for diarrhea and bisacodyl for constipation permitted.	The dose of B. infantis 35624 $1x10^{8}$ was found to provide the most benefit for a variety of symptoms including pain, bloating, gas, and had increased bowel habit satisfaction.
Guyonnet (2007)	France RCT, DB, 35 centers	N=274 65%female. C 100%	Bifidobacterium animalis DN-173 010 with S. thermophilus and L. bulgaricus (1.2 x 10^{9} cfu/container for 6 weeks.	Prebiotics and other probiotic were stopped	Increase in reported quality of life measures, bloating and abdominal pain improved and increase in the amount of BM/wk in IBS-C with <3BM/wk.

N= number of participants; C= constipation predominant; D= diarrhea predominant; M= mixed pattern; RCT= randomized control trial; DB= double blind; NC= no concealment; VAS= visual analog scale; BM= Bowel Movement.

Appendix B

Figure 1

Bristol Stool Chart



(Lewis & Heaton, 1997)

Appendix C

Figure 2

Irritable Bowel Syndrome Diagnosis Algorithm