Gut Instincts: The Science and Treatment of the Irritable Bowel Syndrome

A Panel Discussion by
Jean Harvey-Berino, PhD
Peter L. Moses, MD
Gary M. Mawe, PhD
10 NUTRITION DO’S AND DON’TS FOR GI HEALTH

JEAN HARVEY-BERINO, PHD, RD
HIGH FAT FOODS
MILK PRODUCTS
High-octane beverages: Caffeine is the new ingredient of choice for beverage companies. How high-energy drinks compare with coffee:

- **Coffee**: 128 mg
- **Propel Invigorating Water**: 20 mg
- **Coke**: 23 mg
- **Diet Pepsi**: 24 mg
- **Coke Blak**: 46 mg
- **Diet Pepsi Max**: 46 mg
- **SoBe Essential Energy**: 48 mg
- **Energy drinks**: 50 to 145 mg
ARTIFICIAL SWEETENERS

sugar alcohols

Not a sugar...
Not an alcohol...

So - What are they?
CABBAGE, BEANS, ETC...
AVOID LARGE MEALS
EAT MEALS LOWER IN FAT AND HIGHER IN CARBOHYDRATE
DIETARY FIBER?

**HIGH-FIBER SUPER STARS**

1 medium baked potato with skin 5 grams

1 pear 4 grams

1 cup lentil soup 14 grams

1/2 cup FIBER ONE® Cereal 13 grams

1 cup strawberries 4 grams

1 medium orange 3 grams

3 cups popcorn 4 grams

1 serving Brown Rice & Vegetable Stuffed Squash (page 90) 11 grams

1/4 cup oatmeal 3 grams
PROBIOTICS?

400+ Species Of Probiotics In Your Body
FODMAP DIET?
FERMENTABLE OLIGOSACCHARIDES, DISACCHARIDES, MONOSACCHARIDES, AND POLYOLS

<table>
<thead>
<tr>
<th>FODMAP</th>
<th>Richest Food Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fructo-oligosaccharides</td>
<td>Wheat, rye, onions, garlic artichokes</td>
</tr>
<tr>
<td>Galacto-oligosaccharides</td>
<td>Legumes</td>
</tr>
<tr>
<td>Lactose</td>
<td>Milk</td>
</tr>
<tr>
<td>Fructose</td>
<td>Honey, apples, pears, watermelon, mango</td>
</tr>
<tr>
<td>Sorbitol</td>
<td>Apples, pears, stone fruits, sugar-free mints/gums</td>
</tr>
<tr>
<td>Mannitol</td>
<td>Mushrooms, cauliflower, sugar-free mints/gums</td>
</tr>
</tbody>
</table>
Process of Elimination

To determine if certain foods are triggering symptoms of irritable bowel syndrome, some specialists recommend a low-Fodmaps diet, which stands for Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols. After six to eight weeks, the foods are gradually reintroduced at low levels to see what patients can tolerate.

### SOME FOODS CONTAINING FODMAPS TO ELIMINATE:

**FRUIT**
- Apples
- Apricots
- Cherries
- Pears
- Watermelon
- Dried Fruit

**VEGETABLES**
- Asparagus
- Broccoli
- Cabbage
- Eggplant
- Garlic
- Mushrooms
- Onions

**CEREALS / GRAINS**
- Wheat, rye in large quantities
- Pasta
- Bread
- Cookies

**Milk Products**
- Cow's milk
- Custard
- Ice cream
- Yogurt
- Soft cheeses

**Other**
- Sweeteners: sorbitol, mannitol, isomalt
- Fructose, corn syrup, honey

**Beans / Legumes**
- Chick peas
- Kidney beans
- Lentils
- Soy beans

### SOME SUITABLE FOODS ON A LOW-FODMAP DIET:

**FRUIT**
- Bananas
- Blueberries
- Grapefruit
- Lemons
- Raspberries

**VEGETABLES**
- Carrots
- Celery
- Green beans
- Potatoes
- Pumpkin
- Zucchini

**Grains**
- Gluten-free bread or cereal
- Rice
- Oats
- Polenta
- Tapioca

**Milk Products**
- Lactose-free milk and yogurt
- Hard cheeses

**Other**
- Tofu
- Sugar
- Maple syrup
- Molasses

Source: Shepherd Works and the IBS Self Help and Support Group Photos: Getty Images (Soy beans); iStockphoto (Apples, Lemons); F. Martin Ramin for The Wall Street Journal (5)
LOW FODMAPS GROCERY LIST

Always recheck ingredients. Manufacturers modify on an ongoing basis to ensure ingredients are FODMAPs-friendly.

GRAINS
- Oats
- Oat bran
- Quinoa
- Rice: Brown and White
- Rice bran
- Gluten free pasta: rice, quinoa, and corn

BRAND NAME CEREALS
- Ancient Harvest Quinoa Flakes
- Bob's Red Mill Mighty Tasty Hot Cereal
- Cheerios
- Eden Organics Brown Rice Flakes Hot Cereal
- Erewhon Gluten Free Corn Flakes
- Erewhon Gluten Free Crispy Brown Rice
- Environdz Kidz Tortilla Munch
- Environdz Kidz Peanut Butter Panda Puffs
- Gluten Sensitive Beginnings Cereal

BREADS
- Udi's White Sandwich Bread
- Food for Life Brown Rice tortillas
- Food for Life Multi Seed English muffins
- Food for Life Organic Sprouted Whole Kernel Flourless corn tortillas

FLOURS AND BAKING MIXES
- King Arthur Multi-Purpose flour
- Namaste Perfect Flour Blend
- Namaste Foods Waffle and Pancake mix
- Barqui Gluten-Free Pancake and Baking Mix
- Namaste Foods Brownie Mix
- Namaste Foods Blonde Mix
- Namaste Foods Muffin Mix

PROTEIN
- Beef
- Chicken
- Fish
- Egg
- Tofu

NUTS (allow one handful per sitting)
- Almonds
- Macadamias
- Peanuts
- Pecans
- Pine nuts
- Pumpkin seeds
- Sesame seeds
- Sunflower seeds
- Walnuts

NUT BUTTER
- Smucker's Peanut Butter
- Skippy Peanut Butter
- Teddie Peanut Butter
- 365 Everyday Value Almond Butter (Whole Foods)

DAIRY
- Cheddar
- Swiss
- Parmesan
- Brie
- Feta
- Camembert
- Mozzarella

MILK
- Lactose free
- Almond milk
- Coconut milk
- Rice milk
- Yogurt/Kefir
- Green Valley yogurt
- Lifeway kefir (strawberry or blueberry)

FRUIT (limit to one serving per meal)
- Avocado (limit to ¼)
- Banana (small)
- Blueberries
- Cantaloupe
- Grapefruit
- Grapes
- Honeydew melon
- Kiwi fruit
- Lemon
- Lime
- Orange
- Passion fruit
- Pineapple
- Rhubarb
- Strawberries
- Tangerine
- dried fruit: raisins, blueberries or other acceptable fruit. (limit to 1 TB)
- Orange juice or grapefruit juice (limit to 1/3 cup)

PRODUCE

VEGETABLES
- Alfalfa Sprouts
- Bamboo shoots
- Bean sprouts
- Beets (limit to 4 slices)
- Bok choy
- Bell Peppers: red, yellow, orange
- Broccoli (limit ½ cup)
- Brussels sprouts (limit ½ cup)
- Butternut squash (limit to ½ cup)
- Bok Choy
- Carrots
- Corn (half a cob)
- Celery (limit to 1 stick)
- Chives
- Cucumber
- Eggplant
- Endive
- Ginger
- Green beans
- Lettuce
- Olives
- Parsnip
- Peas (limit to 1/3 cup)
- Potato, white
- Scallions (green part only)
- Spinach
- Summer squash
- Sweet potato (limit to 1/4 cup)
- Tumips
- Tomato
- Water chestnuts
- Zucchini

SNACKS + SWEETS

Rice Cakes
- Blue Diamond Almond Nut Thins
- Lundberg Rice Chips (sea salt)
- Schar Cheese bits
- Mary's Gone Crackers (original)
- Real Food corn thins
- Kettle Brand Potato Chips (sea salt)
- Tortilla Chips
- Gluten Free Pretzels
- Almond chocolate chip biscotti
- Aleia’s almond horn cookies
- Aleia’s peanut butter cookies
- Gilbert’s Super Dooper Snickerdoodles
- Gilbert’s Sensational Sugar cookies
- Sarabeth’s Cranberry Relish
- Sarabeth’s Strawberry Rhubarb Spreadable Fruit

Compiled by © Kate Scarlata, RD.
Gut Instincts:
Food Facts and Fiction in IBS
Community Medical School
Fall 2012

Peter L. Moses, MD
Professor
UVM College of Medicine
What Gastroenterologists Do

• We treat gastrointestinal and digestive disorders.
  – GI Cancers
  – Bleeding
  – Liver Disease
  – Inflammatory Bowel Disease
  – Functional GI Disorders

• We fix things with minimally invasive techniques

• We screen healthy individuals for common cancers.
“As many as 20 percent of the adult population, or one in five Americans, have symptoms of IBS, making it one of the most common disorders diagnosed by doctors. It occurs more often in women than in men, and it begins before the age of 35 in about 50 percent of people”.

NIDDK
NIH Publication No. 07–693
September 2007

“Approximately 20 to 40 percent of all visits to gastroenterologists are due to IBS symptoms”.

A. Lembo, MD
# Prevalence of IBS

Percentage of population reporting symptoms of IBS in various studies from various geographic areas

<table>
<thead>
<tr>
<th>Country</th>
<th>Prevalence</th>
<th>Author/Year</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>6%</td>
<td>Boivin, 2001</td>
<td>Study measured prevalence of GI abdominal pain/cramping</td>
</tr>
<tr>
<td>Japan</td>
<td>10%</td>
<td>Quigley, 2006</td>
<td></td>
</tr>
<tr>
<td>United Kingdom</td>
<td>8.2% 10.5%</td>
<td>Ehlin, 2003 Wilson, 2004</td>
<td>Prevalence increased substantially 1970-2004</td>
</tr>
<tr>
<td>United States</td>
<td>14.1%</td>
<td>Hungin, 2005</td>
<td>Most undiagnosed</td>
</tr>
<tr>
<td>United States</td>
<td>15%</td>
<td>Boivin, 2001</td>
<td>Much more common in 16-30 age range. Of IBS patients, 56% male, 44% female</td>
</tr>
<tr>
<td>Pakistan</td>
<td>14%</td>
<td>Jafri, 2007</td>
<td>College students</td>
</tr>
<tr>
<td>Pakistan</td>
<td>34%</td>
<td>Jafri, 2005</td>
<td>n=324. Also measured functional diarrhea and functional vomiting. High rates attributed to &quot;stress of living in a populated city.&quot;</td>
</tr>
<tr>
<td>Mexico City</td>
<td>35%</td>
<td>Schmulson, 2006</td>
<td>Study measured prevalence of GI abdominal pain/cramping</td>
</tr>
<tr>
<td>Brazil</td>
<td>43%</td>
<td>Quigley, 2006</td>
<td></td>
</tr>
<tr>
<td>Mexico</td>
<td>46%</td>
<td>Quigley, 2006</td>
<td>Study measured prevalence of GI abdominal pain/cramping</td>
</tr>
</tbody>
</table>
Genetic Polymorphisms

Altered 5-HT Signaling

Neuroplasticity

Stress, CRF, Anxiety

Increased Mucosal Permeability

Dysbiosis

Food Sensitivity

Mucosal Immune Activation
ROME III

The Functional Gastrointestinal Disorders

THIRD EDITION

Douglas A. Drossman, M.D., Senior Editor
with Editors

Enrico Corazziari, M.D. Michel Delvaux, M.D., Ph.D.
Robin Spiller, M.D. Nicholas J. Talley, M.D., Ph.D.
W. Grant Thompson, M.D. William E. Whitehead, Ph.D.
and the Rome III Committees

www.RomeCriteria.org
Rome III Criteria
Irritable Bowel Syndrome

Recurrent abdominal pain or discomfort at least 3 days/month
In the last 3 months associated with 2 or more:

- Improvement with defecation and/or
- Onset associated with a change in frequency of stool and/or
- Onset associated with a change in appearance or form of stool

Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.

Longstreth GF, Gastroenterology
Evaluation: Concerning Features

History:
• Unintentional and unexplained weight loss
• Rectal bleeding
• A family history of bowel or ovarian cancer
• Bowel habit change for > 6 weeks in person over 60 years

Examination and Lab Data:
• Anemia or iron deficient
• Abdominal or rectal masses
• Rectal masses
• Inflammatory markers
Proposed New Subtyping Based on Stool Consistency Alone

- IBS with constipation - IBS-C
- IBS with diarrhea - IBS-D
- IBS mixed type - IBS-M
- Alternating IBS - Patients who change subtype over periods of weeks and months
- Also: Functional Abdominal Pain Syndrome
In people who meet the IBS diagnostic criteria, the following tests should be undertaken to exclude other diagnoses:

- CBC
- ESR or CRP
- Antibody testing for Celiac Disease (endomysial antibodies [EMA] and/or tissue transglutaminase [TTG])
Potentially Unnecessary Testing in IBS

The following tests may not be necessary to confirm a diagnosis where IBS diagnostic criteria are met and alarm symptoms are absent:

• sigmoidoscopy
• Colonoscopy, barium enema, CT scan, ultrasound
• fecal ova and parasite test
• fecal occult blood test
How the GI Tract Works, with an Emphasis on The *Amazing* Enteric Nervous System

Gary M. Mawe, PhD
Department of Anatomy and Neurobiology
For better or for worse, the structure and functions of the gut are exquisitely designed to acquire every calorie out of every meal.
Physiological Processes of the Digestive Tract in a Nutshell

- Lumen of digestive tract
- Wall
- Interstitial fluid
- Blood

- Food
- DIGESTION
- SECRETION
- ABSORPTION
- MOTILITY
Divisions of the Nervous System

CNS
- Brain
- Spinal cord

PNS
- Somatic
- Autonomic
  - Sympathetic
  - Parasympathetic
  - Enteric
Somatic vs. Autonomic Reflexes

Somatic

CNS

Sensory ganglion

Skeletal Muscle

Autonomic

CNS

Sensory ganglion

Parasympathetic ganglion

Cardiac Muscle
Smooth Muscle Glands
Dual innervation of organs

- Parasympathetic ganglion
- Sympathetic ganglion
- ACh
- NE
- Inhibitory
- Excitatory
"Local stimulation of the gut produces excitation above and inhibition below the excited spot. These effects are dependent on the activity of the local nervous mechanism."

THE ENTERIC NERVOUS SYSTEM IS SPECIAL

There are A LOT of neurons in the gut.

There are A LOT of neurotransmitters and associated receptors in the gut.

Enteric neurons independently regulate gut functions.

There is intrinsic reflex circuitry in the gut.
Intrinsic reflex circuits exist in the gut.

The diagram illustrates the structure of the gut wall, showing layers such as the mucosa, submucosal plexus, circular muscle, and longitudinal muscle, as well as the myenteric plexus. It depicts the oral and aboral sides of the gut with arrows indicating a pressure gradient. The gut wall is shown to undergo contraction and relaxation, which are integral to the intrinsic reflex circuits.
The Enteric Nervous System IN ACTION

Physiological Saline

Neurotoxin in the bath

Guinea pig distal colon
Stress-induce changes in gut function

Almy, TP: Gastroenterology 8: 616-626, 1947
ALTERATIONS IN LARGE INTESTINAL MOTILITY AND BLOOD FLOW OCCUR IN RESPONSE TO ACUTE STRESS IN HUMANS

Contractile Activity

Early Phase Colonic Exam

Mucosal Engorgement

Time (Min)
The Gut-Brain Axis: Pathways of communication

- **Neural**
  ENS, CNS through vagus and/or spinal afferents

- **Humoral**
  Cytokines, hormones/neuropeptides, Microbial bioactive substances

**Gut-brain axis pathways**

**Microbiota/probiotic targets**

- Immune system
- Epithelial function and barrier
- Neurotransmission
- Muscle function

*Neurogastroenterology and Motility 24:405-413*
What’s going on at the lab bench now that might make it to the bedside?

Can motility be normalized by reversing neuroplastic changes?
Inflammation-induced changes in the motor circuitry of the colon

Linden et al., 2003 Am J Physiol 285: G207-G216
O’Hara et al., 2004, Am J Physiol 287: G998 – G1007
Coates et al., 2004, Gastroenterology 126:1657-1664
Linden et al., 2005, Neurogastro & Motility 17:565-574
Wheatcroft et al., 2005, Neurogastro & Motility 17:863-870
Bertrand et al., 2010 Am J Physiol 298: G446-G455
Strong et al., 2010 J. Physiol. 588: 847–859

Linden et al., 2005 Neurogastro & Motility 17:751-760
Gulbransen et al., 2012 Nature-Med 18:600-604
Linden et al., 2003 J. Physiol. 547:589-601
Lomax et al., 2005 J. Physiol. 564:863-875
Krauter et al., 2007 J. Physiol. 581: 787-800
Linden et al., 2003 J. Physiol. 547:589-601
Linden et al., 2004 J. Physiol. 557:191-205
Lomax et al., 2005 J. Physiol. 564:863-875
Krauter et al., 2007 Neurogastro & Motility, 19:990-1000
Evaluation of propulsive motility in the guinea pig distal colon with the GIMM

Developed at Med Associates, St. Albans, VT
Propulsive motility in the healthy guinea pig distal colon
Disrupted motility in TNBS colitis
Disrupted motility in TNBS colitis

Obstructed motility in TNBS colitis
Ionic currents that contribute to excitability in colonic afferent neurons

The Action Potential

- TTX-sensitive and -insensitive voltage-gated sodium channels
- N-type voltage-gated calcium channels
- Potassium channels

Ca$^{2+}$-activated Potassium (IK) channels

Ca$^{2+}$-induced Ca$^{2+}$ release

Ryanodine receptors

Ca$^{2+}$

The Afterhyperpolarization

Hyperpolarization-activated cation (I_h) channels

ZD-7288

TRAM 34

TNBS colitis

T. spiralis

Dave Linden
Inhibition of sensory neuron hyperexcitability promotes propulsive motility in the inflamed colon

Free radical scavenger treatment promotes propulsive motility in TNBS colitis
What is at the bench now that might make it to the bedside?

Can motility be normalized by reversing neuroplastic changes?

Could epithelial 5-HT$_4$ receptors be targeted for constipation and/or IBD?
Distribution of 5-HT$_4$ receptor in the colon

Jill Hoffman et al., Gastroenterology, 2012
Mucosal 5-HT\textsubscript{4} receptors appear to be protective

Jane Roberts & Brigitte Lavoie, new, unpublished data
What is at the bench now that might make it to the bedside?

1. Can motility be normalized by reversing neuroplastic changes?

2. Could epithelial 5-HT4 receptors be targeted for constipation and/or IBD?

3. Does increased mucosal 5-HT contribute to bone loss associated with colitis?
It Takes a Village

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Sarah MacEachern
Keith Sharkey, PhD

University of Oklahoma
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Anthony Johnson
Beverley Greenwood, PhD

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Hong Zhao, PhD
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Jill Hoffman, PhD
Jane Roberts
Onesmo Balemba, PhD
Elice Brooks
Neil McKnight
Hannah Foote
Brigitte Lavoie, PhD

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